



Team Progress Updates

SU2C–National Science Foundation–Lustgarten Foundation Pancreatic Cancer Convergence Research Team:

“Liberating T-Cell Mediated Immunity to Pancreatic Cancer”



Pancreatic ductal adenocarcinoma (PDAC) currently is the third most common cause of cancer death in the United States, and it is expected to become the second most common cause within the next few years. Unlike virtually all other major cancers, pancreatic cancer both is increasing in incidence and has shown essentially no improvement in five-year survival over the past two decades. The exceptional lethality of pancreatic cancer is due to several factors, including an intrinsically aggressive biology, lack of effective means of early detection, and poor responsiveness to systemic chemotherapy. Clearly, novel approaches to this disease are needed.

The team is building on previous findings to further explore potential approaches to pancreatic cancer that engage the body's immune system. Extensive analysis of existing specimens will assess patients' immune responses to their tumors. The group, comprising physicians, cancer immunobiologists, computational biologists, and biophysicists, strives to better understand the unique immunological microenvironment of pancreatic cancer, develop the technologies needed to take advantage of cancer cell vulnerabilities, and form a multi-institution clinical consortium to readily implement new strategies that could change the course of this deadly disease.

The team reported the following progress:

April 2019

- The team has made significant progress in developing an assay to distinguish between different subtypes of pancreatic cancer, depending on how the cancer reacts to paracalcitriol (vitamin D). This would be a fundamental advance that could have great impact in classifying pancreatic tumors and discerning who will benefit from the inclusion of paracalcitriol in their treatment regimen.
- The ongoing trial of neoadjuvant gemcitabine/paclitaxel + paracalcitriol is nearing completion, and the study should yield valuable information regarding this treatment combination.
- An adjuvant trial with treatment of gemcitabine/nab-paclitaxel versus FOLFIRINOX has been completed. Researchers will use samples from this study to try to better define which patients may be responsive to which intervention.





Team Progress Updates

January 2018

- *In vivo* testing of T cell reactivity to neoantigens in exceptional survivors.
- Developed a novel RNA-ISH for repeat RNAs to determine the relative expression level of repeat RNAs correlated with T-cell infiltrates across colon, liver, pancreas, and melanoma samples.
- Developing computational methods to unravel the statistical nature of T cell responses to pancreatic cancer neoantigens in the clinical context.
- Tested the neoantigen fitness model on three independent datasets to predict patient response to checkpoint blockade immunotherapy. Applied same predictive model to predict long term survival in pancreatic ductal adenocarcinoma.

May 2017

- New immune response techniques and computational models have been generated.
- Neoantigens resemble microbial proteins in long-term survivors post-surgically in PDAC patients.

January 2017

- Computer model to identify immunogenic neoantigens to predict long term survival and to predict responses to checkpoint blockade.
- Long term survivors of pancreatic cancer being evaluated.
- New clinical trials planned.

June 2016

- Studies of the immune cell diversity have begun and computational approaches to understanding the microenvironment have yielded early results.