Team Progress Updates

SU2C–Lustgarten Foundation Pancreatic Cancer Convergence Research Team:

"Computational Deconstruction of Neoantigen-TCR Degeneracy for Cancer Immunotherapy"

The SU2C–Lustgarten Foundation Pancreatic Cancer Convergence Research Team is exploring the underpinnings of pancreatic survivorship. By looking at a few individuals who survive pancreatic cancer for long periods of time (5-12 years), the team has identified an initial set of high-quality neoantigens, or protein tags, on cancer cells that the immune system recognizes.

In this project, researchers are using artificial intelligence computational approaches to understand what makes a neoantigen high-quality and how the microbiome influences how the immune system recognizes it. The goal is to develop a method for creating vaccines to treat pancreatic cancers. If successful, this research will have a significant impact on understanding neoantigen T-cell immunobiology and could improve the treatment prospects of pancreatic cancer patients.

The team reported the following progress:

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- To better understand the association of neoantigen fitness with evolution during latent metastases in long-term pancreatic cancer survivors, the team has completed sample retrieval, sequencing, and in silico processing of 134 primary and metastatic pancreatic cancer samples. Team members will identify the most likely clone to originate each metastatic event, allowing them to determine whether clones with more immunogenic neoantigens are more or less likely to result in a metastatic event.

- The team is building a statistical model predictive of epitope-receptor affinity based on samples collected and sequenced from 87 short- and long-term pancreatic cancer survivors.

- The team has completed analysis of 20,100 neoantigen-specific memory CD8+ T cells in two very long-term pancreatic survivors, with the goal of identifying T cell states associated with long-term neoantigen-specific memory. Interestingly, team members found that a subset of circulating CD8+ T cells and clones shared identical T-cell receptor sequences with tumor-infiltrating lymphocytes found in the primary tumor. This suggests that these T cells are in fact neoantigen-specific memory CD8+ T cells originating in the patient's primary tumor.