

Environmental Exposures and Biomarkers of Pancreatic Cancer

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Abstract:

Pancreatic ductal adenocarcinoma (PDAC) is the 4th most common cause of cancer-related mortality in the US. Outcomes are among the worst of all cancers, with 5-year survival rates estimated between 0.4 and 4%. Little is known about mechanisms of cigarette smoke induced pancreatic carcinogenesis. Cigarette smoke is the major known environmental risk factor for PDAC. The tobacco-specific nitrosamine (TSNA) 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and its chiral metabolite, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL), are known pancreatic carcinogens. Elevated serum NNAL level has been shown to be an independent risk factor for lung cancer. Furthermore, exposure of rats to cigarette smoke has been shown to induce pancreatic fibrosis, a finding characteristic of pancreatic stellate cell activation. The proposed studies will use an innovative approach to study the gene-environment interactions induced by cigarette smoke on the pancreas, and identify biomarkers of susceptibility. In Specific Aim 1 NNK and NNAL levels will be determined in an *in vitro* model of cigarette smoke exposure in the pancreas. Protein biomarkers of exposure will also be identified. In Specific Aim 2, NNK, NNAL and protein biomarkers identified in Aim 1 will be measured in patient serum samples. We are confident these studies will identify clinically applicable biomarkers of smoke exposure and susceptibility to PDAC. Furthermore, these studies will elucidate mechanisms of pancreatic carcinogenesis.