



## Team Progress Updates

### SU2C–Lustgarten Foundation CAR T Research Team:

#### “Chimeric Antigen Receptor T Cell (CAR T) Therapy for Pancreatic Cancer”



The goal of the SU2C–Lustgarten Foundation Chimeric Antigen Receptor T Cell (CAR T) Research Team is to understand why immunotherapy does not cause tumor regression in all patients. They are studying the genetic and epigenetic markings in immune cells called CAR T cells to identify ways to optimize their cancer-killing features.

They have two overarching aims. First, they are isolating CAR T cells from patients with ovarian cancer, mesothelioma, and metastatic pancreatic cancer and analyzing them using state-of-the-art cellular assays. Second, they are studying the CAR T cells obtained from patients to understand how to prolong and enhance the cells' activity. They expect that these studies will shed light on approaches to optimize the combination of CAR T cells with checkpoint therapies that block the function of CTLA-4 and PD-1, proteins on cell surfaces that inhibit normal immune response.

The Team has been able to successfully manufacture CAR T cells from 6 mesothelioma and ovarian cancer patients and safely treat the patients without overt off-tumor on-target toxicity against normal tissues. They confirmed that the many CAR T cells were able to home in on the tumor.

The team has reported the following progress:

#### January 2019

- The development of an effective immunotherapy for pancreatic cancer remains a critical clinical need, and this team's project should determine if targeting mesothelin with a CAR-T cell will be a viable approach for patient care.
- The team has now acquired regulatory approval for a modified protocol (following instances of severe toxicity with the higher dose of T cells plus cyclophosphamide, administered intravenously in the original version of the protocol). The protocol is now open (ClinicalTrials.gov Identifier: NCT03323944). The first patient is scheduled to be treated in mid-March under the new protocol.
- The team has been profiling mono-nuclear blood cells from pancreatic cancer patients to optimize CAR-T therapy. They found, based on molecular profiling, 31 distinct clusters of CD8 T-Cells, which includes six clusters that appear different from CD8 T cells in normal individuals.
- The team also looked at the distribution of T cells in pancreatic cancer patients by taking advantage of the opportunity to evaluate spleens from PDA patients that have undergone splenectomy. They found that the effector subset of CD8 T cells seem to be proportionally





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increased in the spleen but not in the blood. This observation was further validated in a mouse model. These studies highlight the importance of looking at the tissue site, as peripheral blood may not adequately reflect cancer cells in the patients.

### **June 2018**

- The team has opened a clinical trial in patients with metastatic pancreatic cancer to test CAR T cells at two different doses.
- The team has successfully manufactured CAR T cells from six mesothelioma and ovarian cancer patients and safely treated the patients without overt off-tumor on-target toxicity against normal tissues. The team confirmed that the CAR T cells were able to home in on the tumor.
- The team is continuing to enroll pancreatic cancer patients in the clinical trial and analyzing pre- and post-CAR T therapy samples.

