Diseases of the Pancreas

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Research Goal 1

Determine the biologic and genetic factors involved in the pathogenesis of acute pancreatitis with particular emphasis on mechanisms of tissue necrosis and systemic complications.

Research Goal 1 Objectives

- Understand how noxious insults such as ethanol or gallstones initiate pancreatic injury and inflammation.
- Understand the role of obesity, sphincter of Oddi dysfunction, and anatomic variations of the pancreas in the development of pancreatitis.
- Identify the biologic mechanisms leading to necrosis in acute pancreatitis.

Research Goal 1
Objectives (continued)

- Understand the biologic mechanisms responsible for post-ERCP pancreatitis.

- Understand the role of specific cytokines and other inflammatory factors including enteric bacteria and their products in the development of systemic complications and multi-organ failure.

Research Goal 2

Understand the transition from acute to chronic pancreatic injury, particularly with respect to the role of alcohol.

Research Goal 2 Objectives

- Understand how ethanol, smoking and other putative etiologic factors contribute to chronic injury.
- Determine the biology of pancreatic fibrosis and chronic injury including the role of stellate cells and other co-factors.
- Understand the nature and mechanism of endocrine cell loss in chronic pancreatitis.

Research Goal 2
Objectives (continued)

- Understand mechanisms of parenchymal and islet cell regeneration in response to chronic injury.

- Understand the biologic nature and importance of islet-parenchymal communication in the pancreas.

Research Goal 3

Understand genetic factors and how they interact with exogenous insults with respect to pathogenesis, complications, and natural history of pancreatitis and other pancreatic disorders.

Research Goal 3 Objectives

- Understand genetic factors that predispose to increased risk or severity of acute pancreatitis.
- Understand the role of genetic factors that predispose to chronic injury and/or impaired recovery from acute insults.
- Understand gene-environmental interactions in the development of benign and cystic neoplasms as well as pancreatic cancer arising in the context of chronic pancreatitis.

Research Goal 3
Objectives (continued)

- Understand the genetic factors that predispose to sensitization and pain in the setting of pancreatic injury.

- Develop novel models of pancreatic disease derived from targeting of specific genes.

Research Goal 4

Develop and validate therapeutic interventions for treatment and/or progression of pancreatitis and its complications.

Research Goal 4 Objectives

- Study the effects of specific pharmacologic therapies, including anti-cytokine agents for the treatment of acute pancreatitis, prevention, and treatment of necrosis and multi-organ failure.

- Study novel and more effective pharmacologic and/or endoscopic approaches to prevent ERCP-induced pancreatitis.

Research Goal 4
Objectives (continued)

- Study the effect of endoscopic approaches (e.g. stents, stone removal and stricture formation), surgery, and radiologic interventions for the treatment of organized necrosis, pseudocysts, pain and other complications of acute and pancreatitis.

- Study novel pharmacologic approaches for the reversal of fibrosis and prevention of islet and parenchymal cell loss including islet cell and stem cell transplant strategies.

Research Goal 4
Objectives (continued)

- Study the role of immunosuppressive therapy for the treatment of autoimmune pancreatitis.

Research Goal 5

Understand the neurobiology of the pancreas with respect to mechanisms of pain and neurogenic inflammation.

Research Goal 5 Objectives

- Study the biologic basis and mechanisms responsible for peripheral sensitization in chronic pancreatitis.

- Study changes in central sensitization and the underlying mechanisms in patients with painful chronic pancreatitis.

Research Goal 5
Objectives (continued)

- Understand the biologic basis of narcotic dependence and resistance in patients with chronic pancreatitis.

- Identify novel therapeutic targets for more effective analgesic therapy.

- Understand the mechanisms by which autonomic, spinal, and neurohormonal factors influence the course of acute and chronic pancreatitis and their complications.

Research Goal 6

Define the epidemiology and clinical course of acute and chronic pancreatitis, including alcoholic pancreatitis, autoimmune pancreatitis, and cystic fibrosis through population-based studies in adults and children.

Research Goal 6 Objectives

- Identify reliable prognostic factors of severity of acute pancreatitis at admission that can be utilized to stratify patients that can be enrolled in studies that evaluate new therapies.

- Understand the co-factors necessary for development of fibrosis in patients with recurrent pancreatitis and rate of disease progression in chronic pancreatitis.

Research Goal 6
Objectives (continued)

- Understand the natural history of disease in patients with chronic pancreatitis due to various etiologies including autoimmune pancreatitis.

- Understand demographic, ethnic, genetic and environmental factors enhancing risk of disease development and rate of disease progression.

Research Goal 6
Objectives (continued)

- Develop and validate reliable measures of pain and quality of life in patients with chronic pancreatitis.

Research Goal 7

Develop more accurate and useful approaches to the diagnosis of chronic pancreatitis by functional, radiologic, endoscopic, or pathologic/cytologic means.

Research Goal 7 Objectives

- Develop and validate unequivocal criteria for diagnosis of chronic pancreatitis (histologic and non-histologic) and distinguish etiopathologic subsets, such as autoimmune or genetic pancreatitis.

- Study novels methods including minimally invasive biopsy methods to help identify patients with early chronic pancreatitis and distinguish etiopathologic subsets.

Research Goal 7
Objectives (continued)

- Develop and validate novel and less invasive methods to recognize and monitor fibrosis.
- Develop and validate more accurate and convenient tests to assess and monitor pancreatic function.
- Develop and validate reliable non-invasive methods for the diagnosis and monitoring of autoimmune pancreatitis.

Research Goal 8

Define the role of pathologic lesions, such as pancreatic intraepithelial neoplasms (PanINs) and other factors that may correlate with the risk of malignant transformation in chronic pancreatitis and cystic neoplasms and map their morphologic and molecular progression.

Research Goal 8 Objectives

- Study the epidemiology and natural history of cystic disorders of the pancreas and correlation with results of imaging and fluid analysis.

- Identify biomarkers in cystic fluid and tissue aspirates for providing unequivocal diagnoses and pathologic distinction.

Research Goal 8
Objectives (continued)

- Study the role of invasive and non-invasive methods for surveillance of patients at risk for malignancy.
- Study of clinico-pathologic correlations involving PanINs, small cystic lesions, and IPMN.
- Studies on the genetic and morphologic progression between precursor lesions and pancreatic cancer particularly in the context of chronic pancreatitis.

Major Challenges/Steps To Achieve Goals

- Standards for diagnosis
- National resources for pancreas research
- Animal models
- Alignment of research and clinical forces

Major Challenges/Steps To Achieve Goals

Standards for Diagnosis

- Consensus guidelines for diagnosis of chronic pancreatitis and (including histologic and clinical criteria)
- Reliable tools to measure of pain and quality of life in patients with chronic pancreatitis

National Resources for Pancreas Research

- National database of acute pancreatitis to define mortality and morbidity and to develop reliable prognostic factors of severity at admission
- Patient registry and a repository of biologic samples
- Multicenter consortia for the study of chronic pancreatitis in adults and children

Major Challenges/Steps To Achieve Goals

Animal Models

- Animal models of both acute and chronic pancreatitis (alcoholic and non-alcoholic) and its complications

Alignment of Research and Clinical Forces

- Rapid development of endoscopic and other relatively non-invasive approaches to the pancreas has resulted in some divergence between the biologic and clinical approaches to understanding diseases of the pancreas. A concerted effort to re-align these forces is important.