Team Progress Updates

SU2C-CRUK-Lustgarten Foundation Pancreatic Cancer Dream Team:

"Reprogramming of Transcriptional Circuitry to Control Pancreatic Cancer"

The Dream Team's approach is rooted in the idea that pancreatic cancers are, in essence, "wounds" that never heal.

Research by members of this Dream Team, and others in the field, has uncovered gene networks in tumors that are similar to those in injured tissues, where repair and regenerative mechanisms are essential to restoration of normal function. Unlike the normal system of wound healing, which has a shut-off mechanism, in tumors the process remains active, "hijacked" to constantly drive growth. The Team believes that the biological machinery involved is controlled through hot spots in a cell's DNA called super enhancers (SE), which control not only the cancer cell but also surrounding noncancerous cells on which the cancer cells rely for support.

The SU2C–CRUK–Lustgarten Foundation Pancreatic Cancer Dream Team is working to develop new approaches to reset malfunctioning SEs in pancreatic tumors, thereby increasing the sensitivity to chemotherapy and to anticancer immune cells and pushing pancreatic tumors into lasting remission.

The team has reported the following progress:

June 2018

- The team has discovered a protein that becomes more abundant when a patient develops pancreatic cancer and has developed a blood test to measure the levels of this protein. The team is gathering evidence that measuring levels of this protein can be used to assess whether a patient is responding to therapy.
- The team has opened a clinical trial testing the oral form of the anti-super-enhancer drug Minnelide.
- The team has enrolled 25 patients in a clinical trial to test adding immunotherapy and the anti-super-enhancer drug paricalcitol to chemotherapy.
- The team has reported that certain types of white cells can make pancreatic cancer more aggressive, a finding that if validated may provide additional avenues for therapies against the disease.

Team Progress Updates

December 2017

- More patients joined a clinical trial of the anti-superenhancer agent paricalcitol plus chemo-immuno-oncology agents.
- Found that the superenhancer modulating agent Entinostat can reprogram tumor cells and cancer associated fibroblasts in the tumor.
- In preclinical studies, the anti-superenhancer agent Minnelide was found to add strong preclinical antitumor activity to the existing treatment regimen.

June 2017

- The team has identified several potential drug candidates to treat effectively pancreatic cancer stem cells.
- A phase II clinical trial for patients who have progressed on two or more prior regimens for pancreatic cancer has started.
- Two other clinical trials for patients with advanced disease are about to start in the next 2 months.

December 2016

- The Team developed a new animal model of late stage pancreatic cancer for investigation of specific new treatments including a synthetic vitamin D and the new agent, Minnelide.
- The Team has demonstrated that anti-superenhancer agents are active against pancreatic cancer stem cells and improves the efficacy of chemotherapeutics against those stem cells.

June 2016

- The Team developed new methods to identify changes in metabolism when anti-SE super enhancer agents are applied.
- The Team identified a gene that is a potential target for drug treatment of pancreatic cancer.