Team Progress Updates

SU2C-CRI Cancer Immunology Dream Team:

"Immunologic Checkpoint Blockade and Adoptive Cell Transfer in Cancer Therapy"

Cancer immunotherapy is based on getting a patient's own immune system to attack their cancer. This Dream Team has worked on two cancer immunotherapy approaches. In one approach, the team uses drugs called checkpoint inhibitors to foil the "tricks" that cancers rely on to escape natural immune cell attack. In the other approach, known as adoptive cell transfer (ACT), the team takes patients' own immune cells to the lab, makes these cells into more efficient cancer killing machines, and then returns the cells to the patient.

Work by members of this Dream Team contributed to the 2017 FDA approval of two new checkpoint inhibitors, pembrolizumab and nivolumab. The team analyzed tumor samples to determine how checkpoint inhibitors work and to identify biomarkers—molecules that can be measured in patients' blood, tumor samples, or other biological specimens to predict which patients will respond to immune therapy.

To make better T cells for ACT, the team studies the antigens—the substances that trigger an immune response—expressed by tumor cells to find out how best to improve the efficiency of the T cell attack.

The Team's progress is as follows:

December 2017

- The Team found a new protein, SLC45A2, in melanoma cells. They found that cancer-killing T cells that target this new protein does not attack normal cells, and therefore, can reduce potential toxic side-effects. The Team has started a clinical trial to treat patients with uveal melanoma with these SLC45A2-targeting T cells.
- The Team has successfully used a new method to identify the different types of cancer-killing T cells that a patient has, before and after adoptive T cell therapy. With this knowledge, they were able to identify the more effective and persistent cancer-killing T cells. They hope to understand what makes a particular cancer-killing T cell effective and hopefully, treat patients with more effective T cells.
- The Team identified the characteristics of a T cell that can hone in on a protein that is found in large amounts in pancreatic, breast, head and neck, NSCLC, and prostate cancer. They plan to use this knowledge in developing new adoptive cell therapy.

Team Progress Updates

June 2017

- The Team continued to co-develop technology with Berkeley Lights that will allow them to isolate T cells in a way that will require less blood sample from patients.
- The Team continued to develop a microchip that can help identify the cancer-specific "flags" that a patient's tumor has. Because each patient's tumor has a unique set of "flags," this microchip can help in designing more personalized cancer vaccines.

December 2016

- In a study of 20 patients with metastatic prostate cancer treated with anti-CTLA4 plus hormonal therapy, the Team has identified a predictive marker for immune-related toxicities. These data provide a potential strategy for close, clinical monitoring of patients at risk for toxicity from checkpoint inhibitor therapy.

June 2016

- They have identified new checkpoint molecules in prostate tumors that may allow these tumors to circumvent current checkpoint blockade treatments, which are targeted at CTLA4 and PD-1. These data may allow development of new checkpoint blockage drugs that can be used to enhance the effects of CTLA1 and PD-1 blockers.
- They have developed two new "flags" on cancer cells – one in uveal melanoma and the other in a range of non-melanoma solid tumors – for adoptive cell therapies to test in combination with checkpoint blockade in first-in-human clinical trials.
- They have determined that there are larger than expected numbers of anti-cancer immune T cells that appear to be naturally active against cancer-specific "flags," called neoantigens, in tumors where the number of neoantigens is generally low. These data are encouraging that difficult-to-treat cancers may be responsive neoantigen-targeted immunotherapies.
- The Dream Team's Phase 2 clinical trial of the PD-1 blocker nivolumab (Opdivo) as a pre-surgical treatment in early stage non-small cell lung cancer has produced positive results with >90% reduction in tumor size in almost half of patients tested (six of 13 patients). Based on these promising results a Phase 3 trial is planned.

December 2015

- They have gathered new information on how some patients are resistant, or become resistant, to checkpoint blockers like nivolumab (Opdivo) and pembrolizumab (Keytruda).
- They have made progress in improving the quality and activity of genetically engineered anti-tumor T cells and are adapting this therapy for patients with common solid tumors such as lung cancer.

Team Progress Updates

December 2014

- The Team developed new approaches to predict who will benefit from checkpoint inhibitor drugs.
- The Team identified "flags" that appear specifically on cancer cells and can signal to immune cells activating them to attack the cancer. By understanding these "flags," strategies to specifically activate anti-cancer immune cells and to personalize immune therapeutic approaches to individual patient's tumors, can be developed.

June 2014

- The Team developed algorithms to identify and predict the best "flags," called antigens on cancer cells that can be used to target T-cell therapies in a range of cancers.
- The Team sought to identify the best approaches to increase the strength of immune cells for adoptive cell therapy.

December 2013

- The Team conducted an initial clinical trial of 10 patients with metastatic melanoma. The patients underwent adoptive cell transfer (ACT) combined with checkpoint blockade (anti-CTLA-4; ipilimumab). Tumor regression or disease stabilization was observed in 7 of the 10 patients.
- The Team identified a molecule called mesothelin as a potential biomarker and a candidate for targeted ACT in lung cancer.

June 2013

- The Team began implementation of a bioinformatics system (Prometheus) that can merge clinical data and laboratory data from the analyses of specimens that are collected across different sites.