Molecular Analysis of Pancreatic Cancer

Most of the estimated 103,000 patients with a new diagnosis of pancreatic adenocarcinoma (PDAC) in the US and Europe will die within the year of diagnosis. The poor prognosis is due to a number of factors including the aggressive biology of disease, advanced stage at the time of diagnosis, and poor response to current chemotherapy. Patients with locally advanced or metastatic disease have a median survival of less than 12 months, with current Gemcitabine-based chemotherapeutic regimens extending survival by only a median of 5 weeks. There is an urgent need to develop new and better strategies for the prevention and treatment of PDAC. Determining the genetic and molecular changes associated with PDAC is a key component to understanding the initiation and aggressiveness of these tumors. Our lab is interested in identifying the “malignant” molecular signature of PDAC by linking an extensive array analysis (DNA, miRNA, and mRNA) with clinical prognosis, and using key genes/pathways as markers of earlier disease and targets for therapy. My lab is closely affiliated with Dr. Hong Wu MD, PhD, Professor of Molecular and Medical Pharmacology, and is located in the Institute for Molecular Medicine (IMED). To examine the molecular genetics of PDAC, we have developed a number of transgenic mouse models that recapitulate human PDAC with well-defined kinetics. We have a number of ongoing projects. We are examining the role of micro-RNAs (miRNA) on regulation of key PDAC-associated gene expression changes, and are examining whether PDAC-associated miRNA can be detected in precursor lesions, mucinous cystic neoplasms (MCN) and intraductal papillary mucinous neoplasms (IPMN). We are collecting the serum from patients with PDAC and will probe the serum for promising PDAC-associated miRNA as early markers of disease. We have identified a novel cell surface profile that can isolate a PDAC “cancer stem cell” population of cells, and are examining key pathways within these cells that are responsible for PDAC initiation and progression. We are testing biologic agents that target key pathways in the stem cell population in a high-throughput manner using human in vivo xenograft models and in vitro sphere-forming assays. We are working closely with Dr. Dennis Slamon, MD Professor of Medical Oncology, who has developed a large clinical network to translate our laboratory findings to patients in rapidly accruing clinical trials. Our overall goal is to use the malignant PDAC molecular signature (DNA, miRNA, and mRNA) to improve the prognosis associated with PDAC.