JOHNS HOPKINS
TECHNOLOGY VENTURES

# JOHNS HOPKINS UNIVERISTY
# PANCREATIC CANCER RESEARCH

***Highlighted Faculty Members:***
Laura Wood, Michael Goggins, Nilofer Azad, Linda Chu, Lei Zheng, and Ralph Hruban

## Laura Wood, MD, PhD

*Associate Professor of Oncology and Medicine; Deputy Director of the Sol Goldman Pancreatic Research Center*
*Intercepting Pancreatic Cancer Progression: Molecular, Immune, and Organoid-Based Strategies for Early Detection and Risk Stratification*

**Overview:**
Wood's research centers on the early stages of pancreatic ductal adenocarcinoma (PDAC), focusing on the molecular and immunologic evolution of precursor lesions such as intraductal papillary mucinous neoplasms (IPMNs) and mucinous cystic neoplasms (MCNs). Using an integrated approach that combines multiregion genomic analysis, morphology-guided transcriptomics, and advanced immunohistochemistry, she has uncovered significant genetic heterogeneity and dynamic changes in the immune microenvironment that accompany lesion progression. Her studies identify immune checkpoint expression and macrophage infiltration as key hallmarks of high-risk lesions, offering new avenues for early detection, risk stratification, and potential immunopreventive interventions. The development of cyst fluid biomarkers and noninvasive diagnostic assays further positions her work at the intersection of molecular pathology and clinical translation.

Wood also leverages patient-derived organoid models and single-cell technologies to elucidate the role of stromal and immune cell signaling in shaping tumor behavior. Her investigations into hypoxia-induced pathways, epigenetic alterations like 5-hydroxymethylcytosine loss, and invasion-associated molecular programs driven by stromal ligands such as TGF-β1 and IL-6 have revealed critical mechanisms of early tumor progression. These insights inform strategies for therapeutic interception and provide a strong foundation for collaborations aimed at cancer prevention and minimally invasive diagnostics. Collectively, her work offers transformative potential in shifting pancreatic cancer management toward earlier, biologically guided intervention.

**Areas of Potential Collaboration:**
1. Decoding Progression Pathways in Precursor Lesions:
    - Utilize morphology-guided transcriptomics and spatial analysis to reveal invasion-driving pathways in IPMNs and MCNs.
    - Identify early epigenetic changes, including 5-hydroxymethylcytosine downregulation, as potential biomarkers of malignant transformation.
2. Immune Landscape and Tumor Microenvironment Modulation:
    - Characterize immune checkpoint expression (e.g., PD-L1, TIM-3, VISTA) and macrophage infiltration in precursor lesions to identify immune evasion mechanisms.

   - Develop immune-based prognostic tools and stratification frameworks for high-risk IPMNs.
3. Organoid-Based Functional Platforms:
   - Advance PDO models with microenvironmental components to study stromal signaling (e.g., TGF-β1, IL-6) and hypoxia-driven invasion (e.g., P4HA1 expression).
   - Screen candidate agents targeting invasion, immune modulation, and epigenetic reprogramming.
4. Translational Biomarker Development:
   - Develop and validate cyst fluid biomarkers for distinguishing high-risk mucinous cysts from benign lesions.
   - Create integrated risk assessment tools combining genomic, transcriptomic, and immune data to guide clinical decision-making.

**Selected Publications:**

*Predictive ability of pancreatic cyst fluid biomarkers: A systematic review and meta-analysis*. Pancreatology. 2023 Nov;23(7):868-877
*Downregulation of 5-hydroxymethylcytosine is an early event in pancreatic tumorigenesis*. J Pathol. 2021 Jul;254(3):279-288
*Tumor immune microenvironment alterations associated with progression in human intraductal papillary mucinous neoplasms*. J Pathol. 2025 May;266(1):40-50
*P4HA1 Mediates Hypoxia-Induced Invasion in Human Pancreatic Cancer Organoids*. Cancer Res Commun. 2025 May 1;5(5):881-895
*3D genomic mapping reveals multifocality of human pancreatic precancers*. Nature volume 629, (2024), 679–687
*Multiregion Genomic Analysis of Human Pancreatic Mucinous Cystic Neoplasms*. Modern Pathology, Volume 38, Issue 7 (2025)

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## Michael Goggins, MD

*Professor of Pathology, Medicine, and Oncology; Director of the Pancreatic Cancer Early Detection Laboratory; Attending physician in medicine in the Division of Gastroenterology and Hepatology; The Sol Goldman Professor of Pancreatic Cancer Research*

*Integrated Biomarker, Genetic, and Microbiome-Based Platforms for Early Detection and Risk Stratification in Pancreatic Cancer*

**Overview:**

Goggins, The Sol Goldman Professor of Pancreatic Cancer Research and Director of the Pancreatic Cancer Early Detection Laboratory at Johns Hopkins, is a prominent leader in advancing early detection and risk assessment for pancreatic ductal adenocarcinoma (PDAC). His multidisciplinary research spans genetic susceptibility, biomarker development, and microbiome analysis, with a focus on integrating basic science discoveries into clinically actionable tools. Dr. Goggins investigates inherited genetic variants, including ER stress-related genes like CEL, to better understand their roles in pancreatic tumorigenesis, metabolic dysfunction, and immune evasion. This work underpins the development of personalized genetic screening and surveillance protocols designed to identify high-risk individuals for earlier intervention and cancer interception.

In parallel, Goggins leads efforts in biomarker innovation, creating serum-based panels incorporating markers such as CA19-9 and carboxypeptidase activity, enhanced by AI-driven analytics to improve noninvasive early detection accuracy. He pioneers liquid biopsy diagnostics for detecting pre-invasive lesions and minimal residual disease, aiming to augment or replace more costly imaging surveillance methods. Additionally, his exploration of the pancreatic and duodenal microbiome offers novel predictive models linking microbial signatures to cancer risk and therapeutic response. By establishing integrated biospecimen and clinical-microbiome platforms, Dr. Goggins is poised to accelerate translational research and broaden diagnostic accessibility for populations at risk of PDAC.

**Areas of Potential Collaboration:**

1. Genetic Susceptibility and Risk Stratification
    1. Investigation of ER stress-related gene variants, including *CEL* (carboxyl ester lipase), linked to inherited pancreatic disease and metabolic dysfunction.
    2. Development of personalized genetic screening protocols for early identification of individuals at elevated PDAC risk.
    3. Characterization of germline variants and their mechanistic roles in tumorigenesis, metabolic stress, and immune evasion.
    4. Collaboration on therapeutic modulation of ER stress pathways as a cancer prevention or interception strategy.
2. Biomarker Development and Diagnostic Innovation
    - Creation and validation of serum-based biomarker panels, including CA19-9 and carboxypeptidase activity, tailored to genetic backgrounds.
    - Application of AI-driven analytics to interpret complex biomarker datasets, supporting non-invasive, high-throughput early detection tools.
    - Design of molecular diagnostics for pre-invasive neoplasia and minimal residual disease using liquid biopsy platforms.
3. Surveillance and Early Detection in High-Risk Populations
    - Implementation of risk-adjusted screening protocols based on family history, genetic testing, and biomarker profiling.
    - Clinical infrastructure development for personalized surveillance and longitudinal monitoring of high-risk individuals.
    - Strategic evaluation of cost-effective diagnostic alternatives to imaging-based surveillance (e.g., EUS, MRI), enabling broader population access.
4. Microbiome-Driven Diagnostics and Tumor Profiling
    - Analysis of duodenal fluid microbiota as a surrogate for intratumoral microbial signatures in PDAC.
    - Development of microbiome-based predictive models for cancer risk, immune environment modulation, and therapeutic response.
    - Establishment of biospecimen pipelines and clinical-microbiome integration platforms for diagnostic innovation and research scalability.

**Selected Publications**

*Endoplasmic stress-inducing variants in CPB1 and CPA1 and risk of pancreatic cancer: A case-control study and meta-analysis*. Int J Cancer. 2022 Apr 1;150(7):1123-1133
*Alterations in the Duodenal Fluid Microbiome of Patients with Pancreatic Cancer*. Clin

Gastroenterol Hepatol. 2022 Feb;20(2): e196-e227
*Pancreatic Cancer Surveillance and Survival of High-Risk Individuals*. JAMA Oncol. 2024;10(8):1087–1096
*Inherited Pancreatic Cancer Syndromes and High-Risk Screening*. Surg Oncol Clin N Am. 2021 Oct;30(4):773-786

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## Linda Chu, MD

*Associate Professor in the Johns Hopkins Medicine Department of Radiology and Radiological Science*

*Artificial Intelligence and Advanced Imaging Integration for Early Detection of Pancreatic Ductal Adenocarcinoma (PDAC)*

**Overview:**
Chu leads transformative research in radiology with a focus on leveraging artificial intelligence (AI) and advanced imaging to enhance early detection and precision diagnostics in pancreatic ductal adenocarcinoma (PDAC). Her work aims to reduce diagnostic delays and variability by developing and validating deep learning algorithms that augment radiologic interpretation across modalities such as MRI, conventional CT, and photon-counting CT. By automating tumor localization and integrating imaging biomarkers with clinical risk factors, Dr. Chu is building AI-driven workflows that support timely and accurate screening, especially in asymptomatic and high-risk populations.

A core strength of Chu's research lies in the integration of radiologic and molecular diagnostics to improve risk stratification and early detection. She is actively developing predictive models that combine imaging features with liquid biopsy data—including ctDNA, exosomes, and protein biomarkers—to detect PDAC at earlier, more treatable stages. Her exploration of next-generation imaging technologies and refined protocols further supports detection of small-volume lesions. By tailoring precision imaging strategies to individuals with genetic predispositions or chronic pancreatic conditions, Dr. Chu's work offers significant potential for collaborative efforts in building comprehensive, multimodal diagnostic platforms for PDAC.

**Areas of Potential Collaborative:**

1. AI-Augmented Imaging for PDAC Detection
    - Design and validation of deep learning algorithms to enhance detection sensitivity and specificity across MRI, conventional CT, and photon-counting CT modalities
    - Automation of tumor localization and risk stratification to reduce diagnostic delay and variability in radiologic interpretation
    - Development of AI-driven clinical workflows for PDAC screening in asymptomatic or at-risk cohorts
2. Imaging Biomarkers and Risk Stratification

- Identification and validation of quantitative imaging biomarkers to characterize tumor biology, assess disease stage, and monitor progression
- Integration of AI-generated imaging features with clinical risk factors and patient history to support personalized screening strategies

3. Multimodal Diagnostic Integration
   - Fusion of imaging data with liquid biopsy platforms, including circulating tumor DNA (ctDNA), exosomes, and protein biomarkers
   - Development of predictive diagnostic models combining radiologic and molecular insights to detect PDAC at earlier, more treatable stages
4. Photon-Counting CT and Advanced MRI Optimization
   - Exploration of next-generation imaging technologies to enhance spatial and contrast resolution in pancreatic tissue
   - Protocol refinement for optimized performance in early-stage and small-volume lesion detection
5. Targeted Screening in High-Risk Populations
   - Implementation of precision imaging tools tailored to individuals with familial PDAC syndromes, chronic pancreatitis, or other elevated-risk conditions
   - Use of AI to support screening decision support and reduce false positives in surveillance programs

**Selected Publications**

*Early detection of pancreatic cancer in the era of precision medicine*. Abdom Radiol (NY). 2024 Oct;49(10):3559-3573

*Advancements in early detection of pancreatic cancer: the role of artificial intelligence and novel imaging techniques*. Abdom Radiol (NY). 2025 Apr;50(4):1731-1743

*Radiomics machine learning algorithm facilitates detection of small pancreatic neuroendocrine tumors on CT*. Diagn Interv Imaging . 2025 Jan;106(1):28-40

*CT Radiomics-Based Preoperative Survival Prediction in Patients with Pancreatic Ductal Adenocarcinoma*. AJR Am J Roentgenol. 2021 Nov;217(5):1104-1112

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## Lei Zheng, MD, PhD

*Professor of Oncology and Surgery in the Gastrointestinal Oncology Program; Director of the Pancreatic Cancer Precision Medicine Center of Excellence; Director of the Multidisciplinary Hepato-Panreato-Biliary Research Laboratory*

*Enhancing Immunotherapy and Tumor Microenvironment Modulation in Pancreatic Ductal Adenocarcinoma*

**Overview:**

Zheng leads innovative research focused on overcoming the formidable immune resistance of pancreatic ductal adenocarcinoma (PDAC) by targeting its complex tumor microenvironment (TME). Utilizing cutting-edge preclinical models such as patient-derived xenografts, humanized mice, and single-cell transcriptomics, his work dissects immune-stromal interactions and develops novel immunotherapeutic strategies including checkpoint inhibitors, STING agonists, and engineered T cell therapies. Dr. Zheng's research also addresses stromal and immune cell

heterogeneity—particularly cancer-associated fibroblasts (CAF) and tumor-associated macrophages (TAM)—alongside mechanisms of metastasis driven by KRAS mutations and inflammatory pathways like the IL-8 axis. His expertise extends to epigenetic modulation and combinatorial approaches that enhance immune priming, such as TGF-β inhibition and radiation-immunotherapy synergy.

Zheng's comprehensive approach integrates immunotherapy development with precision oncology and translational multi-omics to advance biomarker-guided patient selection and therapeutic optimization. His work on reprogramming the TME leverages targeted inhibitors and receptor pathway modulation to enhance T-cell infiltration and treatment efficacy. Additionally, he models organ-specific metastasis and KRAS-driven pathways to identify molecular biomarkers predictive of disease progression. Through integrated RNA sequencing, spatial transcriptomics, and neoantigen discovery, Dr. Zheng builds platforms for biomarker validation and clinical trial stratification. His translational efforts support the design of neoadjuvant and adjuvant immunotherapy protocols, advancing early-phase clinical trials that bridge preclinical insights with patient care in PDAC.

**Areas of Potential Collaboration:**

1. Immunotherapy Development & Optimization
    - Design of novel immune-based combinations (e.g., anti-PD-1 + GVAX + CD137 agonists)
    - Development of BiTEs and engineered TCR therapies for low-antigen-density tumors
    - Systemic delivery platforms for innate immune agonists such as STING and TLR ligands
2. Tumor Microenvironment (TME) Modulation
    - CAF and TAM reprogramming strategies using TGF-β traps, GARP inhibitors, or epigenetic agents
    - CCR2/CCR5 pathway targeting to enhance T-cell infiltration and radiation response
    - Preclinical modeling of stromal remodeling therapies using GEMMs and co-culture systems
3. Metastasis and Precision Oncology
    - Organo-specific metastasis modeling, including liver- and lung-tropic PDAC
    - KRAS-targeted interventions and inflammation-driven pathways (e.g., IL-8 axis)
    - Development of molecular biomarkers for predicting and monitoring metastatic progression
4. Translational Multi-Omics Platforms
    - Neoantigen discovery through integrated RNA-seq, DNA methylation, and mass spectrometry pipelines
    - Single-cell and spatial transcriptomics to map tumor-stroma-immune interactions
    - Biomarker discovery pipelines to support clinical trial stratification and response tracking
5. Clinical Trial Infrastructure
    - Neoadjuvant and adjuvant immunotherapy protocols in resectable PDAC
    - Validation of immune-stromal biomarkers in human biospecimens
    - Integration of preclinical findings into early-phase trial designs

**Selected Publications**

*The impact of KRAS mutations on the clinical outcome and immune response following immunotherapy for pancreatic cancer*. Ann Pancreat Cancer 2024;7 1-9
*CLDN18.2 BiTE Engages Effector and Regulatory T Cells for Antitumor Immune Response in Preclinical Models of Pancreatic Cancer*. Gastroenterology. 2023 Nov;165(5):1219-1232
*Cancer-associated fibroblast heterogeneity is associated with organ-specific metastasis in pancreatic ductal adenocarcinoma*. J Hematol Oncol. 2021 Nov 2;14(1):184
*Neoadjuvant radioimmunotherapy in pancreatic cancer enhances effector T cell infiltration and shortens their distances to tumor cells*. Sci. Adv.10,eadk1827(2024)

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## Ralph Hruban, MD

*Baxley Professor of Pathology; Director of the Sol Goldman Pancreatic Cancer Research Center; Director, Department of Pathology*

*Transforming Early Detection and Molecular Stratification in Pancreatic Cancer: A Genomics-Driven Precision Approach*

**Overview:**

Hruban's research centers on unraveling the genetic and histological basis of pancreatic cancer, with a strong emphasis on early detection, risk stratification, and molecular diagnostics. His work highlights the critical role of precursor lesions—particularly intraductal papillary mucinous neoplasms (IPMNs)—in the progression to pancreatic ductal adenocarcinoma (PDAC), especially among individuals with familial or germline mutations (e.g., *BRCA*, *CDKN2A*).
By integrating pathology with large-scale genomic data from initiatives like TCGA and ICGC, Hruban's research provides a foundation for translational efforts aimed at catching PDAC early, when it is still potentially curable. He is also advancing the evaluation and development of biomarkers, including circulating tumor DNA (ctDNA) and liquid biopsy platforms, to increase diagnostic accuracy and guide clinical decision-making.

**Areas of Potential Collaboration:**

1. Molecular Diagnostics Development
    - Design and validation of assays to detect high-risk precursor lesions.
    - Integration of genomic, proteomic, and imaging data for early PDAC detection.
2. Genetic Risk Stratification
    - Development of tools that combine germline mutation profiles and familial history for targeted screening.
    - Implementation of precision oncology workflows for high-risk cohorts.
3. Biomarker Discovery and Validation
    - Exploration of novel biomarkers (e.g., ctDNA, proteomic signatures) to enhance or replace CA19.9.
    - Clinical validation of biomarker panels in real-world settings.
4. Target Discovery and Functional Genomics
    - Identification and validation of therapeutic targets from somatic mutation data.
    - Use of TCGA/ICGC data to guide translational studies and preclinical modeling.
5. Scalable Early Detection Frameworks

- Development of liquid biopsy-based screening programs deployable in both academic and community health settings.
- Partnerships for implementing and assessing new detection technologies at scale.

**Selected Publications**

*Precursor lesions in familial and hereditary pancreatic cancer*. Familial Cancer (2024) 23:267–278
*Screening for pancreatic cancer has the potential to save lives, but is it practical?* Expert Rev Gastroenterol Hepatol. 2023 Jan-Jun;17(6):555-574
*The genetics of ductal adenocarcinoma of the pancreas in the year 2020: dramatic progress, but far to go*. Mod Pathol. 2020 Dec;33(12):2544-2563
*Tissue clearing and 3D reconstruction of digitized, serially sectioned slides provide novel insights into pancreatic cancer*. Med. 2023 Feb 10;4(2):75-91
*Pathology of intraductal papillary mucinous neoplasms*. Langenbecks Arch Surg. 2021 Dec;406(8):2643-2655