Cancer of the Pancreas Screening (CAPS) Program
at Johns Hopkins
Translational Research Project Description

With a gift of $10,000 annually for three years, the support of Mr. & Mrs. Hugh Victor would initially be directed towards a specific study that is considered the next step towards developing a clinical test for pancreatic screening following the identification of a bio-marker.

SIGNIFICANCE: Diagnosis of early pancreatic cancer (PC) and benign high grade precursors is the ultimate goal of pancreatic cancer screening and surveillance. Early detection and treatment of these neoplasms might lead to decreased mortality. Identification of biomarkers of pancreatic neoplasia in pancreatic juice collected at the time of screening or surveillance endoscopic ultrasound (EUS) could be an effective strategy compared to serum markers. The information gained from this pilot study could potentially lead to the prospective clinical validation of specific biomarkers in screening and surveillance programs.

GENERAL AIM: To perform a translational pilot study of biomarkers in pancreatic juice of high risk individuals with an inherited predisposition for pancreatic cancer who underwent EUS screening and surgical resection of suspected neoplasia.

SPECIFIC AIM: 1) To measure the levels of quantity and quality of KRAS and p53 in the banked pancreatic juice of high risk individuals prior to surgical resection and correlate these with EUS and CT/MRI findings and the highest grade of prevalent neoplasia in resection specimens. 2) To determine the potential predictive value of KRAS and p53 in pancreatic juice for high grade neoplasia in patients undergoing surgery for suspected neoplasms.

DESIGN: Nested case-control study.

PATIENTS: Consented patients seen at the Johns Hopkins Hospital with a strong family history of pancreatic cancer (with at least 2 or more first degree relatives affected) or a known genetic mutation associated with pancreatic cancer enrolled in prior CAPS (Cancer of the Pancreas Screening) screening studies who had surgical treatment between 2000-2010. Approximately 32 individuals will be recruited from the CAPS Registry and CAPS study databases.

METHODS:
Year 1: Cases and controls will be selected based upon the highest grade of neoplasia in resected pancreata. Cases (case group 1) will consist of patients with at least carcinoma-in-situ or invasive adenocarcinoma in the main pancreatic duct or branch ducts (intraductal papillary mucinous neoplasms) and/or pancreatic intraepithelial neoplasia (PanIN). Controls will consist of patients with only PanIN 1 and 2 or IPMN adenomas with low grade dysplasia. Patients with IPMNs and moderate grade dysplasia will be analyzed separately as an intermediate risk case group (case group 2). Banked secretin-

stimulated pancreatic juice specimens collected at the time of screening EUS and/or ERCP during CAPS 1,2, 3, and 4 studies and stored in the Johns Hopkins Pancreatic Cancer Early Detection Laboratory (c/o translational scientist Dr. Michael Goggins) will be selected for analysis. Levels of KRAS and p53 will be assayed using Digital melt curve analysis.

The mean and 95% confidence intervals for measurable levels of KRAS and p53 for case groups 1 and 2 will be compared with those of controls. ROC analysis to determine the optimal threshold for distinguishing patients with early PC and high-grade precursors from those with only low-grade precursors will be performed. Biomarker levels will be correlated with preoperative radiographic (CT, MRI) and EUS abnormalities.

The sensitivity, specificity, accuracy, PPV, and NPV for prediction of high grade neoplasia will be determined for clinical and imaging tests alone, biomarkers alone, and combined clinical + imaging + biomarkers.

Years 2-3: The preoperative clinical, EUS, and radiographic diagnoses for high risk patients undergoing pancreatic surveillance within ongoing CAPS studies with suspicious pancreatic lesions will be recorded. The sample of the pancreatic juice of these patients will be assayed “for KRAS and p53. The final pathologic diagnosis for patients who undergo surgery will be recorded and compared with biomarker levels, using the cut-off points from specific aim 1.