Scientific Abstract

SU2C-CRUK-Lustgarten Foundation Pancreatic Cancer Dream Team:

"Reprogramming of Transcriptional Circuitry to Control Pancreatic Cancer"

[This abstract was provided by the scientists when their application was accepted.]

Although pancreatic ductal adenocarcinoma (PDAC) looks diverse (morphologically complex, variable responses to therapeutic regimens, etc.) we think this diversity obscures a remarkable underlying commonality that PDAC evolution is highly channeled (e.g. highly conserved drivers, unique environment, capacity for self-renewal, unique "feeding" mechanisms, etc). Our Dream Team Collaborative Vision is that pancreatic cancer is the result of a regenerative program that has been "hacked" into.

The overall goal for this effort is to

(a) At least double the one year survival rate for patients with metastatic pancreatic cancer
(b) To double the time to tumor regrowth in a maintenance setting after maximal responses

Our Hypothesis is:

PDAC Is driven/maintained by superenhancer (SE) regulated regenerative programs in the pancreas:

- Epithelial compartment (including cancer stem cells)
- Stromal compartment
- Immune compartment

(1) These deregulated SE networks mediate cellular communications in pancreatic cancer
(2) Reprogramming (resetting) SE Networks (transcriptional circuitry) in PDAC epithelial (including stem cells) stromal, and immune compartments will halt tumor progression.

Our Specific Aims are as follows:

Aim 1. Define superenhancer networks in the cellular milieu of pancreatic cancer
Aim 2. Determine the mechanisms that mediate crosstalk between superenhancer networks both within cells and between them
Aim 3. Determine the utility of superenhancer disruption in treating pancreatic cancer.