STAND UP TO CANCER



SCIENTIFIC SUMMIT



JANUARY 26-29 CORONADO, CALIFORNIA For further information, pleasevisit us at:

www.StandUpToCancer.org



January 2024

Dear Members of the Stand Up To Cancer Family,

Welcome to the SU2C Scientific Summit 2024. We are thrilled to come together, once again, in Coronado to celebrate the groundbreaking research, advances in clinical and translational medicine, and efforts towards health equity that have taken place over the past year.

We feel incredibly fortunate to welcome not only team members from new and active teams, but also the leaders and co-leaders from past teams who have helped us create an incredible network of cancer researchers. It is a testament to the collaborative spirit of this organization and groups of researchers past and present that we have witnessed such dramatic and innovative breakthroughs across the past 15 years. It is our hope that during this SU2C Scientific Summit, you have time to collaborate, network, and forge new partnerships with scientists and clinicians in different fields of research than your expertise.

The overarching goal of SU2C is to help people with cancer as quickly as possible, but we cannot do it alone. We are indebted to many individuals and organizations for their long-standing commitment and contributions to our ever-growing portfolio of pioneering clinical trials and research projects.

We must first thank the members of our Scientific Advisory Committee (SAC) led by Nobel laureate, Dr. Phillip A. Sharp, and vice-chairs Dr. John Carpten, Dr. Arnie Levine, and Dr. William Nelson. Their tireless guidance and rigorous oversight continue to be the keystone of SU2C's scientific review process.

We must also thank our scientific partner, the American Association of Cancer Research. Led by Dr. Margaret Foti, the AACR has been with SU2C since the beginning, and all of this is possible with the support and professional guidance of their remarkable staff.

Thanks also to our generous donors. Thank you for your trust, your support, and your patience as we work together to help as many people as we possibly can. All of this is possible with your financial contribution.

Finally, we want to thank the entire SU2C community for your continued support of this collaborative research model and for working together toward a time when all cancer patients become long-term survivors. On behalf of the Founders and Advisors Committee, we look forward to an exciting SU2C Scientific Summit 2024.

Julian Adams, Ph.D. Chief Executive Officer

Standboocancer.org

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Stand Up To Cancer is a division of the Entertainment Industry Foundation (EIF), a 501(c)(3) charitable organization. Federal ID 95-1644609



Dear Colleagues and Friends:

We are pleased to welcome you to Coronado for the 2024 Stand Up To Cancer Scientific Summit. Once more, we gather to hear from colleagues about their exciting research, celebrate the many accomplishments, and dedicate ourselves to the profound mission that lies ahead in our fight against cancer.

Stand Up To Cancer's many successes during the past 15 years give us great hope and confidence that we will continue to make more progress and save more lives from cancer.

We have come a long way since 2008 when Stand Up to Cancer was formed with the American Association for Cancer Research as its Scientific Partner. The AACR was thrilled then, and still is today, to work collaboratively with the Co-Founders, the extraordinary group of women who are determined to advance cancer research and improve treatment.

We are also honored to work with the stellar group of scientists who serve on the Scientific Advisory Committee, led with distinction by Nobel Laureate Dr. Phil Sharp and the Vice Chairs. Their tireless dedication to this important cause is truly inspiring.

The AACR is proud of our ongoing partnership with SU2C CEO Dr. Julian Adams, Chief Financial Officer Shawn Burke, Chief Development Officer Stephanie Herron, General Counsel and Human Resources Officer Dana Hirsch Lipman, and the entire SU2C staff. We look forward to forging ahead as SU2C's dedicated Scientific Partner in our collective endeavor to conquer cancer in all its forms.

As we begin this Summit, we encourage you to seize every opportunity to embrace the spirit of collaboration and innovation, and to direct your passion to the mission we all share — to deliver new and effective therapies to patients and cure all cancers.

Have a productive meeting!

Sincerely,

w gt

Margaret Foti, PhD, MD (hc) Chief Executive Officer, AACR

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I stand up for myself...

and all those fighting cancer.



FRIDAY, JANUARY 26, 2024

11:30 A.M. - 6:00 P.M. REGISTRATION Constellation Foyer

12:30 P.M. - 6:00 P.M.

SU2C CONVERGENCE 3.1416 Review Meetings (Closed) Constellation A

SATURDAY, JANUARY 27, 2024

9:30 A.M. - 11:00 A.M.

SU2C CONVERGENCE 3.1416 Review Meetings (Closed) Constellation A

12:00 P.M. - 6:00 P.M.

REGISTRATION AND SPEAKER CHECK-IN Commodore Ballroom Foyer

2:10 P.M. - 3:00 P.M.

PANCREATIC CANCER COLLECTIVE VITAMIN D RECEPTOR AGONIST TRIAL Leader: Brian M. Wolpin, MD, MPH Update Meeting (Closed) Aurora

3:05 P.M. - 4:10 P.M.

SU2C HEALTH EQUITY BREAKTHROUGH TEAM Leader: Nina Bickell, MD, MPH Review Meeting (Closed) Sovereign

3:15 P.M. - 4:00 P.M.

PANCREATIC CANCER COLLECTIVE – NEW THERAPIES CHALLENGE: EXPLOITING DNA REPAIR GENE MUTATIONS IN PANCREATIC CANCER Leader: Alan D. D'Andrea, MD Review Meeting (Closed) Aurora

3:55 P.M. - 4:45 P.M.

SU2C CATALYST® RESEARCH TEAMS WITH SUPPORT FROM ZENTALIS PHARMACEUTICALS Leader: Bruce E.Clurman, MD, PhD Review Meeting (Closed) Constellation B

3:55 P.M. - 5:00 P.M.

VAI - SU2C CANCER EPIGENETICS DREAM TEAM Leader: Peter A. Jones, PhD, DSc (hon) Review Meeting (Closed) Constellation A

4:15 P.M. - 5:00 P.M.

PANCREATIC CANCER COLLECTIVE - NEW THERAPIES CHALLENGE: TARGETING SHP2 IN PANCREATIC CANCER Leader: René Bernards, PhD Review Meeting (Closed) Aurora

4:25 P.M. - 5:10 P.M.

SU2C LUNG CANCER HEALTH EQUITY RESEARCH TEAM Leader: Robert A. Winn, MD Review Meeting (Closed) Sovereign

5:00 P.M. - 5:45 P.M.

SU2C - FARF - FFF HEAD AND NECK CANCER RESEARCH TEAM Leader: Agata Smogorzewska, MD, PhD Review Meeting (Closed) Constellation B

5:15 P.M. - 6:00 P.M.

SU2C CANADA - LUSTGARTEN FOUNDATION - PANCREATIC CANCER CANADA PASS CONVERGENCE DREAM TEAM Leaders: Jennifer J. Knox, MD, and Elizabeth M. Jaffee, MD Review Meeting (Closed) Aurora

5:15 P.M. - 6:00 P.M.

SU2C CATALYST® RESEARCH TEAM WITH SUPPORT FROM MERCK Leaders: Kurt Weinhold, PhD, and David G.Kirsch, MD, PhD Review Meeting (Closed) Constellation A

5:25 P.M. - 6:10 P.M.

LUNG CANCER HEALTH EQUITY SU2C CATALYST® RESEARCH TEAM Leader: Vamsidhar Velcheti, MD Review Meeting (Closed) Sovereign

5:25 P.M. - 6:30 P.M.

SU2C - CRUK PEDIATRIC NEW DISCOVERIES CHALLENGE ROUND 2 RESEARCH TEAMS Leaders: John M. Anderson, MBBS, MRCP, PhD, and Martin McCabe,MB/BChir, PhD Review Meeting (Closed) Brittania/Cambria

6:00 P.M. - 8:00 P.M.

DINNER AVAILABLE Commodore F

6:00 P.M. - 6:45 P.M.

SU2C CATALYST® RESEARCH TEAM WITH SUPPORT FROM MIRATI THERAPEUTICS Leader: Ryan B. Corcoran, MD, PhD Review Meeting (Closed) Constellation B

6:15 P.M. - 7:00 P.M.

PANCREATIC CANCER COLLECTIVE - NEW THERAPIES CHALLENGE: IMMUNOTHERAPY TARGETING MUTANT KRAS Leader: Robert H. Vonderheide, MD, DPhil Review Meeting (Closed) Aurora

6:15 P.M. - 7:45 P.M.

SU2C CATALYST® RESEARCH TEAM WITH SUPPORT FROM GENENTECH Leaders: Sean M. McBride, MD, Elizabeth A. Mittendorf, MD, PhD, and Matthew S. Block, MD, PhD Review Meeting (Closed) Constellation A

6:25 P.M. - 7:45 P.M.

SU2C DIVERSITY IN EARLY DEVELOPMENT CLINICAL TRIALS RESEARCH GRANTS Leaders: Walter M. Stadler, MD, David E. Gerber, MD, Anthony El-Khoueiry, MD, and Martin J. Edelman, MD Review Meeting (Closed) Sovereign

6:45 P.M. - 7:45 P.M.

SU2C CATALYST® RESEARCH TEAM WITH SUPPORT FROM JAZZ PHARMACEUTICALS Leaders: Patrick J. Grohar, MD, PhD, and Fred R. Hirsch MD, PhD Review Meeting (Closed) Brittania/Cambria



7:00 P.M. - 9:00 P.M.

SU2C GASTROESOPHAGEAL DREAM TEAM COLLECTIVE

Leaders: Yelena Y. Janjigian, MD, Anil K. Rustgi, MD, and William R. Sellers, MD Review Meeting (Closed) Constellation B

7:15 P.M. - 8:00 P.M.

PANCREATIC CANCER COLLECTIVE – NEW THERAPIES CHALLENGE: MOLECULARLY TARGETED RADIONUCLIDE THERAPY VIA THE INTEGRIN AVSS6 Leader: Julie L. Sutcliffe, PhD Review Meeting (Closed) Aurora

8:00 P.M. - 9:00 P.M.

PEDIATRIC SU2C CATALYST® RESEARCH TEAMS WITH SUPPORT FROM BRISTOL MYERS SQUIBB Leaders: Kimberly Stegmaier, MD, and Uri Y. Tabori MD Review Meeting (Closed) Brittania/Cambria

8:00 P.M. - 9:00 P.M.

SU2C COLORECTAL CANCER HEALTH EQUITY DREAM TEAM Leader: Jennifer S. Haas, MD, MSPH Review Meeting (Closed) Sovereign

8:00 P.M. - 9:00 P.M.

SU2C GASTRIC CANCER INTERCEPTION RESEARCH TEAM Leader: Andrew T. Chan, MD, MPH Review Meeting (Closed) Constellation A

8:15 P.M. - 9:00 P.M.

SU2C - LUSTGARTEN FOUNDATION PANCREATIC CANCER INTERCEPTION DREAM TEAM Leader: Anirban Maitra, MBBS Review Meeting (Closed) Aurora

SUNDAY, JANUARY 28, 2024

7:00 A.M. - 6:30 P.M. REGISTRATION AND SPEAKER CHECK-IN Commodore Ballroom Foyer

7:30 A.M. - 8:15 A.M.

BREAKFAST Commodore E

7:30 A.M. - 8:15 A.M.

SU2C HEALTH EQUITY COMMITTEE MEETING (CLOSED) Brittania/Cambria

8:15 A.M. - 8:30 A.M.

BREAK/TRANSFER

8:30 A.M. - 8:55 A.M.

WELCOME AND INTRODUCTIONS Sherry Lansing , Chair, Founders and Advisors Committee, Stand Up To Cancer Julian Adams, PhD, CEO, Stand Up To Cancer Margaret Foti, PhD, MD (hc), CEO, American Association for Cancer Research Plenary Session Commodore Ballroom ABCD

8:55 A.M. - 9:10 A.M.

TARGETING EPIGENETIC DYSREGULATION IN PEDIATRIC CANCER Speaker: Kimberly Stegmaier, MD Pediatric SU2C Catalyst® Research Team With Support From Bristol Myers Squibb Plenary Session Commodore Ballroom ABCD

9:10 A.M. - 9:15 A.M.

9:15 A.M. - 9:30 A.M.

TARGETING PAEDIATRIC SOLID CANCERS WITH DEGRON REGULATED CAR-T CELLS Speaker: John M. Anderson, MBBS, MRCP, PhD Plenary Session Commodore Ballroom ABCD

9:30 A.M. - 9:35 A.M.

DISCUSSION Plenary Session Commodore Ballroom ABCD

9:35 A.M. - 9:50 A.M.

BRAINATOMY: MECHANISMS AND IMAGE-DEFINED LOCI OF COGNITIVE AND ENDOCRINE DAMAGE AFTER CHILDHOOD THERAPEUTIC BRAIN RADIATION Speaker: Martin McCabe, MB/BChir, PhD SU2C - CRUK Pediatric New Discoveries Challenge Round 2 Research Team Plenary Session Commodore Ballroom ABCD

9:50 A.M. - 9:55 A.M.

DISCUSSION Plenary Session Commodore Ballroom ABCD

9:55 A.M. - 10:15 A.M.

BREAK Commodore Ballroom ABCD

10:15 A.M. - 10:30 A.M.

COLORECTAL CANCER DREAM TEAM PROGRESS INTO THE FUTURE Speakers: : Ryan B. Corcoran, MD, PhD, Andrea Cercek, MD, and Zsofia K. Stadler, MD Plenary Session Commodore Ballroom ABCD

10:30 A.M. - 10:35 A.M.

DISCUSSION Plenary Session Commodore Ballroom ABCD

10:35 A.M. - 10:50 A.M.

MOLECULARLY GUIDED IMAGING FOR EARLY INTERCEPTION OF GASTRIC CANCER Speaker: David A. Drew, PhD SU2C Gastric Cancer Interception Research Team: Early Detection and Interception of Diffuse and Intestinal Gastric Cancer Plenary Session Commodore Ballroom ABCD

10:50 A.M. - 10:55 A.M.

DISCUSSION Plenary Session Commodore Ballroom ABCD

10:55 A.M. - 11:10 A.M.

GASTROESOPHAGEAL CANCERS: UNVEILING CELL SURFACE TARGETS AND FUNCTIONAL GENOMIC INSIGHTS FOR THERAPEUTIC INTERVENTION Speaker: William R. Sellers, PhD SU2C-Torrey Coast Gastroesophageal Cancer Dream Team CollectiveResearch Team: Therapeutics for Gastroesophageal Adenocarcinoma: Application, Translation and Discovery Plenary Session Commodore Ballroom ABCD

11:10 A.M. - 11:15 A.M.



11:15 A.M. - 11:25 A.M.

NEOADJUVANT COMBINATION TARGETED AND IMMUNOTHERAPY FOR HIGH RISK STAGE III MELANOMA: NEOACTIVATE (NCT03554083) Speaker: Matthew S. Block, MD, PhD, and Tina Hieken, MD SU2C Catalyst® Research Team With Support From Genentech: Neoadjuvant Therapy for Patients With High-Risk Stage III Melanoma Plenary Session Commodore Ballroom ABCD

11:25 A.M. - 11:30 A.M.

DISCUSSION Plenary Session

Commodore Ballroom ABCD

11:30 A.M. - 11:40 A.M.

PEMBROLIZUMAB AND RADIATION THERAPY TO IMPROVE OUTCOME IN HIGH-RISK SARCOMA Speaker: David G. Kirsch, MD, PhD SU2C Catalyst® Research Team With Support From Merck: Pembrolizumab and Radiation Therapy to Improve Outcome in High- Risk Sarcoma Plenary Session Commodore Ballroom ABCD

11:40 A.M. - 11:45 A.M.

DISCUSSION Plenary Session Commodore Ballroom ABCD

11:45 A.M. - 12:00 P.M.

GROUP PHOTO

Location to be announced and placards to be distributed in the Plenary Session

12:00 P.M. - 1:30 P.M.

LUNCH Commodore E

1:30 P.M. - 1:45 P.M. BREAK/TRANSFER Commodore Ballroom ABCD

1:45 P.M. - 2:20 P.M.

KEYNOTE PRESENTATION AND DISCUSSION: THE MOLECULAR AND THE GENETIC DIFFERENCES IN MULTIPLE MYELOMAS FROM INDIVIDUALS OF AFRICAN AND EUROPEAN ANCESTRY Introduction: John D. Carpten, PhD, City of Hope Keynote Speaker: Arnold J. Levine, PhD, Institute for Advanced Study Plenary Session Commodore Ballroom ABCD

2:20 P.M. - 2:35 P.M.

REVERSE-TRANSLATION OF PATIENT-IDENTIFIED EPIGENETIC REGULATORS FOR DURABLE IMMUNOTHERAPY Speaker: Ben Youngblood, PhD VAI - SU2C Epigenetics Dream Team Plenary Session Commodore Ballroom ABCD

2:35 P.M. - 2:40 P.M.

DISCUSSION Plenary Session Commodore Ballroom ABCD

2:40 P.M. - 2:55 P.M.

LSD1 INHIBITION: AUGMENTING IMMUNOTHERAPY FOR PATIENTS WITH SMALL CELL LUNG CANCER Speaker: Charles M. Rudin, MD, PhD VAI - SU2C Epigenetics Dream Team Plenary Session Commodore Ballroom ABCD

2:55 P.M. - 3:00 P.M.

3:00 P.M. - 3:15 P.M.

TRANSLATIONAL RESULTS FROM THE GEMCITABINE/NAB-PACLITAXEL PLUS OR MINUS VDR AGONIST PARICALCITOL TRIAL IN PATIENTS WITH METASTATIC PANCREATIC CANCER Speaker: Brian M. Wolpin, MD, MPH SU2C - Lustgarten Foundation Vitamin D Receptor Agonist Team Plenary Session Commodore Ballroom ABCD

3:15 P.M. - 3:20 P.M.

DISCUSSION Plenary Session Commodore Ballroom ABCD

3:20 P.M. - 3:30 P.M.

ZISKIN PRIZE ANNOUNCEMENT Plenary Session Commodore Ballroom ABCD

3:30 P.M. - 3:40 P.M.

MLB RECOGNITION Plenary Session Commodore Ballroom ABCD

3:40 P.M. - 4:00 P.M. BREAK

4:00 P.M. - 6:30 P.M.

POSTER SESSION AND RECEPTION Constellation

5:00 P.M.

SHARP AWARD APPLICATION SUBMISSION DEADLINE

6:30 P.M. - 7:00 P.M. BREAK

7:00 P.M. - 9:00 P.M. CALIFORNIA DREAMIN' EVENT

The Pavilion

MONDAY, JANUARY 29, 2024

7:00 A.M. - 3:00 P.M. REGISTRATION AND SPEAKER CHECK-IN Commodore Ballroom Foyer

7:30 A.M. - 8:15 A.M. BREAKFAST

Commodore E

8:15 A.M. - 8:30 A.M. BREAK/TRANSFER

8:30 A.M. - 8:35 A.M.

INTRODUCTORY REMARKS Julian Adams, PhD, CEO, Stand Up To Cancer Plenary Session Commodore Ballroom ABCD

8:35 A.M. - 9:45 A.M.

PANEL AND DISCUSSION: AI IN CANCER RESEARCH, DIAGNOSIS, AND TREATMENT Thomas J. Albert, PhD, Roche Diagnostics Christina Curtis, PhD, Stanford University Aviv Regev, PhD, Genentech Peter K. Sorger, PhD, Harvard Medical School Plenary Session Commodore Ballroom ABCD

9:45 A.M. - 9:50 A.M.

2023 SU2C MAVERICK AWARD PRESENTATION ARTIFICIAL INTELLIGENCE FOR TARGETING UNDEFINED MOLECULAR SUBTYPES OF HEAD/NECK CANCER Speaker: Alexander T. Pearson, MD, PHD Plenary Session Commodore Ballroom ABCD

9:50 A.M. - 9:55 A.M.



9:55 A.M. - 10:15 A.M. BREAK

10:15 A.M. - 10:30 A.M.

TITLE: TO MRNA VACCINES FOR PANCREATIC CANCER Speaker: Vinod P. Balachandran, MD SU2C-Lustgarten Foundation Convergence Research Team: Computational Deconstruction of Neoantigen-TCR Degeneracy for Cancer Immunotherapy Plenary Session Commodore Ballroom ABCD

10:30 A.M. - 10:35 A.M.

DISCUSSION Plenary Session Commodore Ballroom ABCD

10:35 A.M. - 10:50 A.M.

ENGINEERING TCR-T CELLS TO BE AN EFFECTIVE THERAPY FOR PANCREATIC CANCER Speaker: Phil Greenberg, MD SU2C-Lustgarten Foundation Pancreatic Cancer Team: Transforming Pancreatic Cancer to Treatable Disease Plenary Session Commodore Ballroom ABCD

10:50 A.M. - 10:55 A.M.

DISCUSSION Plenary Session Commodore Ballroom ABCD

10:55 A.M. - 11:00 A.M.

SU2C MAVERICK AWARD: FINALIST #1 Plenary Session Commodore Ballroom ABCD

11:00 A.M. - 11:05 A.M.

DISCUSSION Plenary Session Commodore Ballroom ABCD

11:05 A.M. - 11:10 A.M.

SU2C MAVERICK AWARD: FINALIST #2 Plenary Session Commodore Ballroom ABCD

11:10 A.M. - 11:15 A.M.

DISCUSSION Plenary Session Commodore Ballroom ABCD

11:15 A.M. - 11:20 A.M.

POSTER AWARD PRESENTATION Plenary Session Commodore Ballroom ABCD

11:20 A.M. - 11:25 A.M.

DISCUSSION Plenary Session Commodore Ballroom ABCD

11:25 A.M. - 11:30 A.M.

HEALTH EQUITY POSTER PRESENTATION Plenary Session Commodore Ballroom ABCD

11:30 A.M. - 11:35 A.M.

DISCUSSION Plenary Session Commodore Ballroom ABCD

11:35 A.M. - 11: 50 A.M. BREAK/TRANSFER

11:50 A.M. - 1:20 P.M.

LUNCH Commodore E

11:50 A.M. - 1:20 P.M.

PHILLIP A. SHARP INNOVATION IN COLLABORATION AWARDS, GERHARD CLESS GASTRIC CANCER INNOVATION IN COLLABORATION AWARD, AND NINA NICOLAI PANCREATIC CANCER INNOVATION IN COLLABORATION AWARD Brittania/Cambria

1:20 P.M. - 1:35 P.M.

BREAK/TRANSFER Plenary Session Commodore Ballroom ABCD

1:35 P.M. - 1:45 P.M.

MICROFLUIDIC APPROACHES FOR STUDYING TUMOR-HOST INTERACTIONS IN VIVO AND IN VITRO Speaker: Scott Manalis, PhD

Speaker: Scott Manalis, PhD SU2C Convergence 3.1416 Research Team: Molecular and Biophysical Definition of Tumor-Host Interactions and Impact on Tumorigenesis and Therapeutic Response Plenary Session Commodore Ballroom ABCD

1:45 P.M. - 1:50 P.M.

DISCUSSION Plenary Session Commodore Ballroom ABCD

1:50 P.M. - 2:00 P.M.

TITLE: HITTING A MOVING TARGET: TREATING EVOLVING TUMORS

Speaker: Karuna Ganesh, MD, PhD SU2C Convergence 3.1416 Research Team: Multi-omic Analysis of Immune System and Microbiota Influence on Temporal and Spatial Evolution of Tumor Microenvironments Plenary Session Commodore Ballroom ABCD

2:00 P.M. - 2:05 P.M.

DISCUSSION Plenary Session Commodore Ballroom ABCD

2:05 P.M. - 2:40 P.M.

KEYNOTE PRESENTATION AND DISCUSSION: WHICH IS VACCINE BOOSTING NATURAL AND SYNTHETIC T CELLS Darrell Irvine, PhD, Massachusetts Institute of Technology Plenary Session Commodore Ballroom ABCD

2:40 P.M. - 2:50 P.M.

AWARD PRESENTATION PHILLIP A. SHARP INNOVATION IN COLLABORATION AWARDS, GERHARD CLESS GASTRIC CANCER INNOVATION IN COLLABORATION AWARD, NINA NICOLAI PANCREATIC CANCER INNOVATION IN COLLABORATION AWARD, AND SU2C MAVERICK AWARD Plenary Session Commodore Ballroom ABCD

2:50 P.M. - 3:00 P.M.

SCIENTIFIC ADVISORY COMMITTEE CONFERENCE SUMMARY William Nelson, MD, PhD, Johns Hopkins University Plenary Session Commodore Ballroom ABCD

3:00 P.M. - 3:20 P.M. BREAK

3:20 P.M. - 4:20 P.M. SU2C SCIENTIFIC ADVISORY

COMMITTEE DEBRIEF MEETING (CLOSED) Brittania/Cambria

4:20 P.M. - 4:30 P.M. BREAK

4:30 P.M. - 5:45 P.M.

SU2C FAC/SAC EXECUTIVE COMMITTEE MEETING (CLOSED) Brittania/Cambria

5:15 P.M. - 5:30 P.M. BREAK/TRANSFER

5:30 P.M. - 6:15 P.M.

SU2C SAC EXECUTIVE COMMITTEE MEETING (CLOSED) Brittania/Cambria

6:15 P.M. - 6:30 P.M. BREAK/TRANSFER

6:30 P.M. - 8:30 P.M.

DINNER FOR SU2C SCIENTIFIC ADVISORY COMMITTEE

Avalon Avalon

ADVISORY COMMITTEES

SU2C SCIENTIFIC ADVISORY COMMITTEE EXECUTIVE COMMITTEE

Phillip A. Sharp, PhD Chairperson

Institute Professor Koch Institute for Integrative Cancer Research Massachusetts Institute of Technology Cambridge, MA

John D. Carpten, PhD Vice Chairperson

Chief Scientific Officer Irell & Manella Cancer Center Director's Distinquished Chair Morgan & Helen Chu Director's Chair Beckman Research Institute Professor, Integrative Translational Sciences City of Hope Duarte, CA

Arnold J. Levine, PhD Vice Chairperson

Professor Emeritus Institute for Advanced Study and Cancer Institute of New Jersey Princeton, NJ

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Vice Chairperson Director Sidney Kimmel Comprehensive Cancer Center Johns Hopkins University Baltimore, MD

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Senior Director of Proteomics and Institute Scientist Broad Institute Cambridge, MA

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Emily Herrmann Chair in Cancer Research and Director Methodist Cancer Center at Houston Methodist Hospital Houston, TX

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Director Susan F. Smith Center for Women's Cancers Dana-Farber Cancer Institute Cambridge, MA

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Michael Fischbach, PhD

Liu (Liao) Family Professor of Bioengineering Stanford University Stanford, CA

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President of Research and Development BioNTech Cambridge, MA

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Director Duke Cancer Institute Durham, NC

David Kaufman, MD, PhD

Partner Third Rock Ventures Boston, MA

David Kirsch, MD, PhD

Senior Scientist Peter and Shelagh Godsoe Chair in Radiation Medicine Princess Margaret Cancer Centre Toronto, Ontario Canada

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Chairman and Professor University of Texas MD Anderson Cancer Center Houston, TX

Lecia Sequist, MD, MPH

Landry Family Professor of Medicine Harvard Medical School Program Director, Cancer Early Detection and Diagnostics Clinic Massachusetts General Cancer Center Cambridge, MA

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George Fabyan Professor of Comparative Pathology Co-Director, Harvard Institute of Translational Immunology Co-Director, Evergrande Center for Immunologic Diseases Harvard Medical School Boston, MA

Laura K. Shawver, PhD

President and Chief Executive Officer Capstan Therapeutics San Diego, CA

Peter Sorger, PhD

Otto Krayer Professor Department of Systems Biology Head of the Harvard Program in Therapeutic Sciences - HiTS Harvard Medical School Cambridge, MA

David A. Tuveson, MD, PhD

Professor and Director Cold Spring Harbor Laboratory Cancer Center Cold Spring Harbor, NY



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Chief, Laboratory of Genome Integrity NIH Distinguished Investigator Center for Cancer Research National Cancer Institute Bethesda, MD

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President, R&D (retired) Biogen Inc. Sarasota, FL

Carol L. Prives, PhD

Da Costa Professor Columbia University New York, NY

HEALTH EQUITY COMMITTEE John D. Carpten, PhD Chairperson

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Andrew T. Chan, MD, MPH

Professor of Medicine Harvard Medical School Cambridge, MA

Margaret Foti, PhD, MD (hc)

Chief Executive Officer American Association for Cancer Research Philadelphia, PA

Shawna Hudson, PhD

Professor and Research Division Chief, Department of Family Medicine and Community Health Rutgers Robert Wood Johnson Medical School New Brunswick, NJ

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David R. Wilson, PhD

Associate Vice President Health Research Chair Department of Indigenous Health School of Medicine and Health Sciences University of North Dakota Grand Forks, ND

Karen M. Winkfield, MD, PhD

Executive Director Meharry-Vanderbilt Alliance Nashville, TN

Robert A. Winn, MD

Director Massey Cancer Center Virginia Commonwealth University Richmond, VA







THOMAS J. ALBERT V.P. Global Head of Research and Early Development Roche Diagnostics

Tom received his BS in Chemistry from the University of Michigan and a PhD in Molecular Toxicology from the University of Wisconsin. Tom was an early employee of NimbleGen Systems, which was acquired by Roche in 2007. Since then, Tom has held various R&D leadership positions in Roche Diagnostics. He has led teams that have developed and commercialized several important novel genomics technologies, including whole genome sequencing methods, hybrid capture for targeted sequencing, whole exome sequencing, and whole proteome peptide arrays. Tom is currently Global Head of Research and Early Development for Roche Diagnostics, leading the development of next generation clinical diagnostic technologies, workflows, and assays.



JOHN D. CARPTEN, PHD

Chief Scientific Officer Irell & Manella Cancer Center

Director's Distinquished Chair Morgan & Helen Chu Director's Chair of the Beckman Research Institute

Professor, Department of Integrative Translational Sciences City of Hope

Dr. John D. Carpten currently serves as Chief Scientific Officer for the City of Hope, where he also serves as Director of the Comprehensive Cancer Center and Director of Beckman Research Institute. Prior to his current appointment, he served as Professor and Chair for the Department of Translational Genomics, Keck School of Medicine, University of Southern California (USC), Los Angeles, CA. From 2003-2015, he served as Professor and Deputy Director of Basic Sciences at the Translational Genomics Research Institute (TGen), Phoenix, AZ. Dr. Carpten attended Lane College, a Historically Black College, in Jackson, TN where he completed his BS. degree in Biology in 1988. He received his PhD in Molecular, Cellular and Developmental Biology from the Ohio State University in 1994. After completing his postdoctoral fellowship at the National Human Genome Research Institute (NHGRI) at the NIH, Bethesda, MD in 1999, he was promoted to the tenure track at NHGRI in 1999.

Dr. Carpten's expertise spans a very broad range of research disciplines including genome science, tumor profiling, cancer cell biology, functional genomics, health disparities, and precision medicine. The primary goal of Dr. Carpten's research program is to discover molecular alterations in cancer and to translate these findings into new approaches for prevention, diagnosis, and treatment. In support of this goal, his program is actively involved in the development and application of cutting edge technologies and novel bioinformatics approaches for discovery research. His work has impacted our understanding of a variety of cancer types particularly those that disproportionately affect underrepresented minorities including prostate cancer, breast cancer, colorectal cancer, multiple myeloma, and pediatric cancers. Dr. Carpten has co-authored over 200 peer reviewed publications in scientific journals that include Science, Nature, Nature Genetics, Cancer Cell, Cancer Research, Molecular Cancer Therapeutics, and the New England Journal of Medicine.

Dr. Carpten has been honored with numerous awards. He was named a Science Trailblazer by Spectrum Magazine in 2006, and was awarded Susan G. Komen Distinguished Lectureship on the Science of Cancer Health Disparities in 2014 for his untiring work in ensuring that all people are equally represented in science and innovative healthcare. Dr. Carpten was also awarded the 2018 AACR MICR Jane Cooke Wright Lectureship for his outstanding research in cancer disparities and his efforts in developing the careers of minority scientists. In 2019, he serves as Program Committee Chair for the AACR Annual Conference in Atlanta, GA, which included over 21,500 international participants. In 2021 he was inducted into the AACR Fellows of the Academy, and also became a member of the AACR Board of Directors. He also currently serves as a member of the National Cancer Institute Board of Scientific Counselors, a member of the Scientific Advisory Committee for Stand Up To Cancer, a member of the Board of Directors for Tower Cancer Research Foundation, and as a member of the Scientific Advisory Board for Break Through Cancer Foundation. In 2021, Dr. Carpten received a presidential appointment to serve as Chair for the National Cancer Advisory Board.







CHRISTINA CURTIS, PHD RZ Cao Professor of Medicine, Genetics, and Biomedical Data Science Director, Al Cancer Genomics Standord University

Christina Curtis, PhD is the RZ Cao Professor of Medicine, Genetics, and Biomedical Data Science and Director of AI and Cancer Genomics at Stanford University. Her research has led to new paradigms in understanding how human tumors evolve and metastasize and has redefined the molecular map of breast cancer.

Dr. Curtis has been the recipient of multiple awards, including the NIH Director's Pioneer Award and the AACR Award for Outstanding Achievement in Basic Science. She is a Kavli Fellow of the National Academy of Sciences, a Susan G. Komen Scholar, and a Chan Zuckerberg Biohub Investigator.

Dr. Curtis serves on the editorial boards of numerous journals, including Science and Cancer Discovery, as an advisor to biotech and biopharma, and as a member of the AACR Board of Directors.



DARRELL IRVINE, PH.D.

Professor, Departments of Biological Engineering and Materials Science & Engineering Koch Institute for Integrative Cancer Research Massachusetts Institute of Technology Ragon Institute of MGH, MIT, and Harvard

Investigator

Howard Hughes Medical Institute

Darrell Irvine, PhD, is a Professor at the Massachusetts Institute of Technology and an Investigator of the Howard Hughes Medical Institute. He also serves on the steering committee of the Ragon Institute of Massachusetts General Hospital, MIT, and Harvard. His research is focused on the application of engineering tools to problems in cellular immunology and the development of new materials for vaccine and drug delivery. Major efforts of the laboratory are directed toward vaccine development for HIV and cancer immunotherapy.

Dr. Irvine's work has been recognized by numerous awards, including election as a Member of the National Academy of Medicine, Fellow of the Biomedical Engineering Society, Fellow of the American Institute for Medical and Biological Engineering, and appointment as an investigator of the Howard Hughes Medical Institute. He is the author of over 200 publications, reviews, and book chapters, and an inventor on numerous patents.





ARNOLD J. LEVINE, PH.D Professor Emeritus Institute for Advanced Study

Arnold J. Levine, PhD, Professor Emeritus at the Institute for Advanced Study in Princeton, N.J., received his BA in Biology from Harpur College, SUNY, his PhD from the University of Pennsylvania, and trained as a Postdoctoral Fellow at the California Institute of Technology in the laboratory of Robert Sinsheimer. In 1968, Dr. Levine joined Princeton University as an Assistant Professor, becoming a Professor of biochemistry in 1976. In 1979, he moved to the SUNY Stony Brook School of Medicine to Chair the Department of Microbiology, the same year he and others discovered the p53 tumor suppressor protein, a molecule that inhibits tumor development. He returned to Princeton in 1984. Between 1984 and 1996, he presided over a major expansion of Princeton's life sciences programs as Chairman of the Department of Molecular Biology. From 1998 to 2002, Dr. Levine was President of The Rockefeller University.

Professor Levine established the Simons Center for Systems Biology at the Institute for Advanced Study, concentrating on research at the interface of molecular biology and the physical sciences. He helped shape U.S. science priorities as chairman of an influential 1996 review panel on federal AIDS research funding. He also chaired the National Cancer Advisory Board, which advises the National Academy of Sciences and its Institute of Medicine on cancer policy. Levine's work has been recognized with numerous honors and awards. He was elected to the National Academy of Sciences in 1991, and to its Institute of Medicine in 1995. In April 2001, Levine received the first Albany Medical Center Prize in Medicine and Biomedical Research, then the largest annual prize in science or medicine offered in the United States.

The research paths of the Levine group have provided clear evidence that the p53 pathway plays a central role in the prevention of human cancers and that polymorphic variations in components of the pathway can influence individual responses to environmental mutagens, age of cancer onset, sexual dimorphisms in cancers, response to therapy and survival times. This research has helped to uncover the genetic origins of cancer and focus drug discovery on a rational path to treat cancers.



AVIV REGEV, PH.D. Executive Vice President, Head Genentech Research and Early Development

Aviv Regev is the head of Genentech Research and Early Development. Prior to Genentech, Regev served as Chair of the Faculty and Core Member at the Broad Institute of MIT and Harvard, and as Professor of Biology at MIT and Investigator at the Howard Hughes Medical Institute. She is a founding co-chair of the Human Cell Atlas.

Regev is a leader in deciphering molecular circuits that govern cells, tissues and organs in health and their malfunction in disease. Her lab has pioneered foundational experimental and computational methods in single-cell genomics, working toward greater understanding of the function of cells and tissues in health and disease, including autoimmune disease, inflammation and cancer.

She is a member of the National Academy of Sciences and National Academy of Medicine, and a Fellow of the International Society of Computational Biology. She is a recipient of multiple prizes and honors, including most recently the 2023 L'Oreal Women In Science award.







PETER K. SORGER, PH.D Otto Krayer Professor Department of Systems Biology

Head

Harvard Program in Therapeutic Sciences - HiTS

Harvard Medical School

Peter Sorger is a Professor of Systems Biology at Harvard Medical School and Head of the Harvard Program in Therapeutic Sciences. an interinstitutional effort to advance the fundamental science used to develop and test therapeutic hypotheses, identify and prioritize active molecules, and evaluate new drugs via precision clinical trials. He received his PhD from Trinity College, Cambridge U.K. for research on heat shock genes under the supervision of Hugh Pelham and trained as postdoctoral fellow at the University of California, San Francisco with Harold Varmus. Sorger has co-founded software and biopharmaceutical companies and is an advisor to multiple public and private corporations and research institutes in the US and Europe. Prior to joining HMS, Peter served as a Professor of Biology and Biological Engineering at MIT.

Peter's research focuses on the signal transduction networks controlling cell proliferation and death, dysregulation of these networks in cancer and inflammatory diseases, and the interplay between tumor cell intrinsic mechanisms and immune surveillance in response to therapy. This involves the use of both classical algorithms and machinelearning/AI to create quantitative models of disease processes in cell lines, mouse models, and human specimens. The Sorger group also develops open-source software for analyzing biological networks and drug mechanism of action and it participates in multiple collaborative programs working to improve data access and reproducibility. Recent research extends the groups measuremodel approach to the development of drug response biomarkers using highly multiplexed tissue imaging and digital pathology.

ABOUT SU2C

STAND UP TO CANCER: A GROUNDBREAKING MOVEMENT TRANSFORMING CANCER RESEARCH

Founded in 2008 by women leaders in the entertainment and media industries, Stand Up To Cancer is a groundbreaking movement that accelerates cancer research and gets new therapies to patients quickly to save lives now.

Since our founding, Stand Up To Cancer has supported more than 236 science projects with nearly \$800 million pledged for these efforts. We have funded 142 team science projects, as well as 94 individuals through our Innovative Research Grants for earlycareer researchers and other grants. And more than 270 clinical trials enrolling more than 292,350 patients have been launched.

SU2C's research projects bring together top investigators from different institutions to accelerate the discovery and delivery of new therapies, and they have evolved to include an array of industry collaborations, as well.

Focusing on accelerating the development of new therapies, new methods of cancer interception, and new approaches to making these treatments and screening available to all, we have created grant mechanisms that fund meaningful team-based research projects. Collectively, they offer opportunities for cancer science and cancer treatment questions to be answered using a variety of techniques.

- Our flagship Dream Team grants fund multidisciplinary, multi-institutional, collaborative teams to take innovative ideas from concept to patient.
- Research Teams bring together scientists from different institutions answering important questions about cancer research and treatment.

- SU2C Convergence[™] Grants unite physical and computational scientists with oncologists to ask fundamental questions about cancer biology, producing insights that can be rapidly applied for patient benefits.
- SU2C Catalyst[®] teams use funding, compounds, and other materials from the pharmaceutical and biotechnology industries to rapidly assess new treatment combinations.
- Innovative Research Grants support cuttingedge cancer research that might not receive funding through traditional channels.
- And the Phillip A. Sharp Innovation in Collaboration Award, the Ziskin Prize, the Jim Toth Sr. Breakthrough Lung Cancer Research Award, the Peggy Prescott Early Career Award, and the Golden Arrow Award provide support for smaller projects to rapidly explore the newest and most exciting ideas emerging from the cancer research community.

To further support development of cancer treatments that are effective across all communities, the SU2C Health Equity Committee continues to help us find ways to lower the barriers of access to new treatments for all cancer patients.

With mounting evidence for the need to develop precision medical treatments and interventions to serve diverse patient populations, we are supporting the inclusion of historically under-represented racial and ethnic minority populations in clinical trials that we fund. SU2C staff continue to produce educational materials for the public to drive awareness of clinical trials and participation, as well.



STAND UP TO CANCER

DREAM TEAMS

SU2C DREAM TEAMS

SU2C COLORECTAL CANCER HEALTH EQUITY DREAM TEAM DT6214

Community Collaboration to Advance Racial/Ethnic Equity in CRC Screening GRANT TERM: September 2021– August 2024

KEY PERSONNEL

Team Leader: Jennifer Haas, MD, MSc Massachusetts General Hospital

Co-Leader: Anton Bilchik, MD, PhD, MBA Providence Saint John's Cancer Institute Saint John's Cancer Institute

Co-Leader: Folasade P. May, MD, PhD University of California, Los Angeles



HAAS



BILCHIK



MAY

Principal: Sapna Syngal, MD, MPH Dana-Farber Cancer Institute

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Project Manager: Jennifer Rountree, PhD Providence Research Network

Project Manager: Jessica Tuan, MPH University of California, Los Angeles

Advocate: Marsha Baker Fight CRC

Advocate: Anjee Davis Fight CRC

Advocate: Cathy Jeffries Great Plains Tribal Leaders Health Board

Advocate: Kimberly Schoolcraft Fight CRC

Advocate: Helena L Williams, RN, BSN Board Chair, Gailen and Cathy Reevers Center for Community Empowerment



SU2C DREAM TEAMS

PURPOSE

This project is identifying communities near anchor medical institutions that serve minority and medically underserved communities to pinpoint unique local needs and turn at-risk communities into Stand Up To Cancer Zones® with high rates of colorectal cancer screening. The Team will provide free colorectal cancer testing in the zones and develop better approaches to colorectal cancer interception.

SPECIFIC AIMS

Aim 1. Develop and conduct a two-arm, multilevel, multicomponent, pragmatic trial randomized at the level of the community health center to compare two population outreach approaches, Cologuard or fecal immunochemical test (FIT), to increase CRC screening.

Aim 2. Conduct patient follow-up after an abnormal Cologuard or FIT screening test result.

Aim 3. Mentor a new generation of underrepresented researchers in medicine and public health focused on CRC prevention and control.

Aim 4. Design and deploy a community-based campaign to increase CRC screening rates in a demographically diverse impact zone within Los Angeles County.

KEY PROGRESS

The Team has successfully launched the CARES trial. Patients will receive a FIT or Cologuard kit in the mail. Any patient who returns a positive screening test (FIT or Cologuard) will be offered patient navigation to help them complete a diagnostic colonoscopy and the opportunity to complete a family cancer risk assessment. In March 2023, the CHATs launched their community outreach campaign to increase CRC screening rates in the South LA and Santa Monica impact zones, targeting community members of color who may be eligible for CRC screening.

CLINICAL TRIALS

Community Collaboration to Advance Racial/ Ethnic Equity in CRC Screening; NCT05714644; Enrolling by invitation



A larger version of this graphic is available in the appendix.

ADDITIONAL FUNDERS



HEARST foundations

SU2C DREAM TEAMS

SU2C HEALTH EQUITY BREAKTHROUGH TEAM BT6209

DISRUPT: Diversity and IncluSion in Research Underpinning Prevention and Therapy Trials Grant Term: May 2021 - April 2025

KEY PERSONNEL

Team Leader: Nina A. Bickell, MD, MPH Icahn School of Medicine at Mount Sinai

Co-Leader: Karen Hubbard, PhD The City College of New York





BICKELL

HUBBARD

Principal: Bruce Rapkin, PhD Albert Einstein College of Medicine

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Project Manager: Rita Ravichandar Albert Einstein College of Medicine rita.ravichandar@einsteinmed.edu

Project Manager: Radhi M. Yagnik, MS Icahn School of Medicine at Mount Sinai Radhi.Yagnik@mountsinai.org

PURPOSE

The Breakthrough Team is working to combat low BIPOC (Black Indigenous People of Color) participation in clinical trials in the US caused by the healthcare system, availability and knowledge of clinical trials, among many other reasons. Multidisciplinary teams from four New York City institutions are working together to improve diversity and inclusion in clinical trials through disruptive approaches at the community, provider, system and patient levels, and basic and translational scientist levels.

SPECIFIC AIMS

Aim 1. Disrupt and address community norms regarding participation in cancer research.

Aim 2. Disrupt current clinical trial recruitment making cancer clinical trials an easy and accessible choice for patients.

Aim 3. Disrupt norms in clinical trial design and methods by supporting basic science discovery that will increase its relevance to questions essential to reducing cancer health inequities.


KEY PROGRESS

The Team's Community, Care Delivery and Research Community Work Groups (WG) are establishing inter-institutional and community collaborations to: integrate community perspectives and approaches to message about clinical trials and medical research, develop a robust website for outreach and public information about clinical trials; create a generalizable IT approach to identify patients at times when trials are most relevant and find trials that may be most relevant for patients; and, implement a pilot award program incorporating community scientists into the research question development. In the past 6 months, in addition to the 25+ educational outreach sessions on messaging about clinical trials our community members, researchers and oncologists have conducted, community members across a broad sweep of our catchment areas are preparing a video for expanded wide-scale outreach that will further enhance our impact on community norms regarding cancer clinical trials. In April 2023, the Care Delivery WG began a trial using algorithms to identify patients at treatment decision points and recruit breast cancer patients. We started at Mount Sinai and have recruited 24 patients to date of whom 2 enrolled in a clinical trial. The Research Community team completed the inaugural Community Scientist Certificate course and launched a health equity seminar series for undergraduate, graduate, and postdoctoral trainees. They have awarded and funded two pilot awards (Cohort 1) and have recently announced 3 new pilots (Cohort 2) to be funded.

CLINICAL TRIALS

DISRUPT: Diversity and IncluSion in Research Underpinning Prevention and Therapy Trials NCT05146297. Recruiting.



A larger version of this graphic is available in the appendix.

SU2C CANADA-LUSTGARTEN FOUNDATION-PANCREATIC CANCER CANADA PASS CONVERGENCE DREAM TEAM CV6179, CV6185

PASS-01- Pancreatic Adenocarcinoma Signature Stratification for Treatment-01 Grant Term: August 2020 - October 2024

KEY PERSONNEL

Team Leader: Jennifer Knox, MD University Health Network

Co-Leader: Elizabeth Jaffee, MD John Hopkins University





KNOX

JAFFEE

Principal: Andrew Aquirre, MD, PhD Dana-Farber Cancer Institute

Principal: Steven Gallinger, MD Ontario Institute for Cancer Research

Principal: Daniel King, MD Northwell Health Center for Advanced Medicine

Principal: Daniel Laheru, MD Johns Hopkins University

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Principal: Daniel Renouf, MD, MPH British Columbia Cancer Agency

Principal: Kenneth Yu, MD Memorial Sloan Kettering Cancer Center

Collaborator: David Tuveson, MD, PhD Cold Spring Harbor Laboratory

Project Manager: Anna Dodd University Health Network Anna.Dodd@uhn.ca

PURPOSE

The PASS-01 team is working to identify patientspecific biomarkers predictive of greater benefit with modified FOLFIRINOX (mFFX) versus gemcitabine/nab-paclitaxel (GA), the two first-line combination chemotherapy regimens given to patients with advanced pancreatic cancer with good performance status. Using a suite of correlative studies including WGTS and, PDO drug sensitivity and immune markers, the team is not only using information gathered for each patient's clinical trajectory but is also building a rich discovery set for future analysis. While patients move through first-line therapy, the team turns around WGTS and PDO data guickly in order to provide useful information to clinicians at time of progression. This is followed by second-line therapy that is potentially directed to match the molecular or PDO profile if targetable vulnerabilities are identified.



SPECIFIC AIMS

Aim 1. Determine the PFS benefit of modified FOLFIRINOX (mFFX) compared with gemcitabine/nab- paclitaxel (GA) as first-line treatment in metastatic pancreatic ductal adenocarcinoma (PDAC) in a randomized phase II trial.

Aim 2. Explore biomarker correlation to treatment response and patient outcomes.

Aim 3. Evaluate concordance between patient response and outcomes with model (PDO) profiles, signatures, and pharmacotyping.

Aim 4. Compile a detailed genomic annotation of advanced PDAC patients on first-line chemotherapy.

KEY PROGRESS

For the clinical trial, all PASS-01 subsites have been activated; over 110 patients have been enrolled. This is a complex study requiring significant and timely coordination between centers to perform analyses on patient samples within the planned time frames. To maximize learnings and clinical impact, all patient results are presented and discussed at molecular rounds. This provides clinicians with a consensus opinion as to how best to move forward with precision treatment when possible. For these patients, as targetable vulnerabilities are identified, treatment is followed by second-line therapy that is potentially directed to match the molecular profile and/or drug sensitivity shown in the PDO models.

CLINICAL TRIALS

A Randomized Multicentre Phase II Trial to Evaluate the Two Standard Chemotherapy Regimens, Modified FOLFIRINOX (mFFX) and Gemcitabine/ Nab-Paclitaxel (GA), in Patients With Untreated Metastatic Pancreatic Ductal Adenocarcinoma; NCT04469556; Recruiting



A larger version of this graphic is available in the appendix.

SU2C CANADA METASTATIC BREAST CANCER DREAM TEAM DT5745

Targeting mRNA Translation to Effectively Treat Metastatic Breast Cancer

Grant Term: July 2019 - September 2022, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Nahum Sonenberg, PhD McGill University

Co-Leader: Michael N. Pollak, MD Lady Davis Institute for Medical Research





SONENBERG

POLLAK

Principal: Lynne-Marie Postovit, PhD Queens University

Principal: Poul H. B. Sorenson, MD, PhD BC Cancer Research Institute

Project Manager: Harvey W. Smith, PhD McGill University harvey.smith2@mcgill.ca

Advocate: Candace Cook

Advocate: Lynn Gentile Lynn and Joe Gentile Hope Fund

PURPOSE

The SU2C Canada Metastatic Breast Cancer Dream Team focused on a novel drug candidate that blocks abnormal translation: the dual MNK1/2 inhibitor eFT508 (tomivosertib). A Phase Ib trial of eFT508 in eligible patients with metastatic breast cancer (any subtype) not responsive to standard-of-care therapies was completed.

SPECIFIC AIMS

Aim 1. Run clinical trial of the MNK inhibitor EFT508 in patients with metastatic breast cancer.

Aim 2. Conduct pharmacodynamic studies of the MNK inhibitor EFT508 in patients with metastatic breast cancer.

KEY PROGRESS

The Team established the safety and tolerability of the tomivosertib/paclitaxel combination, in the first clinical trial that tested the combination of a MNK inhibitor with a cytotoxic agent. Preliminary correlative analyses showed that cytotoxic immune cells were recruited to metastastic tumors in tomivosertib-treated patients.

CLINICAL TRIALS

Trial to Assess the Safety, Pharmacodynamic Effects, Pharmacokinetics, and Efficacy of the MNK Inhibitor Tomivosertib (eFT508) in Combination With Paclitaxel, Following a Run-In Period of Tomivosertib Monotherapy, in Patients With Advanced Breast Cancer; NCT04261218; Completed

FUNDERS







SU2C MEG VOSBURG T-CELL LYMPHOMA DREAM TEAM DT6164

Tailoring CAR-based Immunotherapy Strategies to T-Cell Lymphoma

Grant Term: March 2019 - August 2023, administered by the American Association for Cancer Research

KEY PERSONNEL Team Leader: Helen E. Heslop, MD Baylor College of Medicine

Co-Leader: Gianpietro Dotti, MD University of North Carolina at Chapel Hill



HESLOP

DOTTI

Principal: Bayard L. Powell, MD Wake Forest University Health Sciences

Principal: Katy Rezvani, MD, PhD The University of Texas MD Anderson Cancer Center

Project Manager: Reynaldo Herrera Baylor College of Medicine Reynaldo.Herrera@bcm.edu

Advocate: Gustavo Ayala University of Texas Health Science Center at Houston **Advocate:** Bambi Grilley Baylor College of Medicine

Advocate: Ruth Sorelle Baylor College of Medicine

Advocate: Patty Spears University of North Carolina at Chapel Hill

PURPOSE

The T-Cell Lymphoma Dream Team is testing the safety and potency of different types of CARengineered immune cells directed to different target molecules on the lymphoma cells. In addition to CAR-engineered immune cell-based therapies, they are also working to determine whether such therapies can be made available as a banked "off-the-shelf" product.

SPECIFIC AIMS

Aim 1. Conduct a series of phase I clinical trials of CAR-ACT targeting different T-cell antigens in patients with resistant TCLs.

Aim 2. Identify factors that shape responses to CAR-ACT and thus inform the next generation of immune cell engineering.

Aim 3. Test additional modifications of CAR-ACT to improve their function against resistant TCLs.

KEY PROGRESS

The Team continues to enroll patients in their clinical trial testing the sequential administration of CART cells targeted to a protein called CD30. This sequential administration is being explored to prolong the therapeutic benefit of CAR T-cells. They developed an alternative clinically applicable method to manufacture functional CD7 CAR Tcells which can resist CAR-directed fratricide. After confirming that the CD7 CAR T cells manufactured using this method can expand, persist and lead to tumor responses without evidence of fratricide, the Team has moved forward with this approach in a clinical trial called CRIMSON-NE. In addition, the team has developed a novel strategy to genetically modify cord blood (CB)derived natural killer (NK) cells to express a CAR. In light of promising laboratory results, they are designing a phase I trial to study the safety and efficacy of these CAR-NK cells.

CLINICAL TRIALS

Phase I Study of Relapsed CD30 Expressing Lymphoma Treated With CD30 CAR T Cells (RELY-30); NCT02917083; Recruiting

Phase I Study of the Administration of T Lymphocytes Co-expressing the CD30 Chimeric Antigen Receptor (CAR) and CCR4 for Relapsed/Refractory CD30+ Hodgkin Lymphoma and CD30+ Non-Hodgkin Lymphoma; NCT03602157; Recruiting

Phase II Study of the Administration of T Lymphocytes Expressing the CD30 Chimeric Antigen Receptor (CAR) for Relapsed/Refractory CD30+ Peripheral T-Cell Lymphoma; NCT04083495; Recruiting

Phase I Study Evaluating the Safety and Activity of Allogeneic Chimeric Antigen Receptor Epstein-Barr Virus-Specific T Lymphocytes (CD30. CAR-EBVSTs) in Patients With Relapsed or Refractory CD30-Positive Lymphomas; NCT04288726; Recruiting

Cell Therapy for High Risk T-cell Malignancies Using CD7-Specific CAR Expressed on Non-Edited T Cells (CRIMSON-NE);NCT03690011; Recruiting



SU2C MULTIPLE MYELOMA DREAM TEAM DT6046

Screening and Interception of Precursor Myeloma

Grant Term: September 2018 - August 2022, administered by the American Association for Cancer Research

KEY PERSONNEL Team Leader: Irene M. Ghobrial, MD Dana-Farber Cancer Institute

Co-Leader: Ivan M. Borrello, MD Johns Hopkins University School of Medicine





GHOBRIAL

BORRELLO

Principal: Gad A. Getz, PhD Broad Institute

Principal: Jeremiah A. Johnson, PhD Massachusetts Institute of Technology

Principal: Prashant Kapoor, MBBS Mayo Clinic

Principal: Timothy R. Rebbeck, PhD Harvard T. H. Chan School of Public Health

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Advocate: Cheryl A. Boyce (deceased)

Advocate: Marie Cherisol

Advocate: Rebecca A. Nutley

Advocate: Kelly Smith

Advocate: Yaphet Smith

PURPOSE

The SU2C Multiple Myeloma Dream Team's overarching hypothesis is that early detection of precursor myeloma conditions (MGUS/SM) in a high-risk population, along with a good understanding of the molecular and immune factors that lead to disease progression, will lead to effective strategies that intercept disease progression and improve survival.

SPECIFIC AIMS

Aim 1. Establish a screen-detected prospective cohort study of monoclonal gammopathy of undetermined significance (MGUS)/smoldering multiple myeloma (SMM) patients at risk for multiple myeloma (MM) (Predicting Progression of Developing Myeloma in a High-Risk Screened Population, PROMISE).

Aim 2. Dissect genomic characteristics of clonal evolution from MGUS/SMM to MM and germline variants of high-risk individuals at risk of developing MGUS/SMM.

Aim 3. Evaluate the role of race, obesity, and health-related comorbidities on progression from pre-MM states to MM.

Aim 4. Define the permissive tumor microenvironment in MGUS/SMM.

Aim 5. Develop novel imaging and therapeutic approaches to detect and intercept disease progression at the precursor stages of the disease.

KEY ACCOMPLISHMENTS

The Team's PROMISE Study is the largest US screening study, screening individuals over age 30 who are at higher risk for myeloma and its precursors, such as individuals of African descent and individuals who have a first degree relative with a blood cancer. The Team observed a prevalence of 36% monoclonal gammopathies in the high-risk population screened age 50 and older and identified a new category of monoclonal gammopathy termed monoclonal gammopathy of indeterminant potential, or MGIP, in 29% of high-risk individuals age 50 and older. The Team used single-cell RNA sequencing, wholegenome sequencing, ATAC sequencing, plasma proteomic profiling, and MALDI-TOF mass spectrometry to analyze the molecular underpinnings of disease in tumor and immune cells. They differentiated malignant from normal plasma cells, uncovered novel associations between tumor immunophenotype and cytogenetics, developed a framework to prioritize novel targets for therapeutics development, described differences between marrow-resident and circulating plasma cells, and discovered abnormal proliferation in the marrow-resident normal plasma cells of patients.

CLINICAL TRIALS

Predicting Progression of Developing Myeloma in a High-Risk Screened Population (PROMISE); NCT03689595; Recruiting

FUNDER





SU2C-LUNGEVITY FOUNDATION-AMERICAN LUNG ASSOCIATION LUNG CANCER INTERCEPTION DREAM TEAM DT6045

Intercept Lung Cancer Through Immune, Imaging, and Molecular Evaluation (InTIME) Grant Term: March 2018 - February 2023, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Avrum E. Spira, MD Boston University

Co-Leader: Steven M. Dubinett, MD University of California, Los Angeles



SPIRA



DUBINETT

Principal: Charles Swanton, MD, PhD Francis Crick Institute

Principal: Carina Mari Aparici, MD Stanford University

Principal: Julie R. Brahmer, MD Johns Hopkins University

Principal: Matthew L. Meyerson, MD, PhD Dana-Farber Cancer Institute

Project Manager: Erin E. Kane, PhD Boston University erinkane@bu.edu

Advocate: Marcia Horn, JD International Cancer Advocacy Network

Advocate: Kim Norris Lung Cancer Foundation of America

PURPOSE

The Lung Cancer Interception Dream Team is applying novel molecular, imaging, and immunological approaches prospectively collected biospecimens to understand the biology of lung cancer precursor lesions, early-stage tumors, and the associated airway field to develop non-invasive biomarkers that predict progression, recurrence or response to therapy. The hypothesis is that premalignant lesions bear specific genomic and transcriptomic aberrations, and a subset of these lesions escape immune surveillance and progress to invasive cancer.

SPECIFIC AIMS

Aim 1. Establish a Pre-Cancer Genome Atlas (PCGA) to identify genomic, transcriptomic, and immune determinants of lung squamous and adenomatous premalignancy.

Aim 2. Identify molecular and imaging markers that distinguish malignant from benign indeterminate pulmonary nodules and circulating DNA markers that predict tumor recurrence.

Aim 3a. Develop molecular biomarkers to enable precision interception approaches in ongoing clinical trials of lung cancer interception.

Aim 3b. Discover baseline biomarkers predictive of therapeutic response to neoadjuvant therapy with immune checkpoint inhibitors and temporal markers of therapeutic efficacy.

Aim 3c. Assess therapeutic efficacy of adjuvant chemotherapy and immunotherapy among patients with subclinical evidence of lung cancer recurrence using ctDNA.

KEY ACCOMPLISHMENTS

The Team assembled unique cohorts of premalignant lung squamous and adenocarcinoma lesions. Analyses of these samples indicated that the immune microenvironment is an important determinant of premalignant progression for both lung squamous and adenocarcinoma. As part of the Team's effort to develop diagnostic tools to detect lung cancer early, they have been analyzing nasal swabs. Preliminary results showed that nasal gene expression was similar in lung cancer patients regardless of whether they smoked or not. The Team developed an assay for detecting circulating DNA called the Archer Diagnostics MRD assay. This assay has been used in two international phase III trials (MERMAID-01 and MERMAID-02) where the presence of ctDNA was used to determine whether the patient will be given additional treatment (combination chemotherapy and immunotherapy, immunotherapy or chemotherapy alone).

CLINICAL TRIALS

Neoadjuvant Nivolumab, or Nivolumab in Combination with Ipilimumab, in Resectable Nonsmall Cell Lung Cancer; NCT02259621; Active, not recruiting

18F-FSPG PET/CT and Integrated Biomarkers for Early Lung Cancer Detection in Patients With Indeterminate Pulmonary Nodules; NCT03824535; Recruiting

Phase III, Randomized, Multicenter, Double-Blind, Placebo-Controlled Study to Determine the Efficacy of Adjuvant Durvalumab in Combination With Platinum-Based Chemotherapy in Completely Resected Stage 2-3 NSCLC (MERMAID-1); NCT04385368; Completed

FUNDERS





SU2C-LUSTGARTEN FOUNDATION PANCREATIC CANCER INTERCEPTION DREAM TEAM DT6047

Intercepting Pancreatic Cancer in High-Risk Cohorts

Grant Term: February 2018 - July 2023, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Anirban Maitra, MBBS The University of Texas MD Anderson Cancer Center

Co-Leader: Michael G. Goggins, MD Johns Hopkins University

Co-Leader: Scott M. Lippman, MD University of California, San Diego







GOGGINS



LIPPMAN

Principal: Tyler Jacks, PhD Massachusetts Institute of Technology

Principal: Gloria M. Petersen, PhD (deceased) Mayo Clinic

Principal: Sapna Syngal, MD Dana-Farber Cancer Institute

Project Manager: Pamela Constantinou Papadopoulos, PhD The University of Texas MD Anderson Cancer Center pcpapadopoulos@mdanderson.org

Advocate: Barbara J. Kenner, PhD Kenner Family Research Fund

Advocate: Scott Nelson

PURPOSE

The SU2C-Lustgarten Foundation Pancreatic Cancer Interception Dream Team's goal is to intercept pancreatic cancer in high-risk patients through early detection and targeted immune prevention. Working first with relatives of people with pancreatic cancer, this team seeks to create a test to screen people at risk for pancreatic cancer to potentially detect cancer earlier and offer the most effective treatment options.

SPECIFIC AIMS

Aim 1. Enhance access to germline testing and screening protocols for cancer interception in high- risk cohorts and combine this with novel imaging algorithms to diagnose early PDAC lesions that are currently undetectable.

Aim 2. Intercept pancreatic cancer in high-risk cohorts using targeted immune prevention.

Aim 3. Develop a blood test for identifying individuals at risk for PDAC who would be candidates for early detection using imaging.

KEY PROGRESS

The Team embarked on the GENetic Education Risk Assessment and Testing (GENERATE) study, designed to increase early PDAC diagnosis by enhancing access to germline testing and screening in high-risk cohorts. Close to 90% of the 601 participants assigned to one of two study arms opted to undergo genetic screening. In addition, the Team is testing the potential of a peptide vaccine in individuals who have a higher risk of developing pancreatic cancer. Preliminary results confirmed that the immune system of these vaccinated individuals was activated against KRAS mutations. The Team continues to develop a blood-based test to predict whether or not an individual will develop pancreatic cancer. The sensitivity of the test is improving as more biomarkers are analyzed.

CLINICAL TRIALS

Pooled Mutant KRAS-Targeted Long Peptide Vaccine Combined with Nivolumab and Ipilimumab for Patients with Resected MMR-p Colorectal and Pancreatic Cancer; NCT04117087; Recruiting

Mutant KRAS-Targeted Long Peptide Vaccine for Patients at High Risk of Developing Pancreatic Cancer; NCT05013216; Recruiting

GENetic Education Risk Assessment and Testing Study (GENERATE); NCT03762590; Active, not recruiting

FUNDERS







ST. BALDRICK'S FOUNDATION-SU2C PEDIATRIC CANCER DREAM TEAM DT6065

Immunogenomics to Create New Therapies for High-Risk Childhood Cancers

Grant Term: December 2017 - May 2022, administered by the American Association for Cancer Research

KEY PERSONNEL Team Leader: John M. Maris, MD

Children's Hospital of Philadelphia

Co-Leader: Crystal L. Mackall, MD Stanford University



MARIS



MACKALL

Principal: Nabil M. Ahmed, MD Baylor College of Medicine

Principal: Lia Gore, MD University of Colorado

Principal: Rimas Orentas, PhD Seattle Children's Hospital

Principal: Paul M. Sondel, MD, PhD University of Wisconsin, Madison

Principal: Poul H. B. Sorenson, MD, PhD BC Cancer Research Institute

Principal: Michael D. Taylor, MD, PhD The Hospital for Sick Children **Investigator:** Kenneth B. DeSantes, MD University of Wisconsin, Madison

Investigator: Dimiter Dimitrov, PhD University of Pittsburgh

Investigator: Terry J. Fry, MD University of Colorado

Investigator: Stephan Grupp, MD, PhD Children's Hospital of Philadelphia

Investigator: Rosandra N. Kaplan, MD National Cancer Institute

Investigator: Michelle Monje, MD Stanford University

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Investigator: Julie R. Park, MD Seattle Children's Hospital

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Advocate: Kelly Forebough Seattle Children's Hospital

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Advocate: Gavin Lindberg Children's Hospital of Philadelphia

Advocate: Melanie Frost Moll Baylor College of Medicine

Advocate: Antonia Palmer The Hospital for Sick Children

Advocate: Kevin Reidy University of Colorado

Advocate: Carlos Sandi Stanford University and the National Cancer Institute

Advocate: Lori Schultz University of Wisconsin

Advocate: Patrick J. Sullivan, LLB, BC Cancer Research Institute

PURPOSE

The St. Baldrick's Foundation-SU2C Pediatric Cancer Dream Team brought together pediatric cancer researchers in cancer genomics and immunotherapeutics. The overall focus was to identify lineage restricted cell surface molecules not present on normal tissues which may be targeted with synthetic immunotherapeutics. The objective of this multi-institutional team from ten institutions was to develop and conduct paradigm changing early phase clinical trials of immunotherapies.

SPECIFIC AIMS

Aim 1. Discover and validate cell surface proteins as immunotherapeutic targets for high-risk pediatric cancers.

Aim 2. Perform preclinical optimization of candidate immunotherapeutics and IND-enabling studies to support the development of clinical trials for pediatric cancers with few therapeutic options.

Aim 3. Conduct pivotal pediatric cancer immunotherapy trials.

KEY ACCOMPLISHMENTS

The Team set out to develop and conduct early phase clinical trials of immunotherapies directed toward prioritized targets emerging from the first phase of their Dream Team project. In addition to continued support from St. Baldrick's and matching funds from their home institutions, the Team has leveraged two recent NCI initiatives emerging from the Biden Moonshot Initiative to accelerate efforts by creating two research networks: 1) Pediatric Cancer Immunotherapy Discovery and Development network (PI-DDN) and 2) the Pediatric Cancer Immunotherapy Trials Network (PedCITN). The Team has 45 early phase clinical trials in its Dream Team portfolio and has enrolled 1,371 children. They continue to design novel CART cells for a number of pediatric cancers plus a variety of tumor cell targets. The Team is generating and evaluating antibody-drug conjugates and antibody- radioconjugates with multiple payloads.

CLINICAL TRIALS

Phase I Study of HER2-Specific CAR T Cell Locoregional Immunotherapy for HER2-Positive Recurrent/ Refractory Pediatric Central Nervous System Tumors; NCT03500991; Recruiting

Phase I Dose-Escalation Study of CD19/CD22 Chimeric Antigen Receptor T Cells in Children and Young Adults With Recurrent or Refractory CD19/CD22-Expressing B-Cell Malignancies; NCT03448393; Recruiting



Pediatric and Young Adult Leukemia Adoptive Therapy (PLAT)-06: Phase I/II Study of CD19-Specific CAR T Cells With a Fully Human Binding Domain for CD19+ Leukemia or Lymphoma; NCT03684889; Active, not recruiting

Phase 1 Study of EGFR806-Specific CAR T Cell Locoregional Immunotherapy for EGFR-Positive Recurrent or Refractory Pediatric Central Nervous System Tumors; NCT03638167; Active, not recruiting

Phase I Study of EGFR806 CAR T Cell Immunotherapy for Recurrent/Refractory Solid Tumors in Children and Young Adults; NCT03618381; Recruiting

Phase II Study of Humanized CD19-Directed Chimeric Antigen Receptor-Modified T Cells (huCART19) for Very High Risk Subsets of B-Cell Acute Lymphoblastic Leukemia (B-ALL); NCT03792633; Active, not recruiting

Treatment of CMV Infections With Viral-Specific T Cells Against CMV in Pediatric and Adult Immunocompromised Patients or Recipients of Allogeneic Stem Cell Transplantation; NCT03798301; Recruiting

Phase I Dose-Escalation Study Evaluating Safety and Tolerability of Viral-Specific T Cells Against CMV in Adult Solid Organ Transplant Recipients; NCT03950414; Recruiting

GD2-CAR PERSIST: Production and Engineering of GD2-Targeted, Receptor-Modified T Cells (GD2CART) for Sarcoma and Neuroblastoma to Increase Systemic Tumor Exposure; NCT04539366; Suspended

An Open-Label Dose-Escalation, Efficacy, and Safety Study of CLR 131 in Children, Adolescents, and Young Adults With Select Solid Tumors, Lymphoma, and Malignant Brain Tumors; NCT03478462; Active, not recruiting Phase I Study of B7-H3-Specific CAR T Cell Locoregional Immunotherapy for Diffuse Intrinsic Pontine Glioma/Diffuse Midline Glioma and Recurrent or Refractory Pediatric Central Nervous System Tumors; NCT04185038; Recruiting

Phase I/II Study of Anti-CD33 Chimeric Antigen Receptor-Expressing T Cells (CD33CART) in Children and Young Adults With Relapsed/Refractory Acute Myeloid Leukemia; NCT03971799; Active, not recruiting

Phase I Study of B7H3 CAR T Cell Immunotherapy for Recurrent/Refractory Solid Tumors in Children and Young Adults; NCT04483778; Active, not recruiting

Phase Ib Clinical Trial of Autologous CD22 Chimeric Antigen Receptor (CAR) T Cells in Children and Young Adults With Recurrent or Refractory B-Cell Malignancies; NCT04088864; Suspended

Phase I Clinical Trial of Autologous GD2 Chimeric Antigen Receptor (CAR) T Cells (GD2CART) for Diffuse Intrinsic Pontine Gliomas (DIPG) and Spinal Diffuse Midline Gliomas (DMG); NCT04196413; Recruiting

Phase I Trial of Autologous HER2-Specific CAR T Cells in Pediatric Patients With Refractory or Recurrent Ependymoma; NCT04903080; Active, not recruiting

FUNDERS





SU2C COLORECTAL CANCER DREAM TEAM DT6044

Targeting Genomic, Metabolic, and Immunological Vulnerabilities of Colorectal Cancer Grant Term: August 2017 – January 2024, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Luis A. Diaz Jr., MD Memorial Sloan Kettering Cancer Center

Co-Leader: Lewis C. Cantley, PhD Harvard Medical School

Co-Leader: Zhenghe J. Wang, PhD Case Western Reserve University



DIAZ, JR.



CANTLEY



WANG

Principal: Nilofer S. Azad, MD Johns Hopkins University

Principal: Ryan B. Corcoran, MD, PhD Massachusetts General Hospital

Project Manager: Mitesh Patel Memorial Sloan Kettering Cancer Center patelm2@mskcc.org

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Advocate: Joanna R. Fuchs, MD Dana-Farber/ Harvard SPORE

Advocate: Manju George Paltown Development Foundation

Advocate: Ivelisse Page Believe Big

Advocate: Martha Raymond Michael's Mission

Advocate: Nancy Roach Fight Colorectal Cancer

Advocate: Steven Schwarze Paltown Development Foundation

PURPOSE

The SU2C Colorectal Cancer Treatment Dream Team is working to integrate molecular science, cancer genomics, and metabolomics with targeted and immune approaches for more effective treatments, investigating new approaches, and "precision prevention" strategies for colorectal cancer, thereby preventing cancer recurrence after initial treatments.

SPECIFIC AIMS

Aim 1. Harness the immune system to treat colorectal cancer.

Aim 2. High impacted targeted pathway blockade in colorectal cancer.

Aim 3. Develop high-dose vitamin C as a therapy for KRAS/BRAF mutant colorectal cancer.

Aim 4. Target the glutamine dependence of PIK-3CA mutant CRC in combination therapy with novel glutaminase inhibitor CB-839 plus capecitabine.



Aim 5. "Precision prevention" for colorectal cancer.

KEY PROGRESS

The team tested an approach to increase tumor mutation burden and augment anti-tumor immune responses which could be intensified by administration of immune checkpoint inhibitors. The Team also launched a prospective study of the clinical utility of minimal residual disease (MRD) detection using circulating tumor DNA (ctDNA) assays for stage 3 colorectal cancer. The Team is also running a single-arm, Phase 2 study to evaluate the effect of 6 months of neoadjuvant dostarlimab-gxly treatment in patients with dMMR/MSI-H locally advanced rectal cancer. At the 2022 ASCO Annual Meeting and in the NEJM, the Team reported clinical complete responses in all of the first 14 patients. During its tenure, the Team accrued 736 subjects to therapeutic trials, authored more than 300 manuscripts, and secured one patent. This team's work contributed 2020 FDA approval of pembrolizumab (Merck) for microsatellite instability-high or mismatch repair deficient metastatic colorectal cancer.

CLINICAL TRIALS

Phase II Study of MK-3475 in Patients With Microsatellite Unstable (MSI) Tumors; NCT01876511; Completed

Phase III Study of Pembrolizumab (MK-3475) Versus Chemotherapy in Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Stage 4 Colorectal Carcinoma (KEY-NOTE-177); NCT02563002; Completed

Phase I/II Study of CB-839 and Capecitabinein Patients With Advanced Solid Tumors and Fluoropyrimidine Resistant PIK3CA Mutant Colorectal Cancer; NCT02861300; Active, not recruiting

Nivolumab and Ipilimumab and Radiation Therapy in Microsatellite Stable (MSS) and Microsatellite Instability (MSI) High Colorectal and Pancreatic Cancer; NCT03104439; Recruiting Phase II Study of High-Dose Vitamin C Intravenous Infusion in Patients With Resectable or Metastatic Solid Tumor Malignancies; NCT03146962;Completed

Phase II Study of Dabrafenib and Trametinib in Combination With PDR001 in Patients With BRAFV600E Metastatic Colorectal Cancer; NCT03668431; Recruiting

Phase Ib/II Open-Label Dose Escalation Study of Entinostat in Combination With Pembrolizumab in Patients With Non-small Cell Lung Cancer, With Expansion Cohorts in Patients With Non-small Cell Lung Cancer, Melanoma, and Mismatch Repair-Proficient Colorectal Cancer; NCT02437136; Active, not recruiting

Phase I/II Study of PI3Kinase Inhibition (Copanlisib) and Anti-PD-1 Antibody Nivolumab in Relapsed/ Refractory Solid Tumors With Expansions in Mismatch Repair-Proficient (MSS) Colorectal Cancer; NCT03711058; Active not recruiting

Early Identification and Treatment of Occult Metastatic Disease in Stage 3 Colon Cancer; NCT03803553; Recruiting

Phase II Study of Induction PD-1 Blockade in Subjects With Locally Advanced Mismatch Repair-Deficient Solid Tumors; NCT04165772; Recruiting

Phase II Study of Temozolomide, Cisplatin, and Nivolumab in MMR-Proficient Colorectal Cancer; NCT04457284; Active, not recruiting

SU2C CANADA-CANADIAN CANCER SOCIETY BREAST CANCER DREAM TEAM DT6144

Translational Development of Novel Drugs Targeting Tumor Vulnerabilities

Grant Term: January 2016 - June 2022, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Tak W. Mak, PhD Campbell Family Institute for Breast Cancer Research at Princess Margaret Cancer Centre

Co-Leader: Samuel Aparicio, BM, BCh, PhD University of British Columbia





ΜΑΚ

APARICIO

Principal: Karen A. Gelmon, MD British Columbia Cancer Agency

Principal: Morag Park, PhD Goodman Cancer Research Centre and McGill University

Principal: Kathleen I. Pritchard, MD University of Toronto, Sunnybrook Health Sciences Centre of Toronto

Project Manager: Thorsten Berger, PhD University Health Network Thorsten.Berger@uhnresearch.ca

Advocate: Wendie den Brok, MD BC Cancer Agency Research Centre

Advocate: Randy Mellon Think Pink Direct

Advocate: Zuri Scrivens The Beautiful Gift

PURPOSE

The goal of the SU2C Canada–Canadian Cancer Society Breast Cancer Dream Team was to develop new treatments for triple-negative/basal-like breast cancer (TNBC) and other aggressive breast cancers which currently need more efficacious targeted therapies. The Team developed three biomarker-driven drugs: CFI-400945 (PLK4 inhibitor), CFI-402257 (TTK inhibitor), and CX5461 (G-quadruplex binder).

SPECIFIC AIMS

Aim 1. Pursue basic and translational development of CFI-400945, CX5461, and CFI-402257.

Aim 2. Conduct proof-of-concept clinical trials of CFI-400945, CX5461, and CFI-402257.

KEY ACCOMPLISHMENTS

Discoveries made in the laboratory component of the project identified new opportunities to expand the use of CFI-400945 and CFI-402257 into the large group of patients with metastatic breast cancer resistant to current standard first line treatment (CDK4/6 inhibitors). The Team completed accrual to their clinical trials which were carried out in collaboration with the Canadian Cancer Trials Group. They identified safe and tolerable recommended Phase 2 doses of each agent, as well as combinations of CFI-400945 and durvalumab, and CFI-402257 and paclitaxel. Promising clinical activity, including durable responses were observed with all agents in patients with metastatic breast cancer. These results have supported the further development of these agents in ongoing and planned biomarker-directed trials.



CLINICAL TRIALS

Phase I Study of CX5461; NCT02719977; Completed

Open-Label Dose-Escalation, Safety, and Pharmacokinetic Study of CFI-400945 Fumarate Administered Orally to Patients With Advanced Cancer; NCT01954316; Completed

Open-Label Dose-Escalation, Safety, and Pharmacokinetic Study of CFI-402257 Administered Orally to Patients With Advanced Solid Tumors; NCT02792465; Active, not recruiting

Phase Ib and Open-Label Phase II Study of CFI-402257 in Combination With Weekly Paclitaxel in Patients With Advanced/Metastatic HER2-Negative Breast Cancer; NCT03568422; Completed

Phase II Study of CFI-400945 in Patients With Advanced/Metastatic Breast Cancer; NCT03624543; Active, not recruiting

Phase II Study of CFI-400945 and Durvalumab in Patients With Advanced/Metastatic Triple-Negative Breast Cancer (TNBC); NCT04176848; Completed FUNDERS







SU2C-CANCER RESEARCH UK-LUSTGARTEN FOUNDATION PANCREATIC CANCER DREAM TEAM DT6014

Reprogramming of Transcriptional Circuitry to Control Pancreatic Cancer

Grant Term: January 2016 - June 2020, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Daniel D. Von Hoff, MD Translational Genomics Research Institute (TGEN)

Co-Leader: Gerard I. Evan, PhD University of Cambridge

Co-Leader: Ronald M. Evans, PhD Salk Research Institute for Biological Studies



VON HOFF



EVAN



EVANS Principal: David J. Propper, MBChB, MD, PhD Barts Cancer Institute and London NHS Trust

Principal: Joshua D. Rabinowitz, MD, PhD Princeton University **Project Manager:** Jatan Clark TGEN jclark@tgen.org

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Advocate: Suzanne Berenger Bain & Company, Inc.

Advocate: Devah Pager, PhD, (deceased) Harvard University

Advocate: Jill E. Pechacek, MD (deceased)

Advocate: Howard Young General Wholesale Beer Company

PURPOSE

The Dream Team's goal was to significantly improve pancreatic cancer patient survival by targeting super-enhancer (SE) regulated regenerative programs in the pancreas, including cellular communication between the epithelial compartment (including cancer stem cells), stromal compartment, and immune compartment.

SPECIFIC AIMS

Aim 1. Define super-enhancer networks in the cellular milieu of pancreatic cancer.

Aim 2. Determine the mechanisms that mediate crosstalk between super-enhancer networks both within cells and between them, including metabolic dependencies.

Aim 3. Determine the utility of super-enhancer disruption in treating pancreatic cancer. (Work on this Aim is continuing as an SU2C subproject.)



KEY ACCOMPLISHMENTS

The Team showed how super-enhancer networks control tumor behavior and the behavior of individual cell types within the tumor microenvironment. These findings support the team's model of pancreatic cancer as a normal regenerative program that has been "hacked" into, suggesting the possibility of reversing the program. Therapeutic targets identified include LIF [stromal compartment], MICAL2 [tumor compartment], ROR gamma, and Musashi [stem cell compartment]). Building on these findings, the investigators developed therapeutic strategies. Studies on metabolism have begun to reveal pancreatic cancer sensitivity to metabolic perturbations ("electron overloading," ketogenic diet). A continuing clinical trial led by Dr. Wolpin is evaluating the therapeutic potential of targeting the Vitamin D receptor with paricalcitol.

CLINICAL TRIALS

A Phase II Pilot Trial of Nivolumab + Albumin-Bound Paclitaxel +Paricalcitol + Cisplatin + Gemcitabine (NAPPCG) in Patients With Previously Untreated Metastatic Pancreatic Ductal Adenocarcinoma; NCT02754726; Active, not recruiting

A Phase II Study of Cabiralizumab (BMS-986227, FPA008) Administered in Combination With Nivolumab (BMS-936558) With and Without Chemotherapy in Patients With Advanced Pancreatic Cancer; NCT03336216; Completed

Phase Ib/II Trial of High-Dose Ascorbic Acid (AA) + Nanoparticle Paclitaxel Protein Band + Cisplatin + Gemcitabine (AA NABPLAGEM) in Patients Who Have Received No Prior Therapy for Their Metastatic Pancreatic Cancer; NCT03410030; Completed Phase II Pilot Trial of Paclitaxel Protein Bound Plus Cisplatin Plus Gemcitabine and the Addition of Paricalcitol Upon Disease Progression in Patients With Previously Untreated Metastatic Pancreatic Ductal Adenocarcinoma (NABPLAGEMD); NCT03415854; Active, not recruiting

Vitamin D Receptor Agonist Paricalcitol Plus Gemcitabine and Nab-Paclitaxel in Patients With Metastatic Pancreatic Cancer; NCT03520790; Active, not recruiting

A Phase Ib/II Randomized Clinical Trial of Chemotherapy With Nab-Paclitaxel/Gemcitabine/ Cisplatin +/- the AXL Inhibitor Bemcentinib for Patients With Metastatic Pancreatic Cancer; NCT03649321; Terminated

A Phase I Multicenter, Open-Label, Dose-Escalation and Dose-Expansion Study to Evaluate the Safety, Pharmacokinetics, Pharmacodynamics, Immunogenicity, and Antitumor Activity of MSC-1 in Patients With Advanced Solid Tumors; NCT03490669; Complered

MinPAC: Phase II, International, Open-Label Trial of Minnelide™ in Patients With Refractory Pancreatic Cancer; NCT03117920; Completed

FUNDERS





SU2C CANADA CANCER STEM CELL DREAM TEAM DT6145

Targeting Brain Tumor Stem Cell Epigenetic and Molecular Networks Grant Term: October 2015 - March 2021, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Peter B. Dirks, MD, PhD The Hospital for Sick Children

Co-Leader: Samuel Weiss, PhD University of Calgary





DIRKS

WEISS

Principal: Cheryl H. Arrowsmith, PhD University of Toronto

Principal: Gary D. Bader, PhD University of Toronto

Principal: Nada Jabado, MD, PhD McGill University

Principal: Mathieu Lupien, PhD University Health Network

Principal: Marco A. Marra, PhD University of British Columbia

Principal: Michael W. Salter, MD, PhD The Hospital for Sick Children

Principal: Michael D. Taylor, MD, PhD The Hospital for Sick Children **Principal:** Michael Tyers, PhD Université de Montreal

Project Manager: Tracey Richards The Hospital for Sick Children tracey.richards@sickkids.ca

Advocate: Wendy M. Durigon Jessica's Footprint Foundation

Advocate: Patrick J. Sullivan, LLB Team Finn Foundation

PURPOSE

The Team sought to understand the basic biology of brain tumor stem cells and expose their vulnerabilities, with the ultimate goal of developing new therapies.

SPECIFIC AIMS

Aim 1. Conduct a comprehensive investigation of genomic, epigenomic, and metabolomic profiles of BTSCs to define networks of self-renewal, therapeutic resistance, and targetable vulnerabilities.

Aim 2. Identify targets whose pharmacological inhibition is efficacious on BTSCs from GBM and PFA ependymoma.

Aim 3. Preclinically test five targets to accelerate translation to the clinic.



KEY ACCOMPLISHMENTS

The Team completed sequencing and functional characterization of 89 adult glioblastomas (GBM), 4 pediatric GBM, 16 pediatric ependymomas, and 6 control neural stem cell cultures. In adult GBM, the investigators converged on two tumor subgroups defined by developmental and inflammatory signals. They also found two promising clinically-actionable targets - one epigenetic (PRMT5) and the other metabolic (GLS) - both targets of promising drug candidates. The Team also characterized the posterior fossa A and supratentorial subtypes of pediatric ependymoma using brain tumor stem cells grown from patient tumor samples and screened them in various ways to identify therapeutic vulnerabilities. In pediatric GBM, they characterized Histone 3 mutant tumors, specially focusing their efforts to target H3K27 mutant tumors with an ALK inhibitor, which showed promise for clinical translation. The Team has been conducting a phase I/Ib trial of combined 5'azacitidine and carboplatin for recurrent/refractory brain tumors.

CLINICAL TRIALS

Phase I/Ib Trial of Combined 5-Azacitidine and Carboplatin for Recurrent/Refractory Pediatric Brain and Solid Tumors; NCT03206021; Active, not recruiting

FUNDERS





Cancer Stem Cell Consortium (CSCC)







SU2C-AMERICAN CANCER SOCIETY LUNG CANCER DREAM TEAM DT5977

Targeting KRAS-Mutant Lung Cancers

Grant Term: August 2015 - January 2021, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Jedd D. Wolchok, MD, PhD Weill Cornell Medical College

Co-Leader: Pasi A. Jänne, MD, PhD Dana-Farber Cancer Institute

Co-Leader: Justin F. Gainor, MD Massachusetts General Hospital Cancer Center







WOLCHOK

JÄNNE

GAINOR



Principal: Gad A. Getz, PhD Broad Institute

Principal: Roy S. Herbst, MD, PhD Yale University

Principal: John V. Heymach, MD, PhD The University of Texas MD Anderson Cancer Center

Principal: Frank McCormick, PhD University of California, San Francisco

Principal: Drew M. Pardoll, MD, PhD Johns Hopkins University

Principal: Charles M. Rudin, MD, PhD Memorial Sloan Kettering Cancer Center

Project Manager: Lalitha Ramanathapuram, PhD Memorial Sloan Kettering Cancer Center

Project Manager: Cam Anh Tran Dana-Farber Cancer Institute

Advocate: Andrea F. Ferris LUNGevity Foundation

Advocate: Jeffrey L. Wigbels Cypress Group at Morgan Stanley



PURPOSE

The Targeting KRAS-Mutant Lung Cancers Team established a collaborative, rigorous, multidisciplinary program that brings together two highly promising treatment approaches: targeted therapy – in this case targeting the KRAS gene – and immunotherapy. This combined approach may lead to novel treatments that will markedly improve outcomes for KRAS-mutant non-small lung cancer patients.

SPECIFIC AIMS

Aim 1. Target KRAS and downstream pathways.

Aim 2. Target the immune system for treatment of KRAS-mutant lung cancers. (Work on this Aim is continuing as an SU2C subproject.)

Aim 3. Integrate targeted therapies with immunotherapies for KRAS-mutant lung cancers.

KEY ACCOMPLISHMENTS

The Team amassed a large data set of NSCLC tumors derived from patients treated with checkpoint inhibitors which served as a rich resource, especially for the identification of predictive and prognostic markers of checkpoint inhibitor response. This is an important resource to aid in the design of future studies. The Team demonstrated that NSCLC patients with KRAS-mutant cancers with concomitant LKB1/STK1 mutations derived little benefit from immune checkpoint inhibitors when used as single agents and that there was no benefit from the addition of immune checkpoint inhibitors to chemotherapy. This was in contrast to patients with KRAS- or KRAS/TP53-mutant cancers. Mechanistic insights into the role of the LKB1/STK11 mutations demonstrated immune defects dependent on dysregulation of metabolic and STING pathways. This work contributed to the understanding of the role of KRAS G12C inhibitors in the treatment of these patients relative to the role of checkpoint blockade. The Team has significantly contributed to the development of KRAS G12C inhibitors and investigations of resistance mechanisms to KRAS G12C inhibitors. This Team continued its work with support from The Mark Foundation for Cancer Research.

CLINICAL TRIALS

Identifying Genetic Predictors of Durable Clinical Benefit to Pembrolizumab in Advanced Nonsmall Cell Lung Cancer Alone and in Combination With Chemotherapy; NCT02710396; Terminated

Phase Ib Trial of Pembrolizumab (MK-3475) and Trametinib Focused on Advanced KRAS-Mutant Non-small Cell Lung Cancer; NCT03299088; Active, not recruiting

BATTLE-2 Program: Biomarker-Integrated Targeted Therapy Study in Previously Treated Patients With Advanced Non-small Cell Lung Cancer; NCT03225664; Active, not recruiting

Phase I Trial of RO5126766 (CH5126766) in Patients With Advanced KRAS-Mutant Lung Adenocarcinomas; NCT03681483; Active, not recruiting

Phase I Trial of Trametinib and Ponatinib in Patients With KRAS-Mutant Advanced Non-small Cell Lung Cancer; NCT03704688; Completed

Open-Label, Two-Part, Phase Ib/II Study to Investigate the Safety, Pharmacokinetics, Pharmacodynamics, and Clinical Activity of the MEK Inhibitor Trametinib and the BCL-2-Family Inhibitor Navitoclax (ABT-263) in Combination in Subjects With KRAS or NRAS Mutation-Positive Advanced Solid Tumors; NCT02079740; Active, not recruiting

Neoadjuvant Nivolumab, or Nivolumab in Combination With Ipilimumab, in Resectable Nonsmall Cell Lung Cancer. NCT02259621; Active, not recruiting

Phase I/II Trial Immunotherapy With Durvalumab and Tremelimumab With Continuous or Intermittent MEK Inhibitor Selumetinib in NSCLC; NCT03581487; Recruiting

A Phase I/II Open-Label Study Evaluating the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Efficacy of AMG 510 Monotherapy in Subjects With Advanced Solid Tumors With KRAS p.G12C Mutation and AMG 510 Combination Therapy in Subjects With Advanced NSCLC With KRAS p.G12C Mutation (CodeBreaK 100); NCT03600883; Active, not recruiting

Phase I/II Multiple Expansion Cohort Trial of MRTX849 in Patients With Advanced Solid Tumors With KRAS G12C Mutation; NCT03785249; Recruiting Phase I Open-Label, Multi-Centre Study to Assess the Safety, Tolerability, and Preliminary Anti-tumour Activity of Ascending Doses of Selumetinib (AZD6244 Hyd-sulfate) in Combination With MEDI4736 and Selumetinib in Combination With MEDI4736 and Tremelimumab in Patients With Advanced Solid Tumours; NCT02586987; Completed

A First in Human Phase I trial of a Vaccine Targeting Mutant KRAS and Mesothelin Epitopes in Combination with an anti-PD-1 Antibody in Patients with Previously Treated, Metastatic, KRAS mutant NSCLC;NCT03371381;Terminated

FUNDERS



🖑 Bristol Myers Squibb



SU2C-OVARIAN CANCER RESEARCH ALLIANCE-NATIONAL OVARIAN CANCER COALITION OVARIAN CANCER DREAM TEAM DT5978

DNA Repair Therapies for Ovarian Cancer

Grant Term: July 2015 - June 2019, administered by the American Association for Cancer Research

KEY PERSONNEL Team Leader: Alan D. D'Andrea, MD Dana-Farber Cancer Institute

Co-Leader: Elizabeth M. Swisher, MD University of Washington





D'ANDREA

SWISHER

Principal: Gini F. Fleming, MD University of Chicago

Principal: Maria Jasin, PhD Memorial Sloan Kettering Cancer Center

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Principal: Karen H. Lu, MD The University of Texas MD Anderson Cancer Center **Project Manager:** Alexandra Feinstein Dana- Farber Cancer Institute

Project Manager: Donald R. Watson Dana- Farber Cancer Institute

Advocate: Jamie Crase University of Washington

Advocate: Sue Friedman FORCE

Advocate: Kathleen A. Gavin Minnesota Ovarian Cancer Alliance

Advocate: Deborah Polinsky SHARE

PURPOSE

The SU2C-Ovarian Cancer Research Alliance-National Ovarian Cancer Coalition Ovarian Cancer Dream Team was assembled to develop new therapies targeting DNA repair pathways and expand on recent clinical advances to a larger group of ovarian cancer patients, including those without mutations in BRCA1 or BRCA2. The Team also worked to develop novel cancer prevention strategies through the development of ovarian cancer genetic testing and surgical prevention models.

SPECIFIC AIMS

Aim 1. Characterize mechanisms of sensitivity and resistance to PARPi that can identify individual ovarian cancers that are hypersensitive to PARPi monotherapy.

Aim 2. Evaluate novel drug combinations that extend the use of PARPi to HR-proficient ovarian cancers.

Aim 3. Develop ovarian cancer genetic testing and surgical prevention models, which could increase access to ovarian cancer genetic testing and ovarian cancer prevention.

KEY ACCOMPLISHMENTS

The Team identified new biomarkers of sensitivity and resistance to PARP inhibitors, including PTIP, EZH2 MUS81, and REV7. The Team's TOPACIO study, which tested the combination of the PARP inhibitor Niraparib and the anti-PD1 antibody Pembrolizumab, showed an improved objective response in ovarian cancer patients with advanced platinum-resistant tumors. Analysis of patient samples revealed novel biomarkers that were predictive of patient responses. Findings from the team have also contributed to the 2016 FDA approval of rucaparib, the second PARP inhibitor approved by the FDA, for treatment of BRCA1/2 mutated ovarian cancer. The Team's MAGENTA trial, which enrolled 3822 patients, demonstrated the benefits of genetic counseling for individuals who have been found to have a pathogenic mutation.

CLINICAL TRIALS

Phase 1 Trial of ABT-888 and SCH727965 in Patients With Advanced Solid Tumors; NCT01434316; Active, not recruiting

Stand Up To Cancer: MAGENTA (Making Genetic Testing Accessible); NCT02993068; Recruiting WISP (Women Choosing Surgical Prevention); NCT02760849; Active, not recruiting

Phase I Study of the Oral PI3kinase Inhibitor BKM120 or BYL719 and the Oral PARP Inhibitor Olaparib in Patients With Recurrent Triple-Negative Breast Cancer or High Grade Serous Ovarian Cancer; NCT01623349; Completed

Phase I/II Clinical Study of Niraparib in Combination With Pembrolizumab (MK-3475) in Patients With Advanced or Metastatic Triple-Negative Breast Cancer and in Patients With Recurrent Ovarian Cancer; NCT02657889; Completed

A Phase II, Open-Label Study of Rucaparib in Patients With Platinum-Sensitive, Relapsed, High-Grade Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer (ARIEL2); NCT01891344; Completed

FUNDERS





SU2C-DUTCH CANCER SOCIETY COLORECTAL CANCER EARLY DETECTION DREAM TEAM DT5916

Molecular Early Detection of Colorectal Cancer (MEDOCC)

Grant Term: April 2015 - September 2022, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Gerrit A. Meijer, MD, PhD Netherlands Cancer Institute

Co-Leader: Victor E. Velculescu, MD, PhD Johns Hopkins University





MEIJER

VELCULESCU

Principal: Veerle Coupé, PhD VU University Medical Center

Principal: Evelien Dekker, MD, PhD University of Amsterdam

Principal: Manon van Engeland, PhD Maastricht University Medical Center

Principal: James G. Herman, MD University of Pittsburgh

Principal: Miriam Koopman, MD, PhD University Medical Center Utrecht

Principal: Ernst J. Kuipers, MD, PhD Erasmus University Medical Center **Project Manager:** Meike de Wit, PhD Netherlands Cancer Institute m.d.wit@nki.nl

Advocate: Joop Kroes (deceased) Foundation for Patients With Cancer of the Digestive Tract (Stichting Voor Patiënten met Kanker aan het Spijsverteringskanaal, SPKS)

Advocate: Marcia Horn, JD International Cancer Advocacy Network

Advocate: Huig Schipper (inactive)

PURPOSE

The SU2C-Dutch Cancer Society Colorectal Cancer Early Detection Dream Team aims to bring highly sensitive molecular tests from the lab bench to the bed side. The Molecular Early Detection Of Colorectal Cancer (MEDOCC) project has two aims. The first aim is to improve molecular stool-based tests by using the best combination of protein biomarkers. The second aim is to develop a molecular blood test for circulating cancer-associated DNA that identifies early-stage colorectal cancer patients whose survival may be improved by chemotherapy after surgery.

SPECIFIC AIMS

Aim 1. Develop and clinically validate a costeffective molecular screening test for CRC that outperforms the current state-of-the-art FIT.

Aim 2. Develop and clinically validate a better test for residual disease detection and monitoring in stage II and III colorectal cancer patients.

KEY ACCOMPLISHMENTS

The currently used stool test, fecal immunochemical test (FIT), that is used in nationwide screening programs, has been proven to be successful in helping identify patients with CRC. Unfortunately, the test is not sensitive enough to identify individuals with precancerous lesions. The Team developed an improved and potentially cost-effective stool test (called mtFIT) that is more sensitive than the traditional test, without increasing the probability of false positives. In addition, the Team developed and optimized approaches for detection of circulating tumor DNA (ctDNA) in patients with early stage cancers. They have shown that a tumor-guided approach for detection of ctDNA may be useful for clinical identification of minimal residual disease in stage II and III colorectal cancer patients.

CLINICAL TRIALS

Clinical Validation of a Multi-target Faecal Immunochemical Test (mtFIT) Versus a Faecal Immunochemical Test (FIT) for Detecting Advanced Neoplasia in Population Screening for CRC: a Prospective Cohort Study With Paired Design; NCT05314309; Active, not recruiting

Prospective Data Collection Initiative on Colorectal Cancer–A Prospective Observational Cohort Study; sub-study of NCT02070146; Recruiting.

FUNDER





VAN ANDEL INSTITUTE-SU2C CANCER EPIGENETICS DREAM TEAM DT5957

Team Project Name

Grant Term: January 2023 - December 2025

KEY PERSONNEL Team Co-Leader: Peter Jones, PhD, DSc (hon) Van Andel Institute

Co-Leader: Stephen Baylin, MD

John Hopkins University and Van Andel Institute





JONES

BAYLIN

Principal: Anthony B. El-Khoueiry, MD University of Southern California

Principal: Kirsten Grønbæk, MD, DMSc Rigshospitalet and Biotech Research and Innovation Centre (BRIC)

Principal: Jean-Pierre Issa, MD Coriell Institute for Medical Research **Principal:** Kenneth P. Nephew, PhD Indiana University School of Medicine

Principal: Feyruz V. Rassool, PhD University of Maryland School of Medicine

Principal: Charles Rudin, MD, PhD Memorial Sloan Kettering Cancer Center

Principal: Benjamin A. Youngblood, PhD St. Jude Children's Research Hospital

Project Manager: Ryan Burgos, MBA Van Andel Institute Ryan.Burgos@vai.org

Advocates: Beth Flory and Rick Bangs

PURPOSE:

Epigenetic therapy is an approach to cancer treatment that involves switching key genes on or off to help destroy cancer cells. The Van Andel Institute (VAI)-Stand Up To Cancer Epigenetics Dream Team II, funded by the Van Andel Institute, continues the original Epigenetics Dream Team's work to restore normal function to damaged epigenetic mechanisms by exploring immune sensitization, chemo sensitization and novel target strategies.

SPECIFIC AIM

Bring epigenetic therapy to the forefront of cancer management.

KEY PROGRESS:

Baylin and Jones labs defined what became a well-known theme followed by many groups termed "viral mimicry" (Chiappinelli et al, Cell, 2015), (Roulois et al, Cell, 2015) representing a molecular viral defense-like response to the epigenetics drugs being studied and have extended the understanding of the concept of "viral mimicry" for DNMTi-induced upregulation of repeat sequences. The current Team has conducted 14 clinical trials and treated more than 700 patients. The composition of the Team was leveraged to receive a discipline-based NCI SPORE focused on epigenetic therapies. Additionally, they were able to show that DNMTis induce PD1 expression, and so when they are combined with Atezolizumab in MDS patients resistant to DNMTis, the result is a tripling of the expected median overall survival from 5 to 15 months (O'Connell, Casey L et al, Clinical Cancer Research, 2022). The Team is working with orally bioavailable DNMTis, where they are running the first two solid tumors trials using ASTX727. The Team has designed novel interception trials in Denmark focusing on using oral Vitamin C with the goal to augment DNMTi efficacy and slow clonal cytopenia of undetermined significance (CCUS) progression.

CLINICAL TRIALS

Trials Completed:

A phase I study of SGI-110 combined with irinotecan followed by a randomized phase II study of SGI-110 combined with irinotecan versus regorafenib or TAS-102 (lonsurf) in previously treated metastatic colorectal cancer patients

Lee, Valerie et al. "A Phase I Trial of a Guadecitabine (SGI-110) and Irinotecan in Metastatic Colorectal Cancer Patients Previously Exposed to Irinotecan." Clinical Cancer Research : an official journal of the American Association for Cancer Research vol. 24,24 (2018): 6160-6167. doi:10.1158/1078-0432.CCR-18-0421

Pilot Study Restoring Physiological Vitamin C Levels to the Normal Range: Influence on Epigenetic Regulation in Normal and Malignant Hematopoiesis

Gillberg L, Ørskov AD, Nasif A, et al. Oral vitamin C supplementation to patients with myeloid cancer on azacitidine treatment: Normalization of plasma vitamin C induces epigenetic changes. Clin Epigenetics. 2019;11(1):143. Published 2019 Oct 17. doi:10.1186/s13148-019-0739-5. PMID 31623675.

Multicenter phase 1/2 study of combination therapy with the DNA methyltransferase inhibitor decitabine and the poly ADP ribose polymerase (PARP) inhibitor talazoparib (BMN 673) for untreated acute myeloid leukemia (AML) in adult patients unfit for cytotoxic chemotherapy or relapsed/refractory AML

Baer, Maria R et al. "Phase I Clinical Trial of DNA Methyltransferase Inhibitor Decitabine and PARP Inhibitor Talazoparib Combination Therapy in Relapsed/Refractory Acute Myeloid Leukemia." Clinical cancer research : an official journal of the American Association for Cancer Research vol. 28,7 (2022): 1313-1322. doi:10.1158/1078-0432. CCR-21-3729

A Phase I/II multicenter study combining guadecitabine, a DNA methyltransferase inhibitor, with Atezolizumab, an immune checkpoint inhibitor, in patients with intermediate or high-risk myelodysplastic syndrome or chronic myelomonocytic leukemia.



O'Connell, Casey L et al. "Safety, Outcomes, and T-Cell Characteristics in Patients with Relapsed or Refractory MDS or CMML Treated with Atezolizumab in Combination with Guadecitabine." Clinical cancer research : an official journal of the American Association for Cancer Research vol. 28,24 (2022): 5306-5316. doi:10.1158/1078-0432.CCR-22-1810

SU2C Genentech Catalyst: GU-114: Overcoming Checkpoint Inhibitor Resistance With Epigenetic Therapy in Urothelial Cancer

Jang, H Josh et al. "A Phase II Trial of Guadecitabine plus Atezolizumab in Metastatic Urothelial Carcinoma Progressing after Initial Immune Checkpoint Inhibitor Therapy." Clinical cancer research : an official journal of the American Association for Cancer Research vol. 29,11 (2023): 2052-2065. doi:10.1158/1078-0432. CCR-22-3642

Active, Enrollment Complete:

A Phase II Study of Epigenetic Therapy With Azacitidine and Entinostat With Concurrent Nivolumab in Subjects With Metastatic Non-Small Cell Lung Cancer (NCT01928576)

Epigenetics, Vitamin C, and Abnormal Hematopoiesis - Role of Vitamin C in Epigenetic Regulation in Hematopoiesis Sub-Study on CCUS, Low-Risk MDS, and CMML-0/1 (NCT03682029)

A Phase Ib Study of Guadecitabine (SGI-110) and Durvalumab (MEDI 4736) in Patients With Advanced Hepatocellular Carcinoma, Pancreatic Adenocarcinoma, and Cholangiocarcinoma/Gallbladder Cancer (NCT03257761)

SU2C Merck Catalyst: Phase I/Ib Study of Combined Pembrolizumab Plus Guadecitabine and Mocetinostat for Patients With Advanced NSCLC (NCT03220477) A Phase I/II Study of DS-3201b, an EZH1/2 Inhibitor, in Combination With Irinotecan in Patients With Recurrent Small Cell Lung Cancer (NCT03879798)

Trials Enrolling:

Combining Active and Passive DNA Hypomethylation: A Randomized, Placebo-Controlled Phase II Study of the Efficacy and Safety of Oral Vitamin C in Combination With Azacitidine in Patients With Higher-Risk MDS, CMML-2 or Low-Blast Count AML (NCT03999723)

A Phase I Dose-Escalation Study of E7727, an Oral Cytidine Deaminase Inhibitor (CDAi) With Oral Decitabine in Subjects With Solid Tumors (NCT03875287)

A Phase I Study of ASTX727 Plus Talazoparib in Patients With Triple Negative or Hormone Resistant/ Human Epidermal Growth Factor Receptor 2 (HER2)-Negative Metastatic Breast Cancer (NCT04134884)

STOP-LEUKEMIA: Repurposing Metformin as a Leukemia-preventive Drug in CCUS and LR-MDS (NCT04741945)

Trial Upcoming:

CAR T cells gene-edited for improved PERSIS-Tence for pediatric and young adult patients with CD19- and/or CD22-positive leukemia (Drs. Caitlin Zebley, Benjamin Youngblood, and Stephen Gottschalk)

FUNDER



SU2C-LUSTGARTEN FOUNDATION PANCREATIC CANCER DREAM TEAM DT5915

Transforming Pancreatic Cancer to Treatable Disease

Grant Term: July 2014 - December 2023, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Elizabeth M. Jaffee, MD Johns Hopkins University

Co-Leader: Robert H. Vonderheide, MD, DPhil Abramson Cancer Center University of Pennsylvania





JAFFEE

VONDERHEIDE

Principal: Philip Greenberg, MD Fred Hutchinson Cancer Research Center

Principal: Robert D. Schreiber, PhD Washington University in St. Louis

Project Manager: Stephanie Porter Johns Hopkins University sporter@jhmi.edu

Advocate: Betty Booher Oregon Health & Science University

Advocate: Stuart Rickerson University of California, San Francisco

PURPOSE

The goal of the SU2C-Lustgarten Foundation Pancreatic Cancer Dream Team is to demonstrate that the immune suppressive tumor environment (TME) in pancreatic cancer (PDA) can be converted into an immuno-stimulatory environment resulting in improved treatment response and prognosis.

SPECIFIC AIMS

Aim 1. Conduct a multicenter phase 2 study designed to test the safety and clinical activity of a PD-1 inhibitor (cemiplimab) with a CXCR4 inhibitor (plerixafor).

Aim 2. Conduct a trial to treat patients with their own T cells engineered to recognize mesothelin, a clinical target expressed specifically by pancreatic cancer cells.

Aim 3. Conduct a trial to explore whether vaccinating PDA patients with neoantigens derived from their own tumors can reactivate preexisting neoantigen specific T cells, induce T-cell responses to additional vaccine induced tumor neoantigens, and induce a measurable clinical response.



KEY PROGRESS

The Team completed their phase 2 clinical trial of combining plerixafor and cemiplimab in patients with metastatic PDA. Although only limited clinical activity has been observed, their correlative studies are anticipated to provide insights into the mechanisms behind the observed resistance to plerixafor/cemiplimab. The Team has reached their target of treating 10 patients with their neoantigen epitope vaccine. Laboratory studies confirmed that the immune system responded to at least some of the protein fragments that were used in the personalized vaccines. The Team is continuing to enroll in their clinical trial where they are testing adoptive cell therapy in pancreatic cancer. No adverse events have been observed.

CLINICAL TRIALS

A Phase II Study of Plerixafor and Cemiplimab in Metastatic Pancreatic Cancer; NCT04177810; Completed

Phase I Study of Autologous Transgenic T Cells Expressing High Affinity Mesothelin-Specific T-Cell Receptor (TCR) (FH-TCR TMSLN) in Patients With Metastatic Pancreatic Ductal Adenocarcinoma; NCT04809766; Recruiting

A Phase I Clinical Trial to Evaluate the Safety and Immunogenicity of a Neoantigen Peptide Vaccine Strategy in Pancreatic Cancer Patients Following Surgical Resection and Adjuvant Chemotherapy; NCT03956056; Terminated Study to Assess the Safety of Continuous IV Administration of the CXCR4 Antagonist Plerixafor (Mozobil) and Assess Its Impact on the Immune Microenvironment in Patients With Advanced Pancreatic, High- Grade Serous Ovarian, and Colorectal Adenocarcinomas; NCT02179970; Completed

First-in-Human Phase I Dose-Escalation Trial of Hu5F9-G4 in Patients With Advanced Solid Malignancies; NCT02216409; Completed

Randomized Phase II Study of the Safety, Efficacy, and Immune Response of GVAX Pancreas Vaccine (With Cyclophosphamide) and CRS-207 With or Without Nivolumab in Patients With Previously Treated Metastatic Pancreatic Adenocarcinoma; NCT02243371; Completed

Study of the Safety, Immunopharmacodynamics and Anti-tumor Activity of Ibrutinib Combined With Gemcitabine and Nab-Paclitaxel in Patients With Metastatic Pancreatic Adenocarcinoma; NCT02562898; Completed

Phase I Study of Neo-adjuvant RO7009789 Alone or Neo-adjuvant RO7009789 Plus Nab-Paclitaxel and Gemcitabine Followed by Adjuvant RO7009789 Plus Nab-Paclitaxel and Gemcitabine for Patients With Newly Diagnosed Resectable Pancreatic Carcinoma; NCT02588443; Completed

FUNDER



SU2C-DUTCH CANCER SOCIETY TUMOR ORGANOIDS DREAM TEAM DT5906

A New Preclinical Model for Drug Sensitivity Analysis

Grant Term: April 2014 - April 2019, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Hans C. Clevers, MD, PhD Hubrecht Institute

Co-Leader: Johannes L. Bos, PhD University Medical Center Utrecht





CLEVERS

BOS

Principal: Sir Michael R. Stratton, PhD Wellcome Trust Sanger Institute

Principal: Lodewyk Wessels, PhD Netherlands Cancer Institute

Project Manager: Johan H. van Es, PhD Hubrecht Institute j.es@hubrecht.edu

Advocate: Pauline Evers Leven Met Kanker

Advocate: Jeannette Janzen Leven Met Kanker

Advocate: Margreet Jonker Leven Met Kanker **Advocate:** Catherine Transler Leven Met Kanker

PURPOSE

The SU2C-Dutch Cancer Society Tumor Organoids Dream Team established and analyzed a large collection of long-term cultures of tumours (tumor organoids) in an effort to capture the genetic spectrum of tumours. This strategy allows the stratification of tumours based on their genomic footprint and drug sensitivity and facilitates correlations between drug sensitivity and this footprint. The ultimate goal of this Team is to design novel, more sophisticated clinical trials that test treatment regimens tailored to a patient's tumor.

SPECIFIC AIMS

Aim 1. Build and validate a large "living" biobank for colon, pancreatic, and breast cancer using organoid technology, thus capturing the genetic variability of these three tumor types.

Aim 2. Correlate drug sensitivity with genotype and gene expression in vitro to identify putative biomarkers of drug sensitivity.

Aim 3. Validate the dual "genetic/organoid" approach as a predictor of drug response for individual cancer patients.

Aim 4. Identify molecular mechanisms of drug sensitivity and resistance.


KEY PROGRESS

The Team developed a groundbreaking technology that allows tumor samples isolated from patients to be maintained and grown in the laboratory setting. These tumor organoids provide an unprecedented opportunity to combine DNA sequence analyses with functional studies of tumors from individual patients. Importantly, tumor organoids have allowed studies of sensitivity and resistance to a large number of anticancer drugs in the lab. The Team has developed organoids from multiple cancer types, including colorectal, pancreas, liver, esophageal, and breast. In addition to the abovementioned studies, the Team has used CRISPR with organoids to pinpoint genetic mutations responsible for a given patient's cancer.

CLINICAL TRIALS

N/A



SU2C-ST. BALDRICK'S FOUNDATION PEDIATRIC CANCER DREAM TEAM DT5908

Immunogenomics to Create New Therapies for High-Risk Childhood Cancers Grant Term: July 2013 – June 2018, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: John M. Maris, MD Children's Hospital of Philadelphia

Co-Leader: Crystal L. Mackall, MD Stanford University





MARIS

MACKALL

Principal: Nabil M. Ahmed, MD Baylor College of Medicine

Principal: Michael C. Jensen, MD Seattle Children's Research Institute

Principal: Paul M. Sondel, MD, PhD University of Wisconsin, Madison

Principal: Poul H. B. Sorenson, MD, PhD BC Cancer Research Institute

Principal: Michael D. Taylor, MD, PhD The Hospital for Sick Children

Project Manager: Jennifer L. Baldi Children's Hospital of Philadelphia baldij@email.chop.edu Advocate: Beth Anne Baber, PhD Nicholas Connor Institute

Advocate: Kelly Cotter

Advocate: Jay Scott Alex's Lemonade Stand Foundation

Advocate: Liz Scott Alex's Lemonade Stand Foundation

Advocate: Patrick J. Sullivan, LLB Team Finn Foundation

Advocate: Lisa Tichenor QuadW Foundation

Advocate: Mac Tichenor QuadW Foundation

PURPOSE

The SU2C-St. Baldrick's Foundation Pediatric Cancer Dream Team brought together the fields of cancer genomics and immuno-oncology to rethink curative therapies for malignancies afflicting children. The Team focused on developing innovative new immunotherapies, discovering basic mechanisms of effectiveness (or lack thereof) in both antibody and cellular engineering, and devising novel methods to monitor clinical effectiveness and toxicity. The Team's work continues through a renewal project awarded in 2017.



SPECIFIC AIMS

Aim 1. Discover and validate cell surface targets for immunotherapy of high-risk pediatric cancers.

Aim 2. Generate and develop therapeutic proteins targeting prioritized cell surface molecules.

Aim 3. Conduct pivotal multi-institution pediatric cancer immunotherapy trials.

KEY ACCOMPLISHMENTS

Team investigators developed antibodies, antibody-drug conjugates and chimeric antigen receptor- arm T cells to attack new targets for immunotherapy, discovering basic mechanisms of effectiveness (or lack thereof), made significant progress in both antibody and cellular engineering, and developed novel methods to monitor clinical effectiveness and toxicity. They demonstrated the potency of immunotherapy against childhood acute lymphoblastic leukemia (ALL), as well as defined mechanisms for how these cancers cells can adapt and avoid the modified immune cells designed to target ALL. They also made progress against childhood solid cancers, with emerging therapeutics against diseases such as neuroblastoma, glioblastoma, medulloblastoma, osteosarcoma, Ewing sarcoma, and rhabdomyosarcoma. The Team's work contributed to two 2017 FDA approvals for refractory leukemia, a first-of-its-kind CD19 CAR T therapy that trains patient's immune cells to eliminate cancer in children and young adults with ALL and treatment for cytokine release syndrome, a potential life-threatening complication of CAR T therapies.

CLINICAL TRIALS

Pediatric and Young Adult Leukemia Adoptive Therapy (PLAT)-02: A Phase I/II Feasibility and Safety Study of CD19-CAR T-cell Immunotherapy for CD19+ Leukemia; NCT02028455; Active, not recruiting

A Phase 1 Feasibility and Safety Study of Cellular Immunotherapy for Recurrent/Refractory Neuroblastoma Using Autologous T-cells Lentivirally Transduced to Express CD171-specific Chimeric Antigen Receptors; NCT02311621; Active, not recruiting

Phase I Dose Escalation Study of Anti-CD22 Chimeric Receptor T Cells in Pediatric and Young Adults With Recurrent or Refractory CD22expressing B-cell Malignancies; NCT02315612; Recruiting

Phase I Study of Intracranial Injection of T Cells Expressing HER2-specific Chimeric Antigen Receptors (CAR) in Subjects With HER2-Positive Tumors of the Central Nervous System (iCAR); NCT02442297; Active, not recruiting

TCR alpha/beta+ and CD19+ Depleted KIR/KIR Ligand-Mismatched Haploidentical Hematopoietic Stem Cell Transplant and Zolendronate for Pediatric Relapsed/Refractory Hematologic Malignancies and High-Risk Solid Tumors; NCT02508038; Recruiting

Pilot Study of Autologous Anti-CD22 Chimeric Antigen Receptor Redirected T Cells in Pediatric Patients With Chemotherapy-Resistant or Refractory Acute Lymphoblastic Leukemia; NCT02650414; Recruiting

A Phase I Study of 131-1 mIBG Followed by Nivolumab and Dinutuximab Beta in Children With Relapsed/ Refractory Neuroblastoma; NCT02914405; Recruiting

Pediatric and Young Adult Leukemia Adoptive Therapy (PLAT)-03: A Pilot Feasibility and Safety Study of CD19t T-Antigen Presenting Cells (T-APCs) Following CAR T Cell Immunotherapy for CD19+ Leukemia; NCT03186118; Active, not recruiting

Treatment of Relapsed or Refractory Neuroblastoma With Ex Vivo Expanded and Activated Haploidentical NK Cells and Hu14.18-IL2; NCT03209869; Withdrawn

Phase I Dose Escalation Study of CD19/CD22 Chimeric Antigen Receptor (CAR) T Cells in Children and Young Adults With Recurrent or Refractory B Cell Malignancies; NCT03241940; Recruiting

Pediatric and Young Adult Leukemia Adoptive Therapy (PLAT)-05: Phase I Feasibility and Safety Study of Dual Specificity CD19 and CD22 CAR T Cell Immunotherapy for CD19+CD22+ Leukemia and Lymphoma; NCT03330691; Recruiting

Pediatric Leukemia Adoptive Therapy (PLAT)-01: Phase I Feasibility and Safety Study of Cellular Immunotherapy for Relapsed Pediatric CD19+ Acute Lymphoblastic Leukemia Using Autologous T Cells Lentivirally Transduced to Express a CD19-Specific Chimeric Antigen Receptor; NCT01683279; Active, not recruiting A Phase II, Single-Arm, Multicenter Trial to Determine the Efficacy and Safety of CTL019 in Pediatric Patients With Relapsed and Refractory B-Cell Acute Lymphoblastic Leukemia; NCT02435849; Completed

A Two-Cohort Pilot Study of the Tocilizumab Optimization Timing for CART19 Associated Cytokine Release Syndrome (CRS) Management in Pediatric Patients With CD19 Expressing Relapsed/Refractory B-cell Acute Lymphoblastic Leukemia (ALL); NCT02906371; Completed.

Administration of HER2 Chimeric Antigen Receptor Expressing T Cells for Subjects With Advanced Sarcoma (HEROS); NCT00902044; Active, not recruiting

Pediatric and Young Adult Leukemia Adoptive Therapy (PLAT)-04: Phase I Feasibility and Safety Study of CD22-CAR T Cell Immunotherapy for CD22+ Leukemia and Lymphoma; NCT03244306; Active, not recruiting

Pilot Study of Nonviral, RNA-Redirected Autologous T Cells Engineered to Contain Anti-CD19 Linked to TCR and 4-1BB Signaling Domains in Patients With Refractory or Relapsed Hodgkin Lymphoma; NCT02624258; Terminated

Administration of HER2 Chimeric Receptor and TGF Beta Dominant Negative Receptor (DNR) Expressing EBV Specific Lymphocytes for Subjects With Advanced HER2-Positive Malignancy (HERCREEM); NCT00889954; Completed

Administration of HER2 Chimeric Antigen Receptor Expressing CMV-Specific Cytotoxic T Cells in Patients With Glioblastoma Multiforme (HERT-GBM); NCT01109095; Completed



Phase I Study of T Cells Expressing an Anti-CD19 Chimeric Receptor in Children and Young Adults With B-cell Malignancies; NCT01593696; Completed

CHP959-Phase I/IIa Study of Redirected Autologous T Cells Engineered to Contain Anti-CD19 Attached to TCR Zeta and 4-1BB Signaling Domains in Patients With Chemotherapy-Resistant or Refractory CD19+ Leukemia and Lymphoma; NCT01626495; Completed

Phase I Trial of T Cells Expressing an Anti-GD2 Chimeric Antigen Receptor in Children and Young Adults With GD2+ Solid Tumors; NCT02107963; Completed

Phase II, Single-Arm, Multicenter Trial to Determine the Efficacy and Safety of CTL019 in Pediatric Patients With Relapsed and Refractory B-Cell Acute Lymphoblastic Leukemia; NCT02228096; Completed

Phase I, Open-Label, Dose-Escalation Study of MGA271 in Pediatric Patients With B7-H3-Expressing Relapsed or Refractory Solid Tumors; NCT02982941; Completed

Pilot Study of Redirected Autologous T Cells Engineered to Contain Humanized Anti-CD19 Attached to TCR and 4-1BB Signaling Domains in Patients With Relapsed or Refractory CD19+ Leukemia and Lymphoma Previously Treated With Cell Therapy; NCT02374333; Completed





SU2C-CANCER RESEARCH INSTITUTE CANCER IMMUNOLOGY DREAM TEAM DT5907

Immunologic Checkpoint Blockade and Adoptive Cell Transfer in Cancer Therapy Grant Term: March 2013 - February 2018, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: James P. Allison, PhD The University of Texas MD Anderson Cancer Center

Co-Leader: Drew M. Pardoll, MD, PhDJ ohns Hopkins University

Co-Leader: Antoni Ribas, MD, PhD University of California, Los Angeles

Co-Leader: Cassian Yee, MD The University of Texas MD Anderson Cancer Center



ALLISON



PARDOLL



RIBAS



YEE

Principal: Glenn E. Dranoff, MD Dana-Farber Cancer Institute

Principal: Philip D. Greenberg, MD Fred Hutchinson Cancer Research Center

Principal: James R. Heath, PhD California Institute of Technology

Principal: F. Stephen Hodi, MD Dana-Farber Cancer Institute

Principal: Michel Sadelain, MD, PhD Memorial Sloan Kettering Cancer Center

Principal: Ton N. Schumacher, PhD Netherlands Cancer Institute

Principal: Jedd D. Wolchok, MD, PhD Memorial Sloan Kettering Cancer Center

Project Manager: James J. Mancuso The University of Texas MD Anderson Cancer Center JJMancuso@mdanderson.org

Advocate: Robert E. Behrens REB Investments, Inc.

Advocate: Debra Black Melanoma Research Alliance

Advocate: Roy Doumani, JD (deceased) University of California, Los Angeles

Advocate: Valerie Guild AIM at Melanoma



Advocate: Jonathan W. Simons, MD Prostate Cancer Foundation

Advocate: Mary Elizabeth Williams Salon.com

PURPOSE

The members of the. SU2C-Cancer Research Institute Cancer Immunology Dream Team led the pre-clinical and clinical development of antibodies that block two immune inhibitory (checkpoint) pathways, the cornerstones of molecularly based immunotherapy, and identified additional inhibitory checkpoints and co-stimulatory molecules which are "druggable" targets.

SPECIFIC AIMS

Aim 1. Interrogate immune responses within the tumor microenvironment before and after treatment with immune checkpoint blockade.

Aim 2. Interrogate the targets of T and B-cell responses after checkpoint blockade.

Aim 3. Provide therapeutic benefit to patients with advanced tumors by improving the quality of cancer-specific T lymphocytes generated for adoptive cell transfer (ACT) therapy.

Aim 4. Develop novel combinatorial therapies based on immune checkpoint blockade.

KEY ACCOMPLISHMENTS

Work by members of this Dream Team contributed to several approvals of the PD-1 checkpoint inhibitors pembrolizumab and nivolumab for patients with different cancers starting in 2014. The Team made the landmark demonstration of the benefits of administering immunotherapy prior to surgical treatment of non-small cell lung cancer. The report was published in the New England Journal of Medicine. The Team conducted a clinical trial to assess combined CTLA-4 and PD-1/PD-L1 blockade in patients with advanced melanoma.

CLINICAL TRIALS

Neoadjuvant Nivolumab, or Nivolumab in Combination With Ipilimumab, in Resectable Nonsmall Cell Lung Cancer; NCT02259621; Active, not recruiting

A Phase I/II Clinical Trial of Malignant Pleural Disease Treated With Autologous T Cells Genetically Engineered to Target the Cancer-Cell Surface Antigen Mesothelin; NCT02414269; Active, not recruiting

Phase Ib Study of Cellular Adoptive Immunotherapy Using Autologous Cd8+ Antigen-Specific T Cells and Anti-CTLA4 For Patients With Metastatic Uveal Melanoma; NCT03068624; Active, not recruiting

Adoptive Transfer of NY-ESO-1 TCR Engineered Peripheral Blood Mononuclear Cells (PBMC) After a Nonmyeloablative Conditioning Regimen, With Administration of NY-ESO-1157-165 Pulsed Dendritic Cells and Interleukin-2, in Patients With Advanced Malignancies; NCT01697527; Active, not recruiting

A Phase I/II, Open-Label Study of Nivolumab Monotherapy or Nivolumab Combined With Ipilimumab in Subjects With Advanced or Metastatic Solid Tumors; NCT01928394; Active, not recruiting

Phase II Study of Cellular Adoptive Immunotherapy Using Autologous CD8+ Antigen-Specific T Cells and Anti-CTLA4 for Patients With Metastatic Melanoma; NCT02027935; Active, not recruiting

A Pilot Randomized Tissue-Based Study Evaluating Anti-PD1 Antibody or Anti-PD1 +Bevacizumab or Anti- PD1 + Anti-CTLA-4 in Patients With Metastatic Renal Cell Carcinoma Who Are Eligible for Cytoreductive Nephrectomy, Metastasectomy, or Post-treatment Biopsy; NCT02210117; Unknown

Phase I/II Study in WT1-Expressing Non-small Cell Lung Cancer and Mesothelioma, Comparing Cellular Adoptive Immunotherapy With Polyclonal Autologous Central Memory to Naive CD8+ T Cells That Have Been Transduced to Express a WT1-Specific T-cell Receptor; NCT02408016; Terminated (Terminated due to loss of funding)

Pilot Study of Feasibility and Safety of Personalized Autologous CD8+ T-cell Therapy Plus Anti-PD-1 Antibody in Advanced Solid Malignancies; NCT02757391; Terminated Phase II, Single-Arm Clinical Trial of Nivolumab (BMS-936558) in Subjects With Metastatic or Unresectable Urothelial Cancer Who Have Progressed or Recurred Following Treatment With a Platinum Agent; NCT02387996; Completed

Phase Ib Safety and Dose-Assessment Study of Neoadjuvant Ipilimumab Monotherapy in Patients With Urothelial Carcinoma Undergoing Surgical Resection; NCT00362713; Completed

Neoadjuvant Phase IIa Study of Ipilimumab (Formerly known as MDX-010 [BMS-734016]) Plus Hormone Ablation in Men With Prostate Cancer Followed by Radical Prostatectomy; NCT01194271; Completed

Phase II Study of Ipilimumab Plus Androgen Deprivation Therapy in Castrate-Sensitive Prostate Carcinoma; NCT01377389; Completed

Exploratory Study of the Biologic Effects of Nivolumab and Ipilimumab Monotherapy and Nivolumab in Combination With Ipilimumab Treatment in Subjects With Advanced Melanoma (Unresectable or Metastatic); NCT01621490; Completed

Feasibility Study to Determine T-Cell Responses to Neoantigens Following Treatment With Ipilimumab in Men With Metastatic Castration-Resistant Prostate Carcinoma; NCT02113657; Completed

NY-ESO-1 TCR Engineered Adoptive Cell Transfer Therapy With Nivolumab PD-1 Blockade; NCT02775292; Completed







SU2C-PROSTATE CANCER FOUNDATION PROSTATE CANCER DREAM TEAM DT5904

Targeting Adaptive Pathways in Metastatic Castration-Resistant Prostate Cancer

Grant Term: January 2013 - December 2016, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Eric J. Small, MD University of California, San Francisco

Co-Leader: Owen N. Witte, MD University of California, Los Angeles





SMALL

WITTE

Principal: Tomasz M. Beer, MD Oregon Health & Science University

Principal: Christopher P. Evans, MD University of California, Davis, Comprehensive Cancer Center

Principal: Martin E. Gleave, MD University of British Columbia

Principal: Joshua M. Stuart, PhD University of California, Santa Cruz

Project Manager: Kelly McNeill University of California, San Francisco kelly.mcneill@ucsf.edu

Advocate: Roy Doumani, JD (deceased) University of California, Los Angeles

Advocate: Arthur H. Kern (deceased) University of California, San Francisco

PURPOSE

The SU2C-Prostate Cancer Foundation Prostate Cancer Dream Team was formed to explore the molecular basis of adaptive mechanisms of treatment resistance exhibited by men with castration-resistant prostate cancer (CRPC).

SPECIFIC AIMS

Aim 1. Identify adaptive pathways to abiraterone and enzalutamide active in resistant mCRPC tumors.

Aim 2. Validate that identified adaptive pathways cause resistance.

Aim 3. Demonstrate the efficacy of co-targeting adaptive pathways.

KEY ACCOMPLISHMENTS

The Team studied metastatic biopsies to understand why patients become resistant to hormone therapy. The active signaling pathway that they identified in enzalutamide-resistant patients can potentially be blocked by drugs. They found that the MEK/ERK pathway, which is being targeted already in other cancers with new drugs, is also a linchpin in metastatic prostate cancer. They conducted a clinical trial on a MEK pathway inhibitor in mCRPC patients. The Team has developed blood tests that can be used to monitor the response of patients to treatment. These methods can keep patients from having to have tumor biopsies. They also found certain genetic characteristics in patients with treatment-emergent small-cell neuroendocrine prostate cancer (t-SCNC) (a highly aggressive subtype), that can potentially be targeted with drugs.

CLINICAL TRIALS

Radiologically Guided Biopsies of Metastatic Castration-Resistant Prostate Cancer (mCRPC) to Identify Adaptive Mechanisms of Resistance; NCT02432001; Completed

Phase Ib/II Study of the Oral CDK4/6 Inhibitor LEE011 in Combination With Docetaxel Plus Prednisone in Metastatic Castration-Resistant Prostate Cancer; NCT02494921; Completed

Phase I/II Trial of Concurrent Chemohormonal Therapy Using Enzalutamide (MDV-3100) and Cabazitaxel in Patients With Metastatic Castration-Resistant Prostate Cancer; NCT02522715; Active, not recruiting

Single-Arm, Open-Label, Two-Stage Phase II Study of the MEK 1/2 Inhibitor Trametinib in Men With Progressive Metastatic Castrate-Resistant Prostate Cancer; NCT02881242; Active, not recruiting

Phase II Study Combining Ipilimumab With Abiraterone Acetate Plus Prednisone in Chemotherapy and Immunotherapy-Naive Patients With Progressive Metastatic Castration-Resistant Prostate Cancer; NCT01688492; Active, not recruiting

Multicenter, Randomized, Double-Blind, Placebo-Controlled, Phase III Study of ARN-509 in Men With Non- Metastatic (M0) Castration-Resistant Prostate Cancer; NCT019462904; Active, not recruiting

Genetic and Molecular Mechanisms Underlying Tumor Progression Despite Enzalutamide Treatment; NCT02099864; Active, not recruiting

Phase III Trial of Enzalutamide (NSC # 766085) Versus Enzalutamide, Abiraterone, and Prednisone for Castration-Resistant Metastatic Prostate Cancer; NCT01949337; Active, not recruiting

A Phase II Randomized, Multicenter Study of Cabazitaxel Versus Abiraterone or Enzalutamide in Poor Prognostic-Metastatic Castration-Resistant Prostate Cancer; NCT02254785; Unknown

Addition of Pembrolizumab Upon Progression on Enzalutamide in Men With mCRPC; NCT02312557; Active, not recruiting

Phase II Study of MAOA Inhibitor Plus Docetaxel in Patients Receiving and Progressing on Docetaxel Therapy; NCT01253642; Terminated (low enrollment)

Phase II Single-Agent Study of Selinexor (KPT-330) in Patients With Metastatic Castration-Resistant Prostate Cancer (mCRPC) and Prior Therapy With Abiraterone and/or Enzalutamide; NCT02215161; Terminated (risk-to-benefit ratio was not acceptable)

An Open-Label Study of Rovalpituzumab Tesirine in Subjects With Delta-Like Protein 3-Expressing Advanced Solid Tumors; NCT02709889; Terminated (strategic considerations)

PREVAIL: A Multinational Phase III, Randomized, Double-Blind, Placebo-Controlled Efficacy and Safety Study of Oral MDV3100 in Chemotherapy-Naive Patients With Progressive Metastatic Prostate Cancer Who Have Failed Androgen Deprivation Therapy; NCT01212991; Completed

Phase I Trial of ADIPEG 20 Plus Docetaxel in Advanced Solid Tumors With Emphasis on Castration- Resistant Prostate Cancer (CRPC) and Advanced Non-small Cell Lung Cancer (NSCLC); NCT01497925; Completed



Randomized Phase III Study Comparing Cabazitaxel/Prednisone in Combination With Custirsen (OGX- 011) to Cabazitaxel/Prednisone for Second-Line Chemotherapy in Men With Metastatic Castrate- Resistant Prostate Cancer; NCT01578655; Completed

Phase II Study of Increased-Dose Abiraterone Acetate in Patients With Castration-Resistant Prostate Cancer (CRPC); NCT01637402; Completed

Randomized Phase II Trial of Immediate Versus Delayed Anti-CTLA4 Blockade Following Sipuleucel-T Treatment for Prostate Cancer Immunotherapy; NCT01804465; Completed

Randomized, Double-Blind, Multicenter, Parallel-Group, Phase III Study to Evaluate Efficacy and Safety of DCVAC/Pca Versus Placebo in Men With Metastatic Castration-Resistant Prostate Cancer Eligible for First-Line Chemotherapy; NCT02111577; Completed

Randomized Phase II Study of Sequencing Abiraterone Acetate and Enzalutamide in Metastatic Castration-Resistant Prostate Cancer; NCT02125357; Completed

Identifying Mechanisms of Resistance to Enzalutamide (MDV3100) Treatment in Men With Castration- Resistant Prostate Cancer; NCT02228265; Completed

Phase I Study of Cabazitaxel, Mitoxantrone, and Prednisone (CAMP) for Patients With Metastatic Castration-Resistant Prostate Cancer and No Prior Chemotherapy; NCT01594918; Completed STRIVE: A Multicenter Phase II, Randomized, Double-Blind Efficacy and Safety Study of Enzalutamide Versus Bicalutamide in Men With Prostate Cancer Who Have Failed Primary Androgen Therapy; NCT01664923; Completed

Phase II Study of Recombinant Glycosolated Human IL7 (CYT107) After Completion of Standard FDA-Approved Therapy With Sipuleucel-T (Provenge®) for Patients With Asymptomatic or Minimally Symptomatic Metastatic Castration-Resistant Prostate Cancer; NCT01881867; Completed

Three-Arm, Randomized, Open-Label, Phase II Study of Radium-223 Dichloride 50 kBq/kg (55 kBq/kg After Implementation of NIST Update) Versus 80 kBq/kg (88 kBq/kg After Implementation of NISTUpdate), and Versus 50 kBq/kg (55 kBq/kg After Implementation of NIST Update) in an Extended Dosing Schedule in Subjects With Castration-Resistant Prostate Cancer Metastatic to the Bone; NCT02023697; Completed

Phase I Safety and Tolerability Study of ZEN003694 in Patients With Metastatic Castration-Resistant Prostate Cancer; NCT02705469; Completed

FUNDER



THE S^{+2C} SCIENTIFIC SUMMIT 81

SU2C-PROSTATE CANCER FOUNDATION PROSTATE CANCER DREAM TEAM DT5903

Precision Therapy of Advanced Prostate Cancer

Grant Term: August 2012 - July 2016, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Arul M. Chinnaiyan, MD, PhD University of Michigan

Co-Leader: Charles L. Sawyers, MD Memorial Sloan Kettering Cancer Center





CHINNAIYAN

SAWYERS

Principal: Johann S. de Bono, MBChB, MD Institute of Cancer Research, Royal Marsden NHS Foundation Trust

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Principal: Philip W. Kantoff, MD Dana-Farber Cancer Institute

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Principal: Mark A. Rubin, MD Weill Cornell Medical College of Cornell University

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Advocate: Thomas A. Farrington Prostate Health Education Network

Advocate: W. Grant Gregory Memorial Sloan Kettering Cancer Center

Advocate: James Kiefert, EdD Us TOO International, Inc.

Advocate: Stanley Klein Boston Prostate Cancer Support Group

Advocate: Ian S. Liston (deceased)

Advocate: Douglas Pergament (deceased)

PURPOSE

The SU2C-Prostate Cancer Foundation Prostate Cancer Dream Team's goal was to apply genome analysis technologies/techniques to biopsy tissues collected from a large cohort study of men with castration-resistant prostate cancer (CRPC).

SPECIFIC AIMS

Aim 1. Establish a multi-institutional infrastructure incorporating five leading prostate cancer clinical sites and two sequencing and computational analysis sites, linked with appropriate sample and data coordination.

Aim 2. Establish a prospective cohort of 500 patients (the "CRPC 500") utilizing the multi-institutional infrastructure to support the clinical use of integrative prostate cancer sequencing, analysis, and clinical trial decision making.



Aim 3. Conduct parallel, preclinical in vivo functional studies of resistance biomarkers and of SU2C/PCF- sponsored combination therapies.

Aim 4. Identify molecular determinants of abiraterone sensitivity and acquired resistance in patients.

Aim 5. Conduct clinical trials of novel combinations targeting AR and/or the PTEN pathway based on existing preclinical data and an understanding of resistance mechanisms.

Aim 6. Identify molecular determinants of sensitivity and acquired resistance to PARP inhibitors in patients.

KEY PROGRESS

The team's work resulted in the largest collection of genomic data on clinical mCRPC patients to date. The Team determined the molecular landscape of metastatic CRPC and defined a "long tail" of alterations in clinically relevant genes that may inform treatment strategies. Further, the Team's standardized analytical pipeline serves as a vital infrastructure for cross-institutional genomics studies of therapeutic resistance. The Team also found that men with somatic loss of DNA repair genes have enhanced responses to PARPi and determined that 12% of men with mCRPC have germline aberrations in DNA repair genes. This research contributed to the 2020 FDA approval of Olaparib for homologous recombination repair gene-mutated metastatic castration-resistant prostate cancer.

CLINICAL TRIALS

Phase II Trial of Olaparib in Patients With Advanced Castration-Resistant Prostate Cancer (TOPARP); NCT01682772; Not recruiting

Phase II Clinical Trial of Abiraterone Acetate Without Exogenous Glucocorticoids in Men With Castration- Resistant Prostate Cancer With Correlative Assessment of Hormone Intermediates; NCT02025010; Active, not recruiting Randomized Phase II Study of Enzalutamide (MDV3100) in Combination With AZD5363 in Patients With Metastatic Castration-Resistant Prostate Cancer (RE-AKT); NCT02525068; Unknown

Open-Label Pharmacodynamic Study of Abiraterone Acetate in the Treatment of Metastatic, Castration- Resistant Prostate Cancer; NCT01503229; Completed

Randomized Gene Fusion Stratified Phase II Trial of Abiraterone With or Without ABT-888 for Patients With Metastatic Castration-Resistant Prostate Cancer; NCT01576172; Completed

ARMOR 2: A 2-Part, Phase II Trial of Galeterone in the Treatment of Castration-Resistant Prostate Cancer; NCT01709734; Completed

Phase Ib Study of ARN509 Plus Everolimus in Men With Progressive Metastatic Castration-Resistant Prostate Cancer After Treatment With Abiraterone Acetate; NCT02106507; Completed

Phase II Trial of Enzalutamide for Castrate-Resistant Prostate Cancer (CRPC) With Correlative Assessment of Androgen Receptor (AR) Signaling and Whole-Exome and Transcriptome Sequencing; NCT01942837; Completed

Phase I Study of Crizotinib in Combination With Enzalutamide in Metastatic Castration-Resistant Prostate Cancer Before or After Progression on Docetaxel; NCT02207504; Complete

FUNDING



SU2C-MELANOMA RESEARCH ALLIANCE MELANOMA DREAM TEAM DT5913

Personalized Medicine for Patients With BRAF Wild-Type (BRAFwt) Cancer

Grant Term: April 2012 - June 2017, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Jeffrey M. Trent, PhD Translational Genomics Research Institute

Co-Leader: Patricia M. LoRusso, DO Yale Cancer Center





TRENT

LORUSSO

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Principal: Svetomir N. Markovic, MD, PhD Mayo Clinic

Principal: Brian J. Nickoloff, MD, PhD Michigan State University

Principal: Emanuel F. Petricoin, PhD George Mason University

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Advocate: Tracy L. Bame Freeport-McMoRan Copper & Gold Foundation

Advocate: Mark Gorman, JD National Coalition for Cancer Survivorship

Advocate: Derrick M. Hall Arizona Diamondbacks

Advocate: Cornelius A. McGillicuddy III Liberty Partners Group

Advocate: Jane Perlmutter, PhD Gemini Group



PURPOSE

The goal of this Team was to examine the genome of metastatic melanoma patients whose tumors do not bear a BRAF mutation to identify specific genetic alterations that would help match patients with an appropriate targeted therapy. The Team tested whether this personalized medicine approach would lead to more appropriate treatments and spare patients from unnecessary treatments, which are often highly toxic with uncertain benefit.

SPECIFIC AIMS

Aim 1. Conduct a randomized pilot study to assess the feasibility and safety of characterizing BRAFwt MM tumors to design a molecularly informed therapeutic regimen.

Aim 2. Iteratively refine and standardize a set of statistical and informatics methodologies for matching treatments to the patient's tumor, based on its molecular profile.

Aim 3. Evaluate whether molecularly informed personalized therapy selection, based on a tumor's molecular profile (potentially enhanced by the refined methodology for predicting drug response developed in Aim 2), will improve outcomes relative to standard of care therapy in BRAFwt MM.

KEY ACCOMPLISHMENTS

The Team developed and optimized a methodology for molecular characterization of BRAF wildtype melanomas. This optimization decreased the time for the clinical and molecular profiling from biopsy to tumor board from five weeks to 22 days. The Team successfully conducted a pilot study, followed by a larger-scale clinical trial, to assess the feasibility of tumor molecular characterization to guide the selection of appropriate treatments.

CLINICAL TRIALS

Stand Up To Cancer Consortium Genomics-Enabled Medicine for Melanoma (G.E.M.M.): Using Molecularly Guided Therapy for Patients With BRAF Wild-Type (BRAFwt) Metastatic Melanoma; NCT02094872; Completed



SU2C PANCREATIC DREAM TEAM DT5921

Cutting Off the Fuel Supply: A New Approach to the Treatment of Pancreatic Cancer Grant Term: December 2009 - October 2017, administered by the American Association for Cancer Research

KEY PERSONNEL Team Leader: Craig B. Thompson, MD, (2009-2011) University of Pennsylvania

Team Leader: Jeffrey A. Drebin, MD, PhD (2011-2015) University of Pennsylvania

Co-Leader: Daniel D. Von Hoff, MD Translational Genomics Research Institute



THOMPSON



DREBIN



VON HOFF

Principal: Chi Van Dang, MD, PhD University of Pennsylvania

Principal: Joshua D. Rabinowitz, MD, PhD Princeton University

Principal: Geoffrey M. Wahl, PhD Salk Institute for Biological Studies

Advocate: Julie M. Fleshman, JD Pancreatic Action Network

Advocate: Barton A. Kamen (deceased) Leukemia and Lymphoma Society

Advocate: Kerri Kaplan Lustgarten Foundation

Advocate: Randall M. Katz Milestone Entertainment

Advocate: Howard Young

PURPOSE

The Pancreatic Dream Team aimed to develop new clinical tests to determine how pancreatic cancer cells fuel their growth and survival to allow tailored clinical therapies challenging the tumor cell's fuel supply. Clinical trials were initiated of drugs to inhibit pancreatic cancer cells from effectively using either stromal cell-derived cytokines or glucose and/or glutamine to maintain their survival.



SPECIFIC AIMS

Aim 1. Imaging glucose and/or glutamine uptake in pancreatic tumors.

Aim 2. Investigating clinical therapies to impair tumor metabolism and stromal support.

KEY ACCOMPLISHMENTS

The Team has transformed how pancreatic cancer patients could be treated by developing a new way to take an image of the tumor inside a patient's body, showing the efficacy of a new drug regimen that is now being used as the standard of care, demonstrating how circulating DNA in the blood can be used to detect cancer recurrence, and developing a new cancer-killing strategy using a vitamin D-like compound. The results of the Team's Phase III trial testing Gemcitabine +/- Albumin-bound paclitaxel provided key evidence leading to the FDA approval of the combination of nab-paclitaxel with gemcitabine for the treatment of advanced pancreatic cancer -- changing the standard of care.

CLINICAL TRIALS

Phase I Study: PET Imaging of Cancer Patients Using [18F] 4-L-Fluoroglutamine (2S,4R); NCT01697930; Recruiting

Randomized Phase III Study of Weekly ABI-007 Plus Gemcitabine Versus Gemcitabine Alone in Patients With Metastatic Adenocarcinoma of the Pancreas; NCT00844649; Completed

Stand Up To Cancer Consortium: Phase II Study of Therapy Selected by Molecular/Metabolic Profiling in Patients With Previously Treated Metastatic Pancreatic Cancer; NCT01196247; Completed

Phase I/II Pharmacodynamics Study of Hydroxychloroquine in Combination With Gemcitabine/ Abraxane to Inhibit Autophagy in Pancreatic Cancer; NCT01506973; Completed

Randomized Pilot/Pharmacodynamic/Genomic Study of Neoadjuvant Paricalcitol to Target the Microenvironment in Resectable Pancreatic Cancer; NCT02030860; Completed

Exploratory Study of Metformin With or Without Rapamycin as Maintenance Therapy After Induction Chemotherapy in Subjects With Metastatic Pancreatic Adenocarcinoma Cancer; NCT02048384; Completed

SU2C EPIGENETICS DREAM TEAM DT5917

Bringing Epigenetic Therapy to the Forefront of Cancer Management Grant Term: December 2009 – January 2015, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Stephen B. Baylin, MD Johns Hopkins University

Co-Leader: Peter A. Jones, PhD, DSc (hc) Van Andel Institute





BAYLIN

JONES

Principal: Steven A. Belinsky, PhD Lovelace Respiratory Research Institute

Principal: Nancy E. Davidson, MD Fred Hutchinson Cancer Research Center

Principal: Jean-Pierre J. Issa, MD Coriell Institute for Medical Research

Advocate: Diana T. Chingos National Cancer Institute

Advocate: Lillie D. Shockney Johns Hopkins University

PURPOSE

The Epigenetics Dream Team tested the hypothesis that drugs targeting DNA demethylation and histone deactylation can potently change the management of advanced NSCLC.

SPECIFIC AIMS

Aim 1. Develop molecular markers that predict and monitor the efficacy of cancer epigenetic therapies.

Aim 2. Perform clinical trials to bring epigenetic therapy to the forefront of cancer management.

Aim 3. Determine whether a key mechanism for efficacy of epigenetic therapy is the targeting and exhaustion of self-renewing cancer cells.

Aim 4. Develop a clinical trial with a new drug designed to circumvent the instability of 5-AC and DAC.

Aim 5. Determine targets in addition to promoter DNA hypermethylation that may be utilized in new cancer epigenetic therapy approaches.



KEY ACCOMPLISHMENTS

The Epigenetics Dream Team explored the therapeutic potential of different epigenetic drugs; namely, 5-azacitidine (5-AC), decitabine (DAC), entinostat, and a novel DNA demethylating agent SGI-110 (guadecitabine), in clinical trials for non-small cell lung cancer, colorectal cancer, AML, breast cancer and MDS/AML. They observed objective, durable responses in patients with solid tumors treated with low-dose azacitidine and entinostat in their phase I/II clinical trial. Correlative analyses of lung cancer clinical trial samples, along with results from preclinical studies, indicated that epigenetic therapy may prime tumors for responsiveness to immune checkpoint blockade.

CLINICAL TRIALS

A Phase II Study of Epigenetic Therapy With Azacitidine and Entinostat With Concurrent Nivolumab in Subjects With Metastatic Non-Small Cell Lung Cancer; NCT01928576; Completed

A Phase I/II Study of Entinostat in Combination With 5-Azacitidine in Patients With Recurrent Advanced Non- small Cell Lung Cancer; NCT00387465; Completed

Phase II Study of Azacitidine and Entinostat in Patients With Metastatic Colorectal Cancer; NCT01105377; Completed

Phase 1-2, Dose Escalation, Multicenter Study of Two Subcutaneous Regimens of SGI-110, a DNA Hypomethylating Agent, in Subjects With Intermediate or High-Risk Myelodysplastic Syndromes (MDS) or Acute Myelogenous Leukemia (AML); NCT01261312; Completed

Phase II Study of Azacitidine and Entinostat (SNDX-275) in Patients With Advanced Breast Cancer; NCT01349959; Completed

Randomized Phase II Trial of Adjuvant Combined Epigenetic Therapy With 5-Azacitidine and Entinostat in Resected Stage 1 Non-small Cell Lung Cancer Versus Standard Care; NCT01207726; Terminated

Randomized Phase II Trial of Cytotoxic Chemotherapy With or Without Epigenetic Priming in Patients With Advanced Non-small Cell Lung Cancer; NCT01935947; Terminated

SU2C CIRCULATING TUMOR CELL (CTC) DREAM TEAM DT5919

Bioengineering and Clinical Applications of Circulating Tumor Cell Chip

Grant Term: December 2009 - November 2013, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Daniel A. Haber, MD, PhD Massachusetts General Hospital

Co-Leader: Mehmet Toner, PhD Massachusetts General Hospital





HABER

TONER

Principal: Sangeeta N. Bhatia, MD, PhD Massachusetts Institute of Technology

Principal: John V. Heymach, MD, PhD The University of Texas MD Anderson Cancer Center

Principal: Bruce E. Johnson, MD Dana-Farber Cancer Institute

Principal: Mark G. Kris, MD Memorial Sloan Kettering Cancer Center

Advocate: Rebecca Douglass Douglass Family Foundation

Advocate: Jeane Ungerleider Boston IVF

PURPOSE

The SU2C Circulating Tumor Cell Dream Team generated the prototype Herringbone-CTC-Chip, which allows initial molecular analysis of Circulating Tumor Cells (CTCs) and enables pilot clinical trials in cancers of the lung, prostate, breast, and pancreas, as well as melanoma. It also laid the groundwork for the next-generation CTC-iChip.

SPECIFIC AIMS

Aim 1a. Examine bioengineering optimization and nanosensing for increased sensitivity.

Aim 1b. Perform molecular characterization of CTCs.

Aim 2. Investigate clinical applications of the CTC-chip.

KEY ACCOMPLISHMENTS

The Team created a silicon chip that captures CTCs in a blood sample, allowing them to be analyzed, and laid the groundwork for a more sensitive, next-generation chip. The Team continued to develop techniques for studying CTCs and growing them in the laboratory. With these new methods, a doctor can learn about a patient's tumor by studying CTCs in a simple blood sample, rather than having to order a biopsy.



CLINICAL TRIALS

Circulating Tumor Cell Analysis in Patients With Localized Prostate Cancer Undergoing Prostatectomy; NCT01961713; Unknown

Phase II Study of Lapatinib in Combination With Trastuzumab in Patients With HER2-Positive, Metastatic Breast Cancer; NCT00470704; Active, not recruiting

First-Line Erlotinib Therapy and the Subsequent Development of Mechanisms of Secondary Resistance in Patients With Non-small Cell Lung Cancer and Known Sensitizing EGFR Mutations; NCT00997334; Completed

Detecting EGFR T790M Mutations From Circulating Tumor Cells; NCT01734915; Completed Phase II Single-Arm, Open-Label Study to Evaluate the Efficacy and Safety of Trastuzumab and Vinorelbine in Advanced Breast Cancer Patients With Human Epidermal Growth Factor-2 (HER2) Negative Primary Tumors and HER2-Positive Circulating Tumor Cells; NCT01185509; Terminated

SU2C PI3K DREAM TEAM DT5918

Targeting the PI3K Pathway in Women's Cancers

Grant Term: November 2009 - October 2013, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Lewis C. Cantley, PhD Beth Israel Deaconess Medical Center

Co-Leader: Gordon B. Mills, MD, PhD The University of Texas MD Anderson Cancer Center

Co-Leader: Charles L. Sawyers, MD (2009-2012) Memorial Sloan Kettering Cancer Center





CANTLEY

MILLS

SAWYERS



Principal: José Baselga, MD, PhD (deceased) Vall d'Hebron Institute of Oncology

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Principal: Thomas M. Roberts, PhD Dana-Farber Cancer Institute

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Advocate: Patricia Lee Vanderbilt University

Advocate: Don Listwin Canary Foundation

Advocate: Jane Perlmutter Gemini Group

Advocate: Sara Weiss Dana-Farber Cancer Institute



PURPOSE

The goal of the PI3K Dream Team was to discover approaches that predict which patients will respond positively to PI3K pathway inhibitors. This project's aims allowed clinicians to use biomarkers and imaging techniques to predict which patients would benefit from specific PI3K pathway inhibitors, leading to the development of therapeutic combinations that would hit multiple targets in the complex pathways that contribute to cancer cell growth.

SPECIFIC AIMS

Aim 1. Develop molecular markers and/or imaging modalities that predict the subset of cancers that are likely to respond to PI3K pathway inhibitors.

Aim 2. Design and conduct single-agent, molecular marker-driven adaptive trial(s).

Aim 3. Develop rational therapeutic combinations of PI3K pathway-targeted drugs.

Aim 4. Design and conduct two multi-arm, molecular marker-driven adaptive trials using a rational combination of a PI3K pathway inhibitor with another targeted therapy.

KEY ACCOMPLISHMENTS

The PI3K Dream Team developed a set of biomarkers, PI3K pathway inhibitors, and AKT inhibitors which were studied in 15 clinical trials. Promising early results from PI3K pathway or AKT inhibitor combinations in breast, ovarian, and endometrial cancers led to follow-on studies supported by pharmaceutical companies. Studies of olaparib drug combinations in BRCA1 ovarian and triple negative breast cancers informed the later work of the SU2C-Ovarian Cancer Research Alliance-National Ovarian Cancer Coalition Ovarian Cancer Dream Team. Results of one clinical trial developed by the team contributed to the FDA approval of alpelisib combined with fulvestrant for advanced or metastatic HR+/HER2-, PIK-3CA-mutated breast cancer in postmenopausal women and in men. The SU2C PI3K Dream team has continued the team science concepts and collaborative model developed during the SU2C-supported grant with continued collaborations on preclinical studies and clinical trials. The trials initiated with SU2C's support of the PI3K Dream team have demonstrated marked benefit for patients and have driven the development of multiple ongoing clinical trials.

CLINICAL TRIALS

Phase Ib Trial of BYL719 (an a-Specific PI3K Inhibitor) in Combination With Endocrine Therapy in Post- menopausal Patients With Hormone Receptor-Positive Metastatic Breast Cancer; NCT01791478; Active, not recruiting

Three-Arm, Randomized, Phase II Study of Paclitaxel/Carboplatin/Bevacizumab (NSC #704865), Paclitaxel/Carboplatin/Temsirolimus (NSC #683864), and Ixabepilone (NSC #710428)/ Carboplatin/ Bevacizumab as Initial Therapy for

Measurable Stage 3 or 4a, Stage 4b, or Recurrent Endometrial Cancer; NCT00977574; Active, not recruiting

Randomized Phase I Study With a Safety Lead-In to Assess the Antitumor Efficacy of the MEK Inhibitor Trametinib Alone or in Combination With GSK2141795, an AKT Inhibitor, in Patients With Recurrent or Persistent Endometrial Cancer; NCT01935973; Completed

Phase Ib Trial of BKM120 (a PI3K Inhibitor) or BEZ235 (a PI3K/mTOR Inhibitor) in Combination With Endocrine Therapy in Post-menopausal Patients With Hormone Receptor-Positive Metastatic Breast Cancer; NCT01248494; Completed

Phase Ib Dose-Escalation and Biomarker Study of MK-2206 in Combination With Standard Doses of Weekly Paclitaxel in Patients With Locally Advanced or Metastatic Solid Tumors With an Expansion in Advanced Breast Cancer; NCT01263145; Completed

Phase II Trial of AKT Inhibitor MK2206 in Patients With Advanced Breast Cancer Who Have Tumors With a PIK3CA Mutation, or an AKT Mutation, and/or PTEN Loss/PTEN Mutation; NCT01277757; Completed

Phase II Study of MK-2206 in the Treatment of Recurrent High-Grade Serous Platinum-Resistant Ovarian, Fallopian Tube, or Primary Peritoneal Cancer; NCT01283035; Completed

Phase II Trial of BKM120 (a PI3K Inhibitor) in Patients With Triple-Negative Metastatic Breast Cancer; NCT01629615; Completed

Phase I Study of the Oral PI3kinase Inhibitor BKM120 or BYL719 and the Oral PARP Inhibitor Olaparib in Patients With Recurrent Triple-Negative Breast Cancer or High-Grade Serous Ovarian Cancer; NCT01623349; Completed Phase II, Two-Stage, Two-Arm PIK3CA Mutation Stratified Trial of MK-2206 in Recurrent or Advanced Endometrial Cancer; NCT01312753; Completed

Phase II Evaluation of AZD6244 (NSC#748727) in the Treatment of Recurrent or Persistent Endometrial Carcinoma; NCT01011933; Completed

Phase I/II Study of XL147 (SAR245408) Administered in Combination With Trastuzumab or Paclitaxel and Trastuzumab in Subjects With Metastatic Breast Cancer Who Have Progressed on a Previous Trastuzumab-Based Regimen; NCT01042925; Completed

Phase I/II Dose-Escalation Study of XL147 (SAR245408) or XL765 (SAR245409) in Combination With Letrozole in Subjects With Hormone Receptor-Positive and HER2-Negative Breast Cancer Refractory to a Nonsteroidal Aromatase Inhibitor; NCT01082068; Completed

Multicenter, Single-Arm, Open-Label, Phase II Study of GDC-0980 for the Treatment of Recurrent or Persistent Endometrial Carcinoma; NCT01455493; Completed

Phase II, Randomized, Double-Blind, Placebo-Controlled Study of Letrozole With or Without BYL719 or Buparlisib for the Neoadjuvant Treatment of Postmenopausal Women With Hormone Receptor-Positive, HER2-Negative Breast Cancer; NCT01923168; Completed

A Phase Ib Study of the Oral PARP Inhibitor Olaparib With the Oral mTORC1/2 Inhibitor AZD2014 or the Oral AKT Inhibitor AZD5363 for Recurrent Endometrial, Triple Negative Breast, and Ovarian, Primary Peritoneal, or Fallopian Tube Cancer; NCT02208375; Active, not recruiting



SU2C BREAST CANCER DREAM TEAM DT5920

An Integrated Approach to Targeting Breast Cancer Molecular Subtypes and Their Resistance Phenotypes

Grant Term: October 2009 - September 2014, administered by the American Association for Cancer Research

KEY PERSONNEL Team Leader: Dennis J. Slamon, MD, PhD University of California, Los Angeles

Co-Leader: Joe W. Gray, PhD Oregon Health & Science University



SLAMON

GRAY

Principal: Alan Ashworth, PhD UCSF Helen Diller Family Comprehensive Cancer Center

Principal: Joan S. Brugge, PhD Harvard Medical School

Principal: Arul M. Chinnaiyan, MD, PhD University of Michigan

Principal: Gregory J. Hannon, PhD Cold Spring Harbor Laboratory

Principal: David Haussler, PhD University of California, Santa Cruz **Principal:** Craig V. Jordan, DSc, PhD Fox Chase Cancer Center

Principal: C. Kent Osborne, PhD Baylor College of Medicine

Principal: Peter K. Sorger, PhD Harvard Medical School

Principal: Terence P. Speed, PhD University of California, Berkeley

Principal: Zena Werb, PhD (deceased) University of California, San Francisco

Principal: Max S. Wicha, MD University of Michigan

Advocate: Janice Barlow (Retired) Zero Breast Cancer

Advocate: Cindy Geoghegan Patient & Partners, LLC

Advocate: Ellen L. Stoval (deceased) National Coalition for Cancer Survivorship

Advocate: Frances M. Visco National Breast Cancer Coalition

PURPOSE

The SU2C Breast Cancer Dream Team studied the mechanisms of resistance to treatment in three major subtypes of breast cancer – ER-positive, HER2-positive, and triple negative. It used its findings to develop less toxic therapies with the potential to improve treatment outcomes.

SPECIFIC AIMS

Aim 1. Expand the understanding of the known "driving" initial molecular mechanisms responsible for the pathogenesis and clinical behavior of the three known therapeutic breast cancer subtypes, i.e., estrogen (E2)/estrogen receptor (ER-positive), HER2-positive, and triple-negative (TN) subtypes of breast cancer.

Aim 2. Study the "driving" mechanisms responsible for de novo as well as acquired resistance to appropriately targeted treatments of the three known therapeutic breast cancer subtypes, i.e., estrogen (E2)/estrogen receptor (ER-positive), HER2-positive, and triple-negative (TN) breast cancers.

Aim 3. Investigate the potential initial "driving" pathogenetic as well as de novo or acquired "resistance" mechanisms mediated by "stem/progenitor" breast cancer cells within each or across all of the three known breast cancer subtypes, with the ultimate objective being the design, development, and clinical testing of new and innovative therapies for the "tumorigenic" and "resistance" phenotypes potentially mediated by these stem/progenitor cells.

Aim 4. Develop new and/or characterize existing relevant and representative cell line and xenograft models, as well as utilize annotated clinical material to query the contributions of "normal" and "malignancy-derived" matrix/stromal components of each breast cancer subtype, including those that might contribute to or mediate the "resistance" phenotype to targeted therapeutics.

Aim 5. Develop an integrated discovery and informatics research unit that cuts across the above aims that is designed to deploy, inform, and facilitate implementation of relevant discovery and informatics platforms needed for these aims.

KEY ACCOMPLISHMENTS

The Breast Cancer Dream Team endeavored to develop less toxic therapies with the potential to improve treatment outcomes, study the malignant cancer stem cells' impact of resistance across the three major breast cancer subtypes, and develop a "discovery platform" for identifying and validating new drug combinations and targets that can be pursued in clinical trials by creating a database which integrates existing information about breast cancer. A significant outcome of these efforts contributed to the 2015 FDA approval of the first-in-class CDK4/6 inhibitor palbociclib in combination with letrozole for ER+, HER2- metastatic breast cancer.

CLINICAL TRIALS

Novel (PD 0332991: CDK4/6 Inhibitor, Pfizer) ER-Positive, HER2-Negative Advanced Breast Cancer in Postmenopausal Women; NCT00721409; Completed





SU2C-TORREY COAST FOUNDATION GASTROESOPHAGEAL CANCER RESEARCH TEAM RT6352

Targeting Immune Evasion in Gastroesophageal Cancer

Grant Term: May 2023 - April 2026

KEY PERSONNEL

Team Leader: Yelena Janjigian, MD Memorial Sloan Kettering Cancer Center

Co-Leader: Jedd Wolchok, MD, PhD Weill Cornell Medicine





JANJIGIAN

WOLCHOCK

Principal: Taha Merghoub, PhD Weill Cornell Medicine

Principal: Benjamin Greenbaum, PhD Memorial Sloan Kettering Cancer Center

Project Manager: Fiona Socolow Memorial Sloan Kettering Cancer Center SocolowF@mskcc.org

Clinical Research Manager: Amin Yaqubie Memorial Sloan Kettering Cancer Center YaqubieA@mskcc.org

Advocate: Aki Smith Stomach Cancer Awareness Network

Advocate: Mindy Mordecai, JD Esophageal Cancer Action Network

Advocate: Lynn Degregorio DeGregorio Family Foundation

PURPOSE

This Research Team will define the immunesuppressive mechanisms contributing to ICB resistance in GEC and their relationship to CIN. Specifically, the research aims to delineate subtype-specific features of the pre-treatment tumor neoantigens and tumor immune microenvironment (TME) associated with clinical benefit from ICB and their relationship to CIN as well as assess the potential of cGAS+ micronuclei, an indicator of ongoing CIN, as a biomarker of ICB resistance. Finally, the Team will identify neoantigens in CIN tumor biopsies and evaluate the prevalence of corresponding T cells.

SPECIFIC AIMS

Aim 1. Delineate subtype-specific features of the pre-treatment tumor neoantigens and tumor immune microenvironment (TME) associated with clinical benefit from ICB and their relationship to CIN.

Aim 2. Identify CIN samples and characterize cGAS-STING activation.

Aim 3. Identify neoantigens in CIN tumor biopsies and evaluate the prevalence of corresponding T cells in matched patient PBMCs.

CLINICAL TRIALS

N/A







SU2C-TORREY COAST FOUNDATION GASTROESOPHAGEAL CANCER RESEARCH TEAM RT6353

Novel Therapeutic Approaches for Esophageal Squamous Cell Carcinoma

Grant Term: July 2023 - June 2026

KEY PERSONNEL

Team Leader: Anil K. Rustgi, MD Herbert Irving Comprehensive Cancer Center, Columbia University Irving Medical Center

Co-Leader: Kwok-Kin Wong, MD, PhD NYU Langone Health and NYU Grossman School of Medicine



RUSTIGI

WONG

Principal: J. Alan Diehl, PhD Case Comprehensive Cancer Center, Case Western Reserve University

Project Manager: Emer Smyth, PhD Herbert Irving Comprehensive Cancer Center, Columbia University Irving Medical Center es3551@cumc.columbia.edu

Advocate: Lynn Degregorio DeGregorio Family Foundation

Advocate: Mindy Mordecai, JD Esophageal Cancer Action Network

Advocate: Rhonda Small Esophageal Cancer Awareness Association

PURPOSE

Hypothesizing that eliminating an unfavorable metabolic environment for tumor growth can improve outcomes in ESCC, the Research Team seeks to exploit glutamine dependence of ESCC and calibrate anti-tumor immune cell function by impeding glutamine metabolism in combination with inhibitors of cyclin-dependent kinases. Recent work has identified several mechanisms that may allow ESCCs to evade sustained immunologic control, spanning tumor-immune interactions and intrinsic tumor cell dependencies. This Team is proposing a program of translational studies to parse the differential impact of glutamine pathway blockade on tumor-intrinsic and -extrinsic factors.

SPECIFIC AIMS

Aim 1. To examine the direct anti-tumor impact of DON/DRP-104 and CDK4/6 inhibition in ESCC.

Aim 2. To evaluate the impact of CDK4/6 and glutamine metabolism inhibition on the ESCC tumor microenvironment.

CLINICAL TRIALS

N/A



SU2C-TORREY COAST FOUNDATION GASTROESOPHAGEAL CANCER RESEARCH TEAM RT6354

Therapeutics for Gastroesophageal Adenocarcinoma: Application, Translation and Discovery Grant Term: January 2023 - December 2027

KEY PERSONNEL

Team Leader: William Sellers, MD Broad Institute

Co-Leader: Marcela Maus, MD, PhD Massachusetts General Hospital





SELLERS

MAUS

Project Manager: Maura Charlton Broad Institute charlton@broadinstitute.org

Advocate: Jason Diaz Hope for Stomach Cancer

PURPOSE

The past 10 years have seen a revolution in the development of cancer therapeutics, which created the basis for this Research Team to uncover new therapeutics and initiate new trials in GEA. The Team plans to do this by: 1) defining and targeting the cell surface of gastroesophageal adenocarcinoma and squamous cell carcinoma, and 2) using functional genomic approaches to identify therapeutic targets in gastroesophageal adenocarcinoma. The Team also plans to develop biparatopic claudin 18.2-targeting CAR T cells for clinical development in claudin 18.2-expressing gastric and esophageal cancers.

SPECIFIC AIMS

Aim 1. Defining and targeting the cell surface of gastroesophageal adenocarcinoma

Aim 2. Functional genomic approaches to identify therapeutic targets in GEA and GESC

KEY PROGRESS

Since the inception of funding in May 2023, we have hired and attracted the key personnel that will constitute the research team, worked to characterize the cancer cell surface (the Surfaceome), and completed paralog CRISPR screens with a 168,000-guide library targeting ~7500 paralog pair and 4500 single genes in 5 gastric and 5 esophageal cancer cell lines. In addition, we have generated claudin 18.2- and claudin 18.1-expressing cell lines for immunization and screening, with the aim of generation biparatopic antibodies.

CLINICAL TRIALS

N/A





SU2C DIVERSITY IN EARLY DEVELOPMENT CLINICAL TRIALS **RESEARCH GRANTS PROGRAM RT6342, RT6343, RT6344,** RT6345

Increasing Diversity in Cancer Clinical Trials

Grant Term: January 2023 - December 2024

The Diversity in Early Development Clinical Trials Research Grants Program is supporting four teams to increase diversity among participants in Phase 1 and Phase 2 cancer clinical trials. The objective is to increase accessibility for patients of all racial and ethnic backgrounds and/or medically underserved locations to equally participate in studies. Each Team is bringing together key stakeholders who are deeply connected to the impacted communities, integrating social/ behavioral determinants of health, community engagement and outreach with cancer biology, prevention, and treatment, and realizing the ideal of health equity.

SU2C DIVERSITY IN EARLY DEVELOPMENT CLINICAL TRIALS RESEARCH TEAMS Increasing Diversity in Cancer Clinical Trials Cancer clinical trials need to be available to all potential patients to make new medicines available as widely as possible. SU2C and Janssen Research & Development are supporting teams in Chicago, Dallas, Los Angeles and Philadelphia to increase accessibility for patients of all racial and ethnic backgrounds and/or living in medically underserved locations. The widest possible participation in clinical trials will help bring access to the latest treatments to all patients Los Angeles and help power the studies that will lead to breakthroughs in future cancer treatments.

The teams will focus on specific neighborhoods and cities to increase diversity among participants in Phase 1 and Phase 2 cancer clinical trials, the early trials that often determine whether a potential treatment is tested in large and expensive randomized clinical trials for widespread use by clinicians Each team is independent but the four groups will come together to share strategies and learnings



CREATE A RANDOMIZED **RECRUITMENT STUDY**

• Randomly recruit Black patients for a special clinical trial.

 Keep patients informed about progress through emails, text messages and other electronic messaging systems.

 Work with doctors to use more culturally appropriate communication methods.

 Work with community organizations and hospitals to build a patient database.

UTSouthwestern 2 IMPLEMENT & PROGRAM

FOR SCREENING. **RECRUITING, AND ENROLLING PATIENTS**

• Work with local universities, health centers and community outreach programs to create a program.

 Impact and efficiency of trial enrollment procedures will be studied, and patients will be surveyed and interviewed to find areas of improvement

EXAMINE EXISTING STRUCTURES TO FIND **IMPROVEMENTS**

Cancer Center

3

USC Norris Comprehensive

3

• Work with the county hospital system to enhance referral and enrollment of minority patients.

 Work to address systemic barriers for patients and current early phase cancer clinical trials recruitment.

 Study the demographics, financial and social burdens, geographical barriers, and impact of remote trials on participation in early cancer clinical trials.



CREATING MORE OPPORTUNITIES FOR MINORITIES TO ACCESS CLINICAL TRIALS is the ultimate goal for this initiative. By working in underserved communities in four major metropolitan areas, the teams will be able to reach, educate, better understand, and serve a large population that is historically less engaged in cancer research and treatment. The result will be better outcomes for cancer patients and their families and communities.



Chicago

Δ

Dallas 2

FOX CHASE

IDENTIFY AND OVERCOME

SPECIFIC BARRIERS

Work to address all

barriers patients may have

outreach programs to help

gathered will be shared on

to access a clinical trial

Work with community

Information and data

educate patients.

a public website

(4

Philadelphia

UNIVERSITY OF CHICAGO RT6344

Project: Enhancing Diversity in Early Phase Clinical Trials in an Urban Underserved Community

KEY PERSONNEL

Team Leader: Walter Stadler, MD

Co-Leader: Brisa Aschebrook-Kilfoy, PhD





STADLER

ASCHEBROOK-KILFOY

SPECIFIC AIMS

Aim 1. Conduct a randomized recruitment study for available phase 1 and 2 cancer trials.

Aim 2. Assess the long-term impact of the community engagement program.

KEY PROGRESS

To address the under-representation of African American (AA) cancer patients in clinical trials, we are conducting a randomized recruitment trial to determine if novel patient outreach alone or in conjunction with community outreach enhances accrual above and beyond treating physician outreach only. Using a combination of artificial intelligence and manual approaches, patients potentially eligible for one of more than 130 available clinical trials at the University of Chicago Comprehensive Cancer Center (UCCCC) will be pre-screened and randomized. In the control group, the treating physician will be informed of the specific trial the patient is potentially eligible for. In the patient outreach group, a novel dripmarketing approach more typical of consumer environments utilizing email and text messaging will be utilized to inform and educate the patient about clinical trials. The physicians in this group will also receive additional information on culturally appropriate communication. In the last randomized group, patients will additionally be offered contact with community cancer ambassadors trained to provide support in the clinical trial participation decision. In the first 6 months we have:

- Worked with community-based partners to finalize patient and physician facing informational materials.
- Finalized the computer and AI-based screening methodology for identifying potential trial candidates.
- Finalized the electronic communications tool for drip marketing.
- Obtained IRB approval for the recruitment trial.
- Begun to obtain consent from treating physicians to participate in the recruitment trial.
- Identified community ambassadors and have initiated trainings.
- Developed study related workflows for all 3 study-arms.
- Engaged physician partners whose clinical trials we will be targeting for outreach.

FUNDER



UNIVERSITY OF TEXAS SOUTHWESTERN MEDICAL CENTER RT6342

Project: Transferring Care to Enhance Access to Early-phase Cancer Clinical Trials

KEY PERSONNEL Team Leader: David Gerber, MD

Co-Leader: Sukh Makhnoon, PhD, MS





GERBER

MAKHNOON

SPECIFIC AIMS

Aim 1. Implement a program for screening, recruiting, and enrolling patients from a safety-net medical system on early-phase cancer clinical trials in a university-based NCI-designated cancer center.

Aim 2. Determine program impact and efficiency.

Aim 3. Determine experience with and perceptions of the program.

KEY PROGRESS

The team has made substantial progress during the first six months of the project. The team has hired/appointed three Clinical Trial navigators, engaged with patient advocates, clinicians, and administrative staff leading to successful project development and implementation. Key project implementation milestones include the following: establishing a process with the safety-net medical system to facilitate rapid referral of cancer patients to phase I and II clinical trials; developing logistical process and parameters (including financial support) for timely and effective communication and coordination between the safety-net medical system and the research team. To date, the team has prescreened 17 patients. One patient has been enrolled in a trial (phase 1 trial requiring study-specific biopsies).

FUNDER

UNIVERSITY OF SOUTHERN CALIFORNIA RT6345

Project: Eliminating Enrollment Barriers to Early Phase Trials in a Diverse Population in Los Angeles County

KEY PERSONNEL Team Leader: Anthony El-Khoueiry, MD

Co-Leader: Chanita Hughes-Halbert, PhD





EL-KHOUEIRY

HUGHES-HALBERT

SPECIFIC AIMS

Aim 1. Engage oncology care providers in a safety net hospital system to identify referral barriers and facilitators using key informant interviews.

Aim 2. Create a multicomponent intervention tailored to address barriers at the patient, provider, and system levels and to optimize the referral and enrollment process in early phase therapeutic trials in a safety-net setting.

Aim 3. Evaluate the impact of remote trial enrollment in a funded investigator-initiated trial.

FUNDER



THE RESEARCH INSTITUTE OF FOX CHASE CANCER CENTER RT6343

Project: Accelerating and Diversifying Access to Clinical Trials (adacT)

KEY PERSONNEL Team Leader: Martin Edelman, MD

Co-Leader: Linda Fleisher, PhD





EDELMAN

FLEISHER

PURPOSE

This initiative is designed to combat racial, ethnic and socioeconomic disparities that frequently occur during enrollment to clinical trials. Funded by Stand up to Cancer (SU2C), the ADACT Initiative is a multifaceted approach that aims to identify and overcome widespread barriers to accrual - specifically in early phase clinical trials (EPCTs). It aims to address all levels of the socioeconomic model which encompasses the patient, provider, community and system as a whole, and is driven by community involvement and partnership. The goal is to increase the number and diversity of patients enrolled in EPCTs across the entire Temple University Health System, including at the Fox Chase Cancer Center (FCCC) and Temple University Hospital (TUH), with a particular focus on patients served by the Cancer Center at TUH.

SPECIFIC AIMS

Aim 1. Develop infrastructure/personnel to extend early phase clinical trials

Aim 2. Provide extensive patient support and services in early phase clinical trials

Aim 3. Leverage community and patient engagement for community education and to integrate existing community services to support early phase clinical trials participation.

KEY PROGRESS

Since the start of the ADACT initiative, we have had a significant increase in clinical trial activation and accrual, especially amongst Spanish speakers. This is largely due to the increase in translated clinical trial documents, such as consent forms. Focusing on building infrastructure at TUH in North Philadelphia, we have on-boarded new leadership and staff including a senior investigator. We are in the process of initiating a bi-lingual Clinical Trial Patient Navigator position after thoughtful collaboration with UT Southwestern. Numerous "Listening Sessions" have been conducted with interdisciplinary teams at TUH, including clinical, research, and social work teams, among others, to pinpoint where resources are most needed. We are working with Palliative Care services at TUH and the primary FCCC campus to develop an oncology-centered outpatient palliative care consult service with a focus on supporting patients enrolled on trials. We have reviewed our community grants and revised our community ambassador training, as well as conducted an extensive Geo-mapping analysis to identify which communities to target. Proposals for Spanish translation of the mychoice[™] clinical trial education tool are underway.

FUNDER

SU2C LUNG CANCER HEALTH EQUITY RESEARCH TEAM RT6228

Southeastern Consortium for Lung Cancer Health Equity Grant Term: February 2022 - January 2025

KEY PERSONNEL

Team Leader: Robert A. Winn, MD Virginia Commonwealth University

Co-Leader: Marvella E. Ford, PhD Medical University of South Carolina





WINN

FORD

Principal: Louise Henderson, PhD University of North Carolina at Chapel Hill

Project Manager: Rosuany Vélez Acevedo, PhD Virginia Commonwealth University velezrn@vcu.edu

Advocates: Tomma Hargraves and Vernal Branch UNC Lineberger Comprehensive Cancer Center

Advocate: Rudene Mercer Haynes Virginia Commonwealth University

Advocate: Diane Juitt MUSC Hollings Cancer Center

PURPOSE:

The Southeastern Consortium for Lung Cancer Health Equity Team is focusing on lung cancer disparities within the Black/African American population using a "cell-to-society" approach. They aim to create a sustainable infrastructure to gather relevant data needed to increase lung cancer screening and develop better methods for identifying those at the highest risk for a diagnosis of and/or poor treatment outcomes for lung cancer.

SPECIFIC AIMS

Aim 1. Initiate and evaluate a high-impact, multimodal and multilevel navigation intervention to promote LCS among Black/African American individuals from both rural and urban medically underserved communities in Virginia, North Carolina, and South Carolina.

Aim 2. Develop a robust, shared population-based cohort and biorepository to further support research in understanding biologic determinants or risk factors for poor lung cancer outcomes among Black/African Americans.

KEY PROGRESS

The Consortium has addressed two of the most critical components of patient navigation with their clinical site partners and with the surrounding communities in preparation for study activation. These components include: 1) establishing clear workflow processes for clinical care referral and 2) conducting community asset mapping. Without establishing these components, patient navigation is less supportive and helpful. Additionally, the Team developed and held a comprehensive training for the navigators. Study activation for the navigation aim has occurred. Recruitment for the biorepository aim began in late July 2023.

CLINICAL TRIALS

N/A

FUNDER

\mu Bristol Myers Squibb


STAND UP TO CANCER-FANCONI ANEMIA RESEARCH FUND-FARRAH FAWCETT FOUNDATION HEAD AND NECK CANCER RESEARCH TEAM RT6219

Precision Therapy for Fanconi Anemia and HPV-Related Head and Neck Cancers

Grant Term: October 2021 - September 2024

KEY PERSONNEL

Team Leader: Agata Smogorzewska, MD, PhD The Rockefeller University

Co-Leader: Barbara Burtness, MD Yale School of Medicine





SMOGORZEWSKA

BURTNESS

Principal: Amanda Paulovich, MD, PhD Fred Hutchinson Cancer Research Center

Principal: Markus Grompe, MD Oregon Health & Science University

Principal: Jorge Silvio Gutkind, PhD University of California, San Diego

Project Manager: Anna Arnal Estape, PhD Yale School of Medicine anna.arnal@yale.edu

Advocate: Allison Breininger

Advocate: Peter Krause, MD Yale School of Medicine

PURPOSE

The goal of the Precision Therapy for Fanconi Anemia and HPV-Related Head and Neck Cancers Team is to develop improved treatments for patients with head and neck squamous cell carcinoma. The Team is concentrating on treatments for patients who develop this cancer due to human papillomavirus infection (HPV) or Fanconi anemia (FA). Cancers that develop due to HPV infection are often diagnosed when cancer has already spread, and a quarter of these patients are not cured with current therapies. Standard therapies cannot be used in patients with Fanconi anemia due to their disease, leading to poor outcomes. In both patient groups, successful treatment may be associated with serious side effects resulting in low quality of life.

SPECIFIC AIMS

Aim 1. Perform proteogenomic and digital histologic analysis of FA-related and HPV-related HNSCCs to identify common and cohort-specific therapeutic approaches.

Aim 2. Identify and test novel therapeutic approaches in HPV- related HNSCC.

Aim 3. Identify effective chemoprevention and treatments in FA-associated HNSCC.

Aim 4. Assess the toxicity of potential cancer therapeutics using FA mice bone marrow function assays.

KEY PROGRESS

CLINICAL TRIALS

N/A

HEAD AND NECK CANCER RESEARCH TEAM

Comparing, Exploring and Targeting Head and Neck Cancers

SU2C, Fanconi Anemia Research Fund, Farrah Fawcett Foundation, American Head and Neck Society, and the Head and Neck Cancer Alliance are collaborating to unite researchers who typically take different approaches to understand how head and neck cancers grow. Their research is exploring combinations of existing and emerging treatments for head and neck squamous cell cancers, especially for people with the human papillomavirus (HPV) or Fanconi anemia — a rare disease that primarily affects the bone marrow.

These cancers account for more than 90% of cancers in the head and neck. They are the sixth most common cancer in the world and can appear in the nasal cavity, sinuses, lips, mouth, salivary glands, thyroid gland, throat, or larynx.





SU2C-CRUK PEDIATRIC CANCER NEW DISCOVERIES CHALLENGE RESEARCH TEAM RT6188

Combinatorial Targeting of Oncogene-Driven Childhood Cancer

Grant Term: March 2021 - September 2023

KEY PERSONNEL

Team Leader: John Anderson, MBBS, MRCP, PhD University College London Great Ormond Street Institute of Child Health

Co-Leader: Louis Chesler, MD, PhD, FRCPCH Institute of Cancer Research





ANDERSON

CHESLER

Principal: Paul M. Sondel, MD, PhD University of Wisconsin, Madison

Principal: Darren Hargrave, MD, FRCPCH, MRCP University College London Great Ormond Street Institute of Child Health

Principal: Laura Donovan, PhD University College London Great Ormond Street Institute of Child Health

Project Manager: Jennifer Furman, PhD University College London j.furman@ucl.ac.uk

Advocate: Parker Moss

Advocate: Lori R. Schultz UW Health American Family Children's Hospital

PURPOSE

The Combinatorial Targeting of Oncogene-Driven Childhood Cancer Team is working to overcome the diminished efficacy of immunotherapies in the treatment of pediatric cancers, specifically in neuroblastoma and medulloblastoma, using immune competent models of resistant disease. They are designing CAR T cells to overcome immune evasion and barriers using new compounds to overcome tumor growth and immune barrier formation and are also using a combination of drugs to strengthen immune responses, employing multiparameter proteomics to measure response and resistance.

SPECIFIC AIMS

Aim 1. Evaluate MYC inhibitor combinations with chemotherapy and anti-GD2 antibody in neuro-blastoma model.

Aim 2. Evaluate MYC inhibitor agents with local delivery of CAR T cells in medulloblastoma model.

Aim 3. Optimize CAR T to incorporate into combination studies.

Aim 4. Evaluate MYC inhibitor with in situ vaccine in neuroblastoma.

Aim 5. Evaluate addition of in situ vaccine to MYC targeting in medulloblastoma.

Aim 6. Evaluate addition of in situ vaccine to MYC-targeting and systemic CAR T in neuroblastoma.

Aim 7. Evaluate addition of in situ vaccine to MYC-targeting and systemic CAR T in medullo-blastoma.

KEY PROGRESS

The Team has demonstrated the capacity of synthetic immunotherapy combined with immune modulators to induce endogenous memory response in immune cold neuroblastoma. The Team has generated prototypes for next generation CAR T to target neuroblastoma and medulloblastoma.

The following highlights are of particular note:

Development of an anti-B7H3 CAR T platform built on a novel anti-B7H3 binder and incorporating a novel off-switch mechanism through incorporation of an IMiD drug sensitive degradation tag called iTAG2.

Generation of animal models of neuroblastoma and medulloblastoma built on genetically modified mice that represent human counterparts, suitable for high throughput evaluation of combination immunotherapies.

Completion of combination therapies trials using these models to evaluate small molecule/ synthetic immunotherapy +/- molecular radiotherapy.

Optimisation of spatial imaging of the mouse tumour environment from the therapeutics intervention trials using the Phenocycler platform.

The lead innovation for translation into clinical evaluation is the iTAG2 degron tagged anti-B7H3 CAR T platform. Based on data emerging from the New Discoveries Challenge funding, the group has secured funding for a paediatric brain tumour clinical trial incorporating locoregional administration of repeatedly infused CAR T cells that have been manufactured in the presence of IMiD drug iberdomide to minimize CAR T signaling during manufacture. A second clinical trial of the same construct in neuroblastoma which will involve administration of an IMiD drug to patients to allow transient rest of CAR T has been proposed in the second stage funding application from the Team.

CLINICAL TRIALS



Leader: John Anderson, BA, MBBS, MRCP, PhD, University College London Great Ormond Street Institute of Child Health

Great Ormond Street Institute of Child Health Co-Leader: Louis Chesler, MD, PhD, FRCPCH, Institute of Cancer Research

> CANCER RESEARCH

A larger version of this graphic is available in the appendix.



SU2C-CRUK PEDIATRIC CANCER NEW DISCOVERIES CHALLENGE RESEARCH TEAM RT6187

Targeting R-loop Stability in Ewing Sarcoma

Grant Term: January 2021 - September 2023

KEY PERSONNEL Team Leader: Alexander Bishop, DPhil UT Health San Antonio

Co-Leader: Kevin Hiom, PhD University of Dundee





BISHOP

HIOM

Principal: Chun Wei-Chen, PhD Beckman Research Institute of the City of Hope

Project Manager: Sneha Prabhu, MPH UT Health San Antonio prabhus@uthscsa.edu

Advocate: Laura Jean Rutledge Rutledge Cancer Foundation

Advocate: Gregory Aune UT Health San Antonio

PURPOSE

The Targeting R-loop Stability in Ewing Sarcoma Research Team is investigating the basis for the strong increase in R loops seen in Ewing sarcoma. The long-term goal is to leverage insights gained into Ewing sarcoma biology to identify vulnerabilities that can be targeted with available compounds or new formulations.

SPECIFIC AIMS

Aim 1. Target SF3B1/SRSF2 complex in Ewing sarcoma to induce toxic levels of R-loops.

Aim 2. Disrupt DHX9:EWSR1-FLI1 interaction to promote pathological R-loops.

KEY PROGRESS

The Team created a comprehensive database containing approximately 800 datasets to identify high-quality R-loop sequencing data allowing an in-depth analysis of R-loops; this allowed a novel categorization of these structures in the genome and confirmed that Ewing sarcoma has significantly altered levels of R-loops. Through their CRISPR scanning research, the Team delved into the functional characteristics of potential proteins like BRCA1 and SF3B1 that are involved in R-loop regulation, unveiling crucial insights into their dynamics and discovered that SF3B1 regulates BRCA1 availability in Ewing sarcoma. Leveraging this newfound knowledge, the Team identified a promising therapeutic avenue centered around manipulating BRCA1 protein availability which they are now testing in preclinical models with a goal of translating to the clinic to provide a new much needed therapeutic option for Ewing sarcoma.

CLINICAL TRIALS

N/A





CREATING BETTER TARGETED THERAPIES

is an important step for curing childhood cancers. Three transatlantic teams working on new ways to use gene therapies and radiation against pediatric cancers have promising solutions that could soon change the way these cancers are treated.







SU2C-CRUK PEDIATRIC CANCER NEW DISCOVERIES CHALLENGE RESEARCH TEAM RT6186

BRAINatomy: A Validated Anatomical Atlas of Childhood Neuroradiation Damage

Grant Term: April 2021 - November 2023

KEY PERSONNEL

Team Leader: Martin G. McCabe, MB/BChir, PhD University of Manchester

Co-Leader: Thomas E. Merchant, BS, DO, PhD St. Jude Children's Research Hospital





MCCABE

MERCHANT

Principal: Lara Barazzuol, PhD University Medical Center Groningen

Project Manager: Kate Vaughan, PhD University of Manchester kate.vaughan@manchester.ac.uk

Advocate: James Adams

Advocate: Helen Bulbeck Braintrust

Advocate: Joshua Goddard

Advocate: Adam Thomson Braintrust

PURPOSE

The BRAINatomy: A Validated Anatomical Atlas of Childhood Neuroradiation Damage Team is studying the path radiation travels in treating pediatric brain tumors to link brain regions to long term side effects and to differentiate the damaging effects of radiotherapy from other clinical factors. In parallel, the biological effects of proton and X-ray radiotherapy on single cells and bulk brain regions are being investigated in an animal model. The team hopes to develop an atlas of brain regions to be avoided during radiotherapy.

SPECIFIC AIMS

Aim 1. To analyze brain regions responsible for cognitive and endocrine damage in a large, retrospective cohort of children from St Jude Children's Research Hospital (medulloblastoma clinical trial dataset) and Manchester (multiple histologies, "real world" dataset) treated with cranial radiotherapy.

Aim 2. To prospectively evaluate the functional and biological effects of brain irradiation in a well- characterised juvenile rat model.

Aim 3. To compare the effects on multiple brain compartments of irradiation with X-ray photons and high-energy protons.

KEY PROGRESS

Using a custom supervised machine learning algorithm to examine their real world dataset, the Team has identified novel radiological features centring on midline and hemispheric structures, imaged prior to any treatment, that predict subsequent processing speed and working memory. In the St Jude dataset, image-based data mining has identified a brain region where received radiotherapy dose correlates highly with subsequent abnormalities in processing speed, one of the key mediators of school performance. In the juvenile rat model, they have a behavioural readout that reliably demonstrates cognitive damage after both proton therapy and X-ray radiotherapy and imaging evidence of radiation damage with both MR and PET imaging. Using nuclear RNA sequencing the Team has identified subtle differences in the biological effects of proton therapy and X-ray radiotherapy in the same anatomical regions highlighted by the clinical study data.

CLINICAL TRIALS







SU2C GASTRIC CANCER INTERCEPTION RESEARCH TEAM RT6072

Early Detection and Interception of Diffuse and Intestinal Gastric Cancer Grant Term: September 2020 - August 2024, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Andrew T. Chan, MD, MPH Massachusetts General Hospital

Co-Leader: Sandra W. Ryeom, PhD Columbia University Irving Medical Center





CHAN

RYEOM

Principal: Jeeyun Lee, MD Samsung Medical Center

Principal: Blasé Polite, MD University of Chicago

Principal: Yanghee Woo, MD Beckman Research Institute of City of Hope

Principal: Sam S. Yoon, MD Columbia University Irving Medical Center

Project Manager: Marina Magicheva-Gupta Massachusetts General Hospital mmagicheva-gupta@mgh.harvard.edu

Advocate: Jason Diaz Stomach Cancer Awareness Network

Advocate: Aki Agata Smith Stomach Cancer Awareness Network

PURPOSE

The Early Detection and Interception of Diffuse and Intestinal Gastric Cancer Team is developing ways to intercept intestinal and diffuse-type gastric cancer through identification and treatment of gastric "precancers" and early-stage disease.

SPECIFIC AIMS

Aim 1. Discover and optimize molecularly specific imaging agents and novel circulating biomarkers for early-stage gastric cancer (GC) using mouse models recapitulating the major TCGA GC subtypes.

Aim 2. Translate preclinical findings to humans by assessing the feasibility of molecular endoscopic or capsule-based imaging across the spectrum of gastric premalignancy and refine circulating biomarkers within cohorts of individuals undergoing routine GC screening and surgery for early-stage disease.

Aim 3. Assess initial performance of a molecular and/or capsule imaging platform for detection of GC and validate circulating biomarkers in locally advanced GC patients enrolled in a clinical trial.

KEY PROGRESS

The Team has established the largest global GC consortium to leverage existing blood and tissue specimens from patients with premalignant lesions and early-stage cancers from endoscopic screening populations (Samsung Medical Center) and from high-risk populations undergoing care in the United States (Columbia University Medical Center, City of Hope, MGH, Samsung Medical Center and the NCI). The Team has identified 16 proteins as potential biomarkers in genetic mouse models of early GC. A subset of these proteins has been confirmed to be expressed in both mouse and human stool from

early-stage GC in mice and patients with diffuse GC. The Team is continuing to enroll participants in a clinical trial that tests the feasibility of a molecular-based imaging agent (pegulicianine) to detect early GC and precancerous lesions. The Team is also developing a novel blood-based early detection assay to detect proteins that are overexpressed in early GC.

CLINICAL TRIALS

Feasibility of the LUM Imaging System for Detection of Gastrointestinal Cancers; NCT02584244; Recruiting

A Phase II Study of Neoadjuvant NALIRIFOX Followed by Chemoradiation With Paclitaxel and Carboplatin in Locally Advanced Esophagogastric Cancer; NCT04656041; Recruiting





PANCREATIC CANCER COLLECTIVE RESEARCH TEAMS-COMPUTATIONAL APPROACHES TO IDENTIFYING HIGH-RISK PANCREATIC CANCER POPULATIONS RT6179

Identification of Genomic and Immune Factors in High-Risk Populations for Pancreatic Cancer Grant Term: May 2019 - February 2022

KEY PERSONNEL Team Leader: Raul Rabadan, PhD Columbia University

Co-Leader: Núria Malats, MD, MPH, PhD Spanish National Cancer Research Centre (CNIO)





RABADAN

MALATS

Principal: Tal Korem, PhD Columbia University

Principal: Gulam Manji, MD, PhD Columbia University

Principal: Ken Olive, PhD Columbia University

Project Manager: Paula Ralph-Birkett Columbia University pr2470@cumc.columbia.edu

Project Manager: Evangelina López de Maturana CNIO

Project Manager: Lola Alonso CNIO **Project Manager:** Oleksandr Kravets Columbia University

Project Manager: Ioan Filip (formerly) Columbia University

PURPOSE

Using five patient cohorts, the Pancreatic Cancer Collective Research Team– Identification of Genomic and Immune Factors in High-Risk Populations for Pancreatic Cancer leveraged the power of large datasets to assess the compounded risk of pancreatic cancer based on well-established empirical factors together with novel genomic and microenvironmental markers.

SPECIFIC AIMS

Aim 1A. Identify de novo and germline alterations.

Aim 1B. Annotate the non-coding landscape of alterations in pancreatic tumors.

Aim 2A. Characterize pathogenic infections in the tumor microenvironment.

Aim 2B. Characterize HLA allele-specific expression.

Aim 3. Pursue external validation and integration with other data modalities.

KEY ACCOMPLISHMENTS

Association analysis of HLA loci variation with pancreatic cancer risk allowed the identification of specific HLA alleles and haplotypes, thereby improving the definition of a high-risk pancreatic cancer population when combined with the stabilized epidemiological risk factors (using the PanGen-EU as a discovery data set and the UK Biobank for validation). Association analysis of microbiome diversity (oral and fecal) and pancreatic cancer risk has been completed. Based on two risk prediction methods, the fecal microbiome was proven to predict PDAC risk better than the oral microbiome. HLA and microbiome integrative risk analysis has been carried out yielding moderate predictive ability. Comprehensive analysis of HLA class I allele-specific expression in the TCGA cohort, based on a novel HLA quantification method, showed that the corresponding loss of homozygosity is a pervasive phenomenon in PDAC and is associated with decreased overall survival in the basal-like subtype. The latter association was further validated in a cohort from Columbia University.

CLINICAL TRIALS





PANCREATIC CANCER COLLECTIVE RESEARCH TEAMS-COMPUTATIONAL APPROACHES TO IDENTIFYING HIGH-RISK PANCREATIC CANCER POPULATIONS RT6180

Identifying Individuals at High Risk of Pancreatic Cancer Through Machine Learning Analysis of Clinical Records and Images

Grant Term: May 2019 - April 2022

KEY PERSONNEL

Team Leader: Chris Sander, PhD Dana-Farber Cancer Institute

Co-Leader: Regina Barzilay, PhD Massachusetts Institute of Technology



SANDER



BARZILAY

Principal: Peter Kraft, PhD Harvard T. H. Chan School of Public Health

Principal: Michael Rosenthal, MD, PhD Dana-Farber Cancer Institute

Principal: Brian Wolpin, MD Dana-Farber Cancer Institute

Collaborator: Søren Brunak, PhD University of Copenhagen

Project Manager: Elizabeth Andrews Dana-Farber Cancer Institute ElizabethA_Andrews@dfci.harvard.edu

PURPOSE

The Pancreatic Cancer Collective Research Team– Identifying Individuals at High Risk of Pancreatic Cancer Through Machine Learning Analysis of Clinical Records and Images utilized machine learning to infer predictive patterns of increased risk for pancreatic cancer from structured data tables, unstructured clinical notes, and radiological images. SPECIFIC AIMS

Aim 1. Curate and annotate data.

Aim 2. Extract features from data.

Aim 3. Conduct predictive modeling.

KEY ACCOMPLISHMENTS

Training on disease code trajectories in the Danish National Patient Registry has been completed, and the Team constructed a data query system under this infrastructure for future analyses and modeling. A common data dictionary that includes disease-relevant demographic, laboratory and clinical information has now been completed, and this data framework will allow models to be trained and validated across sites independent of the medical record structure. The Team found that diabetes and weight loss were each independently associated with a moderately increased risk for development of pancreatic cancer. When weight loss co-occurred with recent-onset diabetes, the subsequent risk of pancreatic cancer was substantially elevated, which identifies a very high-risk group who may benefit from early detection strategies.

CLINICAL TRIALS

N/A



PANCREATIC CANCER COLLECTIVE RESEARCH TEAM-NEW THERAPIES CHALLENGE RT6156

Targeting SHP2 in Pancreatic Cancer

Grant Term: November 2018 - October 2024, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: René Bernards, PhD Netherlands Cancer Institute

Co-Leader: Hana Algül, MD, PhD Technical University of Munich

Co-Leader: Emile E. Voest, MD, PhD Netherlands Cancer Institute



BERNARDS



ALGÜL



VOEST

Project Manager: Henri van Luenen, PhD Netherlands Cancer Institute h.v.luenen@nki.nl

Advocate: Ab Doorn The Netherlands Cancer Institute

Advocate: Otto Lutz Arbeitskreis der Pankreatektomierten e.V.

PURPOSE

Members of the Targeting SHP2 in Pancreatic Cancer Research Team previously found that tumors with an activating KRAS mutation are sensitive to the inhibition of SHP2. In its first grant, the Team found that SHP2/ERK inhibitor combination (RMC4550 and LY3214996, respectively) is efficacious and tolerable in preclinical models. With additional funding, they are set to conduct a phase I/ Ib clinical trial of RMC4630 and LY3214996 to treat KRAS mutant pancreatic cancer.

SPECIFIC AIMS

Aim 1. Evaluate the maximum tolerated dose of the SHP2 inhibitor and MEK inhibitor of choice in non-tumor-bearing mice.

Aim 2. Identify qualifying biomarkers for response that will allow us to identify patients most likely to respond to the proposed therapy.

Aim 3. Test different treatment schedules in different mouse models of pancreatic cancer, in order to maximize the antitumor effect and to minimize toxicity.

KEY PROGRESS

The Team confirmed that RMC4550 and LY3214996 can penetrate pancreatic tumors in preclinical laboratory experiments. In addition, the Team has identified different ways by which tumors can become resistant to the RMC4550/ LY3214996 treatment combination. They continue to enroll patients in their clinical trial.

CLINICAL TRIALS

Phase I/Ib Study With the Combination of RMC-4630 (SHP2 Inhibitor) and LY3214996 (ERK Inhibitor) in Metastatic KRAS Mutant CRC, PDAC and NSCLC; NCT04916236; Recruiting





PANCREATIC CANCER COLLECTIVE RESEARCH TEAM-NEW THERAPIES CHALLENGE RT6155

Exploiting DNA Repair Gene Mutations in Pancreatic Cancer

Grant Term: November 2018 - December 2024, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Alan D. D'Andrea, MD Dana-Farber Cancer Institute

Co-Leader: James M. Cleary, MD, PhD Dana-Farber Cancer Institute





D'ANDREA

CLEARY

Principal: Andrew Aguirre, MD, PhD Dana-Farber Cancer Institute

Principal: Geoffrey I. Shapiro, MD, PhD Dana-Farber Cancer Institute

Principal: Brian M. Wolpin, MD Dana-Farber Cancer Institute

Project Manager: Donald R. Watson Dana-Farber Cancer Institute Donald_watson@dfci.harvard.edu

PURPOSE

The Pancreatic Cancer Collective Research Team– Exploiting DNA Repair Gene Mutations in Pancreatic Cancer is testing the hypothesis that targeting DNA repair deficiency and replicative stress are effective therapeutic strategies in the treatment of pancreatic cancer.

SPECIFIC AIMS

Aim 1. Assess DNA damage repair (DDR) deficiency in pancreatic cancer.

Aim 2. Target replicative stress in platinum-resistant pancreatic cancer

KEY PROGRESS

The Team has completed enrollment to its phase 2 trial of PARP inhibitor niraparib in pancreatic cancer patients with mutations in homologous recombination genes. Given the chemotherapy agent gemcitabine's ability to increase replicative stress, the Team is conducting clinical trials testing the combination of gemcitabine with inhibitors of proteins; namely, CHK1, ATR and WEE1. To understand the mechanisms of response/ resistance to the gemcitabine/CHK1 inhibitor combination, the Team has generated 3D cultures called organoids from patient tumors.

CLINICAL TRIALS

Phase Ib/IIa Two-Part, Open-Label, Multicenter Study to Evaluate the Safety and Efficacy of LY2880070 as Monotherapy and in Combination With Gemcitabine in Patients With Advanced or Metastatic Cancer; NCT02632448; Completed

Phase II Proof-of-Concept Trial Testing the PARP Inhibitor Niraparib in Patients With Pancreatic Cancer Harboring Deficiencies in Homologous Recombination DNA Repair; NCT03601923; Completed

Phase I Trial of Gemcitabine Combined With the BAY 1895344 ATR Inhibitor With Expansion Cohorts in Advanced Pancreatic and Ovarian Cancer; NCT04616534; Recruiting



PANCREATIC CANCER COLLECTIVE RESEARCH TEAM-NEW THERAPIES CHALLENGE RT6154

Adoptive Transfer of TGF-B-Resistant TIL to Defeat Immunosuppressive PDAC

Grant Term: November 2018 - September 2020, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Patrick Hwu, MD The University of Texas MD Anderson Cancer Center

Co-Leader: Chantale Bernatchez, PhD The University of Texas MD Anderson Cancer Center

Co-Leader: Cliona M. Rooney, PhD Baylor College of Medicine



HWU



BERNATCHEZ

PURPOSE

The Adoptive Transfer Pancreatic Cancer Collective New Therapies Challenge Research Team planned to engineer tumor-infiltrating lymphocytes (TIL) to make the cells resistant to the suppressive effect of TGF-B, potentially enabling the TILs to attack the cancer tissue within the pancreas.

SPECIFIC AIMS

Aim 1. Optimize PDAC TIL retroviral transduction method.

Aim 2. Test the impact of the expression of TGF BDNRII on PDAC TIL function.

Aim 3. Investigate in vivo efficacy of tumor-specific TGF BDNRII- transduced T cells in patientderived preclinical models of pancreatic cancer.

KEY ACCOMPLISHMENTS

The Team demonstrated that TILs from two pancreatic cancer patients could be transduced with the TGF decoy receptor and expanded.

CLINICAL TRIALS

N/A

FUNDERS



Project Manager: Karen Millerchip The University of Texas MD Anderson Cancer Center KAMillerchip@mdanderson.org

ROONEY





PANCREATIC CANCER COLLECTIVE RESEARCH TEAM-NEW THERAPIES CHALLENGE RT6152

Combined Targeting of MEK1/2 and Autophagy for Pancreatic Cancer Therapy

Grant Term: November 2018 -December 2020, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Martin McMahon, PhD University of Utah

Co-Leader: Eric A. Collisson, MD University of California, San Francisco





MCMAHON

COLLISSON

Principal: Conan G. Kinsey, MD, PhD University of Utah

Project Manager: Karrie Lasater University of Utah

Advocate: Phyllis D. Coley University of Utah

Advocate: Thomas Kursar University of Utah

PURPOSE

The Combined Targeting of MEK1/2 and Autophagy for Pancreatic Cancer Therapy Team tested a combination approach to pancreatic cancer therapy shutting down two cellular pathways. The first pathway (MEK) carries signals that relate to tumor growth, and the second controls a process call autophagy, in which a cell effectively reuses its own interior contents to function. By shutting down both pathways, the Team hoped to slow or stop the growth of pancreatic tumors.

SPECIFIC AIMS

Aim 1. Test if there is a PDA cell genotype-T/ HCQ drug response phenotype in PDA cell lines and PDX models with an initial emphasis on TP53 mutation status.

Aim 2. Explore novel targets and agents to inhibit trametinib-induced autophagy in PDA cells.

Aim 3. Initiate clinical trials of the combination of trametinib plus HCQ (T/HCQ) in PDA patients.

KEY ACCOMPLISHMENTS

The Team completed a phase 1 trial designated THREAD – testing a fixed dose of the MEK inhibitor trametinib and an escalating dose of the autophagy inhibitor hydroxychloroquine (T/HCQ) in patients with chemotherapy refractory PDAC. Two dose levels of HCQ in combination with trametinib were tested in 14 patients. A safe and tolerable dose of this combination was identified and a plan for an expansion cohort was developed.

CLINICAL TRIALS

THREAD: A Phase I Trial of Trametinib and Hydroxychloroquine in Patients With Advanced Pancreatic Cancer; NCT03825289; Recruiting



PANCREATIC CANCER COLLECTIVE RESEARCH TEAM-NEW THERAPIES CHALLENGE RT6157

Targeting Stem Cell Signals in Pancreatic Cancer

Grant Term: November 2018-October 2020, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Tannishtha Reya, PhD University of California, San Diego

Co-Leader: Andrew M. Lowy, MD University of California, San Diego

Co-Leader: Margaret A. Tempero, MD University of California, San Francisco



REYA





LOWY

PURPOSE

The Targeting Stem Cell Signals in Pancreatic Cancer Team tested whether blocking ROR gamma, a protein that regulates inflammation, can slow or stop the growth of pancreatic cancer.

SPECIFIC AIMS

Aim 1. Test inhibition of ROR- γ in combination with chemotherapy in preclinical models.

Aim 2. Identify biomarkers predictive of response and define a molecular signature reflective of response to ROR-γ inhibition.

KEY ACCOMPLISHMENTS

The Team tested whether pharmacologic inhibition of ROR gamma using a small molecule inhibitor AZD-0284 could inhibit this nuclear receptor and alter the growth of pancreatic cancer cells. AZD-0284 exhibited modest activity in the models tested.



TEMPERO

Project Manager: Marcie Kritzik, PhD University of California, San Diego

CLINICAL TRIALS







PANCREATIC CANCER COLLECTIVE RESEARCH TEAM – NEW THERAPIES CHALLENGE RT6153

Molecularly Targeted Radionuclide Therapy via the Integrin α v β 6

Grant Term: November 2018 - June 2024, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Julie L. Sutcliffe, PhD University of California, Davis

Co-Leader: Richard J. Bold, MD, MBA University of California, Davis





SUTCLIFFE

BOLD

Principal: Cameron C. Foster, MD University of California, Davis

Project Manager: Sonal J. Desai, PhD University of California, Davis

Advocate: Lora Kelly, RN

PURPOSE

The Molecularly Targeted Radionuclide Therapy via the Integrin $\alpha\nu\beta6$ Team is working to conduct a phase I, first-in-human study to evaluate the safety and efficacy of a [68Ga]Ga DOTA-5G / [177Lu]Lu DOTA-ABM-5G theranostic pair in patients with locally advanced or metastatic pancreatic cancer.

SPECIFIC AIMS

Aim 1A. Establish that [⁶⁸Ga]Ga DOTA-5G can detect lesions in patients with locally advanced or metastatic pancreas cancer. The ability of [⁶⁸Ga]Ga DOTA-5G to detect lesions will be assessed by increased standard uptake values (SUVmax >2-fold above normal lung or liver) of [⁶⁸Ga]Ga DOTA-5G in at least one lesion assessed by [⁶⁸Ga]Ga DOTA-5G PET/CT.

Aim 1B. Establish the safety and tolerability of the theranostic pair [⁶⁸Ga]Ga DOTA-5G / [¹⁷⁷Lu]Lu DOTA- ABM-5G. Safety and tolerability of [⁶⁸Ga] Ga DOTA-5G / [¹⁷⁷Lu]Lu DOTA-ABM-5G will be assessed by number of patients with treatmentrelated adverse events using CTCAE v5.0.

Aim 1C. Evaluate the maximum tolerated dose (MTD), and determine the recommended phase II dose (RP2D) of ¹⁷⁷Lu- α vß6 -BP. Dose-limiting toxicities (DLT) of 177Lu- α vß6 -BP with activity levels starting from 25 mCi and increasing up to the "standard" PRRT level of 200 mCi will be assessed using SPECT/CT.

Aim 2. Establish an optimal dosing regimen in pre-clinical models. Fractionated dosing with the ¹⁷⁷Lu- $\alpha\nu\beta6$ -BP as well as combination with standard-of-care chemotherapy and novel avb6-BP drug conjugates will be explored in xenograft, orthotopic and metastatic mouse models.

KEY PROGRESS

The integrin $\alpha v\beta 6$ is a protein that can be found on the surface of pancreatic cancer cells but is undetectable on normal cells. Receiving an initial round of funding support, the Team synthesized a pair of compounds, a ⁶⁸Ga-αvβ6-binding peptide ([68Ga]Ga DOTA-5G) to visualize cancer, and a¹⁷⁷Lu-αvβ6 -binding peptide ([¹⁷⁷Lu]Lu DOTA-ABM-5G) to treat cancer, and confirmed that these peptides can home in on the α v β 6 in vitro and in vivo. With the support of Round 2 funding, they have enrolled 27 patients in their Phase I clinical trial where they are determining whether [⁶⁸Ga]Ga DOTA-5G can be used to detect lesions in patients with locally advanced or metastatic pancreatic cancer, establish the safety of the two peptides, and identify the maximum tolerated dose and recommended phase II dose of [¹⁷⁷Lu] Lu DOTA-ABM-5G. To date they have demonstrated that the [68Ga]Ga DOTA-5G can detect lesions and that the [68Ga]Ga DOTA-5G and [177Lu] Lu DOTA-ABM-5G are safe and well tolerated.

CLINICAL TRIALS

First-in-human Study of the Theranostic Pair [⁶⁸Ga]Ga DOTA-5G and [¹⁷⁷Lu] Lu DOTA-ABM-5G in Pancreatic Cancer; NCT04665947; Recruiting







PANCREATIC CANCER COLLECTIVE RESEARCH TEAM–NEW THERAPIES CHALLENGE RT6151

Immunotherapy Targeting Mutant KRAS

Grant Term: November 2018 - September 2024, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Robert H. Vonderheide, MD, DPhil University of Pennsylvania

Co-Leader: Elizabeth M. Jaffee, MD Johns Hopkins University

Co-Leader: Beatriz M. Carreno, PhD University of Pennsylvania





JAFFEE



CARRENO

Principal: Neeha Zaidi, MD Johns Hopkins University

Early-Career Investigator: Adham Bear, MD, PhD University of Pennsylvania

Project Manager: TBD

PURPOSE

KRAS mutations (mKRAS) occur in greater than 90% of pancreatic ductal adenocarcinoma (PDA) tumors. In Round 1 of its funding, the Immunotherapy Targeting Mutant KRAS Team isolated mKRASspecific T-cell receptors (TCRs) from neoantigenreactive T cells. These TCRs have been confirmed in preclinical experiments to confer selective cytotoxicity against mKRAS-expressing PDA tumors. In Round 2, the team is conducting a phase I clinical study of adoptively transferred autologous T cells engineered to express a mKRAS-specific TCR.

SPECIFIC AIMS

Aim 1. To identify novel mKRAS-specific TCRs in PDAC patients.

Aim 2. To initiate a phase I clinical study of adoptively transferred autologous T cells engineered to express a mKRAS-specific TCR.

KEY PROGRESS

The investigators have identified candidate KRAS epitopes using computational, biochemical, and proteomic determinations. The Team continues enrollment in their two vaccine trials, which have enabled epitope validation and provide samples for mKRAS-specific TCR identification and isolation. A candidate TCR has been selected for clinical development and pre-clinical and INDenabling studies are on-going.

CLINICAL TRIALS

Pilot Study of Mature Dendritic Cell Vaccination Against Mutated KRAS in Patients With Resectable Pancreatic Cancer; NCT03592888; Recruiting

Pooled Mutant KRAS-Targeted Long Peptide Vaccine Combined With Nivolumab and Ipilimumab for Patients With Resected MMR-p Colorectal and Pancreatic Cancer; NCT04117087; Recruiting



SU2C-LUSTGARTEN FOUNDATION PANCREATIC CANCER INTERCEPTION RESEARCH TEAM RT6059

Developing Novel Approaches to Detect and Treat Early Pancreatic Cancer

Grant Term: January 2018 - December 2022, administered by the American Association for Cancer Research

KEY PERSONNEL Team Leader: David P. Ryan, MD Massachusetts General Hospital

Co-Leader: Alec C. Kimmelman, MD, PhD New York University

Principal: Richard A. Burkhart, MD Johns Hopkins University

Principal: Daniel Laheru, MD Johns Hopkins University

Principal: Wells A. Messersmith, MD University of Colorado, Denver

Principal: Cullen M. Taniguchi, MD, PhD The University of Texas MD Anderson Cancer Center

Project Manager: Leilana Ly Massachusetts General Hospital LLY2@mgh.harvard.edu

Advocate: Robert A. Ettl (deceased) Harvard Management Co., Inc.

Advocate: Regina Pyle Massachusetts General Hospital

Advocate: Carole Seigel Massachusetts General Hospital

PURPOSE

The Interception Research Team is evaluating in a randomized setting whether the addition of losartan and nivolumab to FOLFIRINOX increases the rate of surgical resection for localized pancreatic cancer. The Team is also utilizing tumor organoid technology in which an individual patient's tumor cells are grown in the laboratory to create "minitumors" that can be used to test treatments. The Team is also studying changes in the tumor microenvironment.

SPECIFIC AIMS

Aim 1. Evaluate novel neoadjuvant approaches in PDAC patients.

Aim 1A. Conduct neoadjuvant clinical trial to increase curability.

Aim 1B. Determine whether therapeutic screening of patient-derived organoids can identify an optimal clinical treatment.

Aim 1C. Conduct primary tumor molecular analysis.

Aim 1D. Determine the ctDNA, CTC, and exosomes at presentation, during treatment, and after surgery.

Aim 1E. Determine the changes in the tumor microenvironment (TME) between arms.

KEY ACCOMPLISHMENTS

The Team aimed to improve the number of pancreatic cancer patients who are curable by pre-treating patients with new combination therapies prior to surgery. They have successfully completed their accrual goal of 160 patients. They were also able to demonstrate the feasibility of assessing the feasibility of a hospital-at-home intervention for a subset of patients in their clinical trial. With additional funding from a SU2C Sharp Challenge grant, pre-treatment biopsies, post-treatment resection, and serial blood samples are being analyzed to uncover new mechanistic insights into pancreatic cancer pathogenesis and to understand how the therapeutic interventions in this trial led to the observed R0 resection rates.

CLINICAL TRIALS

A randomized Phase II Study of Losartan and Nivolumab in Combination With FOLFIRINOX and SBRT in Localized Pancreatic Cancer; NCT03563248; Active, not recruiting





SU2C-LUNGEVITY FOUNDATION-AMERICAN LUNG ASSOCIATION LUNG CANCER INTERCEPTION RESEARCH TEAM RT6058

Blood-Based Early Interception of Lung Cancer

Grant Term: December 2017 - February 2019, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Lecia V. Sequist, MD Massachusetts General Hospital

Co-Leader: Maximilian Diehn, MD, PhD Stanford University



SEQUIST

DIEHN

Project Manager: Elaina PuiYee Chan, PhD Massachusetts General Hospital pchan9@partners.org

Advocate: Chris M. Draft Chris Draft Family Foundation

PURPOSE

The Blood-Based Early Interception of Lung Cancer Team hypothesized that the early detection of invasive lung cancers could be improved through new technological approaches, and that progress on this front can quickly bring about more effective patient treatments.

SPECIFIC AIMS

Develop a multianalyte Lung Cancer Interception Assay (LCIA) incorporating circulating tumor DNA, CTC-derived RNA signatures, and plasma proteomics for use in early-stage lung cancer detection.

KEY ACCOMPLISHMENTS

The investigators laid the groundwork for a multianalyte lung cancer early detection test. They demonstrated promising performance of circulating tumor DNA and further explored circulating tumor cells (CTCs) and patterns of proteins in the plasma of early stage lung cancer patients.

CLINICAL TRIALS

N/A

FUNDERS



THE S†2C SCIENTIFIC SUMMIT129CORONADO, CALIFORNIA JANUARY 26-29 2024

SU2C-LUSTGARTEN FOUNDATION TRANSLATIONAL RESEARCH TEAM RT6116, RT6162

Chimeric Antigen Receptor T-cell (CAR T) Therapy for Pancreatic Cancer Grant Term: April 2017 - November 2022

KEY PERSONNEL Team Leader: Carl H. June, MD University of Pennsylvania

Co-Leader: Shelley L. Berger, PhD University of Pennsylvania

Co-Leader: E. John Wherry, PhD University of Pennsylvania



JUNE



BERGER



WHERRY

Principal: M. Angela Aznar, PhD University of Pennsylvania

Principal: Charly R. Good, PhD University of Pennsylvania

Principal: Mark H. O'Hara, MD University of Pennsylvania

Principal: Janos L. Tanyi, MD, PhD University of Pennsylvania

Project Manager: Regina M. Young, PhD University of Pennsylvania ryoung@upenn.edu

Advocate: James E. Prevor Phoenix Media Network

PURPOSE

The CAR T Therapy for Pancreatic Cancer Team (June, Berger, and Wherry) came together to identify mechanisms of resistance to CAR T cell therapy and discover strategies to enhance the potency of immunotherapies targeting pancreatic cancer. The goals were to open a phase 1 study to evaluate the safety and feasibility of treating metastatic PDAC patients with CART cells directed against mesothelin and conduct research to interrogate CAR T cells and tumor cells in patients.



SPECIFIC AIMS

Aim 1. Carry out clinical trials in cancer immunotherapy for metastatic pancreatic cancer and transcriptionally and epigenetically interrogate samples prior to and following therapy to compare CAR T cell signatures from responsive and resistant patients, with the objective of improving therapeutic response.

Aim 2. Define the epigenetic landscape and sensitivities of pancreatic cancer cells and therapeutic immune cells, with the goal of identifying baseline molecular differences in pancreatic patients that may impede optimal CAR T cell function.

KEY ACCOMPLISHMENTS

The Team has made significant progress on both aims. They opened a trial for patients with metastatic pancreatic cancer to test the safety and feasibility of mesothelin-directed (M5) CAR T cells (NCT03323944) and completed enrollment on cohort 1. Currently, they are enrolling to cohort 2, intraperitoneal infusion of CAR T cells and cohort 3, local infusion via a microcatheter placed into the hepatic artery. Biopsy samples are being examined by flow cytometry, scRNAseq and scATAC-seq for changes in the CAR T cells as they traffic to the tumor site.

CLINICAL TRIALS

Phase I Study of Human Chimeric Antigen Receptor Modified T Cells in Patients With Mesothelin- Expressing Cancers; NCT03054298; Recruiting

Phase I Study of Human Chimeric Antigen Receptor Modified T Cells (CAR T Cells) in Patients With Pancreatic Cancer; NCT03323944; Active, not recruiting





LAURA ZISKIN TRANSLATIONAL AWARD RESEARCH TEAM RT5934

Phosphatidylinositol 3-kinase δ Inhibition to Treat Patients With Relapsed or Refractory Follicular Lymphoma

Grant Term: March 2016 - May 2020

KEY PERSONNEL

Team Leader: Siddhartha Mukherjee, MD Columbia University



MUKHERJEE

Co-Investigator: Abdullah Ali, PhD Columbia University

Co-Investigator: Jafarov Toghrul, PhD Columbia University

Project Manager: Yan Ma Columbia University

PURPOSE

The Phosphatidylinositol 3-kinase δ Inhibition Team investigated PI3K inhibition in the treatment of relapsed or refractory lymphoma. They studied a novel PI3k inhibitor TGR-1202 (umbralisib) while analyzing mechanisms of resistance and response, along with the effects of PI3K inhibition on the tumor cells.

SPECIFIC AIMS

Aim 1. Assess markers of responsiveness versus resistance to PI3K δ inhibition in a population of patients with relapsed or refractory FL using genomic, epigenomic, and metabolomics profiling.

Aim 2. Use cell lines to determine how PI3K δ inhibition affects growth and survival of lymphoma cells and their sensitivity to other drugs active in lymphoma.

Aim 3. Develop mouse models of FL and use these models to study the response of lymphoma to duvelisib in vivo.

KEY ACCOMPLISHMENTS

The clinical trial was launched but due to personnel changes was terminated. Five subjects had been enrolled, and the required blood and tumor samples are being analyzed via genetic and RNA sequencing. Findings have direct clinical implications for the multiple p110 δ inhibitors that are in clinical trials and provide a way to increase treatment efficacy for patients with many types of tumors. Studies of the novel PI3K inhibitor, CUD-207, demonstrated that it is substantially more potent that currently available PI3K inhibitors such as idelalisib, duvelisib, and tenalisib in lymphoma cells.

CLINICAL TRIALS

Study of the Phosphoinositide-3-Kinase-Delta Inhibitor TGR-1202 in Patients With Relapsed or Refractory Follicular Lymphoma; NCT03178201; Terminated







SU2C-FARRAH FAWCETT FOUNDATION HPV RESEARCH TEAM RT5914

Therapeutic CD8 Vaccines Against Conserved E7 HPV Epitopes Identified by MS

Grant Term: July 2014 - February 2020, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Ellis L. Reinherz, MD Dana-Farber Cancer Institute

Co-Leader: Robert I. Haddad, MD Dana-Farber Cancer Institute





REINHERZ

HADDAD

Project Manager: Joanie Lindstrom Dana-Farber Cancer Institute

Project Manager: Farzana Masood, PhD Dana-Farber Cancer Institute

Advocate: Mary-Jo Murphy

PURPOSE

The Therapeutic CD8 Vaccines Against Conserved E7 HPV Epitopes Identified by MS Team focused on patients with HPV-driven cancers, including cervical, anal, and head and neck cancer, who relapse following initial therapy. The Team aimed to develop novel immunotherapy approaches that will address this important unmet clinical need.

SPECIFIC AIMS

Aim 1. Perform a phase IB/II trial of adjuvant E711-19 nanomer vaccine DPX-E7 in 40 HLA-A*0201- positive patients with HPV16+ squamous cancers of the cervix, anus, or oropharynx.

Aim 2. Define additional immunogenic HLAbound tumor antigens on HPV-driven cancers of the cervix, anus, and head and neck.

Aim 3. Investigate clonal heterogeneity and molecular functional avidity of TCRs elicited by vaccination to engender those supporting the most sensitive tumor antigen recognition/tumor cell killing as well as future adoptive cell therapy.

KEY ACCOMPLISHMENTS

The Team identified the E711-19 tumor antigen using miniscule amounts of tumor tissue via fine needle biopsy. The Team, in conjunction with the NCI, explored the possibility of treating patients who did not respond to the vaccine, with T cell receptor gene therapy targeting the same E711-19 epitope.

CLINICAL TRIALS

A Phase Ib/II Trial to Test the Safety and Efficacy of Vaccination With HPV16-E711-19 Nanomer for the Treatment of Incurable HPV16-Related Oropharyngeal, Cervical, and Anal Cancer in HLA-A*02- Positive Patients; NCT02865135; Active, not recruiting



SU2C-TRANSLATIONAL GENOMICS RESEARCH INSTITUTE GRANT RT1234

Next-Generation Sequencing of Small Cell Lung Cancer to identify Actionable Targets for Treatment

Grant Term: August 2014 - July 2016

KEY PERSONNEL

Team Leader: Jeffrey Trent, PhD Translational Genomics Research Institute (TGEN)



TRENT

Principal: Jessica Aldrich TGEN

Principal: Carly Benford, CRC TGEN

Principal: John Carpten, PhD TGEN

Principal: David Craig, PhD TGEN

Principal: Jeff Kiefer, PhD TGEN

Principal: Sara Nasser, PhD TGEN

Principal: Glen Weiss, MD Cancer Treatment Centers of America

Principal: Tim Whitsett, PhD TGEN

PURPOSE

This study sought to understand the molecular factors that lead to progression of advanced small cell lung cancer (SCLC) after at least one line of chemotherapy. The goals were to (1) align best practice clinical and research efforts across TGen and Cancer Treatment Centers of America in Arizona, (2) use novel methods including whole genome and transcriptome next-generation sequencing and bioinformatics analysis to identify individual patients' genomic characteristics, (3) match this information to individual actionable drug treatment plans, and (4) conduct joint Clinical and Molecular Tumor Boards.

SPECIFIC AIMS

Aim 1. Pilot Study.

Aim 2. Treatment Selection.

KEY ACCOMPLISHMENTS

The pilot clinical study completed accrual with 12 patients. All patients had at least two clinically actionable targets identified. The Team planned to continue developing this approach and potentially expand it to other cancer types.

CLINICAL TRIALS N/A





SU2C-DUTCH CANCER SOCIETY TRANSLATIONAL RESEARCH TEAM RT5905

Prospective Use of DNA-Guided Personalized Cancer Treatment

Grant Term: January 2013 - December 2017, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Emile E. Voest, MD, PhD Netherlands Cancer Institute

Co-Leader: René Bernards, PhD Netherlands Cancer Institute



VOEST

BERNARDS

Principal: Trey Ideker, PhD University of California, San Diego

Principal: Stefan Sleijfer, MD, PhD Erasmus MC Rotterdam

Principal: Laura J. van't Veer, PhD University of California, San Francisco

Project Manager: Alice Tondeur Netherlands Cancer Institute

PURPOSE

The aim of the Prospective Use of DNA-Guided Personalized Cancer Treatment Research Team was to refine treatment algorithms for cancer patients based on large-scale mutational analyses of tumor DNA.

SPECIFIC AIMS

Aim 1. Identify DNA-based biomarkers of response to neoadjuvant chemotherapy+/- neratinib in breast cancer through analyses of biopsies from the trial.

Aim 2. Generate genomic selection criteria for patients with KRAS wild-type colorectal tumors to improve the outcome of anti-EGFR antibody treatment using genomic analyses of metastases for a cancer mini-genome of genes.

Aim 3. Deliver systems biology tools to analyze alterations in our cancer mini-genome to refine patient selection criteria for individualized treatment.

Aim 4. Identify DNA- and RNA- based biomarkers of response to chemotherapy + atezolizumab in metastatic lobular breast cancer.

KEY ACCOMPLISHMENTS

The Team demonstrated the value of an integrative genomics approach, combining DNA, RNA, and proteomic analyses on a small series of tumor biopsies to identify pathways relevant for response to targeted cancer agents. The finding that DNA, RNA, or protein individually were unable to predict drug responses underscores the need for an integrative approach. The Team's work on the analyses of biopsies of patients treated with immune-oncology drugs helped deepen understanding of the factors that determine whether patients respond to these therapies. The work of the team contributed to the 2020 FDA approval of encorafenib and cetuximab combination for treatment of metastatic colorectal cancer with the BRAF V600E mutation.

CLINICAL TRIALS

I-SPY 2 Trial (Investigation of Serial Studies to Predict Your Therapeutic Response With Imaging and Molecular Analysis 2); NCT01042379; Recruiting

Development of a Platform for Next-Generation DNA Sequencing-Based Personalized Treatment for Cancer Patients: Protocol to Obtain Biopsies From Patients With Locally Advanced or Metastatic Cancer (CPCT-02 Biopsy Protocol); NCT01855477; Recruiting

Assessing Efficacy of Carboplatin and Atezolizumab in Metastatic Lobular Breast Cancer GELATO Trial; NCT03147040; Terminated

Phase Ib/II Multicenter, Open-Label, Dose-Escalation Study of LGX818 and Cetuximab or LGX818, BYL719, and Cetuximab in Patients With BRAF Mutant Metastatic Colorectal Cancer; NCT01719380; Completed





SU2C CONVERGENCE™

RESEARCH TEAMS

SU2C CONVERGENCE™ 3.1416 RESEARCH TEAM CV6204

Molecular and Biophysical Definition of Tumor- Host Interactions and Impact on Tumorigenesis and Therapeutic Response

Grant Term: January 2021 - December 2023

KEY PERSONNEL

Team Leader: Ileana Cristea, PhD Princeton University



CRISTEA

Team Member: Shawn Davidson, PhD Princeton University

Team Member: Scott Manalis, PhD Massachusetts Institute of Technology

Team Member: Benjamin Neel, MD, PhD New York University

Project Manager: Alice Lustig Stand Up To Cancer alustig@su2c.org

PURPOSE

The Molecular and Biophysical Definition of Tumor-Host Interactions and Impact on Tumorigenesis and Therapeutic Response Team is seeking to provide an understanding of the mechanisms regulating the tumor-host interaction interface and their effects on host immunity, tumorigenesis, and therapeutic response.

SPECIFIC AIMS Cristea Lab/Princeton University

Aim 1. Uncover molecular drivers of tumor-host interactions by developing methods for defining surface proteomes in 3D cell models in conjunction with secretome and intracellular proteome assays.

Aim 2. Define global protein complex dynamics underlying signaling and immune responses in organoids.

Aim 3. Determine how organelle contact sites link lipid metabolism and immune signaling in organoids.

Manalis Lab/Massachusetts Institute of Technology

Aim1. Develop chemostat for organoid culture.

Aim 2. Study mechanisms by which microbiota affect tumor responses to anti-PD-1 therapy.

Aim 3. Understand how microbial peptides alter biophysical properties of mammalian cells.

Aim 4. Use genotype-defined syngeneic organoid models to study tumor/TME interactions and therapy.

Aim 5. Determine if single-cell biophysical measurements can optimize strategies to enhance immunotherapy.



Davidson Lab/Princeton University

Aim 1. Define the metabolic tumor microenvironment by integrating spatial-omics in mouse and organoid models of cancer.

Aim 1A. Define the metabolic and immunologic microenvironment of high-grade serous tubo-ovarian cancer (HGSC).

Aim 1B. Determine the functional metabolic interaction of commensal gut microbiota, T cells, and lung cancer.

Aim 2. Conduct high-throughput metabolic characterization of organoids based on biophysical separation.

Aim 2A. Perform metabolic screening of organoids from primary dissociated tumors separated by biophysical methods

Aim 3. Develop methods for MALDI (3D imaging and improved spatial resolution) and nanoflow-LC-MS.

Aim 3A. Develop 3D MALDI for labeled metabolite distribution in tumors, organs, and organoids.

Aim 3B. Improve MALDI spatial resolution and metabolic pathway coverage.

Aim 3C. Investigate nanoflow metabolomics toward obtaining separation-based single-cell metabolism measurements.

Neel Lab/New York University

Aim 1. Use genotype-defined organoids to delineate cell autonomous/non-autonomous effects on HGSC evolution.

Aim 2. Further characterize tumor/TME interactions and optimize therapy for Ccne1OE and Nf-/- HGSC.

Aim 3. Develop more refined, TME-retaining human and mouse organoid models of HGSC.

KEY PROGRESS

Generated and characterized numerous genetically defined organoid models for poor prognosis high grade serous tubo-ovarian carcinoma (HGSC). Integrative proteomic and microscopy investigations of HGSC models in both two-dimensional monolayers and three-dimensional organoids uncovered HGSC signatures in elevated organelle-organelle membrane contacts (stable mitochondria-ER encapsulations), mitochondrial calcium, oxidative phosphorylation, and lipid biogenesis.

Engineered cancer organoids with distinct copy number abnormality signatures in human HGSC models and investigated tumor evolution upon serial passaging with next generation sequencing.

A proteomic and phosphoproteomic platform was established to analyze cancer organoids at single-organoid and near-single-cell levels. Between 4000 to 6000 proteins were quantified from 1.25 ng (~6 cells equivalent) to 20 nanograms of protein, respectively, complemented by quantification of > 9,000 phosphopeptides. These analyses provided orthogonal support that HGSC exhibits increased mitochondria-associated metabolic processes.

A labeling method was established to investigate cell-cell communication in the virus microenvironment by spatially discriminating and phenotyping cell populations within a local cellular niche upon virus infection. This facilitated the isolation of virus-infected cells, infection-adjacent neighboring ides a more physiologically relevant microenvironment, including oxygen gradient, flow, shear stress, and chemical composition, with assessments on cancer organoid cultures.

A cantilever-based microfluidic sensor (suspended microchannel resonator) was developed that uniquely measures distinct populations of unactivated T cells, providing a platform to further assess label-free biomarker(s) of dysfunctional T cells. A three-dimensional organ analysis of metabolic processes was generated and used to demonstrate the roles of different cell types and how anatomical differences in an organ dictate diverse metabolic pathways and substrate utilization. Cryosectioning protocols and methods to perform imaging mass spectrometry for metabolite detection have been optimized and applied to investigate tumor-immune modulation upon bacterial colonization.

CLINICAL TRIALS

FUNDERS



ThermoFisher

Modeling Cancer within the Human Microbiome

An international collaboration of scientists is working to understand how cancer convinces the body's organs and tissues to support tumor growth. Cancer's interaction with the micro-environments that exist within the human body is a special focus of the work.

Four teams will seek to learn more about the communication between the body and the tumor on a cellular level—and how the microbiome has both positive and negative implications for the effectiveness of cancer therapies. A fifth group will work to create a laboratory tool that can grow gut tumor organoids complete with the surrounding tissue and microbiome. This engineering feat will be a dramatic advance in scientists' ability to model human cancer so new treatments can be more quickly and effectively tested



TEAM 5 CHEMOSTAT GROUP

Build an accurate, stable model of tumors and their surroundings by growing and maintaining gut organoids using stem cells, lymphoid tissue, and the microbiome to provide scientists with a replicable tool that will supercharge the study of the microbiome's effects on tumor development.



that support the growth

cell cultures.

of exceptionally complex

CONVERGENCE 3.1416 MISSION

By better understanding how microbiomes affect the support the human body provides to tumors, these teams of scientists will help accelerate research and treatments across a wide range of cancers and provide tools to spur the next generation of cancer research.





SU2C CONVERGENCE™ 3.1416 RESEARCH TEAM CV6205

Integrating Gnotobiotic, Organoid, and Metabolomic Pipelines to Probe the Cancer-Microbiome Connection

Grant Term: January 2021 - December 2023

KEY PERSONNEL

Team Leader: Kenya Honda, MD, PhD Keio University, Japan



HONDA

Team Member: Hans Clevers, MD, PhD Hubrecht Institute, Netherlands

Team Member: Josh Rabinowitz, MD, PhD Princeton University

Team Member: Toshiro Sato, MD, PhD Keio University, Japan

Project Manager: Alice Lustig

Stand Up To Cancer alustig@su2c.org

PURPOSE

This Integrating Gnotobiotic, Organoid, and Metabolomic Pipelines to Probe the Cancer-Microbiome Connection Team is studying gastrointestinal malignancies using gnotobiotic assays, organoids, and metabolomics to identify the mechanisms by which bacteria interact with the host cells to cause tumor development or regression. **SPECIFIC AIMS Honda Lab/Keio University Aim 1.** Establish an in vivo model appropriate for screening of CRC-promoting bacteria.

Aim 2. Search for bacterial strains that promote CRC development.

Aim 3. Model bacteria-induced colon carcinogenesis using an in vitro organoid co-culture system.

Aim 4. Search for bacterial strains that can prevent CRC development.

Aim 5. Elucidate diet-microbiome-immune connection.

Clevers Lab/Hubrecht Institute

Aim 1. Build on top of our identification of the first bacterially induced mutational signature by screening further bacterial toxins, strains, and species of potentially genotoxic bacteria.

Aim 2. Focus on the impact of colorectal cancerassociated bacteria on cellular behavior beyond mutation accumulation. This will be performed both on individual cancer-associated species and on microbial communities derived from healthy donors and colorectal cancer patients.

Aim 3. Study the role in tumorigenesis of bacteria from the Clostridium genus associated with CRC tumorigenesis by metagenomics studies.

Aim 4. Obtain microbial communities derived from healthy donors and colorectal cancer patients, and expose healthy human colon and colorectal cancer organoids to microbial communities and the metabolites produced by these, to identify community-level effects on colorectal cancer cell behavior.

Rabinowitz Lab/Princeton University

Aim 1. Investigate diet-microbiome connection.

Aim 2. Study diet-microbiome-immune connection.

Aim 3. Explore diet-cancer therapy connection.

Sato Lab/Keio University

Aim 1. Study carcinogenic potential of gut microbes on colonic epithelium in vivo.

Aim 2. Develop new in vivo human CRC model.

Aim 3. Model bacteria-induced colon carcinogenesis using an in vitro organoid co-culture system.

Aim 4. Understand the molecular determinants of invasiveness and metastatic capacity during colon carcinogenesis.

KEY PROGRESS

Team members across the project are reporting progress. At the Hubrecht Institute, a strain of E. coli has been uncovered that has an additional 10-12 genes, E. coli pks, from a foreign source that synthesizes a mutagen that reacts with the DNA of the colon cells and causes mutations in the APC gene, the first gene to acquire mutations in the progression of colon cancer. This is a clear demonstration of the contribution of the microbiome to colon cancer formation. At Keio University, scientists determined the in vivo effect of E. coli pks using the gnotobiotic technique on somatic mutations in the mouse colonic epithelium. Scientists at Princeton University have varied the diet of mice undergoing chemotherapy to reduce or eliminate tumors that they carry and have demonstrated that dietary changes do have a large impact upon the efficiency of tumor reduction or elimination.

CLINICAL TRIALS

FUNDERS



Thermo Fisher



A larger version of this graphic is available in the appendix.


SU2C CONVERGENCE™ 3.1416 RESEARCH TEAM CV6206

Integrating Microbiome and Organoid Analyses of Patient Cohorts for Immuno- oncology Therapeutic Development

Grant Term: January 2021 - December 2023

KEY PERSONNEL Team Leader: Calvin Kuo, MD, PhD Stanford University



KUO

Team Member: Ami Bhatt, MD, PhD Stanford University

Team Member: Michael Fischbach, PhD Stanford University

Team Member: Jennifer Wargo, MD, MMSc The University of Texas MD Anderson Cancer Center

Project Manager: Alice Lustig Stand Up To Cancer alustig@su2c.org

PURPOSE

The Integrating Microbiome and Organoid Analyses of Patient Cohorts for Immuno-oncology Therapeutic Development Team is investigating the limitations of immunotherapy, including both intrinsic and acquired resistance. Their work is integrating microbiome and organoid analyses of immunotherapy patient cohorts to develop novel immunotherapeutic combinations.

SPECIFIC AIMS Kuo Lab/Stanford University

Aim 1. Investigate Air-Liquid Interface (ALI) tumor organoid-based anoxic culture for obligate anaerobes.

Aim 1A. Flow-based anaerobic/aerobic transwell platform for organoid culture.

Aim 1B. Organoid and anaerobic bacterial interaction and growth.

Aim 2. Integrate microbiota into ALI tumor organoids from neoadjuvant anti-PD-1 patient cohorts.

Aim 2A. Combination with candidate microbiota.

Aim 2B. Addition of microbiota-derived small molecules and peptides.

Aim 2C. Effects on anti-PD-1 responses.

Aim 3. Incorporate peripheral immune components with ALI tumor organoids.

Aim 3A. Human ALI tumor organoid co-culture with autologous lymph node organoids.

Aim 3B. Murine ALI tumor organoid co-culture with autologous lymph node organoids.

Bhatt Lab/Stanford University

Aim 1. Leverage culture-free approaches to strain tracking in human microbiome studies.

Aim 1A. Culture-free genome assembly from microbiomes.

Aim 1B. Measuring genomic plasticity.

Aim 1C. Dissecting the role of translated microbial genes in immunotherapy response.

Aim 2. Identify bioactive microbial small peptides that may modulate cancer biology and therapy efficacy.

Aim 2A. Decoding microbial communication.

Aim 2B. Microbial microproteins and their impact on cellular biophysics.

Aim 2C. Mining microbial microprotein communication signals to transform drug discovery.

Fishbach Lab/Stanford University

Aim 1. Study the role of bacterially derived molecules in dictating the fate of an elicited T cell.

Aim 2. Determine whether tumor-specific T cells can be induced by expressing host antigens in bacterial colonists.

Aim 3. Investigate whether we can study the contribution of each strain in a complex community to immune modulation.

Wargo Lab/MD Anderson Cancer Center

Aim 1. Determine characteristics of the gut microbiome associated with optimal response to immunotherapy in a prospective cohort of immunotherapy-treated patients.

Aim 2. Identify optimal strategies to enhance response to immunotherapy via gut microbiota modulation by deep profiling and integrated analysis of data from existing cohorts.

Aim 3. Optimize strategies to enhance immunotherapy response via gut microbiota/ functional interventions with testing in preclinical models.

KEY PROGRESS

The team has successfully created organoid cultures that contain cancer and immune cells, to which microbial components can be added. Based on work at Stanford University, a particular strain of streptococcus has been found to result in the immunization of CD4 cells that protect mice from further infection, whereas the identical bacteria in a wound immunizes CD4 inflammatorv cells and causes tissue destruction. Bacteria in different organ systems lead to diverse immune responses by triggering different CD4 T- cell types which give rise to diverse cytokines. A similar result has been observed with other bacterial strains in laboratories at Keio University and New York University. Different bacteria regulate different CD4 T-cell subtypes and cytokines. Which bacterial species impact CD-8 killing of cancer cells is under intensive study.

CLINICAL TRIALS

FUNDERS



Thermo Fisher S C I E N T I F I C



A larger version of this graphic is available in the appendix.



SU2C CONVERGENCE™ 3.1416 RESEARCH TEAM CV6207

Multi-omic Analysis of Immune System and Microbiota Influence on Temporal and Spatial Evolution of Tumor Microenvironments

Grant Term: January 2021 - December 2023

KEY PERSONNEL

Team Leader: Dan Littman, MD, PhD New York University Grossman School of Medicine



LITTMAN

Team Member: Karuna Ganesh, MD, PhD Memorial Sloan Kettering Cancer Center

Team Member: Tyler Jacks, PhD Massachusetts Institute of Technology

Team Member: Raul Rabadan, PhD Columbia University

Project Manager: Alice Lustig Stand Up To Cancer alustig@su2c.org

PURPOSE

The Multi-omic Analysis of Immune System and Microbiota Influence on Temporal and Spatial Evolution of Tumor Microenvironments Team is working to advance understanding of tumor-intrinsic and -extrinsic factors that contribute to the dynamic interactions between immune system cells and cells in the tumor microenvironment. The Team aims to identify tumor vulnerabilities and new molecular and cellular targets that can be validated in pre-clinical models and then applied to clinical practice.

SPECIFIC AIMS Littman Lab/New York University

Aim 1. Investigate mechanisms by which microbiota influence anti-tumor responses, in the presence and absence of exogenous anti-PD-1 therapy.

Aim 1A: Examination of how gut microbiota exert immune functions at distal sites, including scenarios where epitopes are shared between gut-colonizing flora and tumor neoantigens.

Aim 1B: Characterization of candidate microbiota/diet-derived metabolites and gut microenvironment-derived cytokines/signals in regulation of antitumor responses.

Aim 2. Study effects of microbiota on intra-tumoral T cells and their subsequent differentiation programs, in mice and organoids.

Aim 2A: Mechanisms of microbiota-induced Th1/Th17 cell differentiation, and their effects on anti- tumor immunity.

Aim 2B: Screening of bacterial peptide libraries for effects on the tumor microenvironment and T-cell differentiation in collaboration with Ami Bhatt.

Ganesh Lab/Memorial Sloan Kettering Cancer Center

Aim 1. Develop a prospective functional longitudinal biospecimen platform to dissect tumor, immune, and microbial determinants of metastasis.

Aim 2. Develop a novel fluidic platform for in vitro modeling of epithelial-immune-microbial interactions.

Aim 3. Define molecular determinants of regenerative plasticity and innate immune activation during infection and cancer.

Jacks Lab/Massachusetts Institute of Technology

Aim 1. Investigate the tumor-immune contexture in immunogenic and immune refractory pancreas and colon cancers by single-cell mRNA sequencing (sc-mRNAseq) and spatial analysis of gene expression, protein expression, and metabolites.

Aim 2. Conduct ex vivo and in vivo organoidbased functional studies.

Rabadan Lab/Columbia University

Aim 1. Quantify host expression and microbial abundances for bulk and single-cell data analysis.

Aim 2. Quantify allele-specific HLA class I expression.

Aim 3. Random matrix theory (RMT) for singlecell denoising.

Aim 4. Topological data analysis (TDA) for dissecting dynamical single-cell data.

Aim 5. Gaussian random fields (GRF) approach for studying cell-cell interactions with special protein and transcriptomic data.

KEY PROGRESS

The Team has compiled a large cohort of esophageal and colorectal cancer patients for which primary tumors, metastases, and stool samples are available for study and has performed detailed single cell analyses and identified a noncanonical transcriptional program that resembles a dedifferentiated state that is observed in the colon of normal fetus. They have established new mouse models to study anti-tumor T cell responses and the properties of distinct commensal microbes that elicit effective T cell-mediated control of tumor growth independently of anti-PD-1 therapy.

CLINICAL TRIALS

N/A

FUNDERS



Thermo Fisher



A larger version of this graphic is available in the appendix.



SU2C CONVERGENCE™ RESEARCH TEAM CV6126

Correlating Immunological Health to Cancer Susceptibility Grant Term: January 2018 - December 2021

KEY PERSONNEL

Team Leader: Mark M. Davis, PhD Stanford University



DAVIS

Team Member: David Furman, PhD Buck Institute

Team Member: Thomas Montine, MD, PhD Stanford University

Team Member: Kari Nadeau, MD, PhD Stanford University

Team Member: Stephen Quake, PhD Stanford University

Project Manager: Alice Lustig Stand Up To Cancer alustig@su2c.org

PURPOSE

The Correlating Immunological Health to Cancer Susceptibility Convergence Research Team used blood cells and other markers to intensively monitor the immune system over time in participants in three research cohorts: an aging cohort, a twin cohort, and a cohort with inherited immunodeficiency. The results will be used to determine signatures of poor immune health that might predispose an individual to cancer.

SPECIFIC AIMS

Aim 1. Correlates of cancer susceptibility in the Stanford-Ellison cohort.

Aim 2. Complementary cohorts.

Aim 3. Validation cohorts.

KEY ACCOMPLISHMENTS

The Team undertook a longitudinal analysis of elderly individuals (> 80 years old) from the Stanford-Ellison Cohort that identified an inflammatory signature present 1-2 years before cancer diagnosis. The cancers were primarily UV- mediated skin cancers, including melanoma, squamous cell carcinomas, and basal cell carcinomas. This suggests that some cancers could be identified years before diagnosis and treatment could be initiated at cancer's earliest stages. A consistent elevation of cytokine transcriptional activity was correlated with aging across 10 types of cancer, coinciding with cellular senescence signatures characterized by p53 activation.

CLINICAL TRIALS

N/A



SU2C CONVERGENCE™ RESEARCH TEAM CV6124

Single-Cell Functional Multi-omics to Characterize and Monitor CAR T Therapy Grant Term: January 2018 – November 2022

KEY PERSONNEL

Team Leader: Rong Fan, PhD Yale University



FAN

Team Member: Pablo Gonzalez Camara, PhD University of Pennsylvania Perelman School of Medicine

Team Member: Stephanie Halene, MD, PhD Yale University

Team Member: Carl H. June, MD University of Pennsylvania Perelman School of Medicine

Team Member: J. Joseph Melenhorst, PhD University of Pennsylvania Perelman School of Medicine

Project Manager: Alice Lustig Stand Up To Cancer alustig@su2c.org

PURPOSE

The Single-Cell Functional Multi-omics to Characterize and Monitor CAR T Therapy Team worked to identify biomarkers that will predict the efficacy and potential side effects of CAR T therapy in individual patients. The Team is developing computational models combining topological analysis – looking at multiple data sets across many fields – with machine learning to better understand the causes of therapeutic efficacy and toxicity.

SPECIFIC AIMS

Aim 1. Measure the full spectrum of cytokine functions in pre-infusion CAR T cells upon antigen-specific stimulation, correlating to objective response and adverse effect.

Aim 2. Measure circulating and/or tumor-infiltrating CAR T cells ex vivo to monitor patient outcome and investigate the mechanism of efficacy versus immune-toxicity.

Aim 3. Develop computational models combining topological analysis and machine learning to unveil the molecular characteristics that underlie therapeutic efficacy and toxicity of CAR T therapy, and identify candidate biomarkers.



KEY ACCOMPLISHMENTS

The team is exploring the molecular determinants of ultra-long-term remission in acute lymphoblastic leukemia (ALL) patients treated with CAR T anti CD-19 therapy. They present the first large-scale single-cell multi-omics study of 82 patients and totally they sequenced one million CAR T cells from all these patients and 6 healthy donors, representing the largest single-cell dataset from CAR T cells to date. Comprehensive analysis identified that elevated type-2 functionality in CAR T infusion products was significantly associated with patients maintaining a durable response of >8 years. Both in vitro and in vivo functional experiments were conducted to examine how type 2 cytokine-producing CAR T cells mediate population fitness and anti-tumor capability, providing valuable preclinical data that could be useful to inform innovative strategies to better engineer CAR T products. Their findings provide key insights into the mediators of CAR T longevity and have huge implications for the development of next-generation CAR T therapies to achieve long-term response and cure.

CLINICAL TRIALS

None





SU2C CONVERGENCE™ RESEARCH TEAM CV6123

Machine Learning for Cancer Immunotherapy Grant Term: January 2018 - November 2023

KEY PERSONNEL

Team Co-Leader: Ernest Fraenkel, PhD Massachusetts Institute of Technology

Team Co-Leader: Regina Barzilay, PhD Massachusetts Institute of Technology





FRAENKEL

BARZILAY

Project Manager: Alice Lustig Stand Up To Cancer alustig@su2c.org

PURPOSE

The Machine Learning for Cancer Immunotherapy Team is using artificial intelligence to predict molecular pathways and clinical outcomes for cancer patients. Data scientists are working to reconstruct signaling pathways and identify previously unrecognized regulatory mechanisms that contribute to the development of cancer. Their discoveries may provide new approaches for treatment with immunotherapy.

SPECIFIC AIMS

Aim 1. Conduct integrative modeling of immune health and tumor biology.

Aim 2. Identify pathways conferring resistance to natural killer cells.

Aim 3. Predict CD8+ and CD4+ T-Cell epitopes.

KEY PROGRESS

Collaborating to model NK cell killing pathways. Applied AI to cancer imaging for diagnostic improvements and to the analysis of chemical space and classes for the development of drugs. Work is underway to predict pathways distinguishing responders and non- responders to immunotherapy and to predict immune-tumor interactions.

Published insights into NK cell killing pathways. Developed interpretable representation learning algorithms that integrate multi-omics data to identify pathways and mutational patterns associated with response to immunotherapy.

CLINICAL TRIALS

N/A







SU2C-LUSTGARTEN FOUNDATION CONVERGENCE™ RESEARCH TEAM CV6122

Computational Deconstruction of Neoantigen- TCR Degeneracy for Cancer Immunotherapy

Grant Term: January 2018 - November 2022

KEY PERSONNEL

Team Co-Leader: Benjamin Greenbaum, PhD Memorial Sloan Kettering Cancer Center

Team Co-Leader: Vinod Balachandran, MD Memorial Sloan Kettering Cancer Center



GREENBAUM

BALACHANDRAN

Team Member: Marta Luksza, PhD Icahn School of Medicine at Mount Sinai

Team Member: Eileen M. O'Reilly, MD Memorial Sloan Kettering Cancer Center

Team Member: Jedd Wolchok, MD, PhD Memorial Sloan Kettering Cancer Center

Project Manager: Alice Lustig Stand Up To Cancer alustig@su2c.org

PURPOSE

The Computational Deconstruction of Neoantigen-TCR Degeneracy for Cancer Immunotherapy Team is investigating why a small group of pancreatic cancer patients survive for many years after diagnosis and developing tools to devise new cancer vaccines that will turn all pancreatic cancer patients into long-term survivors.

SPECIFIC AIMS

Aim 1. Identify the origin, clonality, phenotype, and longevity of neoantigen vaccine-induced T cells.

Aim 2. Isolate immunologic correlates of neoantigen vaccine response.

KEY ACCOMPLISHMENTS

Researchers carried out a clinical trial with 16 stage 2 and 3 pancreatic cancer patients who underwent surgery, FOLFIRINOX treatment, and immunization with RNA encoded vaccines that were matched to 20 different neo-antigens that arose in the genomes of the pancreatic cancer. In this trial, half of the patients responded to the vaccines, and have not seen their cancers return. This is the first demonstration of how to immunize pancreatic cancer patients with an mRNA vaccine. A follow up trial is now being planned.

CLINICAL TRIALS

Phase I Clinical Trial of Personalized Neoantigen Tumor Vaccines and Programmed Death-Ligand 1 (PD-L1) Blockade in Patients With Surgically Resected Pancreatic Cancer; NCT04161755; Recruiting





SU2C CONVERGENCE™ RESEARCH TEAM CV6125

Integrating Experimental and Computational Pipelines to Develop Biomarkers of Tumor Cell Resistance to NK Cells

Grant Term: January 2018 - November 2022

KEY PERSONNEL

Team Leader: Constantine S. Mitsiades, MD, PhD Dana-Farber Cancer Institute



MITSIADES

Team Member: Aedin Culhane, PhD Dana-Farber Cancer Institute

Team Member: Olga Dashevsky, PhD Dana-Farber Cancer Institute

Team Member: Todd Golub, MD Broad Institute of MIT and Harvard

Team Member: Ricardo de Matos Simoes, PhD Dana-Farber Cancer Institute

Team Member: Jennifer Roth, MSc, MBA Broad Institute of MIT and Harvard

Team Member: Michal Sheffer, PhD Dana-Farber Cancer Institute

Team Member: Aviad Tshemiak, MSc Broad Institute of MIT and Harvard

Project Manager: Alice Lustig Stand Up To Cancer alustig@su2c.org

PURPOSE

This SU2C team integrated experimental (e.g., CRISPR screens, and novel types of preclinical models in the lab and in living tissues) and computational pipelines to develop biomarkers of tumor cell resistance to NK cells in solid tumors and hematologic malignancies and validate the relevance of these biomarkers in patient-derived samples from diverse neoplasias.

SPECIFIC AIMS

Aim 1. Apply and develop next-level computational resources to optimize identification of biomarkers of tumor cell sensitivity versus resistance to NK cells.

Aim 2. Expand the spectrum of phenotypic data on NK cell responses.

Aim 3. Validate candidate markers in our in vitro and in vivo experimental platforms.

KEY ACCOMPLISHMENTS

Human NK cells are increasingly applied in various immunotherapies, including CAR-NK cells. This SU2C team employed CRISPR systems to identify which genes, when deleted or activated in tumor cells, prevent vs. enhance the antitumor activity of NK cells. They identified many previously underappreciated genes and pathways which regulate NK cell killing in solid tumors or hematologic malignancies; and applied singlecell technologies to understand how tumor cells adapt to NK cell attack. Work from this team was published in Nature Genetics (2021), Nature Cancer (2022 and 2023), and Biorxiv (2022).

CLINICAL TRIALS







SU2C CONVERGENCE™ RESEARCH TEAM CV6128

Responders and Non-Responders to Endometrial Cancers With Mismatch Repair Grant Term: January 2018 - December 2021

KEY PERSONNEL

Team Leader: Alessandro D. Santin, MD Yale University



SANTIN

Team Member: Ludmil Alexandrov, PhD University of California, San Diego

Team Member: Stephania Bellone, PhD Yale University

Team Member: Akiko Iwasaki, PhD Yale University

Project Manager: Alice Lustig Stand Up To Cancer alustig@su2c.org

PURPOSE

The Responders and Non-responders to Endometrial Cancers With Mismatch Repair Team is investigating why only half of all endometrial cancer patients with mismatch repair deficiencies (MMRd) respond to immunotherapy.

Researchers are utilizing patient biopsies from a clinical trial to try to predict response and side effects and potentially design better immunotherapies for endometrial cancer patients.

SPECIFIC AIMS

Aim 1. How can we predict responders from non-responders to checkpoint inhibitors?

Aim 2. Can we predict which patients will develop side effects to these therapies? How can we relate the peptide sequence of antigens to the nucleic acid sequence of T-cell receptor variable regions?

Aim 3. Can we predict peptide antigens from T-cell receptor sequences? Can we determine with some confidence the neoantigens that are expressed by tumors that are recognized by the immune system in an HLA-dependent fashion?

KEY ACCOMPLISHMENTS

The Team completed enrollment in the planned clinical trial (83% clinical benefit) and evaluated samples from 25 hypermutated, MSI-High endometrial cancer patients. Matched recurrent tumor samples from patients with secondary resistance identified multiple mutations in genes affecting antigen presentation. Analysis of T cells showed that the most-prominent clones were more skewed towards the effector CD8 population in the patients responding with CR/PR when compared to those with SD/PD. Patients with mutational (ie, Lynch/Lynch-like) MMRd tumors had higher

response rates and longer survival than those with epigenetic (ie, methylated) MMRd tumors. Mutation burden was higher in tumors with mutational MMRd compared with epigenetic MMRd; however, within each category of MMRd, mutation burden was not correlated with response to immunotherapy. Longitudinal single-cell RNA-seq of circulating immune cells revealed contrasting modes of antitumor immunity for mutational versus epigenetic MMRd cancers. Whereas effector CD8+T cells correlated with regression of mutational MMRd tumors, activated CD16+ NK cells were associated with ICB-responsive epigenetic MMRd tumors. These data highlight the interplay between tumor-intrinsic and tumor-extrinsic factors that influence response to immunotherapy.

CLINICAL TRIALS

Phase II Evaluation of Pembrolizumab, a Humanized Antibody Against PD-1, in the Treatment of Persistent or Recurrent Hypermutated/Ultramutated Endometrial Cancer Identified by Next-Generation Sequencing (NGS) and Comprehensive Genomic Profiling (CGP); NCT02899793; Active, not recruiting.







SU2C CONVERGENCE™ RESEARCH TEAM CV6127

Connecting Immune Health and Tumor Biology in Gynecologic Cancers

Grant Term: January 2018 - November 2022

KEY PERSONNEL

Team Leader: E. John Wherry, PhD University of Pennsylvania

Co-Leader: Claire Friedman, MD Memorial Sloan Kettering Cancer Center





WHERRY

FRIEDMAN

Team Member: Dmitriy Zamarin, MD, PhD Memorial Sloan Kettering Cancer Center

Team Member: Shelley Berger, PhD University of Pennsylvania

Team Member: Erica Carpenter, MBA, PhD University of Pennsylvania

Team Member: Travis Hollman, MD BMS

Project Manager: Alice Lustig Stand Up To Cancer alustig@su2c.org

PURPOSE

The Connecting Immune Health and Tumor Biology in Gynecologic Cancers Team studies immune defects in gynecologic cancer patients with highly mutated tumors to gain insights into immune responsiveness. The scientists are working to predict therapeutic outcomes and tailor treatment regimens for this subset of gynecologic cancers.

SPECIFIC AIMS

Aim 1. Test how tumor-intrinsic factors predispose to response or resistance to checkpoint blockade.

Aim 2. Test how baseline immune function and quality affects response to checkpoint blockade.

Aim 3. Define how on-treatment blood markers may reflect the tumor-immune interaction.

KEY ACCOMPLISHMENTS

The Team collected data from two clinical trials of PD-1 blockade in patients with gynecologic cancers (see below section). Tumor and blood samples were shared with the Wherry lab in order to test the hypothesis that the T-cell intrinsic response to proliferative and genotoxic stress might contribute to the disparity between immunologic and clinical response.

First, we conducted a phase II study of nivolumab in patients with dMMR gynecologic cancers using objective response rate (ORR) and progression-free survival at 24 weeks (PFS24) as endpoints (NCT03241745). We enrolled 35 patients, 34 of whom were evaluable. The ORR was 58.8% and PFS24 rate was 64.7%, meeting the

pre-specified endpoints. In the tumor microenvironment (TME), using multiplexed immunofluorescence, we found that presence of dysfunctional (CD8+PD-1+) or terminally dysfunctional (CD8+PD-1+TOX+) T cells and their interaction with PD-L1+ cells were independently associated with PFS24. On the genetic level, PFS24 was associated with presence of MEGF8 or SETD1B mutations but not with tumor mutational burden or type of dMMR (genetic or epigenetic). Our findings highlight several genetic and TME parameters associated with response to PD-1 blockade in dMMR cancers, generating rationale for their validation in larger cohorts.

In parallel, the Wherry lab developed a highdimensional single cell cytometric platform to simultaneously analyze T cell differentiation with changes in DNA damage and repair (DDR) pathways. In patients with mismatch repair-deficient (dMMR) or microsatellite instable (MSI) uterine cancer treated with nivolumab, we were able to distinguish responders versus non-responders based on the upregulation of phosphorylated-ATM (pATM) in CD8 T cells. This suggests that T cell-intrinsic DDR plays a role in regulating immune responsiveness and thus clinical outcome in patients treated with immunotherapy. These findings are outlines in a paper available on Biorxiv.

CLINICAL TRIALS

Pilot Study of Nivolumab in Combination With Front-Line Neoadjuvant Dose-Dense Paclitaxel and Carboplatin Chemotherapy and Postsurgical Dose-Dense Paclitaxel and Carboplatin Chemotherapy in Patients With High-Grade Serous Ovarian, Fallopian Tube, or Primary Peritoneal Cancer; NCT03245892; Active, not recruiting.

Phase II Trial of Single-Agent Nivolumab in Patients With Microsatellite Unstable/Mismatch Repair Deficient/Hypermutated Uterine Cancer; NCT03241745; Active, not recruiting.







SU2C-BREAST CANCER RESEARCH FOUNDATION CONVERGENCE™ RESEARCH TEAM CV6004

Ecology of the Tumor Microenvironment in Breast Cancer

Grant Term: June 2015 - December 2019

KEY PERSONNEL Team Leader: Peter P. Lee, MD City of Hope



LEE

Team Member: Gurinder S. "Mickey" Singh Atwal, PhD Cold Spring Harbor Laboratory

Team Member: Darrell J. Irvine, PhD Massachusetts Institute of Technology

Team Member: Herbert Levine, PhD Rice University

Team Member: Clare C. Yu, PhD University of California, Irvine

Project Manager: Alice Lustig Stand Up To Cancer alustig@su2c.org

PURPOSE

The goal of the Ecology of the Tumor Microenvironment in Breast Cancer Team was to study the different cell populations within/surrounding human breast tumors to understand their interactions in the tumor microenvironment (TME). The project included participation from experts in breast cancer, immunology, genomics, bioinformatics, mathematical modeling, ecology, and drug delivery to destabilize the TME as novel treatments.

SPECIFIC AIMS

Aim 1. Study the breast cancer TME via deconstruction into key components and 3-D reconstruction.

Aim 2. Study the intact breast cancer TME and TDLN via quantitative, spatial tissue analysis.

Aim 3. Investigate combination therapy targeting multiple components of the TE.

KEY ACCOMPLISHMENTS

The Team used high dimensional histology, image analysis, cell cultures from primary breast tumors, next generation and single cell genomics, bioinformatics, ecology modeling, and nanotechnology to study the ecology of the TME in breast cancer and to develop therapeutic and imaging applications.

CLINICAL TRIALS

Ivermecten and Balstilimab for the Treatment of Metastatic Triple Negative Breast Cancer; NCT05318469; Active, not recruiting

FUNDERS

Histol Myers Squibb







SU2C-NATIONAL SCIENCE FOUNDATION CONVERGENCE™ RESEARCH TEAM CV6006

Rational Design of Anticancer Drug Combinations with Dynamic Multi- Dimensional Input Grant Term: September 2015 - August 2019

KEY PERSONNEL

Team Leader: Anthony G. Letai, MD, PhD Dana- Farber Cancer Institute



LETAI

Team Member: Reka Z. Albert, PhD Pennsylvania State University

Team Member: Raul Rabadan, PhD Columbia University

Team Member: Maurizio Scaltriti, PhD Memorial Sloan Kettering Cancer Center

Team Member: Nikhil Wagle, MD Dana-Farber Cancer Institute/ Harvard Cancer Center

Project Manager: Alice Lustig Stand Up To Cancer alustig@su2c.org

PURPOSE

The Rational Design of Anticancer Drug Combinations with Dynamic Multi-Dimensional Input Team focused on understanding cancer mutations that can be key to developing therapeutic responses. Five biological and computation labs engaged collaboratively to identify how cancer cells distort protein-protein communications and how drug combinations can be used to restore proper function.

SPECIFIC AIMS

Aim 1. Construct dynamic models for signal transduction in PIK3CA-mutant, ER+ breast cancer cells. **Aim 2.** Perform systematic gain-of-function screens to refine and iterate the dynamic models.

Aim 3. Dissect the evolutionary trajectories of acquired cancer drug resistance.

KEY ACCOMPLISHMENTS

Researchers developed a test employing the tissue sections of cancers to measure the BCL-2 family of proteins that regulate the release of cytochrome from mitochondria channel VDAC. This helped to predict whether treatments of the tumor would result in apoptosis or not. A biotech company was initiated to validate and carry out the tests.

CLINICAL TRIALS

Phase I Trial of BYL719 Plus Letrozole or Exemestane for Patients With Hormone Receptor- Positive, Locally Advanced, Unresectable or Metastatic Breast Cancer; NCT01870505; Active, not recruiting

Phase II, Randomized, Double-Blind Study of Neoadjuvant Letrozole Plus GDC-0032 Versus Letrozole Plus Placebo in Postmenopausal Women With ER-Positive/HER2-Negative, Early-Stage Breast Cancer; NCT02273973; Completed

Phase I, Open-Label, Dose-Escalation Study Evaluating the Safety, Tolerability, and Pharmacokinetics of GDC-0077 as a Single Agent in Patients With Locally Advanced or Metastatic PIK3CA-Mutant Solid Tumors and in Combination With Endocrine and Targeted Therapies in Patients With Locally Advanced or Metastatic PIK3CA-Mutant Hormone Receptor-Positive Breast Cancer; NCT03006172; Recruiting

FUNDERS

🖑 Bristol Myers Squibb







SU2C-NATIONAL SCIENCE FOUNDATION CONVERGENCE™ RESEARCH TEAM CV6007

Genetic, Epigenetic, and Immunological Underpinnings of Cancer Evolution Through Treatment

Grant Term: September 2015 - December 2019

KEY PERSONNEL

Team Leader: Ross Levine, MD Memorial Sloan Kettering Cancer Center



LEVINE

Team Member: Steven J. Altschuler, PhD University of California, San Francisco

Team Member: Chang S. Chan, PhD Rutgers Cancer Institute of New Jersey

Team Member: Daniel S. Fisher, PhD Stanford University

Team Member: Aaron Hata, MD, PhD Massachusetts General Hospital

Team Member: Harlan Robins, PhD Fred Hutchinson Cancer Research Center

Team Member: Lecia VanDam Sequist, MD, MPH Massachusetts General Hospital

Project Manager: Alice Lustig Stand Up To Cancer alustig@su2c.org

PURPOSE

: The Genetic, Epigenetic, and Immunological Underpinnings of Cancer Evolution Through Treatment Team focused on Non-small cell lung cancer (NSCLC) and acute myeloid leukemia (AML) where, despite initial beneficial responses to treatment, resistance to further treatment is all too common. Mathematical modeling approaches were used to understand the evolution of drug resistance and to develop novel therapeutic strategies aimed at keeping the cancers from adapting to treatments.

SPECIFIC AIMS

Aim 1. Investigate genetic, epigenetic, and phenotypic diversity in response to cancer therapies.

Aim 2. Examine immune system dynamics in response to cancer therapies.

Aim 3. Conduct functional interrogation of drug response/resistance.

KEY ACCOMPLISHMENTS

Scientists have described clonal hematopoiesis and the increase in the myeloid compartment with aging in some individuals. Team members also described the evolution of mutations in clonal hematopoiesis, their fitness and selection. This described a path in the development of AML in older adults.

CLINICAL TRIALS

Phase II Study of EGF816 and Gefitinib in TKI-Naive EGFR-Mutant Non-small Cell Lung Cancer; NCT03292133; Recruiting

FUNDERS

Histol Myers Squibb





SU2C-NATIONAL SCIENCE FOUNDATION-LUSTGARTEN FOUNDATION CONVERGENCETM RESEARCH TEAM CV6005

Liberating T-Cell Mediated Immunity to Pancreatic Cancer

Grant Term: September 2015 - January 2020

KEY PERSONNEL

Team Co-Leader: Peter O'Dwyer, MD University of Pennsylvania

Team Co-Leader: Jeffrey Drebin, MD Memorial Sloan Kettering Cancer Center

Team Co-Leader: Jedd Wolchok, MD, PhD Memorial Sloan Kettering Cancer Center





O'DWYER

DREBIN



WOLCHOK

Team Member: Curtis G. Callan, PhD Princeton University

Team Member: Benjamin D. Greenbaum, PhD Icahn Medical School at Mount Sinai **Team Member:** Harlan Robins, PhD Fred Hutchinson Cancer Research Center

Team Member: David T. Ting, MD Massachusetts General Hospital/Harvard Medical School

Project Manager: Alice Lustig Stand Up To Cancer alustig@su2c.org

PURPOSE

This group of physicians, cancer immunologists, computational biologists, and biophysicists in the Liberating T-Cell Mediated Immunity to Pancreatic Cancer Team worked to better understand the immunologic microenvironment of pancreatic cancer, develop technologies to take advantage of cancer cell vulnerabilities, and form a multi-institutional consortium to accelerate implementation of new strategies that could change the course of this deadly disease.

SPECIFIC AIMS

Aim 1. Characterize neoadjuvant vitamin D effects on the T-cell repertoire and immunologic milieu in human pancreatic cancer.

Aim 1.1. Understand the interplay of TCR diversity and neoepitopes in PDAC.

Aim 1.2. Characterize pancreatic cancer transcriptional response to immunomodulatory signals.

Aim 2. Conduct exploratory study of neoadjuvant chemoimmunotherapy in pancreatic cancer.



Aim 2.1. Phase I trial of neoadjuvant gemcitabine/nab-paclitaxel/paricalcitol/nivolumab. (Work on this Aim is continuing as an SU2C subproject.)

Aim 2.2. Perform T-cell repertoire analysis and in vitro characterization of neoantigen reactivity.

KEY ACCOMPLISHMENTS

Convergence Team scientists have developed a CLIA certified test employing paraffin embedded tissue sections and in situ hybridization that distinguishes between pancreatic cancer cells that were either of epithelial or mesenchymal morphologies. This work has demonstrated that tumor cells undergo changes between these different epigenetic cell types and showed that many tumors have both cell types, and that FOL-FIRINOX preferentially kills one cell type and albumin- bound-paclitaxel treatment kills the other cell type. This test is now employed at several different cancer centers to provide prognostic information about these tumors.

CLINICAL TRIALS

Phase Ib Pharmacodynamic Study of Neoadjuvant Paricalcitol in Resectable Pancreatic Cancer; NCT03300921; Active, not recruiting

FUNDERS

Bristol Myers Squibb







I stand up for myself...

and all those fighting cancer.

SURVIVOR: KELLY

SU2C CATALYST®

RESEARCH TEAMS

Participants in the clinical trials supported by SU2C Catalyst have also been supported by the Lazarex Cancer Foundation (LCF) through their IMPACT Patient Reimbursement Program, which offers reimbursement to qualifying patients for certain out-of-pocket expenses associated with participation in the clinical trial.



SU2C CATALYST® RESEARCH GRANT PROGRAM WITH SUPPORT FROM ZENTALIS PHARMACEUTICALS CT6360

Therapeutically Targeting WEE1 in HPV+ Head and Neck Cancer Grant Term: TBD

KEY PERSONNEL

Team Leader: Bruce Clurman, MD, PhD Fred Hutchinson Cancer Center

Co-Leader: Devraj Basu, MD, PhD University of Pennsylvania





CLURMAN

BASU

Principal: Cristina Rodriguez, MD University of Washington

Project Manager: Stephanie Boegeman Fred Hutchinson Cancer Center sboegema@fredhutch.org

PURPOSE

HPV oncogenes render HNSCC cells highly sensitive to premature mitosis and death following WEE1 inhibition, and preliminary data using a murine model of HPV+ HNSCC shows that WEE1 inhibition also remodels the tumor microenvironment by enhancing lymphangiogenesis thereby promoting robust antitumor immunity. The SU2C Catalyst Research Team with Support from Zentalis Pharmaceuticals is working to test if blocking lymphangiogenesis can maximize the antitumor efficacy of ZN-c3, a WEE1 inhibitor. They are also assessing rational ZNc3-based immunotherapy combinations as potential therapeutic strategies and working to exploit the replication stress failure induced by WEE1 inhibition in HPV+ cells to optimize less toxic chemotherapy combination regimens using HPV+ HNSCC patient-derived xenografts.

SPECIFIC AIMS

Aim 1. Test WEE1i-induced lymphangiogenesis as a driver of antitumor immunity.

Aim 2. Test the efficacy of WEE1i-based immunotherapy combinations.

Aim 3. Test the efficacy of low-dose GEM chemotherapy combined with WEE1i.

KEY PROGRESS

To be assessed at first review.

CLINICAL TRIALS

N/A





SU2C CATALYST® RESEARCH TEAM WITH SUPPORT FROM JAZZ PHARMACEUTICALS CT6330

The LiFFT Study (Lurbinectedin in FET-Fusion Tumors)

Grant Term: July 2022 - June 2025

KEY PERSONNEL

Team Leader: Patrick Grohar, MD, PhD Children's Hospital of Philadelphia

Co-Leader: Robert Maki, MD, PhD Memorial Sloan Kettering Cancer Center





GROHAR

MAKI

Principal: Brian D. Compton, MD Dana-Farber Cancer Institute

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Senior Co-Investigator: Theodore W. Laetsch, MD The Children's Hospital of Philadelphia

Young Investigator: Jenna Gedminas, MD University of Iowa

Co-Investigator: John W. Glod, MD, PhD National Cancer Institute

Co-Investigator: Julia Glade-Bender, MD Memorial Sloan Kettering Cancer Center

Co-Investigator: Leo Mascarenhas, MD, MS Children's Hospital Los Angeles **Co-Investigator:** Rashmi Chugh, MD University of Michigan

Co-Investigator: Steven DuBois, MD, MS Dana Farber Cancer Institute

Advocate: Carol R. Basso 1 Million 4 Anna Foundation

Advocate: Laurie E. Karl Sean Karl Foundation

PURPOSE

The goal of the proposed study is to translate lurbinectedin to the clinic as an EWS-FLI1 targeted agent for patients with Ewing sarcoma. In addition, the Team seeks to determine if the compound is a targeted agent for any of the more than 18-tumors characterized by EWSR1 fusion proteins. If successful, this will lead to an exciting new agent for the treatment of Ewing sarcoma. In addition, it may yield an active compound for the 18 additional tumors characterized by EWSR1 translocation.

SPECIFIC AIMS

Aim 1. Determine the safety, tolerability, and pharmacokinetic profile of lurbinectedin in patients with FET-fusion tumors.

Aim 2. Determine if lurbinected in inhibits EWS-FLI1 and/or shows antitumor activity in Ewing's sarcoma.

KEY PROGRESS

To be assessed at first review.

CLINICAL TRIALS

Lurbinectedin in FET-Fusion Tumors (LIFFT); NCT05918640; Recruiting



SU2C CATALYST® RESEARCH TEAM WITH SUPPORT FROM JAZZ PHARMACEUTICALS CT6334

Identification of Combination Therapeutics Using JZP-815 for the Treatment of NSCLC Grant Term: July 2022 – June 2025

KEY PERSONNEL

Team Leader: Fred R. Hirsch, MD, PhD Icahn School of Medicine at Mount Sinai

Co-Leader: Kwok-Kin Wong, MD, PhD New York University, Grossman School of Medicine





HIRSCH

WONG

Project Manager: Benjamin Hopkins, PhD Weill Cornell Medicine beh2020@med.cornell.edu

Principal Investigator: Jiehui Deng, PhD New York University Grossman School of Medicine

Principal Investigator: Rajwanth Veluswamy, MD Icahn School of Medicine at Mount Sinai

PURPOSE

To identify more effective treatment options for patients with KRAS-mutant NSCLC, this research is using a functional genomics approach to identify therapeutic agents that cooperate with the pan-RAF inhibitor JZP-815 and to evaluate the therapeutic potential of these combinations in clinically relevant mouse models of KRAS-mutant NSCLC.

SPECIFIC AIMS

Aim 1. Take functional genomics approach to identify JZP-815-based combinations for the treatment of KRAS mutant NSCLC.

Aim 2. Evaluate therapeutic potential of JZP-815-based combination in GEMM models of KRAS mutant NSCLC.

KEY PROGRESS

Using an automated drug screening platform, the scientists have compared JZP-815 as a single agent against a panel of standard of care regimens. They have conducted combination screens with JZP-815 in a panel of genetically defined murine Kras mutant cell lines and are investigating the relationship between drug induced changes in gene expression and tumor specific drug sensitivities.

CLINICAL TRIALS

N/A





LUNG CANCER HEALTH EQUITY SU2C CATALYST® RESEARCH TEAM CT6332

Technology-Enabled Immunotherapy Monitoring in NYC Minority NSCLC Patients Grant Term: May 2022 – April 2025

KEY PERSONNEL

Team Leader: Vamsidhar Velcheti, MD New York University Grossman School of Medicine

Co-Leader: Rajwanth Veluswamy, MD Icahn School of Medicine at Mount Sinai



VELCHETI

VELUSWAMY

Principal: Balazs Halmos, MD, MS Albert Einstein College of Medicine

Principal: Brian Henick, MD Columbia University

Project Manager: Kristen Labbe, MPH New York University Grossman School of Medicine Kristen.Labbe@nyulangone.org

Advocate: Alexandra Awad, RN New York University Grossman School of Medicine

Advocate: Sulaiha Mastan

PURPOSE

The Team is deploying a mobile health intervention application, ApricityRxTM and technologyenabled supportive care services, for monitoring and management of immunotherapy toxicities in patients with lung cancer. The key objective of this study will be to evaluate the impact of a contextually tailored tech-enabled remote monitoring framework on the quality of oncologic care in underserved minority patients with lung cancer.

SPECIFIC AIMS

Aim 1. Evaluate the barriers to adoption and optimal utilization of technology-enabled remote monitoring and adverse event management of underserved minority patients with non-small cell lung cancer (NSCLC) on immunotherapy.

Aim 2. Determine the impact of patient-reported outcome measures collected using ApricityRx[™] and CARE service on the management of NSCLC patients receiving immunotherapy in a highly diverse New York City community.

Aim 3. Utilize technology-enabled monitoring to enhance the overall quality of care and translational research in underserved minority patients with NSCLC.

KEY PROGRESS

The study has received IRB approval across all sites. Additionally, the trial is activated and open to enrollment at Columbia, and soon will be activated and open to enrollment at NYU, Mount Sinai, and Montefiore. While anticipating study activation at the remaining sites, the team has focused on updating educational informational materials for patients and research teams, established an immune related adverse even (irAE) management consortium, and expanded community outreach and awareness through established community partnerships.

CLINICAL TRIALS

A Phase IV Study of Apricity C.A.R.E. Program for Cancer Adverse Events Rapid Evaluation to Improve Treatment Outcomes of Ethnic/Racial Minority Non-small Cell Lung Cancer (NSCLC) Patients Receiving Immunotherapy; NCT05812274; Not yet recruiting

FUNDER

Histol Myers Squibb"

SU2C CATALYST® RESEARCH TEAM GRANT PROGRAM WITH SUPPORT FROM MIRATI THERAPEUTICS CT6331

Targeting Adaptive and Acquired Resistance to Direct KRAS Inhibition

Grant Term: February 2022 - January 2025

KEY PERSONNEL

Team Leader: Ryan B. Corcoran, MD, PhD Massachusetts General Hospital

Co-Leader: Scott Kopetz, MD, PhD

The University of Texas MD Anderson Cancer Center





CORCORAN

KOPETZ

Principal: Rebecca Heist, MD Massachusetts General Hospital

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Principal: Pasi A. Jänne, MD, PhD Harvard Medical School and Dana-Farber Cancer Institute

Project Manager: Stephanie McQueen Massachusetts General Hospital smcqueen1@partners.org

Advocate: Bonnie Addario GO2 Foundation for Lung Cancer

Advocate: Anjee Davis Fight CRC

Advocate: Manju George Colontown

PURPOSE

This team is working to better understand and overcome challenges that limit effectiveness of KRAS inhibitors. The team will aim to understand why some patients do not respond to KRAS inhibitors, develop strategies to increase the number of patients who benefit from therapy, and study tumor biopsies and circulating tumor DNA to determine why some patients only respond to therapy for a short period before developing resistance. The team is also proposing a clinical trial combining a KRASG12C inhibitor with an anti-EGFR and anti-PD1 antibody in KRASG12C colorectal cancer. Finally, the team will perform single cell sequencing of patient tumor biopsies and use novel mouse models with intact immune systems to understand how direct KRAS inhibition may potentiate the tumor immune response.

SPECIFIC AIMS

Aim 1. Elucidate mechanisms of adaptive resistance to direct KRAS inhibition and understand the drug-tolerant persister state.

Aim 2. Identify mechanisms of acquired resistance to KRASG12C inhibition and perform clinical trials to overcome resistance.

Aim 3. Define interactions between direct KRAS inhibition and the tumor immune response and perform preclinical prioritization of novel therapeutic strategies.

KEY PROGRESS To be assessed at first review.

CLINICAL TRIALS





SU2C CATALYST® RESEARCH TEAM WITH SUPPORT FROM GENENTECH CT6181

Atezolizumab, Androgen Receptor (AR) targeted therapy, and SBRT in Hormone Sensitive Prostate Cancer

Grant Term: September 2019 - August 2024, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Sean M. McBride, MD Memorial Sloan Kettering Cancer Center

Clinical Lead: Dana E. Rathkopf, MD Memorial Sloan Kettering Cancer Center





MCBRIDE

RATHKOPF

Principal: Matthew Dallos, MD Memorial Sloan Kettering Cancer Center

Principal: Anuradha Gopalan, MD Memorial Sloan Kettering Cancer Center

Principal: Mark Stein, MD Columbia University Medical Center

Project Manager: Kevin DeRudder Memorial Sloan Kettering Cancer Center deruddek@mskcc.org

Advocate: Jan Manarite Prostate Cancer International

Advocate: Joel Nowark Cancer ABCs

PURPOSE

The Hormone Sensitive Prostate Cancer Team is conducting a single-arm phase II study of androgen receptor targeted therapy in combination with atezolizumab and SBRT in men with newly diagnosed metastatic hormone-sensitive prostate cancer (mHSPC). The goal is to capitalize upon potential synergy between SBRT and anti-PD-L1 immunotherapy to improve outcomes for mHSPC patients who will otherwise succumb to their disease.

SPECIFIC AIMS

Aim 1. Determine if the addition of SBRT and atezolizumab to abiraterone or enzalutamide + leuprolide improves failure-free survival (FFS) at two years relative to the FFS in the STAMPEDE trial.

Aim 2. Evaluate potential immunologic biomarkers of response.

Aim 3. Evaluate whether noninvasive bloodbased and imaging-based biomarkers can be used to monitor and/or predict treatment response.

KEY PROGRESS

Despite an administrative hold soon after opening to enrollment due to a safety concern, 28 of the target 44 patients were enrolled in this study. Twenty of those patients were enrolled to fill Cohort 1 and the additional eight were subjects on hormone therapy at the time of registration and enrolled to Cohort 2. The trial was ultimately closed to enrollment in July 2023 due to a safety event. At the time of the safety event, active patients were reconsented to the trial and elected to continue on treatment.

Significant progress has been made toward correlative objectives. To date, all subjects have had IMPACT (next-gen tissue sequencing) run on baseline tissue samples as well as genome sequencing on the baseline ctDNA samples using the MSK ACCESS platform. Cytokine analyses were also completed on baseline, Cycle 4 (pre-RT), and Cycle 6 (post-RT) plasma smples using the Immune core lab at MSK. Over the course of the next year, the study team plans to review clinical data as well as expand on correlative analyses.

CLINICAL TRIALS

SAABR: Single-Arm Phase II Study of Androgen Receptor (AR) Targeted Therapy + Atezolizumab + GnRH Analog and Stereotactic Body Radiotherapy (SBRT) to the Prostate in Men With Newly Diagnosed Hormone-Sensitive Metastatic Prostate Cancer; NCT04262154; Active, not recruiting

FUNDER



A Member of the Roche Group



SU2C CATALYST® RESEARCH TEAM WITH SUPPORT FROM GENENTECH CT6174

Combination Sacituzumab Govitecan and Atezolizumab to Prevent Recurrence in Triple Negative Breast Cancer (TNBC)

Grant Term: July 2019 - December 2022, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Elizabeth A. Mittendorf, MD, PhD Dana-Farber Cancer Institute

Clinical Lead: Angela M. DeMichele, MD University of Pennsylvania



MITTENDORF



DEMICHELE

Principal: Vandana Abramson, MD Vanderbilt University Medical Center

Principal: Heather L. McArthur, MD Cedars-Sinai Medical Center

Principal: Rita Nanda, MD University of Chicago

Principal: Ben Ho Park, MD, PhD Vanderbilt University Medical Center

Principal: Hope S. Rugo, MD University of California, San Francisco

Principal: Sara M. Tolaney, MD Dana-Farber Cancer Institute

Project Manager: Michelle DeMeo Dana-Farber Cancer Institute Michelle_DeMeo@dfci.harvard.edu **Advocate:** Caroline Abi-Khattar, JD University of Pennsylvania

Advocate: Elizabeth S. Frank Dana-Farber Cancer Institute

PURPOSE

The Team seeks to eradicate micrometastatic disease in patients with triple-negative breast cancer (TNBC) who have minimal residual disease, by conducting a clinical trial testing the combination of sacituzumab govitecan and atezolizumab.

SPECIFIC AIMS

Aim 1. Conduct a single-arm, phase II trial of sacituzumab govitecan in combination with atezolizumab, enrolling TNBC patients with residual disease and cfDNA following NACT.

Aim 2. Perform correlative studies to determine whether PD-L1 expression on CTCs has utility as a pharmacodynamic biomarker, and whether there is an association between molecular and immunobiological features in residual disease after NACT and response to sacituzumab govitecan plus atezolizumab

KEY PROGRESS

The Team has screened 18 patients and has enrolled one.

CLINICAL TRIALS

Single-Arm Phase II Trial of Atezolizumab With Sacituzumab Govitecan to Prevent Recurrence in Triple-Negative Breast Cancer (ASPRIA); NCT04434040; Active, not recruiting

FUNDER

Genentech

PEDIATRIC SU2C CATALYST® RESEARCH TEAM WITH SUPPORT FROM BRISTOL MYERS SQUIBB CT6148

Clinical Translation of Novel Immune- Based Combination Therapies for Pediatric Hypermutant Cancers

Grant Term: June 2019- November 2023

KEY PERSONNEL Team Leader: Uri Tabori, MD The Hospital for Sick Children

Clinical Lead: Daniel Morgenstern, MB, BChir, PhD The Hospital for Sick Children





TABORI

MORGENSTERN

Principal: Crystal Mackall, MD Stanford University

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Advocate: Denise Bebenek Meagan's Hug

Advocate: Karen Haas The Hospital for Sick Children

Advocate: Jenell Holstead, PhD University of Wisconsin

Advocate: Parvathy Krishnan Krishnan Family Foundation

PURPOSE

This Team is exploring combinational immune based therapies for the treatment of childhood hypermutant cancers. Their research builds upon promising preliminary results from the use of single-agent PD-1 inhibition in children with recurrent cancers, as documented in the clinical trial NCT02992964 and recently published by Das et al. (Das et al. Clinical Cancer Research, 2023). The study's findings unveiled a two-year overall survival rate of 50%, a remarkable achievement especially for aggressive cancer types such as recurrent glioma, where such outcomes were previously considered unattainable. Now, the team is striving to identify new therapies that can be given in combination with PD-1 inhibition, to help treat those patients who do not respond or progress on PD-1 inhibition. Using patient derived cells and immunocompetent animal models, the team is screening promising new drug candidates for testing in combination with immunotherapy on preclinical mouse models. Results from these studies will directly feed into the development of a new clinical trial.

SPECIFIC AIMS

Aim 1. Perform a phase lb clinical trial of combinational immune checkpoint inhibitor (ICI) therapies in childhood hypermutant cancers.

Aim 2. Determine the biological aspects and preclinical benefits of combined BMS lead compounds with ICI on replication repair deficiency (RRD) hypermutant immunocompetent mouse models.

Aim 3. Define immediately translatable tumor intrinsic molecular vulnerabilities in replication repair deficient (RRD) hypermutant cancers.



KEY PROGRESS

High-throughput drug screening performed on childhood and adult hypermutant and non-hypermutant glioma cell lines identified 23 common targets and additional unique vulnerabilities (Aim 3). Testing candidates developed by Bristol Myers Squibb for clinical use revealed that the best combination is anti-PD1 and anti-LAG3. We have now completed pre-clinical experiments on our hypermutant RRD animal models which convincingly show that the combination of anti-PD1 and anti-LAG3 result in improved response over PD1 or LAG3 inhibition alone, not only in ultra-hypermutant tumors, but also in tumors with lower mutational burden which are resistant to PD1 blockade (Aim 2), Interestingly, through analyzing the immune content in the tumour microenvironment, we found that treatment with anti-PD1 increases expression of LAG3 (a negative regulator of T cell activation), which may explain the synergy seen in combination anti-PD1 and anti-LAG3 immunotherapy. Importantly, similar results of the combination therapy were observed for ENU-induced mouse gliomas, (which mimic treatment related hypermutation) which are not responsive to anti-PD1 therapy alone. Because of these exciting results, a new combination clinical trial is currently in development with SU2C and BMS, which feeds into Aim1 of this research funding.

CLINICAL TRIALS

3CI Study: Childhood Cancer Combination Immunotherapy. Phase Ib and Expansion Study of Nivolumab Combination Immunotherapy in Children, Adolescent, and Young Adult (CAYA) Patients With Relapsed/Refractory Hypermutant Cancers; NCT04500548; Closed

FUNDER

\mu Bristol Myers Squibb"

PEDIATRIC SU2C CATALYST® RESEARCH TEAM WITH SUPPORT FROM BRISTOL MYERS SQUIBB CT6147

Immunomodulation to Treat Poor-Prognosis Pediatric Brain Tumors

Grant Term: February 2019 - August 2021

KEY PERSONNEL

Team Leader: Maryam Fouladi, MD Nationwide Children's Hospital

Co-Leader: James Olson, MD, PhD Fred Hutchinson Cancer Research Center





FOULADI

OLSON

Principal: Rachid Drissi, PhD Nationwide Children's Hospital

Principal: Annie Huang, MD, PhD The Hospital for Sick Children

Principal: Nada Jabado, MD, PhD McGill University Health Centre

Project Manager: Sara Lawellin Cincinnati Children's Hospital Medical Center Sara.Lawellin@cchmc.org

Advocate: Keith Desserich Cure Starts Now

PURPOSE

The objectives of the Immunomodulation to Treat Poor-Prognosis Pediatric Brain Tumors Team are to: determine the extent to which 5-aza, ribociclib, or other non-cytotoxic FDA approved drugs enhance T-cell mediated PBT cell death; assess the efficacy of 5-aza, ribociclib in combination with nivolumab, and establish a biomarker-based responder hypothesis.

SPECIFIC AIMS

Aim 1. Determine the extent to which 5-aza, ribo, or other non-cytotoxic FDA-approved drugs enhance T-cell mediated PBT cell death in vitro.

Aim 1B. Assess the efficacy of 5-aza, ribo, or a superior candidate in vivo.

Aim 2. Establish a biomarker-based responder hypothesis.

KEY ACCOMPLISHMENTS

Through this collaborative study, the team generated and/or evaluated several important syngeneic mouse models across a spectrum of rare pediatric brain tumors. Additionally, the team has overcome poor tumor penetrance and difficulties using luciferase markers in vivo. Drug efficacy studies have demonstrated improved survival with decitabine and 4H2 in a subset of models - specifically IUE-DIPG-24-C5 and ATRT SU2C_54_i_5. Quantitative IHC and CyTOF analyses is underway to profile immune cell infiltration in tumor models.

CLINICAL TRIALS

N/A

FUNDER

left Bristol Myers Squibb"



PEDIATRIC SU2C CATALYST® RESEARCH TEAM WITH SUPPORT FROM BRISTOL MYERS SQUIBB CT6143

Targeting Epigenetic Dysregulation in Pediatric Cancer

Grant Term: January 2019 - June 2024

KEY PERSONNEL

Team Leader: Kimberly Stegmaier, MD Dana-Farber Cancer Institute

Co-Leader and Clinical Lead: Steven DuBois, MD Dana-Farber Cancer Institute





STEGMAIER

DUBOIS

Principal: Peter Dirks, MD, PhD The Hospital for Sick Children

Principal: David Kirsch, MD, PhD Princess Margaret Cancer Centre

Principal: Elizabeth Lawlor, MD, PhD Seattle Children's Research Institute

Project Manager: Jennifer Perry, PhD Dana-Farber Cancer Institute Jennifer_perry@dfci.harvard.edu

Advocate: Kathleen Malcolmson

PURPOSE

The Targeting Epigenetic Dysregulation in Pediatric Cancer Team was assembled to understand the potential role of BET bromodomain inhibition in pediatric cancer and to identify new targeted agents for a variety of pediatric cancers. If successful, these studies should have a major impact on cancer treatment and outcomes for patients, improving both survival and long-term outcomes.

SPECIFIC AIMS

Aim 1. Conduct a phase I clinical trial testing the BMS BETi BMS-986158 in children with cancer.

Aim 2. Test rational drug combinations with BMS-986158 in preclinical models of pediatric cancer.

Aim 3. Identify novel drug combinations with BMS-986158 through genome-scale CRISPR-Cas9 synergy screens.

KEY PROGRESS

The first-in-child clinical trial of the BET bromodomain inhibitor BMS-986158 is completing an expansion cohort at six sites in the United States and Canada. The trial is now also evaluating a new CNS-penetrant BET inhibitor known as CC-90010 specifically for children with brain tumors or brain metastasis. The Team is also assessing the efficacy of combinations with BET inhibition on pediatric cancer cell line and mouse models of soft tissue sarcoma, Ewing sarcoma, neuroblastoma, and medulloblastoma. Among the successes to date, researchers have demonstrated in vitro synergy with FAK inhibitors in Ewing sarcoma, CBP/P300 inhibitors in neuroblastoma, and HDAC inhibition in soft tissue sarcoma, Ewing sarcoma, and neuroblastoma.

CLINICAL TRIALS

Study of the Bromodomain (BRD) and Extra-Terminal Domain (BET) Inhibitors BMS-986158 and BMS-986378 in Pediatric Cancer; NCT03936465; Recruiting

FUNDER

Histol Myers Squibb

SU2C CATALYST® RESEARCH TEAM WITH SUPPORT FROM GENENTECH CT6054

Neoadjuvant Therapy for Patients With High-Risk Stage III Melanoma

Grant Term: June 2018 - November 2024, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Matthew S. Block, MD, PhD Mayo Clinic

Clinical Lead: Tina J. Hieken, MD Mayo Clinic





BLOCK

HIEKEN

Principal: Jun Chen, PhD Mayo Clinic

Principal: Evidio Domingo-Musibay, MD University of Minnesota

Principal: Roxana S. Dronca, MD Mayo Clinic

Principal: Thomas J. Flotte, MD Mayo Clinic

Principal: Rachel L. Maus, PhD Mayo Clinic

Principal: Vera J. Suman, PhD Mayo Clinic **Project Manager:** Jill Schimke Mayo Clinic schimke.jill@mayo.edu

Advocate: Alisha Birgin

Advocate: Skylar Starling Mayo Clinic

Advocate: Emalie Marion University of Minnesota

PURPOSE

The purpose of the Neoadjuvant Therapy for Patients With High-Risk Stage III Melanoma Team's clinical trial is to study how well drug therapies given prior to surgery work in treating participants with high-risk stage III melanoma. In the first two treatment arms of the study, patients received either the combination of cobimetinib and atezolizumab or the combination of vemurafenib, cobimetinib, and atezolizumab; followed by surgery; followed by atezolizumab treatment. The team has added a third treatment arm to test the combination of atezolizumab and tiragolumab.



SPECIFIC AIMS

Aim 1. Test the safety and efficacy of the neoadjuvant combination of vemurafenib/cobimetinib/ atezolizumab followed by surgery followed by adjuvant atezolizumab in patients with BRAFm high-risk stage III melanoma.

Aim 2. Test the safety and efficacy of neoadjuvant combination of cobimetinib/atezolizumab followed by surgery followed by adjuvant atezolizumab in patients with BRAFwt high-risk stage III melanoma.

Aim 3. Test the safety and efficacy of the neoadjuvant combination of tiragolumab/atezolizumab followed by surgery and adjuvant atezolizumab in patients with high-risk stage III melanoma.

KEY PROGRESS

Accrual is complete for Arms A and B. A promising rate (54%) of pCR/ncCR has been observed, with 75% showing <50% tumor viability at operation post-neoadjuvant treatment. Accrual to Arm C approaches 60% of target accrual.

CLINICAL TRIALS

Neoadjuvant Therapy for Patients With High-Risk Stage III Melanoma: A Pilot Clinical Trial; NCT03554083, Recruiting



SU2C CATALYST® RESEARCH TEAM WITH SUPPORT FROM GENENTECH CT6053

Immunotherapy Combination Strategies in ER-Positive Metastatic Breast Cancer

Grant Term: May 2018 - December 2019, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Ingrid A. Mayer, MD Vanderbilt University

Co-Leader: Justin M. Balko, PharmD, PhD Vanderbilt University





MAYER

BALKO

Principal: Rita Nanda, MD University of Chicago

Principal: Hope S. Rugo, MD University of California, San Francisco

Principal: Melinda E. Sanders, MD Vanderbilt University

Principal: Yu Shyr, PhD Vanderbilt University

Project Manager: Catherine Weir Vanderbilt University

Advocate: Lynn Cargen

Advocate: Linda J. Horton

PURPOSE

The Team proposed new treatment combination strategies, within a clinical trial for ER+ BC, that sought to increase the presence of specific immune system cells (T-cells) around the tumor and increase the presence of immune proteins (MHC and PD-L1) in the surface of the cancer cell, which would allow T-cells to recognize the tumor as "foreign." This should therefore render immunotherapies much more effective against ER+ BC.

SPECIFIC AIMS

Aim 1. Perform preclinical assays to determine the functional effect of MDM2 inhibition on T cells.

Aim 2. Perform preclinical studies to model the molecular and therapeutic effects of MDM2 inhibition with anti-PD-L1 therapy in breast cancer.

Aim 3. Perform a multicenter, open-label, twoarm phase Ib/II clinical trial that will evaluate the antitumor effect of atezolizumab (ATEZ, an anti-PD-L1 mAb) in combination with cobimetinib (COBI, a MEK inhibitor) in patients with TP53mutated ER+ mBC (metastatic breast cancer), or idasanutlin (IDASA, an MDM2 antagonist) in patients with TP53-wt ER+ mBC.

Aim 4. Determine whether IDASA or COBI enhances T-cell infiltration and activation in ER+ breast tumors, and whether this effect is associated with patient-specific clinical response to ATEZ. In addition, molecular correlates both intra-tumoral and in the peripheral blood of patients will be tested as correlative analyses.


Aim 5. Perform active monitoring of T-cell populations in PBMCs from IDASA-treated patients. To ensure that treatment for two weeks with IDASA does not eliminate peripheral effector T-cell populations, we will perform CyTOF to identify expanded or eliminated T-cell populations in the peripheral blood in the phase I portion of the IDASA arm.

KEY ACCOMPLISHMENTS

Twelve patients were enrolled in the trial (5 in the atezolizumab + cobimetinib arm, and 7 in the atezolizumab + idasanutlin arm). Tumor biopsies and blood were collected before treatment initiation and 2 weeks after treatment initiation to perform molecular analysis for better understanding on why these combinations of drugs will be effective in ER+ BC. No unexpected side effects were seen with either combination. The trial was closed due to low accrual.

CLINICAL TRIALS

BRE 17107: Phase Ib/II Trial of Atezolizumab (an Anti-PD-L1 Monoclonal Antibody) With Cobimetinib (a MEK1/2 Inhibitor) or Idasanutlin (an MDM2 Antagonist) in Metastatic ER+ Breast Cancer; NCT03566485; Terminated

FUNDER



A Member of the Roche Group

SU2C CATALYST® RESEARCH TEAM WITH SUPPORT FROM GENENTECH CT6052

Overcoming Urothelial Cancer Atezolizumab Resistance by Epigenetic Therapy

Grant Term: November 2017 - April 2021, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Peter A. Jones, PhD, DSc (hon) Van Andel Institute

Co-Leader: Elizabeth R. Plimack, MD Fox Chase Cancer Center





JONES

PLIMACK

Principal: Stephen B. Baylin, MD Johns Hopkins University

Principal: Noah M. Hahn, MD Johns Hopkins University

Principal: Jean-Pierre J. Issa, MD Coriell Institute for Medical Research

Principal: David I. Quinn, MD USC Norris Comprehensive Cancer Center

Project Manager: Ryan Burgos Van Andel Institute Ryan.Burgos@vai.org

Project Manager: Revathi Penumatsa Van Andel Institute Revathi.Penumatsa@vai.org

Advocate: Rick Bangs

PURPOSE

Extensive preliminary data from the Team has shown that epigenetic modifiers can dramatically affect the immune microenvironment and promote an inflamed phenotype in tumors. A large number of urothelial cancer (UC) patients are or become resistant to immune checkpoint antibodies. The Team explored the therapeutic potential of combining the epigenetic agent called guadecitabine with anti-PDL1 antibody atezolizumab.

SPECIFIC AIMS

Aim 1. Dose selection: Identify a safe, biologically active dose of concurrent guadecitabine and atezolizumab for patients with advanced UC in the safety run-in portion of our phase II study.

Aim 2. Dose expansion: Determine the efficacy (ORR) of the combination in patients with advanced UC who progressed after immune checkpoint therapy in a single-arm phase II expansion cohort.

Aim 3. Correlative science: Use paired pre- and post-treatment biopsies and peripheral blood to explore genomes, genome-wide expression, pathway alterations, and epigenomes in tumor and immune cells.



KEY ACCOMPLISHMENTS

The Team identified a safe, biologically active dose for concurrent guadecitabine and atezolizumab for patients with advanced urothelial cancer. Although the trial was closed for futility, a small subset of patients experienced stable disease with prolonged survival of greater than 17 months. Correlative analysis involving tumor transcriptomics, whole exome sequencing, DNA methylome, immunohistochemistry, and flow cytometry revealed that patient survival associated with immune activation of circulating immune cells and pre-existing levels of CD8 T cells within the tumor. These results suggest that further studies to target the reprogramming of T cells with alternative methodologies may be of benefit in this disease setting.

CLINICAL TRIALS

GU-114: Overcoming Checkpoint Inhibitor Resistance With Epigenetic Therapy in Urothelial Cancer; NCT03179943; Completed

FUNDER

Genentech

A Member of the Roche Group

SU2C CATALYST® RESEARCH TEAM WITH SUPPORT FROM BRISTOL MYERS SQUIBB CT6048

Tumor Infiltrating Lymphocyte Adoptive T-Cell Therapy for Non-small Cell Lung Cancer (NSCLC)

Grant Term: June 2017 - May 2020, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Co-Leader: Eric B. Haura, MD H. Lee Moffitt Cancer Center & Research Institute

Team Co-Leader: Scott J. Antonia, MD, PhD Duke University

Clinical Lead: Benjamin C. Creelan, MD H. Lee Moffitt Cancer Center & Research Institute







ANTONIA



CREELAN Investigator: Frederic J. Kaye, MD University of Florida

Investigator: John M. Koomen, PhD H. Lee Moffitt Cancer Center& Research Institute

Project Manager: Carol Ulge H. Lee Moffitt Cancer Center & Research Institute Carol.Ulge@moffitt.org

Advocate: Rosalynne I. Miller

Advocate: Joan Tashbar

PURPOSE

The Tumor Infiltrating Lymphocyte Adoptive T-Cell Therapy Team's goals were to conduct a clinical trial combining (TIL) therapy with anti-PD1 therapy and to use advanced proteogenomic technologies to characterize the TILs obtained from patients who have clinical response. These efforts can contribute to the optimization of TIL therapy for lung cancer.

SPECIFIC AIMS

Aim 1. Conduct a trial of TIL ACT and a-PD-1 in advanced-stage NSCLC patients.

Aim 2. Characterize tumor and TIL features associated with response using proteogenomics.

KEY ACCOMPLISHMENTS

The Team's work demonstrated that: 1) TIL therapy was logistically feasible and safe in stage 4 lung cancer patients; 2) TIL could provide meaningful and durable responses in stage 4 lung cancer patients; 3) infused TILs therapy could target neoantigens in the tumors of patients with non-small cell lung cancer (NSCLC) and could persist over time; and 4) antigen loss may be a potential cause of acquired resistance.

CLINICAL TRIALS

A Phase I Clinical Trial Combining Nivolumab and Tumor Infiltrating Lymphocytes (TIL) for Patients With Advanced Non-small Cell Lung Cancer; NCT03215810; Completed

FUNDER

Histol Myers Squibb



SU2C CATALYST® RESEARCH TEAM WITH SUPPORT FROM BRISTOL MYERS SQUIBB CT6049

Immunotherapy to Prevent Progression in Multiple Myeloma

Grant Term: May 2017 - October 2021, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader and Clinical Lead: Irene M. Ghobrial, MD Dana-Farber Cancer Institute



GHOBRIAL

Principal: Viktor A. Adalsteinsson, PhD Broad Institute

Principal: Mark W. Bustoros, MD Weill Cornell Medical College

Principal: Marzia Capelletti, PhD Dana-Farber Cancer Institute

Principal: Jihye Park, PhD Dana-Farber Cancer Institute

Principal: Romanos Sklavenitis Pistofidis, MD Dana-Farber Cancer Institute

Principal: Yujia Shen, PhD Dana-Farber Cancer Institute

Principal: Oksana Zavidij, PhD Dana-Farber Cancer Institute **Project Manager:** Alexandra Savell Dana-Farber Cancer Institute asavell@partners.org

Advocate: Jenny Ahlstrom Myeloma Crowd

PURPOSE

This Team's research was based on the idea that treating a precursor state of multiple myeloma called smoldering multiple myeloma (SMM) with immunotherapy can activate the immune system and trigger a response to the tumor to delay or prevent progression to myeloma.

SPECIFIC AIMS

Aim 1. Define the immune-oncogenomic landscape of smoldering multiple myeloma (SMM) in response to immunotherapy.

Aim 2. Characterize somatic aberrations present in cell-free DNA (cfDNA) and circulating tumor cells (CTCs) as biomarkers of response/resistance in SMM enrolled in the trial.

Aim 3. Define markers of the permissive bone marrow microenvironment that characterize risks of progression in SMM patients enrolled in the trial.

KEY ACCOMPLISHMENTS

The Team completed accrual on their phase II trial. They have found that early treatment with elotuzumab, lenalidomide, and dexamathasone is safe and effective. and in patients. They showed that the similarity of a patient's immune cell composition to that of healthy donors may have prognostic relevance at diagnosis and after treatment. They also uncov¬ered similarities between immune alterations observed in the bone marrow and blood, sug¬gesting that bloodbased immune profiling may have diagnostic and prognostic utility

CLINICAL TRIALS

Phase II Trial of Combination of Elotuzumab, Lenalidomide, and Dexamethasone in High-Risk Smoldering Multiple Myeloma; NCT02279394; Completed

FUNDER

Histol Myers Squibb



SU2C CATALYST® RESEARCH TEAM WITH SUPPORT FROM MERCK CT6032

Pembrolizumab and Radiation Therapy to Improve Outcome in High-Risk Sarcoma

Grant Term: May 2017 - February 2024, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader and Clinical Lead (May 2017 -April 2023): David G. Kirsch, MD, PhD Duke University Medical School

Team Leader and Clinical Lead (May 2023 -February 2024): Kent J. Weinhold, PhD Duke University Medical School



KIRSCH

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Principal: Brian E. Brigman, MD Duke Cancer Institute

Principal: George D. Demetri, MD Dana-Farber Cancer Institute

Principal: Richard F. Riedel, MD Duke Cancer Institute

Principal: Matt van de Rijn, MD, PhD Stanford University

Principal: Andrew J. Wagner, MD, PhD Dana-Farber Cancer Institute

Principal: Kent J. Weinhold, PhD Duke University Medical Center

Principal: Steven Young Sarcoma Alliance for Research Through Collaboration

Early Career Investigator: Everett Moding, MD, PhD Stanford University

Early Career Investigator: Yvonne Mowery, MD, PhD Duke Cancer Institute

Project Manager: Erin Kozlowski Sarcoma Alliance for Research Through Collaboration ekozlowski@sarctrials.org

Project Manager: Lindsay Overman Sarcoma Alliance for Research Through Collaboration leoverman@sarctrials.org

Advocate: Corrie A. Painter, PhD Broad Institute

PURPOSE

The High-Risk Sarcoma Team is conducting a clinical trial to test the safety and efficacy of pembrolizumab combined with preoperative radio-therapy to reduce the development of metastatic disease in sarcoma patients.

SPECIFIC AIMS

Aim 1. Test the safety and efficacy of pembrolizumab combined with preoperative radiotherapy to reduce the development of metastatic disease in sarcoma patients.

Aim 2. Characterize immune response to radiotherapy with or without pembrolizumab and identify predictors of pembrolizumab response in patients with soft-tissue sarcoma.

KEY PROGRESS

The clinical trial is enrolling 126 patients at eleven US sites and five international sites (three in Australia, one in Milan, and one in Montreal). Using a method called CAPP-Seq, the Team has observed in an initial cohort of 45 patients, approximately 40% have detectable circulating tumor DNA three months after surgery. This data set is the first of its kind in a sarcoma study and may reveal opportunities for clinical follow-up and stratification/selection for adjuvant therapies.

CLINICAL TRIALS

SU2C-SARC032: Phase II Randomized Controlled Trial of Neoadjuvant Pembrolizumab With Radiotherapy and Adjuvant Pembrolizumab in Patients With High-Risk, Localized Soft-Tissue Sarcoma of the Extremity; NCT03092323; Recruiting

FUNDER





SU2C CATALYST® RESEARCH TEAM WITH SUPPORT FROM BRISTOL MYERS SQUIBB CT6050

Reversing Primary Anti-PD-1 Resistance with Ipilimumab and Nivolumab

Grant Term: May 2017 - October 2022, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Antoni Ribas, MD, PhD University of California, Los Angeles

Clinical Lead: Ari M. Vanderwalde, MD West Cancer Center and Research Institute



RIBAS

VANDERWALDE

Principal: Kenneth F. Grossmann, MD, PhD Huntsman Cancer Institute, University of Utah

Principal: Siwen Hu-Lieskovan, MD, PhD Huntsman Cancer Institute, University of Utah

Principal: Jeffrey A. Sosman, MD Northwestern University

Project Manager: Jia M. Chen, PhD University of California, Los Angeles JiaChen@mednet.ucla.edu

Advocate: Samantha Guild AIM at Melanoma Foundation

PURPOSE

The Team set out to test the hypothesis that adding ipilimumab to continued nivolumab will reverse primary resistance to anti-PD-1/L1 blockade therapy in patients with metastatic melanoma. They tested this hypothesis within a phase II trial at Southwest Oncology Group (SWOG), conducting multiple biopsy analyses to provide mechanistic understanding of the effects of ipilimumab added to nivolumab.

SPECIFIC AIMS

Aim 1. Conduct a phase II study of ipilimumab and nivolumab in patients with metastatic melanoma progressing on prior anti-PD-1 therapy.

Aim 2. Investigate cellular and genomic changes in biopsies when adding ipilimumab to continued PD-1 inhibition.

KEY ACCOMPLISHMENTS

The clinical trial met its accrual target of 94 patients (enrolled across 19 states). Progression Free Survival (PFS) was significantly improved with the combination treatment of nivolumab + ipilimumab compared to ipilimumab alone. Although the number of high-grade adverse events was higher with the nivolumab + ipilimumab combination, most high-grade events were in line with the known safety profile. Overall, the data supports the combination of nivolumab + ipilimumab as an appropriate nextline treatment for patients with advanced melanoma who do not response to anti-PD-1 alone.

CLINICAL TRIALS

Phase II Randomized Study of Nivolumab (NSC-748726) With Ipilimumab (NSC-732442) or Ipilimumab Alone in Advanced Melanoma Patients Refractory to an Anti-PD1 or Anti-PD-L1 Agent; NCT03033576; Active, not recruiting

FUNDER

Histol Myers Squibb

SU2C CATALYST® RESEARCH TEAM WITH SUPPORT FROM MERCK CT6031

Targeting VDR to Make Pancreatic Cancer Competent for Immunotherapy

Grant Term: May 2017 - June 2020, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader and Clinical Lead: Daniel D. Von Hoff, MD Translational Genomics Research Institute



VON HOFF

Principal: Angela T. Alistar, MD Atlantic Health System

Principal: Michael T. Barrett, PhD Mayo Clinic Arizona

Principal: Carlos H. Becerra, MD Baylor University Medical Center

Principal: Erkut H. Borazanci, MD Honor Health Research Institute

Principal: Vincent Chung, MD City of Hope

Principal: Michael R. Downes, PhD Salk Institute for Biological Studies

Principal: Ronald M. Evans, PhD Salk Institute for Biological Studies

Principal: Haiyong Han, PhD Translational Genomics Research Institute

Principal: Anup Kasi, MD University of Kansas Medical Center

Principal: Ronald L. Korn, MD, PhD Imaging Endpoints, LLC

Principal: Winnie Liang, PhD Translational Genomics Research Institute

Principal: Andrew M. Lowy, MD University of California, San Diego

Principal: Hitendra P. Patel, MBBS UCSD Moores Cancer Center

Principal: Paul S. Ritch, MD Medical College of Wisconsin

Project Manager: Jatan Clark Translational Genomics Research Institute jclark@tgen.org

Advocate: Roger E. Magowitz Seena Magowitz Foundation

Advocate: Howard E. Young General Wholesale Beer Company



PURPOSE

The overall goal of the Targeting the Vitamin D receptor (VDR) to Make Pancreatic Cancer Competent for Immunotherapy Team was to see if targeting VDR would unlock the potential of immunotherapies to keep patients in remission after their chemotherapy.

SPECIFIC AIMS

Aim 1. Determine the synergy between the VDR agonist paricalcitol and the PD-1 inhibitor pembrolizumab in effecting an antitumor immune response in clinical trials.

Aim 2. Define the impact of paricalcitol and pembrolizumab combination therapy on the mutational landscapes and transcriptional programs of pancreatic tumors.

Aim 3. Identify cellular and molecular VDR targets in the immune microenvironment that synergize with PD-1 blockade.

KEY ACCOMPLISHMENTS

By conducting a double-blind placebo-controlled clinical trial, the Team demonstrated that maintenance trials can be conducted in stage IV pancreatic cancer patients who have received induction chemotherapy. However, they did not observe an improvement in percentage of patients who were progression-free at 6 months, in patients who were treated with a combination of paricalcitol and pembrolizumab versus those who were treated with pembrolizumab alone.

CLINICAL TRIALS

SU2C Catalyst[®] Randomized Phase II Trial of the PD1 Inhibitor Pembrolizumab With or Without Vitamin D Receptor Agonist Paricalcitol in Patients With Stage IV Pancreatic Cancer Who Have Been Placed in Best Possible Response; NCT03331562; Completed

FUNDER



SU2C CATALYST® RESEARCH TEAM WITH SUPPORT FROM MERCK CT6030

Combined Epigenetic Therapy and Pembrolizumab for Advanced Non-small Cell Lung Cancer (NSCLC)

Grant Term: April 2017 - June 2022, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Stephen B. Baylin, MD Johns Hopkins University

Co-Leader: Kathryn C. Arbour, MD Memorial Sloan Kettering Cancer Center





BAYLIN

ARBOUR

Principal: Hossein Borghaei, DO Fox Chase Cancer Center

Principal: Peter A. Jones, PhD, DSc (hon) Van Andel Institute

Principal: Kristen A. Marrone, MD Johns Hopkins University

Principal: Jarushka Naidoo, MBBCh Johns Hopkins University

Principal: Charles M. Rudin, MD, PhD Memorial Sloan Kettering Cancer Center

Principal: Hui Shen, PhD Van Andel Institute **Principal:** E. John Wherry, PhD University of Pennsylvania

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Project Manager: Kerri Muenkel Calderone Memorial Sloan Kettering Cancer Center muenkelk@mskcc.org

Project Manager: Revathi Penumatsa Van Andel Institute Revathi.Penumatsa@vai.org

Advocate: Beth Flory Van Andel Institute

PURPOSE

The goal of the Combined Epigenetic Therapy and Pembrolizumab Team was to conduct a Phase1b clinical trial to examine the synergy that can be achieved in NSCLC patients by combining epigenetic (mocetinostat and guadecitabine) and immune (pembrolizumab) therapies.

SPECIFIC AIMS

Aim 1. Dose selection: Identify a safe, biologically active dose of concurrent combination pembrolizumab, guadecitabine, and mocetinostat for patients with advanced NSCLC in a Phase I study.



Aim 2. Dose expansion: Determine the efficacy of this triplet combination in patients with advanced NSCLC as part of a Phase Ib dose expansion, in the context of tumor PD-L1 expression.

Aim 3. Use paired pre-and post-treatment biopsies and serial peripheral blood to explore (in collaboration with Merck) the attraction of immune cells to the tumor microenvironment and genome-wide changes in expression, pathway alterations, and epigenome in tumor and host immune cells.

KEY ACCOMPLISHMENTS

The Team identified that patients can be safely treated with 200mg pembrolizumab, 70mg mocetinostat (with options of dose reduction to 45mg if patients did not tolerate), and 24mg/m2 guadecitabine. Out of 23 patients, two experienced partial responses and one experienced a complete response. The patient who experienced a complete response has now remained on trial without progression for 25+ months. Three patients with stable disease are currently in follow up 25+ months after treatment initiation. The Team is finalizing genome-wide data analysis, in collaboration with Merck, which includes methylation, flow cytometry, whole exome sequencing, spatial transcriptomics (Nanostring DSP), and RNA-sequencing. Their overall present goal is to finalize a molecular signature for the best outcome in patients, allowing for a personalized, precision medicine approach for these individuals.

CLINICAL TRIALS

Phase I/Ib Study of Combined Pembrolizumab Plus Guadecitabine and Mocetinostat for Patients With Advanced NSCLC (dose selection); NCT03220477; Active, not recruiting

FUNDER



SU2C CATALYST® RESEARCH TEAM WITH SUPPORT FROM BRISTOL MYERS SQUIBB CT6051

Combined Approaches by Immune Checkpoint Inhibition for Hypermutant Cancers

Grant Term: April 2017 - March 2020, administered by the American Association for Cancer Research

KEY PERSONNEL Team Leader: Uri Y. Tabori, MD The Hospital for Sick Children

Investigator: John M. Maris, MD Children's Hospital of Philadelphia





TABORI

MARIS

Principal: Eric Bouffet, MD The Hospital for Sick Children

Principal: Michael J. Fisher, MD Children's Hospital of Philadelphia

Project Manager: Melissa Edwards, PhD The Hospital for Sick Children melissa.edwards@sickkids.ca

Advocate: Denise Bebenek Meagan's HUG: Creating a Circle of Hope

PURPOSE

The Team tested their hypotheses that: a) childhood cancer patients with a hypermutant tumor phenotype can be identified, and b) tumors in these patients are highly sensitive to immune checkpoint inhibition with rationally selected combination therapy.

SPECIFIC AIMS

Aim 1. Determine the prevalence and type of hypermutant human cancers.

Aim 2. Test three types of combinational ICI therapies using hypermutant cancer mouse models.

Aim 3. Perform pilot case studies of ICI combinational therapies on recurrent hypermutant human cancers.

KEY ACCOMPLISHMENTS

The Team characterized the prevalence of hypermutation in 80,000 adult and pediatric cancers and identified characteristics that can help detect replication repair deficiency in normal cells and predict response to immunotherapy. These findings can improve the diagnosis and treatment of individuals with hypermutant cancers. The Team also developed the first animal models for replication repair deficiency and completed a registry study where they treated patients with 46 different tumor types with immunotherapy as single agents or in combination.

CLINICAL TRIALS

Pilot Study of Nivolumab in Pediatric Patients With Hypermutant Cancers; NCT02992964; Active, not recruiting

FUNDER

Histol Myers Squibb



SU2C CATALYST® RESEARCH TEAM WITH SUPPORT FROM MERCK CT5978

DNA Repair Therapies for Ovarian Cancer

Grant Term: July 2016 - December 2020, administered by the American Association for Cancer Research

KEY PERSONNEL

Team Leader: Alan D. D'Andrea, MD Dana-Farber Cancer Institute

Co-Leader: Elizabeth M. Swisher, MD University of Washington





D'ANDREA

SWISHER

Principal: Panagiotis (Panos) A. Konstantinopoulos, MD, PhD Dana-Farber Cancer Institute

Project Manager: Donald R. Watson Dana-Farber Cancer Institute donald_watson@dfci.harvard.edu

Advocate: Jamie Crase University of Washington

Advocate: Sue Friedman FORCE: Facing Our Risk of Cancer Empowered

Advocate: Kathleen Gavin Minnesota Ovarian Cancer Alliance

Advocate: Deborah Polinsky (deceased) FORCE: Facing Our Risk of Cancer Empowered

PURPOSE

The DNA Repair Therapies for Ovarian Cancer Team was assembled to conduct correlative studies related to the TOPACIO clinical trial with a combination of the PARP inhibitor, niraparib plus the anti-PD1 antibody, pembrolizumab, for ovarian cancer patients with recurrent disease.

SPECIFIC AIMS

Aim 1. Collect and distribute tumor samples and blood samples from TNBC (triple-negative breast cancer) and HGSOC (high-grade serous ovarian cancer) patients enrolled in this joint Tesaro/ Merck/ SU2C clinical trial.

Aim 2. Complete the indicated biomarker studies, from multiple industry-sponsored and academic laboratories, and analyze the collected data.

KEY ACCOMPLISHMENTS

Three important achievements by the team are: i) demonstration that a combination of PARP inhibitor plus anti-PD1 antibody can result in an improved overall response rate, compared to monotherapy with either agent, for patients with recurrent, heavily treated ovarian cancer, ii) identification of predictive biomarkers which identify the patients with an improved response, and iii) use of CyCIF to identify the tumor cell and immune cell architecture which is most likely, or least likely, to respond. The team continued working towards additional funding and secured a SPORE grant in ovarian cancer.

CLINICAL TRIALS

Phase I/II Clinical Study of Niraparib in Combination With Pembrolizumab (MK-3475) in Patients With Advanced or Metastatic Triple-Negative Breast Cancer and in Patients With Recurrent Ovarian Cancer; NCT02657889; Completed

FUNDER



SU2C INNOVATIVE RESEARCH GRANTS

CLASS OF 2017

The 2017 class is specifically focused on immuno-oncology, supported by a grant from Bristol Myers Squibb.

HARNESSING DIPEPTIDYL PEPTIDASE INHIBITION FOR CANCER IMMUNOTHERAPY Daniel A. Bachovchin, PhD,

Memorial Sloan Kettering Cancer Center

RESCUING T-CELL FUNCTION FOR IMMUNOTHERAPY OF PEDIATRIC MALIGNANCIES

David M. Barrett, MD, PhD, Children's Hospital of Philadelphia

TARGETING THE PRO-METASTATIC NICHE IN THE LIVER FOR CANCER IMMUNOTHERAPY

Gregory L. Beatty, MD, PhD, University of Pennsylvania

T-CELL IMMUNOTHERAPY FOR CORE BINDING FACTOR ACUTE MYELOID LEUKEMIA

Marie E. Bleakley, MD, PhD, Fred Hutchinson Cancer Research Center

IMAGING CAR T CELLS WITH A DUAL-FUNCTION PET REPORTER GENE

Michael D. Farwell, MD, University of Pennsylvania

IDENTIFYING AND TARGETING MECHANISMS OF RESISTANCE TO IMMUNOTHERAPY

Rizwan Haq, MD, PhD, Dana-Farber Cancer Institute

REWORKING NEGATIVE RECEPTOR SIGNALS FOR IMPROVED ANTI-GLIOMA T-CELL THERAPY

Meenakshi G. Hegde, MD, Baylor College of Medicine

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POTENTIATING NOVEL ENGINEERED CELLULAR THERAPIES FOR SOLID TUMORS

Marcela V. Maus, MD, PhD, Massachusetts General Hospital

DELINEATING THE ROLE OF THE MICROBIOME IN MODULATING TUMOR AND HOST IMMUNITY

Jennifer A. Wargo, MD, The University of Texas MD Anderson Cancer Center

REPROGRAMMING TUMOR IMMUNOGENICITY WITH STING-ACTIVATING NANOPARTICLES John T. Wilson, PhD, Vanderbilt University

CLASS OF 2016

TARGETING CELLULAR PLASTICITY IN INDIVIDUAL BASAL-TYPE BREAST CANCER CELLS John G. Albeck, PhD,

University of California, Davis

UNCOVERING HOW RAD51 PARALOG MUTATIONS CONTRIBUTE TO CANCER PREDISPOSITION

Kara A. Bernstein, PhD, University of Pittsburgh

PHOSPHOLIPID MESSENGERS AS DRIVERS OF DENDRITIC CELL DYSFUNCTION IN CANCER

Juan R. Cubillos-Ruiz, PhD, Weill Cornell Medicine

METABOLIC REPROGRAMMING USING ONCOLYTIC VIRUSES TO IMPROVE IMMUNOTHERAPY

Greg M. Delgoffe, PhD, University of Pittsburgh

"WEAK LINKS" IN CANCER PROTEOSTASIS NETWORKS AS NEW THERAPEUTIC TARGETS

Martin Kampmann, PhD, University of California, San Francisco



SU2C INNOVATIVE RESEARCH GRANTS

ALGORITHMICALLY DRIVEN QUANTITATIVE COMBINATION CANCER THERAPY ENGINEERING

Dan A. Landau, MD, PhD, Weill Cornell Medicine

DEUBIQUITINATING ENZYMES AS NOVEL ANTICANCER TARGETS

Li Ma, PhD, The University of Texas MD Anderson Cancer Center

IMAGING CELL-LEVEL HETEROGENEITY IN SOLID TUMORS FOR PERSONALIZED TREATMENT

Melissa C. Skala, PhD, Morgridge Institute for Research

DEFINING THE METABOLIC DEPENDENCIES OF TUMORS

Matthew Vander Heiden, MD, PhD, Massachusetts Institute of Technology

DEFINING THE MECHANISTIC CONNECTIONS BETWEEN INJURY, REGENERATION, AND CANCER

Hao Zhu, MD, The University of Texas Southwestern Medical Center

CLASS OF 2011

TARGETING MLL IN ACUTE MYELOID LEUKEMIA

Yali Dou, PhD, University of Michigan

TARGETING GENETIC AND METABOLIC NETWORKS IN T-ALL

Adolfo A. Ferrando, MD, PhD, Columbia University

TARGETING PROTEIN QUALITY CONTROL FOR CANCER THERAPY Estela Jacinto, PhD, Rutgers University

TARGETING PP2A AND THE GLUTAMINE-SENSING PATHWAY AS CANCER TREATMENT

Mei Kong, PhD, Beckman Research Institute, City of Hope

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CHIMERIC RNAS GENERATED BY TRANS-SPLICING AND THEIR IMPLICATIONS IN CANCER

Hui Li, PhD, University of Virginia

ALLAN H. (BUD) AND SUE SELIG STAND UP TO CANCER MELANOMA INNOVATIVE RESEARCH GRANT

EXOME SEQUENCING OF MELANOMAS WITH ACQUIRED RESISTANCE TO BRAF INHIBITORS

Roger S. Lo, MD, PhD, University of California, Los Angeles

IDENTIFICATION AND TARGETING OF NOVEL REARRANGEMENTS IN HIGH-RISK ALL

Charles G. Mullighan, MD, St. Jude Children's Research Hospital

A SYSTEMS APPROACH TO UNDERSTANDING TUMOR-SPECIFIC DRUG RESPONSE

Dana Pe'er, PhD, Columbia University

TARGETING SLEEPING CANCER CELLS

Sridhar Ramaswamy, MD, Massachusetts General Hospital

INHIBITING INNATE RESISTANCE TO CHEMOTHERAPY IN LUNG CANCER STEM CELL

Eric Alejandro Sweet-Cordero, MD, Stanford University

DEVELOPING NEW THERAPEUTIC STRATEGIES FOR SOFT-TISSUE SARCOMA

Amy J. Wagers, PhD, Joslin Diabetes Center

FRAMING THERAPEUTIC OPPORTUNITIES IN TUMOR- ACTIVATED GAMETOGENIC PROGRAMS

Angelique W. Whitehurst, PhD, UT Southwestern Simmons Comprehensive Cancer Center

SU2C INNOVATIVE RESEARCH GRANTS

COUPLED GENETIC AND FUNCTIONAL DISSECTION OF CHRONIC LYMPHOCYTIC LEUKEMIA

Catherine J. Wu, MD, Dana-Farber Cancer Institute

CLASS OF 2009

AN EMERGING TUMOR SUPPRESSOR PATHWAY IN HUMAN CANCER Fernando D. Camargo, PhD, Boston Children's Hospital

MODELING EWING TUMOR INITIATION IN HUMAN NEURAL CREST STEM CELLS

Elizabeth R. Lawlor, MD, PhD, University of Michigan

CANCER CELL-SPECIFIC, SELF-DELIVERING PRODRUGS

Matthew Levy, PhD, Albert Einstein College of Medicine of Yeshiva University

TARGETED INHIBITION OF BCL6 FOR LEUKEMIA STEM CELL ERADICATION

Markus Müschen, MD, PhD, Children's Hospital Los Angeles

IDENTIFYING SOLID TUMOR KINASE FUSIONS VIA EXON CAPTURE AND 454 SEQUENCING

William Pao, MD, PhD, Vanderbilt University

THERAPEUTICALLY TARGETING THE EPIGENOME IN AGGRESSIVE PEDIATRIC CANCERS

Charles M. Roberts, MD, PhD, Dana-Farber Cancer Institute

ENDOGENOUS SMALL MOLECULES THAT REGULATE SIGNALING PATHWAYS IN CANCER CELLS

Rajat Rohatgi, MD, PhD, Stanford University

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GENETIC APPROACHES FOR NEXT GENERATION OF BREAST CANCER TAILORED THERAPIES

Jose M. Silva, PhD, Columbia University

MODULATING TRANSCRIPTION FACTOR ABNORMALITIES IN PEDIATRIC CANCER Kimberly Stegmaier, MD, Dana-Farber Cancer Institute

NONINVASIVE MOLECULAR PROFILING OF CANCER VIA TUMOR-DERIVED MICROPARTICLES

Muneesh Tewari, MD, PhD, Fred Hutchinson Cancer Research Center

A TRANSFORMATIVE TECHNOLOGY TO CAPTURE AND DRUG NEW CANCER TARGETS

Loren D. Walensky, MD, PhD, Dana-Farber Cancer Institute

FUNCTIONAL ONCOGENE IDENTIFICATION David M. Weinstock, MD, Dana-Farber Cancer Institute

PROBING EBV-LMP-1'S TRANSMEMBRANE ACTIVATION DOMAIN WITH SYNTHETIC PEPTIDE

Hang Hubert Yin, PhD, University of Colorado



PHILLIP A. SHARP INNOVATION IN COLLABORATION AWARDS

CLASS OF 2023

THERAPEUTIC BIPARATOPIC ANTIBODIES TARGETING FGFR2 IN GASTRIC CANCER William Sellers, MD, and Sandra Ryeom, PhD

DEFINING IMMUNOTHERAPY POTENTIAL IN GENOME INSTABILITY-DRIVEN SQUAMOUS CELL CARCINOMAS

Agata Smogorzewska, MD, PhD, and Benjamin Greenbaum, PhD

THE PHILLIP A. SHARP - LAURA ZISKIN INNOVATION IN COLLABORATION AWARD

DEVELOPMENT OF MICROFLUIDIC BLOOD EXCHANGE AS A NEXT-GENERATION PARABIOSIS FOR TUMOR/MICROBIOTA IMMUNOLOGY

Raby Upadhyay, MD, and Scott Manalis, PhD

CLASS OF 2020

GENOMIC AND THERAPEUTIC IMPLICATIONS OF SELECTIVE BACTERIAL AND FUNGAL COLONIZATION OF GASTROINTESTINAL MALIGNANCIES Luis A. Diaz Jr., MD, and Florencia McAllister, MD

UTILIZING TUMOR ORGANOIDS TO FACILITATE THE DEVELOPMENT OF EFFECTIVE STRATEGIES TO TARGET PANCREATIC CANCER WITH ENGINEERED T CELLS

Philip D. Greenberg, MD, Tyler E. Jacks, PhD, and William A. Freed-Pastor, MD, PhD

HARNESSING NK CELLS TO TREAT PEDIATRIC CANCERS

David G. Kirsch, MD, PhD, and Michal Sheffer, PhD

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CAN SCRNASEQ-DERIVED GENE PROGRAMS PREDICT ANTI-PD-1 RESPONSE IN HIGH TMB CRC AND NSCLC PATIENTS?

Karin Pelka, PhD, and Matthew D. Hellmann, MD

ENHANCING FERROPTOSIS TO BLOCK EWING SARCOMA METASTATIC CAPACITY Poul H. B. Sorenson, MD, PhD, and Elizabeth Lawlor, MD, PhD

CLASS OF 2019

RESISTANCE TO PARP INHIBITOR PLUS ANTI-PD1 THERAPY DRIVEN BY ER STRESS AND BIOACTIVE LIPIDS IN OVARIAN CANCER Juan R. Cubillos-Ruiz, PhD, and Alan D. D'Andrea, MD

UNCOVERING MUTANT TP53 DEPENDENCIES IN SPONTANEOUSLY ARISING TRIPLE-NEGATIVE BREAST CANCER Denada Dibra, PhD, and Peter P. Lee, MD

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Aaron N. Hata, MD, PhD, an

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Sarah K. Tasian, MD, and Kimberly Stegmaier, MD

ANTIGENICITY OF MUTANT KRAS AND IMPACT ON CANCER EVOLUTION

Robert H. Vonderheide, D Phil, MD, and Vinod P. Balachandran, MD

PHILLIP A. SHARP INNOVATION IN COLLABORATION AWARDS

CLASS OF 2018

DEFINING EFFECTIVE T-CELL RESPONSE IN VIRAL AND NONVIRAL GYNECOLOGIC CANCERS

Claire F. Friedman, MD, and Marta J. Luksza, PhD

CUPID-SEQ-HIGH THROUGHPUT TRANSCRIPTOMIC SPATIAL MAPPING OF IMMUNE-TUMOR INTERACTIONS IN THE MICROENVIRONMENT

Dan Landau, MD, PhD, and Raul Rabadan, PhD

CHARACTERIZING IMMUNE VARIABILITY IN CHILDREN FOLLOWING STANDARD-OF-CARE TREATMENT TO ENABLE PRECISION Trevor J. Pugh, PhD, and David M. Barrett, MD, PhD

STUDIES OF COLORECTAL CANCER PATIENT-DERIVED ORGANOIDS TO VALIDATE CANDIDATE BIOMARKERS OF RESISTANCE TO NATURAL KILLER CELLS Michal Sheffer, PhD, and Hugo J. Snippert, PhD

INTERROGATING IMPACT OF EPIGENETIC MODIFIERS ON DURABLE REPROGRAMMING OF EXHAUSTED CD8 T CELLS IN PATIENTS WITH NSCLC TREATED WITH PD-1 BLOCKADE E. John Wherry, PhD, and Matthew D. Hellmann, MD

CLASS OF 2017

INTERROGATION OF RESISTANCE MECHANISMS TO CHECKPOINT INHIBITORS USING FUNCTIONAL GENOMICS Siwen Hu-Lieskovan, MD, PhD,

and René Bernards, PhD

DISSECTING THE EPIGENETIC MECHANISMS OF REPEAT RNA REGULATION IN CANCER David T. Ting, MD, and Shelley L. Berger, PhD

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PROBING THE METABOLIC INTERACTIONS BETWEEN TUMOR AND STROMA IN PANCREATIC CANCER

Matthew G. Vander Heiden, MD, PhD, and Melissa C. Skala, PhD

APTAMER-BASED DETECTION AND BINDING OF PEPTIDE-MHC COMPLEXES

Cassian Yee, MD, and Bruce A. Sullenger, PhD

CLASS OF 2016

DEFINING THE ROLE OF EPIGENETICS IN CHIMERIC ANTIGEN RECEPTOR T-CELL THERAPY FOR CLL

Shelley L. Berger, PhD, Carl H. June, MD, and Junwei Shi, PhD

TOWARDS PREDICTIVE MODELS OF IMMUNOTHERAPY RESPONSE

Benjamin D. Greenbaum, PhD, and Jedd D. Wolchok, MD, PhD

CHECKPOINT INHIBITION IN CHILDREN WITH ULTRA- MUTATED CANCER DUE TO BIALLELIC MISMATCH REPAIR DEFICIENCY (BMMRD)

Crystal L. Mackall, MD, and Patrick M. Forde, MD

FINGERPRINTING THE SYSTEMIC MICROBIOME IN PLASMA TO PREDICT IMMUNOTHERAPY OUTCOMES IN MELANOMA

Muhammed Murtaza, MBBS, PhD, and Antoni Ribas, MD, PhD

FUNCTIONAL VERIFICATION OF DNA REPAIR MUTATIONS IN PROSTATE AND OVARY TUMORS

Eliezer M. Van Allen, MD, and Maria Jasin, PhD



PHILLIP A. SHARP INNOVATION IN COLLABORATION AWARDS

CLASS OF 2015

DEVELOPMENT OF A HIGH-THROUGHPUT METHOD TO SCREEN DRUGS WITH ORGANOIDS

Hans Clevers, MD, PhD, and David A. Tuveson, MD, PhD

CROSS-TALK BETWEEN HISTONE H3K4 MONO-METHYLATION AND CANCER METABOLISM TO EXPLORE NEW THERAPEUTIC STRATEGIES Yali Dou, PhD, and Mei Kong, PhD

TARGETING EPIGENETIC PLASTICITY AND DRUG RESISTANCE IN PEDIATRIC CANCER

Adolfo Ferrando, MD, PhD, and Kimberly Stegmaier, MD

IDENTIFICATION AND ANALYSIS OF PROSTATE REACTIVE TCRS FOR T-CELL MEDIATED ADOPTIVE CELLULAR IMMUNOTHERAPY OF METASTATIC PROSTATE CANCER

Owen N. Witte, MD, and Padmanee Sharma, MD, PhD

CLASS OF 2014

THE INTERSECTION OF EPIGENETIC AND IMMUNE CHECKPOINT THERAPY Stephen B. Baylin, MD, and James P. Allison, PhD

DETERMINANTS OF SENSITIVITY AND RESISTANCE TO MEK-BASED TARGETED THERAPIES IN NRAS MUTANT MELANOMAS Roger S. Lo, MD, PhD, and

Jeffrey A. Sosman, MD

ANALYSIS OF HIGH-DIMENSION SINGLE-CELL DATA FROM CANCER IMMUNOTHERAPY CLINICAL TRIALS

Dana Pe'er, PhD, and Padmanee Sharma, MD, PhD

CLINICAL DEVELOPMENT OF CFI-400945, A PLK4 INHIBITOR, IN BREAST CANCER

Dennis J. Slamon, MD, PhD, and Tak W. Mak, PhD

CBIOPORTAL FOR STAND UP TO CANCER

David B. Solit, MD, and Nikolaus Schultz, PhD

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ADDITIONAL AWARDS AND PRIZES

THE ZISKIN PRIZE



The Ziskin Prize is named for Laura Ziskin, legendary Hollywood producer, who cofounded SU2C and lived with breast cancer for seven years before she died in 2011.

- The prize provides a oneyear, \$250,000 grant.
- The grant is shared by two scientists at different institutions.
- Funds are used to collaborate on highrisk, high reward breast cancer research.

RECIPIENTS:

- 2012: Stephen B. Baylin, MD, and Feyruz V. Rassool, PhD
- 2014: Taru E. Muranen, PhD, and Gordon B. Mills, MD, PhD
- 2015: Matthew J. Ellis, PhD, and Charles Swanton, PhD
- 2018: Jos Jonkers, PhD, and Helen Piwnica-Worms, PhD
- 2019: Silvia C. Formenti, MD, and Heather L. McArthur, MD, MOH
- 2020: Leisha A. Emens, MD, PhD, and Xiang Zhang, PhD
- 2022: Jane E. Visvader, PhD, and Geoffrey J. Lindeman, MBBS (Hon.), PhD

THE JIM TOTH SR. BREAKTHROUGH LUNG CANCER RESEARCH AWARD

This award is named in honor of Jim Toth Sr., who passed away from lung cancer. It provides funding for highly innovative, clinically focused lung cancer research.

Two awards, covering the period 2014 - 2017

LEADERS:

Stephen B. Baylin, MD, and Peter A. Jones, PhD

PEGGY PRESCOTT EARLY CAREER SCIENTIST AWARD



The SU2C-Peggy Prescott Early Career Scientist Award in Colorectal Cancer Research supports a novel cancer research project with significant potential for advancing key questions in colorectal cancer research.

RECIPIENT: 2019: Karin Pelka, PhD

GOLDEN ARROW EARLY CAREER SCIENTIST AWARD

The SU2C Golden Arrow Early Career Scientist Award supports a novel cancer research project that, through collaboration with a current SU2C project, has significant potential for advancing key questions in cancer research.

RECIPIENT:

2019: William Freed-Pastor, MD, PhD



ADDITIONAL AWARDS AND PRIZES

SU2C SHARP TANK EARLY CAREER SCIENTIST AWARD



The SU2C Sharp Tank Early Career Scientist Award supports an early-career investigator with a novel cancer research proposal incorporating cutting-edge, high-risk ideas and offering the greatest potential impact for cancer patients.

RECIPIENT: 2020: Catherine Marinac, PhD

PHILLIP A. SHARP CHALLENGE AWARD



The Pancreatic Cancer Collective Phillip A. Sharp Challenge Award supports a novel cancer research project that explores synergistic and innovative collaborations exploring pancreatic cancer interception.

RECIPIENTS:

2021: Alec Kimmelman, MD, PhD, and Benjamin Greenbaum, PhD

SU2C MAVERICK AWARD



The SU2C Maverick Award supports an early-career investigator with a novel cancer research proposal incorporating cutting-edge, high-risk ideas and offering the greatest potential impact for cancer patients.

RECIPIENTS:

2022: Anirban Das, MD 2023: Alexander T. Pearson, MD, PhD

EMPEROR SCIENCE AWARDS

From 2016 to 2018 the Emperor Science Award program encouraged high school students to explore careers in cancer research through a unique mentoring opportunity. This education initiative was inspired by the Ken Burns documentary Cancer: The Emperor of All Maladies and supported with grants from Genentech, Bristol-Myers Squibb, and Novartis. Three hundred students were selected in national competitions and received a \$1,500 stipend, a laptop computer, and the opportunity to work alongside an esteemed scientist on a multi-week cancer research project.

ADDITIONAL AWARDS AND PRIZES

SU2C KIMMEL SCHOLARS

Sidney Kimmel CANCER RESEARCH

SU2C Kimmel Scholars were supported in 2009-2011 through a collaboration with the Sidney Kimmel Foundation which provided administration. The program provided funding (\$50,000 or more) to each of forty-three grantees as a bridge in the funding gap for gifted early cancer researchers at the initial outset of their careers. Applicants were required to hold an MD, PhD, or equivalent degree, be appointed at the assistant professor level, and be engaged in basic, clinical, or translational cancer research. In addition, applicants must not have had current R01 funding or a concurrent award for the same project.

Nabeel Bardeesy, PhD Valerie Brown, MD, PhD Barbara Buttin, MD Paul Chang, PhD Clark Chen, MD, PhD Lara Collier, PhD Maximilian Diehn, MD, PhD Muller Fabbri, MD, PhD Danica Galonic Fujimori, PhD Matthew Gamble, PhD Richard Gardner, PhD Michela Garofalo, PhD Zev Gartner, PhD Ramiro Garzon, MD Suzanne Gaudet, PhD Rani George, MD, PhD Roger Greenberg, MD, PhD Geraldine Guasch, PhD Min Guo, PhD A. McGarry Houghton, MD Erich Huang, MD, PhD Patrick Hwu, MD

Dimitrios Iliopoulos, PhD Antoine Karnoub, PhD Tae Hoon Kim, PhD Alec Kimmelman, MD, PhD Mei Kong, PhD Terry Lechler, PhD Karen Liby, PhD Roger Lo, MD, PhD Ivan Maillard, MD, PhD Christine Mayr, MD, PhD Alexander Minella, MD Stephen Oh, MD, PhD Dinesh Rao, MD, PhD Sohail Tavazoie, MD, PhD Andrea Ventura, MD, PhD Narendra Wajapeyee, PhD Bin Wang, PhD Zefeng Wang, PhD Catherine Yan, PhD Eddy Yang, MD, PhD Hongwu Zheng, PhD



REVIEWERS

SU2C's groundbreaking research programs are made possible because of the dedicated efforts of dozens of scientific reviewers. We thank them for their commitment and hard work.

Patrick Hwu, MD

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CONFERENCE MAP



SECOND FLOOR





THANK YOU

Stand Up To Cancer thanks the generous collaborators, donors, and organizations that have helped fund our groundbreaking programs, including:

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| American Lung Association | Lew & Jean Wolff |
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| Arte & Carole Moreno, Angels Baseball Foundation | Lustgarten Foundation |
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APPENDIX

HEAD AND NECK CANCER RESEARCH TEAM

Comparing, Exploring and Targeting Head and Neck Cancers

SU2C, Fanconi Anemia Research Fund, Farrah Fawcett Foundation, American Head and Neck Society, and the Head and Neck Cancer Alliance are collaborating to unite researchers who typically take different approaches to understand how head and neck cancers grow. Their research is exploring combinations of existing and emerging treatments for head and neck squamous cell cancers, especially for people with the human papillomavirus (HPV) or Fanconi anemia — a rare disease that primarily affects the bone marrow.

These cancers account for more than 90% of cancers in the head and neck. They are the sixth most common cancer in the world and can appear in the nasal cavity, sinuses, lips, mouth, salivary glands, thyroid gland, throat, or larynx.







AIM 1: CREATE OPTIONS FOR LOCAL CANCER PATIENTS . **DISRUPT(ing)** Clinical Trials Engage with community and faith-based organizations in targeted Diversity & IncluSion in Research Underpinning Prevention & Therapy Trials neighborhoods in The Bronx and Manhattan to understand local barriers to clinical trial participation, create more options for cancel Despite Black, Indigenous and people of color (BIPOC) experiencing patients as early as possible, and help patients to see clinical trials as worse cancer outcomes, most research in the U.S. is done using a viable option for treating cancer. primarily white participants. Stand Up To Cancer's four-year program will work to increase the number of BIPOC AIM 2: CHANGE APPROACHES TO CANCER CARE participants in clinical trials. The program targets four communities in New York City with high cancer NEW JERSEY mortality rates and will provide important new Using research gathered with the community, organize models for cancer clinical trials nationally. hospital and health agency leaders, doctors, nurses, and other community health influencers to consistently 85% discuss clinical trials as an initial treatment option for cancer patients and their families. **CANCER MORTALITY RATES** of the population in these four New York City neighborhoods, IN TARGETED NEIGHBORHOODS • Survey patients and health care practitioners to THE BRONX create more data-based solutions Rates per 100,000 people which are overly impacted by cance • Provide training for health care practitioners to 🔳 Bronx 📕 East Harlem 📕 Central Harlem prioritize clinical trial options for cancer patients are Hispanic/Latino Washington Heights U.S. or Black. • Create culturally relevant educational videos and resources for patients and families CENTRAL HARLEM EAST HARLEM Breas Q) **AIM 3: RETHINK CLINICAL TRIALS** MANHATTAN The team works with scientists to design clinical trials accessible to Prostate more patients by: • Creating a better database with Developing educational programs for four health institutions help from community organizations Liver • Developing training programs for Creating a network of citizen scientists, citizen scientists, and scientists within the community 10 20 30 40 50 medical students THIS PROGRAM is leading a change in cancer research to put patients

SU2C HEALTH EQUITY BREAKTHROUGH TEAM

and their families first when new treatments are created and tested. When doctors and scientists incorporate considerations of socioeconomic factors, race, and ethnicity at the outset of their work, we can create cancer treatment strategies and clinical trials that benefit all patients and their families.

Genentech

APPENDIX

Modeling Cancer within the Human Microbiome

An international collaboration of scientists is working to understand how cancer convinces the body's organs and tissues to support tumor growth. Cancer's interaction with the micro-environments that exist within the human body is a special focus of the work.

Four teams will seek to learn more about the communication between the body and the tumor on a cellular level—and how the microbiome has both positive and negative implications for the effectiveness of cancer therapies

A fifth group will work to create a laboratory tool that can grow gut tumor organoids complete with the surrounding tissue and microbiome. This engineering feat will be a dramatic advance in scientists' ability to model human cancer so new treatments can be more quickly and effectively tested.



Organoids: Tissue

cultures derived from

actual cancer samples

and human stem cells.

Mouse models: A way to

test microbiome, cancer.

and drug interactions in

real-life conditions.

cell cultures.





a person's gut, with a focus on identifying specific microorganisms that cause or facilitate the treatment of tumors.





TEAM 5 CHEMOSTAT GROUP Build an accurate, stable model of tumors and their surroundings by growing and maintaining gut organoids using stem cells, lymphoid tissue, and the microbiome to provide scientists with a replicable tool that will supercharge the study of the microbiome's effects on tumor development.



CONVERGENCE 3.1416 MISSION

By better understanding how microbiomes affect the support the human body provides to tumors, these teams of scientists will help accelerate research and treatments across a wide range of cancers and provide tools to spur the next generation of cancer research.







Pancreatic Cancer: The Hunt for Precision Therapies

With a five-year survival rate of 10%, the need to find an effective treatment for pancreatic cancer is critical. Currently, there are two leading chemotherapy combinations, but doctors don't have enough knowledge about the different types of pancreatic cancer to know which will be best for an individual patient. A Dream Team is testing ways to use the molecular characteristics of the tumor to predict which medicines should be prescribed, and develop tests to distinguish specific tumor sub-types.



APPENDIX







SU2C DIVERSITY IN EARLY DEVELOPMENT CLINICAL TRIALS RESEARCH TEAMS Increasing Diversity in Cancer Clinical Trials Cancer clinical trials need to be available to all potential patients to make new medicines available as widely as possible. SU2C and Janssen Research & Development are supporting Chicago 4 teams in Chicago, Dallas, Los Angeles and Philadelphia to increase accessibility for patients of all racial and ethnic backgrounds and/or living in medically underserved locations. The widest possible participation in clinical trials will help bring access to the latest treatments to all patients Philadelphia Los Angeles and help power the studies that will lead to breakthroughs in future cancer treatments. 3 2 Dallas The teams will focus on specific neighborhoods and cities to increase diversity among participants in Phase 1 and Phase 2 cancer clinical trials, the early trials that often determine whether a potential treatment is tested in large and expensive randomized clinical trials for widespread use by clinicians. Each team is independent but the four groups will come together to share strategies and learnings. THE FOREFRONT UChicago Medicine USC Norris Comprehensive **FOX CHASE UT Southwestern** 2 3 Cancer Center 4 1 Medical Center Keck Medicine of US TEMPLE HEALTH **CREATE A RANDOMIZED IMPLEMENT A PROGRAM EXAMINE EXISTING IDENTIFY AND OVERCOME** RECRUITMENT STUDY FOR SCREENING, STRUCTURES TO FIND SPECIFIC BARRIERS **RECRUITING, AND IMPROVEMENTS** Randomly recruit Black patients Work to address all ENBOLLING PATIENTS for a special clinical trial • Work with the county hospital system to enhance referral and barriers patients may have to access a clinical trial. • Keep patients informed about · Work with local universities, enrollment of minority patients. progress through emails, text messages and other electronic · Work with community health centers and outreach programs to help educate patients. community outreach Work to address systemic barriers messaging systems. for patients and current early phase programs to create a cancer clinical trials recruitment. Work with doctors to use more program. Information and data culturally appropriate • Study the demographics, financial and social burdens, geographical barriers, and impact of remote trials gathered will be shared on • Impact and efficiency of trial communication methods a public website. enrollment procedures will be studied, and patients will be Work with community organizations and hospitals to surveyed and interviewed to on participation in early cancer clinical trials. find areas of improvement. build a patient database. CREATING MORE OPPORTUNITIES FOR MINORITIES TO ACCESS CLINICAL TRIALS is the ultimate goal for this initiative. By working in underserved



TRIALS is the ultimate goal for this initiative. By working in underserved communities in four major metropolitan areas, the teams will be able to reach, educate, better understand, and serve a large population that is historically less engaged in cancer research and treatment. The result will be better outcomes for cancer patients and their families and communities.



APPENDIX

Detecting Gastric Cancer

The SU2C Gastric Cancer Interception Research Team is pursuing two strategies to develop more effective screening methods so that pre-cancer or early stages of the disease can be found in patients.





ΔΡΡΓΝΟΙΧ

Pediatric New Discoveries Challenge

Three teams of scientists in both the UK and the US work to improve targeted therapies by studying some of the rarest and deadliest cancers for kids. One or two of these first-round teams will be selected to receive a second round of funding based on progress and potential impact.

> TEAM 3 Madison, WI US

TEAM 1 Memphis, TN

TEAM 2 San Antonio, TX

TEAM 1

Atlas of Childhood Neuroradiation Damage

Pediatric brain cancers are the deadliest form of cancers.

Precision radiotherapy is one type of treatment but causes lifelong side effects including cognition and hormone production.

The team will study the paths radiation beams make through tumors, and map out the long-term side effects in the brain. The goal is to create more precise radiotherapy to avoid the most sensitive brain regions.

Leader: Martin McCabe.

MB/BChir, PhD, University of Manchester Co-Leader: Thomas Merchant, BS, DO, PhD, St. Jude Children's Research Hospital



Atlantic Ocean

Childhood Cancer Immunotherapies, while increasingly successful with adults, have so far not been as successful at treating

of Oncogene-driven

childhood cancers.

The team will study the immune system of patients with two types of brain cancer: neuroblastoma or medulloblastoma. They plan to design special CAR-T cells that can boost a child's immune system to overcome tumor growth and other immunity barriers.

Leader: Alexander Bishop, DPhil. UT Health San Antonio Co-Leader: Kevin Hiom, PhD, University of Dundee



CREATING BETTER TARGETED THERAPIES

is an important step for curing childhood cancers. Three transatlantic teams working on new ways to use gene therapies and radiation against pediatric cancers have promising solutions that could soon change the way these cancers are treated.

TEAM 2 Dundee, UK TEAM 1 Manchester, UK TEAM 1 TEAM 3 Grongingen, NL

London, UK EUROPE

TEAM 3 Targeting R-loop stability

in Ewing Sarcoma

Ewing sarcoma is a type of bone cancer that is poorly understood,

with limited treatment. A gene alteration causes a strong increase in the formation of "R-loops," which can cause cancer. The team noticed a higher number of R-loops than usual in Ewing sarcoma patients.

The team will investigate this unique biological hallmark to create a drug. The long-term goal is to develop new ways to target this unusual gene mutation with novel or existing compounds.

Leader: John Anderson, BA,

MBBS, MRCP, PhD, University College London Great Ormond Street Institute of Child Health Co-Leader: Louis Chesler, MD, PhD, FRCPCH, Institute of Cancer Research





GIVE FOR LOVE, GIVE FOR LIFE

With your support, we can realize our goal of turning all cancer patients into long-term survivors.

Donate now at StandUpToCancer.org/Donate.

