The Department of Pediatrics
Division of Gastroenterology

Research Seminar for Faculty Candidate:

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"Drug Induced Pancreatitis: A clinical clue to understanding recovery from acute and chronic pancreatitis"

Tuesday, March 3, 2020
2:00 pm - 2:45 pm
MacNider 321

Hosted by: Dr. Francisco Sylvester; Division Chief, Pediatric Gastroenterology

Pancreatitis is a life-threatening inflammatory disorder that lacks targeted therapies and if left unchecked progresses to a chronic fibrotic disease. A crucial mediator of pancreatic recovery is the mesenchymal cell, the pancreatic stellate cell (PSC). The molecular mechanisms that regulate PSC activation and the return to quiescence are unclear and thus forms the basis for the current proposal. Understanding the molecular underpinnings of PSC quiescence as well as the switch from quiescent to activated PSCs, will have wide ranging therapeutic implications. An emerging mechanism for orchestrating dynamic changes in cellular phenotypes is the epigenetic modification of histones by repressive complexes like *S*wi-*in*dependent transcription regulator family member A (SIN3a), which contains histone deacetylases 1/2. We hypothesize that SIN3a promotes PSC quiescence through HDAC activity. During PSC activation SIN3a is displaced by β-catenin, leading to the removal of epigenetic repressive marks and promoting gene expression characteristic of activated PSCs. To address this hypothesis, our specific aims are to 1) Determine the mechanism by which the SIN3a complex maintains the quiescent PSC phenotype (Aim 1) and 2) Examine the role of β-catenin in regulating activated PSC gene expression (Aim 2) by balanced *in vitro* and *in vivo* studies. The proposal is significant because it will identify novel epigenetic mechanisms that control PSC activation. These studies will investigate a new paradigm to consider therapeutic strategies for pancreatitis that could exploit epigenetic factors to reduce pathologic fibrosis mediated by activated PSCs and therefore the proposal is highly clinically relevant.