



Team Progress Updates

Pancreatic Cancer Collective Research Team:

“Combined Targeting of MEK1/MEK2 and Autophagy for Pancreatic Cancer”



There is no effective, FDA-approved precision therapy for pancreatic cancer (pancreatic ductal adenocarcinoma or PDAC). The standard of care for most PDAC patients remains conventional cytotoxic chemotherapy, which offers high toxicity with little clinical benefit. The Team has discovered that the survival of pancreatic cancer cells relies on two biochemical processes: 1. Intracellular signaling by the RAS pathway and; 2. Autophagic recycling of the cells' interior contents to generate building blocks for cancer cell metabolism.

Blocking either one of these processes alone has been shown to have negligible effects. But combined blockade of both the RAS pathway (with trametinib, T) and autophagy (with hydroxychloroquine, HCQ), has displayed synergistic antigrowth effects against pancreas cancer cells in vivo. Although both of these FDA-approved drugs have previously been tested in pancreatic cancer patients with little or no effect, they have never been tested in combination.

The team is working toward two goals: 1) elucidating the mechanism(s) by which autophagy is regulated by the RAS pathway, in order to identify predictive biomarkers and new autophagy inhibitors that might be tested in clinical trials; and 2) performing a clinical trial of the T/HCQ combination therapy.

This team started its work in November 2018; progress notes will be posted after its first review.

