OK Symposium on Pancreatic Cancer Cachexia

Hosted By

OU Health | Stephenson Cancer Center
The UNIVERSITY of OKLAHOMA

May 15 & 16, 2026

Colcord Hotel – Oklahoma City

WELCOME LETTER

Dear Speakers, Faculties, Scientists, Students, Fellows, Cancer Survivors, Patient Advocates, Educators and Heroes fighting against pancreatic cancer, the symposium organizing committee on behalf of the OU Health Campus is extremely thrilled to welcome you all to the second "OK Symposium on Pancreatic Cancer Cachexia" being held at the Colcord Hotel, Oklahoma City, OK from May 15 to 16, 2026.

This multi-disciplinary two-day conference is carefully planned and will host keynote, plenary and invited lectures by eminent scientists who will discuss under organized thematic sessions new and emerging concepts, and treatment pancreatic cancer cachexia. The purpose of this symposium is to advance our understanding of the basis of pancreatic cancer cachexia and enhance research collaborations on pancreatic cancer.

The conference organizing committee sincerely appreciates and thanks the Presbyterian Health Foundation (PHF), OU Health Stephenson Cancer Center (SCC), and the College of Medicine (COM) at OU Health Campus for their support in hosting the symposium.

We look forward to welcoming you all to the incredible "Sooner" state of Oklahoma and participating in this exciting conference.

Sincerely,

Min Li, PhD
George Lynn Cross Research Professor of Medicine, Surgery, and Cell Biology
Virginia Kerley Cade Endowed Chair in Cancer Treatment
Assistant Dean for International Research Collaboration, College of Medicine
Vice Chair for Research, Department of Medicine
Associate Director for Global Oncology, Stephenson Cancer Center
Co-Leader, Cancer Biology Program, Stephenson Cancer Center
The University of Oklahoma Health Campus

OK Symposium on Pancreatic Cancer Cachexia

May 15–16, 2026, Oklahoma City, OK

Organizing Committee

Conference Chairman

Min Li	Professor, Department of Medicine/Surgery, OU Health Campus

Co-Chairs

Barish Edil	Professor and Chair, Department of Surgery, OU Health Campus
Pankaj Singh	Professor and Chair, Dept of Oncology Sci, OU Health Campus
Ryan Nipp	Associate Professor, Department of Medicine, OU Health Campus

Planning Committee

Courtney Houchen	Professor, Department of Medicine, OU Health Campus
Danny Dhanasekaran	Professor, Department of Cell Biology, OU Health Campus
Rajagopal Ramesh	Professor, Department of Pathology, OU Health Campus
Priyabrata Mukherjee	Professor, Department of Pathology, OU Health Campus
Chinthalapally. V. Rao	Professor, Department of Medicine, OU Health Campus
Kamiya Mehla	Associate Professor, Dept of Oncology Sci, OU Health Campus
Laura Fischer	Associate Professor, Department of Surgery, OU Health Campus
Sue Bodine	Member, Aging & Metabolism Research Program, OMRF
Wei Chen	Professor and Chair, Sch of Biomedical Engineering, OU Norman
Jingxuan Yang	Associate Professor, Department of Medicine, OU Health Campus
Yuqing Zhang	Associate Professor, Department of Medicine, OU Health Campus
Elizabeth Hile	Associate Professor, College of Allied Health, OU Health Campus
Jamie Hur	Assistant Professor, Department of Medicine, OU Health Campus

OK SYMPOSIUM ON PANCREATIC CANCER CACHEXIA

MAY 15-16, 2026 | COLCORD HOTEL

FRIDAY, MAY 15, 2026

7:30 AM – 8:30 AM	**Registration and Breakfast**
8:30 am – 8:55 am	**Welcome Address**
9:00 am – 9:45 am	**Keynote Speech**
9:45 am – 10:45 am	**Session 1**
10:45 am – 11:00 am	**Coffee Break**
11:00 am – 12:00 pm	**Session 2**
12:00 pm – 1:00 pm	**Lunch Break**
1:00 pm – 1:45 pm	**Keynote Speech**
1:45 pm – 2:45 pm	**Session 3**
2:45 pm – 3:00 pm	**Coffee Break**
3:00 pm – 4:40 pm	**Session 4**
4:45 pm – 5:00 pm	**Closing Remarks**

SATURDAY, MAY 16, 2026

7:30 AM – 8:30 AM	**Registration and Breakfast**
8:30 am – 9:30 am	**Session 5**
9:30 am – 9:50 am	**Coffee Break**
9:50 am – 10:50 am	**Session 6**
11:00 am – 11:15 am	**Closing Remarks**

OK SYMPOSIUM ON PANCREATIC CANCER CACHEXIA

MAY 15-16, 2026 | COLCORD HOTEL

FRIDAY, MAY 15, 2026

7:30 AM – 8:30 AM	Registration and Breakfast

OPENING CEREMONY AND WELCOME ADDRESS

8:30 am – 8:40 am	**Min Li, PhD** *Introduction*
8:40 am – 8:45 am	**Gary Raskob, PhD** *Welcome*
8:45 am – 8:50 am	**Robert Mannel, MD**
8:50 am – 8:55 am	**Michael Bronze, MD**

KEYNOTE SPEECH

Moderator: Ashok K. Saluja, PhD

9:00 am – 9:45 am	**Christopher Wolfgang, MD, PhD** *We Will Water the Thorn for the Sake of the Rose: The Interplay of Cachexia and Treatment of Pancreatic Cancer*

SESSION 1

Moderators: Ashok K. Saluja, PhD and Pankaj Singh, PhD

9:45 am – 10:05 am	Plenary Speaker: **Xiling Shen, PhD** *Targeting the Gut-Brain Neuroinflammatory Axis to Combat Cachexia in Pancreatic Cancer*
10:05 am – 10:25 am	**Jose Trevino, MD** *Beyond Weight Loss: The intersection of Cardiac Cachexia, Dysfunction and Pancreatic Adenocarcinoma*
10:25 am – 10:45 am	**Ashok Kumar, PhD** *From ER Stress to Muscle Loss: The IRE1α-XBP1 Pathway in Pancreatic Cancer Cachexia*
10:45 am – 11:00 am	Coffee Break

SESSION 2

Moderators: Christopher Wolfgang, MD, PhD and Michael Bronze, MD

11:00 am – 11:20 am	Plenary Speaker: **Andy Judge, PhD** *Role of the complement system in pancreatic cancer cachexia*
11:20 am – 11:40 am	**Surinder Batra, PhD**

	OncoMucin MUC16-mediated mechanisms and therapy for cancer-associated cachexia in pancreatic cancer
11:40 am – 12:00 pm	**Min Li, PhD** *Pancreatic Cancer Cachexia: Rethink the Biology, Rebuild the Body*
12:00 pm – 1:00 pm	Lunch Break

KEYNOTE SPEECH

Moderator: Min Li, PhD

1:00 pm – 1:45 pm	**Jose Garcia, MD, PhD** *Restoring What Matters: Translational Strategies in Cancer Cachexia*

SESSION 3

Moderators: Surinder Batra, PhD and Yuqing Zhang, PhD

1:45 pm – 2:05 pm	Plenary Speaker: **Yi-Ping Li, PhD** *Neutralizing Circulating Hsp70 and Hsp90 Mitigates Cachexia in a PDX-derived Pancreatic Cancer Model*
2:05 pm – 2:25 pm	**Surendra Shukla, PhD** *Role of Muscle Glucose Homeostasis in Pancreatic Cancer-Associated Cachexia*
2:25 pm – 2:45 pm	**Prasenjit Dey, PhD** *Pancreatic steatosis drives neurogenesis and pancreatic cancer*
2:45 pm – 3:00 pm	Coffee Break

SESSION 4

Moderators: Xiling Shen, PhD, Ryan D. Nipp, MD, MPH, MBA, FASCO, and Jamie Hur, DO

3:00 pm – 3:20 pm	Plenary Speaker: **Sue Bodine, PhD** *The impact of age on skeletal muscle atrophy and its treatment*
3:20 pm – 3:40 pm	**Lu Han, PhD** *Persistence of the fetal splanchnic program in pancreatic cancer associated fibroblasts*
3:40 pm – 4:00 pm	**Jason Pitarresi, PhD** *Pancreatic cancer cachexia is mediated by PTHrP-driven disruption of adipose de novo lipogenesis*
4:00 pm – 4:20 pm	**Kamiya Mehla, PhD** *Novel Regulators of Muscle Wasting in Cancer Cachexia*
4:20 pm – 4:40 pm	**Jie Wu, PhD** *Mitigating Cancer-associated Anorexia and Cachexia with Selpercatinib*

CLOSING REMARKS

4:45 pm	**Ryan D. Nipp, MD, MPH, MBA, FASCO**

SATURDAY, MAY 16, 2026

7:30 AM – 8:30 AM	Registration and Breakfast

SESSION 5

Moderators: Barish Edil, MD, FACS and Kamiya Mehla, PhD

8:30 am – 8:50 am	Plenary Speaker: **Lei Zheng, MD, PhD** *Macrophages: a major player in the inflammation, metabolism, and antitumor immune response in pancreatic cancer*
8:50 am – 9:10 am	**Ram V. Roy, PhD** *UBAP2 acts as scaffolds between RAC and WAVE in the regulation of membrane ruffling*
9:10 am – 9:30 am	**Wei R. Chen, PhD** *Nano-photo-immunotherapy for pancreatic cancer*
9:30 am – 9:50 am	Coffee Break

SESSION 6

Moderators: Lu Han, and PhD, Jingxuan Yang, PhD

9:50 am – 10:10 am	Plenary Speaker: **Christine Chio, PhD** *An Iron-Methionine Redox Axis Drives Adipose Remodeling in Pancreatic Cancer Cachexia*
10:10 am – 10:30 am	**Pankaj Singh, PhD** *Talk Title TBD*
10:30 am – 10:50 am	**Alex Arreola, PhD Candidate** *Tumor-Immune-Neural Circuit Disrupts Energy Homeostasis in Cancer Cachexia*

CLOSING REMARKS

11:00 am – 11:15 am	**Min Li, PhD and Barish Edil, MD, FACS**

Thank you to our Moderators

Ashok K. Saluja, PhD

Professor, Department of Surgery

University of Miami

Min Li, PhD

Professor

OU Health Campus

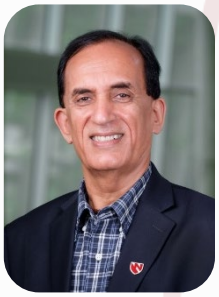
Pankaj Singh, PhD

Professor and Chair, Dept of Oncology Sci

OU Health Campus

Christopher L. Wolfgang, MD, PhD, FACS

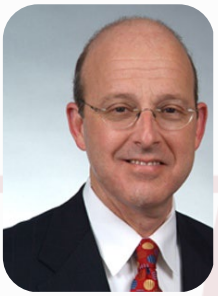
Professor and Chief, NYU; President-Elect, American Pancreatic Association



Surinder Batra, PhD

Professor and Chair

University of Nebraska



Michael Bronze, MD

Associate Dean, COM

OU Health Campus

Ryan Nipp, MD, MPH, MBA, FASCO

Associate Professor and Chair

OU Health Campus

Xiling Shen, PhD

Professor

MD Anderson Cancer Center

Barish H. Edil, MD, FACS

Professor and Chair of Surgery

OU Health Campus

Lu Han, PhD

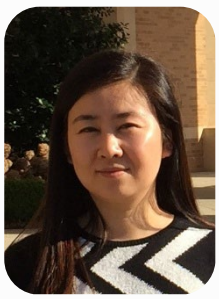
Assistant Professor

Medical University of South Carolina

Kamiya Mehla, PhD

Associate Professor

OU Health Campus



Yuqing Zhang, PhD

Associate Professor

Department of Medicine at the OU Health Campus

Jamie Hur, DO

Associate Professor

OU Health Campus

Jingxuan Yang, PhD

Associate Professor

OU Health Campus

Welcome Address

Min Li, PhD

Professor

OU Health Campus

Gary Raskob, PhD

Provost

OU Health Campus

Robert Mannel, MD

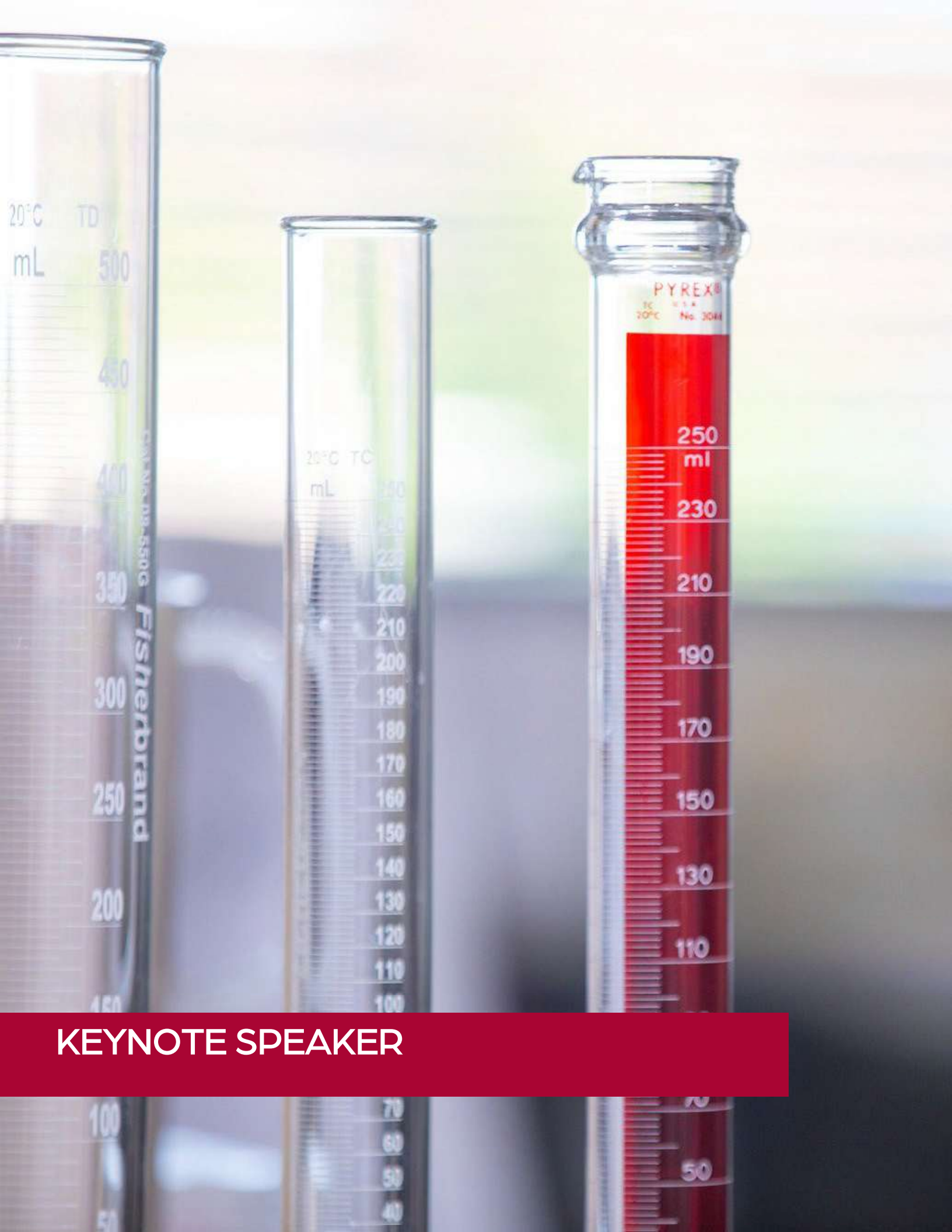
Director

Stephenson Cancer Center

Michael Bronze, MD

Associate Dean, COM

OU Health Campus


KEYNOTE SPEAKER

KEYNOTE

Christopher Wolfgang, MD, PhD

Professor and Chief, NYU; President-Elect, American Pancreatic Association

New York University

Christopher L. Wolfgang, MD, PhD, is the Chief of the Division of Hepatobiliary and Pancreatic Surgery and Vice Chair for Clinical Affairs, Department of Surgery at NYU Langone Health, and serves as the S. Arthur Localio Professor of Surgery and Oncology at the NYU Grossman School of Medicine. He is an internationally recognized leader in hepatobiliary and pancreatic surgery, with particular expertise in the multidisciplinary management of complex diseases of the pancreas including pancreatic ductal adenocarcinoma and cystic neoplasms of the pancreas. Dr. Wolfgang is widely regarded for advancing surgical strategies that expand the safe resection of locally advanced pancreatic cancers involving major vascular structures.

In addition to his clinical leadership, Dr. Wolfgang is a distinguished surgeon-scientist whose research focuses on the biology of pancreatic cancer including circulating tumor cells, minimal residual disease, biomarkers of recurrence, and mechanisms of treatment resistance following resection. His work has helped shape modern approaches to precision cancer care and postoperative surveillance in pancreatic malignancies. Dr. Wolfgang has authored more than 700 peer-reviewed publications, book chapters, and invited reviews in many of the world's leading surgical and oncology journals. He is a frequently invited speaker at national and international meetings and has played a prominent role in shaping contemporary standards in pancreatic cancer surgery and multidisciplinary cancer care. He is a member of all major surgical societies and is one of the directors of the Pancreas Club.

Prior to joining NYU Langone, Dr. Wolfgang held senior leadership positions at Johns Hopkins Medicine, where he helped build one of the nation's premier pancreatic cancer programs. Today, he continues to be recognized as one of the foremost authorities in hepatobiliary and pancreatic surgery, combining innovative research, exceptional clinical outcomes, and dedication to surgical education.

SESSION I

OK SYMPOSIUM ON PANCREATIC CANCER CACHEXIA

FRIDAY, MAY 15, 2026

SESSION 1

Moderators: Ashok K. Saluja, PhD and Pankaj Singh, PhD

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10:45 am – 11:00 am	Coffee Break

PLENARY

Xiling Shen, PhD

Professor

MD Anderson Cancer Center

Dr. Shen is a Professor and CPRIT Scholar in GI Medical Oncology and Co-Director of the CRC Moonshot at MD Anderson Cancer Center. He earned his BS, MS, and PhD from Stanford University and received the NSF Faculty CAREER Award while at Cornell University. He serves on the editorial board of the NIH Director's New Innovator Award (DP2) program and has previously served as a Steering Committee Chair for both the NCI Patient-Derived Models of Cancer Consortium and the Tissue Engineering Collaborative. He also served as Cancer Track Chair of Biomedical Engineering Society Meeting as well as Director of the Woo Center for Big Data and Precision Health at Duke University. Dr. Shen has founded multiple biotechnology startups that have translated discoveries from his laboratory into ongoing clinical trials. His research focuses on cancer biology, stem cells, precision therapeutics, and the gut–brain axis.

Targeting the Gut-Brain Neuroinflammatory Axis to Combat Cachexia in Pancreatic Cancer

Cachexia is an incurable, multifactorial syndrome that is highly prevalent in patients with pancreatic cancer. Traditionally viewed as a nutritional disorder, emerging evidence highlights a critical role for the neuroinflammatory axis in its pathogenesis. We discovered that cancer-induced neuroinflammation profoundly alters specific brain regions and disrupts the liver–brain vagal axis, leading to a rewiring of hepatic protein metabolism and acute-phase inflammatory response. Targeting this neuroinflammatory axis mitigates cachexia progression, alleviates key clinical manifestations, and synergizes with chemotherapy to improve overall well-being and survival.

Jose Trevino, MD

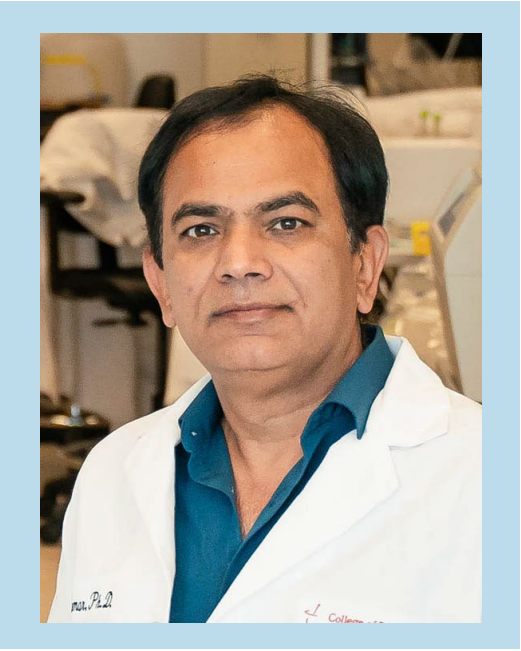
Professor and Chair

Virginia Commonwealth University

Dr. Trevino is presently a tenured Professor in the Department of Surgery. He has a significant published record of accomplishment and academic success in basic/translational and clinical research in cancer. His work has allowed for strong collaborations with top investigators in the country resulting in successful NIH and Foundation grant applications in discovery of new targetable proteins contributing to pancreatic cancer tumor progression. With his successes and national reputation as a clinical surgeon and investigator, he has established work with international groups on pancreatic cancer and has significant efforts on various NIH funded proposals including numerous R01s, R44, U54 and significant foundation awards and Department of Health extramural research grants. Along with his success in R01 submissions, Dr. Trevino the co-PI on a funded grant to develop the first state- wide academic cancer center collaborative dedicated to promoting the early detection and prevention of pancreatic cancer as well as corresponding PI on a NIH/NCI funded U54 mechanism reinforcing his passion for team science. This collaborative highlights his leadership experience in running large-scale, multi-institutional studies. His research interests have led to a fully funded laboratory with a sustained research program focusing on pancreatic carcinogenesis and patient-specific tumor-stromal interactions which affect skeletal muscle atrophy. He has also determined a significant pancreatic health disparity and determined possible initiating mechanisms of cancer cachexia as well as molecular differences amongst underserved populations. His leadership skills, work and laboratory efforts have translated my work directly into novel therapeutic clinical trials, high impact peer-reviewed publications increasing h-index to 47 and rising, national and international presentations, and more than 50 invited speaker engagements at academic institutions across the country. His is a leader and chairperson for regional, national, and international organizations, am on numerous editorial boards and associate editor for academic journals and also a standing member for the National Institute of Health (NIH/NCI) Study Section ATA.

Beyond Weight Loss: The intersection of Cardiac Cachexia, Dysfunction and Pancreatic Adenocarcinoma

Pre-existing cardiac disease is associated with worse overall survival in pancreatic adenocarcinoma patients (PDAC). Patients with PDAC experience significantly lower cardiac-specific median survival compared to those with other GI cancers. While cancer cachexia is known to impact survival through skeletal muscle loss, the contribution of cardiac function to clinical outcomes in PDAC is currently unknown. Data from our group evaluating cardiac status in patients with PDAC before and after initiation of neoadjuvant therapy demonstrate aortic and cardiac abnormalities at baseline, with evidence of significant worsening over time when compared to controls. To further characterize these findings, our studies in cardiac tissue structure and function where defined in the most representative human preclinical model where patient derived tumors where implanted in xenograft models and cardiac structure and function were assessed. We determine that early cardiac dysfunction is a strong possibility in PDAC patients and preclinical models will provide insight into cardiac remodeling associated with PDAC and its clinical implication for possible interventions to improve overall survival.



Ashok Kumar, PhD

Professor

Institute of Muscle Biology and Cachexia

University of Houston

Dr. Ashok Kumar is the Founding Director of the Institute of Muscle Biology and Cachexia (IMBC) at the University of Houston, where he also holds the Else and Philip Hargrove Endowed Professorship in Drug Discovery. Until recently, he served as Chair of the Department of Pharmacological and Pharmaceutical Sciences. Prior to joining the University of Houston in 2019, he was a Professor and Distinguished University Scholar at the University of Louisville School of Medicine.

Dr. Kumar's research focuses on elucidating the molecular and signaling mechanisms that regulate skeletal muscle mass under both physiological and pathological conditions, including cancer-associated cachexia. His work also investigates the signaling pathways that control tumorigenesis and progression of pediatric rhabdomyosarcoma.

Among his major contributions is the identification and characterization of TWEAK as a key cytokine driving muscle wasting. His laboratory has also defined critical roles for signaling molecules such as TRAF6, TAK1, and MyD88 in regulating skeletal muscle mass and muscle stem cell function.

Dr. Kumar has mentored more than 45 graduate students and postdoctoral fellows and has published over 125 peer-reviewed articles in leading journals, including *Nature Communications*, *Journal of Clinical Investigation*, *Cell Reports Medicine*, *Journal of Cell Biology*, *EMBO Reports*, *EMBO Molecular Medicine*, *JCI Insight*, *Molecular and Cellular Biology*, *eLife*, and *Science Signaling*. He serves as a frequent reviewer for more than 70 scientific journals and numerous international funding agencies. His research program has been continuously supported by multiple NIH R01 grants and other funding sources.

From ER Stress to Muscle Loss: The IRE1α-XBP1 Pathway in Pancreatic Cancer Cachexia

Cancer cachexia is a debilitating syndrome characterized by progressive loss of skeletal muscle mass, with or without accompanying fat loss. Emerging evidence implicates dysregulation of endoplasmic reticulum (ER) stress-induced unfolded protein response (UPR) pathways in skeletal muscle under various conditions, including cancer-associated cachexia. However, the specific contribution of the UPR to cancer-induced muscle wasting remains poorly defined.
Our recent studies demonstrate that multiple UPR markers are markedly upregulated across several preclinical models of cancer cachexia. Notably, the inositol-requiring enzyme 1α (IRE1α)/X-box binding protein 1 (XBP1) branch of the UPR is selectively activated in skeletal muscle in the KPC mouse model of pancreatic cancer cachexia and serves as a key driver of muscle wasting. Skeletal muscle-specific deletion of the XBP1 transcription factor significantly attenuates tumor-induced muscle atrophy. The IRE1α-XBP1 axis promotes activation of major proteolytic systems, including the ubiquitin-proteasome pathway and autophagy, enhances JAK-STAT3 signaling, and increases fatty acid oxidation. Transcriptionally active spliced XBP1 protein directly binds to promoter regions of genes encoding proteins that drive muscle proteolysis. Importantly, pharmacological inhibition of IRE1α using a small molecule mitigates cachexia-associated molecular alterations and improves muscle mass and strength in KPC tumor-bearing mice. Collectively, these findings identify the IRE1α-XBP1 pathway as a central regulator of cancer cachexia and support its therapeutic targeting to counteract muscle wasting.

Funding support: This work was supported by NIH funding AR081487 to AK.

SESSION II

OK SYMPOSIUM ON PANCREATIC CANCER CACHEXIA

FRIDAY, MAY 15, 2026

SESSION 2

Moderators: Christopher Wolfgang, MD, PhD and Michael Bronze, MD

11:00 am – 11:20 am	Plenary Speaker: **Andy Judge, PhD** *Role of the complement system in pancreatic cancer cachexia*
11:20 am – 11:40 am	**Surinder Batra, PhD** *OncoMucin MUC16-mediated mechanisms and therapy for cancer-associated cachexia in pancreatic cancer*
11:40 am – 12:00 pm	**Min Li, PhD** *Pancreatic Cancer Cachexia: Rethink the Biology, Rebuild the Body*
12:00 pm – 1:00 pm	Lunch Break

PLENARY

Andy Judge, PhD

Professor

University of Florida

Andy Judge is a Professor in the Department of Physical Therapy, and Director of the Rehabilitation Sciences PhD Program, at the University of Florida. His research is focused on cancer-induced skeletal muscle pathologies, which he studies through patient-derived muscle biopsies and pre-clinical models.

Role of the complement system in pancreatic cancer cachexia

Cancer cachexia is a multifactorial condition characterized by skeletal muscle wasting that impairs quality of life and longevity for many cancer patients. A greater understanding of the molecular etiology of this condition is needed for effective therapies to be developed. We previously performed a quantitative proteomic analysis of skeletal muscle from cachectic pancreatic ductal adenocarcinoma (PDAC) patients and non-cancer controls, followed by immunohistochemical analyses of muscle cross-sections. These data provide evidence of a local inflammatory response in muscles of cachectic PDAC patients, including an accumulation of plasma proteins and recruitment of immune cells into muscle that may promote the pathological remodeling of muscle. Our data further support the complement system as a potential mediator of these processes, which we are testing by injecting murine pancreatic cancer cells into wild type (WT) mice, or mice with genetic deletion of various complement components.

Surinder Batra, PhD

Professor and Chair

University of Nebraska

Dr. Surinder Kumar Batra has built a distinguished career as a leader in cancer biology and translational research. As Professor and Chair of the Department of Biochemistry and Molecular Biology at the University of Nebraska Medical Center, he has also held multiple cross-disciplinary professorships spanning pathology, pediatrics, and urology. His leadership roles extend to serving as Associate Director of Translational Research at the Fred and Pamela Buffett Cancer Center, reflecting his central role in advancing collaborative, bench-to-bedside cancer research initiatives. A hallmark of Dr. Batra's career is his sustained success in securing major extramural funding and leading large, multi-institutional research efforts. He has served as principal investigator or co-principal investigator on numerous NIH R01, P01, SPORE, U54, and U01grants, many of which are focused on pancreatic cancer biology, early detection, and therapeutic development. His work has contributed significantly to understanding tumor microenvironment interactions, biomarker development, and novel treatment strategies, including imaging probes and nanotherapeutics. His long-standing involvement in national research consortia highlights both the impact and recognition of his scientific contributions.

OncoMucin MUC16-mediated mechanisms and therapy for cancer-associated cachexia in pancreatic cancer

The oncomucin MUC16 is a high-molecular-weight transmembrane glycoprotein that plays a role in the progression and metastasis of pancreatic cancer (PC). (i) Depletion of MUC16 significantly decreased the metabolomic genes, including GDF15, a cachexia gene. (ii) MUC16 and GDF15 correlated their expression in PC and metastatic tumors. (iii) MUC16 KO-KPC animals showed increased body weight compared to KPC. (iv) MUC16 and GDF15 play a major role in the survival of PC patients. (v) Loss of Muc16 reduces GDF15 PC progression, decreases tumor weight, and increases mouse survival. (vi) MUC16 reduces the Runx1, a transcription factor for the GDF15 and Runx1 silencing decreased the GDF15 level. (vii) MUC16-mediated muscle atrophy in human and mouse skeletal muscle cells. (viii) MUC16-mediated lipolysis in human and mouse adipocytes. (ix) Targeting MUC16 using a chimeric antibody decreases the PC organoid growth and tumor burden. Overall, these preliminary observations support the hypothesis that MUC16-induced GDF15 promotes muscle atrophy and adipose browning, leading to cancer-associated cachexia in PC; thereby, targeting MUC16 will reduce metastasis and cachexia.

Min Li, PhD

Professor

University of Oklahoma Health Campus

Dr. Min Li is George Lynn Cross Research Professor of Medicine, Surgery, and Cell Biology at The University of Oklahoma Health Campus and holds the Virginia Kerley Cade Endowed Chair in Cancer Treatment. He is the Assistant Dean for International Research Collaboration at College of Medicine, and Associate Director for Global Oncology at the NCI designated Stephenson Cancer Center (SCC). He is the Vice Chair for Research at the Department of Medicine, and Co-Leader of Cancer Biology Program of SCC at OUHealth. He is a leading expert on pancreatic cancer (PC), and his research mainly focus on studying PC pathogenesis and developing new therapies. Dr. Li's group is the first to identify a key zinc transporter ZIP4, which is aberrantly expressed in PC, and promotes cancer growth, drug resistance, muscle wasting, cachexia, and metastasis. Current projects in his laboratory include the role of ZIP4 in PC progression and pathogenesis, the therapeutic potential for ZIP4 silencing, the function of microRNAs in tumor growth, signaling transduction and metabolism in PC, and cancer cachexia. He has published more than 200 papers on high impact journals such as Cancer Cell, PNAS, EMBO Mol Med, Nature, Nature Communications, Gastroenterology, Can Res, Clin Can Res, etc., and has three active NIH/NCI R01 grants, and multiple private foundation grants.

Dr. Li is a member of many NIH study sections, such as Developmental Therapeutics (DT), Cancer Etiology (CE), Basic Mechanism of Cancer Therapy (BMCT), Clinical Oncology (CONC), Mouse Model of Translational Cancer Research (MMTR), GI SPORE, Omnibus R21, DoD Cancer Research Program, AACR Pancreatic cancer action network (PanCAN), French NCI, Austrian Science Fund, Prostate Cancer UK, etc. He also serves as the Editor-in-Chief of Cancer Letters, and Senior Editor and editorial board member for many prestigious journals such as Clin Can Res and BMC Medicine. Dr. Li holds many important administrative positions at OU Health, and he serve on multiple committees locally, nationally, and internationally. Dr. Li is past President of American Pancreatic Association (APA), and the President-Elect of the International Association for Pancreatology (IAP). He received many awards such as the Palade Award of IAP, and

Pancreatic Cancer Cachexia: Rethink the Biology, Rebuild the Body

Cancer-induced cachexia and anorexia are debilitating complications across many cancers, yet effective treatments remain limited due to a poor understanding of the underlying mechanisms. Here, we identify an uncharacterized tumor-immune-neural circuit driving these syndromes, centered on growth and differentiation factor 15 (GDF15). Using genetically engineered mouse models, we find that loss of GDF15 protects against appetite loss, muscle wasting, and fat loss in pancreatic, lung, and skin cancers. Single-cell RNA sequencing reveals macrophages as a major source of GDF15, induced by tumor-derived colony stimulating factor 1 (CSF1). GDF15 acts via the central nervous system to enhance β-adrenergic signaling in the tumor microenvironment, thereby amplifying cachexia. Disruption of this feedforward loop with GDF15-neutralizing antibody, anti-CSF1R antibody, or Rearranged during Transfection (RET) inhibitor markedly reduces both cachexia and anorexia. These findings reveal a non-cell-autonomous mechanism linking tumor signals, macrophage-derived GDF15, and neural pathways, highlighting the tumor-immune-neural triad as a promising therapeutic target. Emerging evidence indicates that cachexia arises from complex and dynamic interactions between tumors and host organ systems, including immune, metabolic, endocrine, and neural networks, that collectively reshape energy balance, immune function, and tissue integrity. We propose a tumor-centric framework in which cachexia represents a progressive collapse of systemic homeostasis and outline translational strategies to guide mechanism-informed therapeutic interventions.

KEYNOTE SPEAKER

KEYNOTE

Jose Garcia, MD, PhD

Professor, University of Washington

President, Cancer Cachexia Society

Dr. Jose M. Garcia, M.D., Ph.D., is a Physician-Scientist at the Puget Sound VA Health Care System and a Professor of Medicine in the Division of Geriatrics at the University of Washington in Seattle, WA, USA. He is also the Director of the Clinical Research Unit and the Director of the Geriatric Research Education and Clinical Center at the Puget Sound VA Health Care System. His current research focuses on the role of ghrelin, androgens, and other anabolic pathways in different wasting conditions including sarcopenia of aging and cancer cachexia. His basic laboratory is focused on understanding the molecular underpinnings of muscle wasting, fat atrophy, and anorexia in these settings, and the development of novel targets for these conditions. His group also participates in several human trials in patients with cancer aiming at characterizing the pathways involved, identifying the mechanisms of action of different potential therapies, and testing them in multicenter trials. He also serves as the President of the Cancer Cachexia Society.

Restoring What Matters: Translational Strategies in Cancer Cachexia

Cancer cachexia is a multifactorial metabolic syndrome marked by progressive loss of muscle and fat mass, impaired physical function, and poor quality of life. To this date, effective therapies remain limited, in part because traditional clinical and biological endpoints do not fully capture outcomes that are considered clinically meaningful. Increasingly, research has highlighted that weight and lean mass alone are insufficient surrogates for functional health, treatment tolerance, and well-being.

This presentation will examine emerging translational research in cancer cachexia through the lens of restoring function and other patient-centered outcomes. Human studies integrating proteomic and metabolic profiling, body composition, and objective measures of physical performance reveal that cachexia is characterized by distinct and heterogeneous alterations in muscle and adipose tissue metabolism. Importantly, pathways associated with physical function appear partially distinct from those linked to weight loss or muscle mass, underscoring the need to target function explicitly as a therapeutic goal.

The talk will also review current and emerging pharmacologic and multimodal approaches, emphasizing why single-agent strategies have yielded limited success and how combination therapies may better address the complex biology of cachexia. Finally, the presentation will discuss practical implications for clinical trial design, including the selection of meaningful endpoints and biomarkers that reflect what patients experience and value.

By bridging mechanistic insight with clinical relevance, this talk aims to reframe cancer cachexia treatment toward restoring what matters most to patients: physical function, independence, and quality of life.

SESSION III

OK SYMPOSIUM ON PANCREATIC CANCER CACHEXIA

FRIDAY, MAY 15, 2026

SESSION 3

Moderators: Surinder Batra, PhD and Yuqing Zhang, PhD

1:45 pm – 2:05 pm	Plenary Speaker: **Yi-Ping Li, PhD** *Neutralizing Circulating Hsp70 and Hsp90 Mitigates Cachexia in a PDX-derived Pancreatic Cancer Model*
2:05 pm – 2:25 pm	**Surendra Shukla, PhD** *Role of Muscle Glucose Homeostasis in Pancreatic Cancer-Associated Cachexia*
2:25 pm – 2:45 pm	**Prasenjit Dey, PhD** *Pancreatic steatosis drives neurogenesis and pancreatic cancer*
2:45 pm – 3:00 pm	Coffee Break

PLENARY

Yi-Ping Li, PhD

Professor

UTHealth

Dr. Yi-Ping Li is a Professor in the Dept of Integrative Biology and Pharmacology at the University of Texas Health Science Center at Houston. He received his Ph.D. degree, postdoctoral training, and academic ranks all in Texas. He has specialized in the molecular mechanisms of striated muscle remodeling associated with disease or injury, particularly muscle wasting in cancer cachexia. With continuous support from the NIH over the past two decades, his research team has identified cancer cell-released extracellular Hsp70 and Hsp90 (eHsp70 and eHsp90) as key mediators of cancer-induced muscle wasting, by acting as Danger-Associated Molecular Patterns (DAMPs) to directly stimulate muscle wasting through the activation of TLR4 on muscle cells. In addition, systemic TLR4 activation increases proinflammatory cytokine production, further enhancing muscle wasting. Intramuscularly, his team identified p38β MAPK as the intracellular signaling node critical for the coordinated activation of ubiquitin-proteasome and autophagy-lysosome pathways in response to eHsp70/90, proinflammatory cytokines, and the TGFb superfamily of cytokines. These findings help shape the current paradigm of cancer cachexia.

Neutralizing Circulating Hsp70 and Hsp90 Mitigates Cachexia in a PDX-derived Pancreatic Cancer Model

Previously, cancer cell-released Hsp70 and Hsp90 were shown to be key mediators of cancer-induced muscle wasting in mouse models of cancer due to their activation of Toll-like receptor 4 (TLR4) as danger-associated molecular patterns (DAMPs). To investigate whether this mechanism also mediates human cancer-induced muscle wasting, we established a modified PDX model of human pancreatic cancer in the immunodeficient NSG mice that developed cachexia in a highly consistent manner, which allowed the testing of interventions. Systemic administration of neutralizing antibodies against Hsp70 and Hsp90 to the human pancreatic tumor-bearing mice ameliorated the development of muscle wasting, including loss of muscle mass and function, due to a blockade of the muscle catabolism pathways (ubiquitin-proteasome and autophagy-lysosome) mediated by the p38b MAPK. The antibody treatment also attenuated the loss of heart weight. These results demonstrate a key role of human pancreatic cancer cell-released Hsp70 and Hsp90 in the development of cachexia.

Surendra Shukla, PhD

Assistant Professor

University of Oklahoma Health Campus

Dr. Surendra Kumar Shukla is an assistant professor at the Department of Oncology Science, University of Oklahoma Health Campus, Oklahoma City, USA. Dr. Shukla completed his PhD at the International Center for Genetic Engineering and Biotechnology (ICGEB), New Delhi, India. Dr. Shukla completed his postdoctoral studies at the University of Nebraska Medical Center, Omaha, NE, USA. Following his training, Shukla became a faculty member in the Department of Oncology Science at OU Health Campus. His research work is basically focused on the role of epigenetic and metabolic crosstalk in pancreatic cancer pathogenesis, therapy resistance, and cancer-associated systemic syndromes such as cachexia. His previous research has demonstrated that altered glycolytic metabolism leads to chemotherapy resistance in pancreatic cancer patients and that targeting glycolytic metabolic regulators, either genetically or pharmacologically, can improve therapeutic efficacy. He has also demonstrated that ketogenic and bioactive molecules mediated metabolic reprogramming of pancreatic cancer cells, leading to reduced cachectic phenotype. Recently, he has also demonstrated that pancreatic cancer-associated fibroblasts regulate tumor cell metabolism through the secretion of acetate, a process that can be blocked by silencing ATP citrate lyase in CAFs. Genetic or pharmacologic inhibition of the ACSS2–SP1–SAT1 axis diminished the tumor burden in mouse models

Role of Muscle Glucose Homeostasis in Pancreatic Cancer-Associated Cachexia

Cancer-induced cachexia is a multifactorial syndrome characterized by systemic inflammation and progressive skeletal muscle and fat wasting. More than 80% pancreatic cancer patients exhibit a cachectic phenotype, which significantly contributes to the overall mortality of cancer patients. Till now, there is no FDA-approved therapy for cancer-associated cachexia that has been developed. In the present study, we have demonstrated the anti-cachectic potential of an anti-malarial compound, atovaquone. We observed that atovaquone inhibits cancer cell-conditioned media-induced myotube atrophy in a dose-dependent manner. Atovaquone treatments lead to reduced cachectic markers expression in conditioned media-treated myotubes. Further, we observed that atovaquone treatment results in reduced reactive oxygen species levels in conditioned media-treated myotubes. Mechanistically, we observed that atovaquone treatment of myotubes leads to enhanced glycolytic capacity of conditioned-media-treated myotubes by upregulating *Glut4* expression. Furthermore, we established that increased Glut4 expression is primarily driven by atovaquone-induced AMPK activation. By utilizing a syngeneic orthotopic implantation model of pancreatic cancer, we have observed that atovaquone can inhibit the cachectic phenotype in tumor-bearing mice, without impacting the overall tumor growth. Overall, we have demonstrated that atovaquone exhibits anti-cachectic properties in both in vitro and in vivo model systems of pancreatic cancer-associated cachexia by modulating glycolytic capacity.

Prasenjit Dey, PhD

Assistant Professor of
Oncology/Immunology

Roswell Park Comprehensive Cancer Center

Prasenjit Dey is an Associate Professor of Oncology and Immunology at the Roswell Park Comprehensive Cancer Center in Buffalo, New York. His research broadly focuses on the complex interplay among genetics, metabolism, and the immune microenvironment in pancreatic ductal adenocarcinoma (PDAC).

Current Research Focus: Neuro-Steatotic Signaling: Investigating how intrapancreatic fat (steatosis) triggers sympathetic neurogenesis, providing the "second hit" that activates dormant KRAS-mutant cells. Mycobiome: Discovering how the fungal microbiome in the pancreas induces IL-33 secretion and type 2 immunity (TH2 cells) to accelerate tumor growth. Immuno-Metabolism: Mapping how cytokines and chemokines synergize with oncogenic pathways like KRAS and c-Myc to reprogram tumor metabolism and evade the immune system.

Pancreatic steatosis drives neurogenesis and pancreatic cancer

The incidence of pancreatic ductal adenocarcinoma (PDAC) is on the rise, and host factors like obesity increase risk by 60% and mortality by two-fold; however, the mechanisms that drive obesity-associated tumorigenesis are poorly understood. Here, we showed that obesity-mediated pancreatic steatosis was associated with increased neo-innervation in PDAC. Neo-innervation was mostly comprised of sympathetic neurons that released catecholamines, which ligated adrenergic receptors on both tumor and immune cells, subsequently activating a downstream signaling cascade that led to a pro-tumorigenic type 2 immune microenvironment, accelerating tumorigenesis. Further, we identified specific neurotrophic factors as major secreted mediators from adipocytes that drive neurogenesis. Targeting neuro-adrenergic signaling by nerve ablation or pharmacologic approaches abolished obesity-related tumor progression. Overall, this study advances our understanding of the fundamental biology underlying obesity-mediated neoinnervation and its causal role in exacerbating PDAC development, providing new avenues for therapeutic intervention.

SESSION IV

OK SYMPOSIUM ON PANCREATIC CANCER CACHEXIA

FRIDAY, MAY 15, 2026

SESSION 4

Moderators: Xiling Shen, PhD, Ryan D. Nipp, MD, MPH, MBA, FASCO, and Jamie Hur, DO

3:00 pm – 3:20 pm	Plenary Speaker: **Sue Bodine, PhD** *The impact of age on skeletal muscle atrophy and its treatment*
3:20 pm – 3:40 pm	**Lu Han, PhD** *Persistence of the fetal splanchnic program in pancreatic cancer associated fibroblasts*
3:40 pm – 4:00 pm	**Jason Pitarresi, PhD** *Pancreatic cancer cachexia is mediated by PTHrP-driven disruption of adipose de novo lipogenesis*
4:00 pm – 4:20 pm	**Kamiya Mehla, PhD** *Novel Regulators of Muscle Wasting in Cancer Cachexia*
4:20 pm – 4:40 pm	**Jie Wu, PhD** *Mitigating Cancer-associated Anorexia and Cachexia with Selpercatinib*

PLENARY

Sue Bodine, PhD

Professor

Oklahoma Medical Research Foundation

Sue Bodine, PhD. is a Professor in the Aging and Metabolism Research Program at the Oklahoma Medical Research Foundation and a Research Health Scientist at the Oklahoma City Veteran's Affairs Medical Center. Her research is focused on the study of the neuromuscular system and its response and adaptation to both positive and negative stressors, including exercise, disuse, and aging. A major focus of her lab has been in understanding the mechanisms underlying skeletal muscle atrophy, with specific investigation of the role of E3 ligases in the regulation of skeletal muscle mass. Her laboratory was instrumental in the identification of two muscle specific E3 Ubiquitin Ligases: MuRF1 and MAFbx, in skeletal muscle, and they continue to examine the role of these ligases in the regulation of skeletal muscle mass, with recent emphasis on identifying the specific substrates regulated by MuRF1 and MAFbx. The lab also investigates the effect of aging on skeletal muscle mass and function, with a focus on identifying the mechanisms underlying the poor recovery of mass and function following atrophy in aged animals. In recent years the lab has been pursuing research to identify the molecular mediators of the health benefits of exercise and are a member of the NIH Common Fund Molecular Transducers of Physical Activity Consortium (MoTrPAC). She has served as Chair and regular member of the Skeletal Muscle and Exercise Physiology panel and as a regular member of the Aging Systems and Geriatrics panel. She served as Editor-In-Chief of the *Journal of Applied Physiology* (2017-2023) and is currently on the editorial board of *Physiological Reviews*. She is currently President of the American Physiological Society.

Lu Han, PhD

Assistant Professor

Medical University of South Carolina

Dr. Lu Han has a long-held research interest in tissue interactions and signaling networks during organogenesis and pathogenesis. Dr. Han conducted her PhD thesis studies at Cincinnati Children's Hospital. Her studies focused on the development of the foregut, which is a fetal structure that gives rise to the respiratory and upper digestive systems, including the pancreas. She and her colleagues discovered the intricate coordination between the epithelium and splanchnic mesenchyme (Rankin*, Han* et al, *Cell Rep*, 2016; Han et al, *Dev Biol*, 2017) and diversification of the splanchnic mesenchyme marked by transcription factors (Han et al, *Nat Commun*, 2020).

In further pursuit of her interests in tissue interactions, she then moved on to develop her expertise in cancer biology for postdoctoral training mentored by Drs. Gustavo Leone and Michael Ostrowski. Pancreatic cancer is one of most devastating malignancies and is characterized by an expansion of the stromal fibroblasts. Cancer associated fibroblasts (CAFs) play important and complex roles in modulating the tumor microenvironment. Dr. Han performed lineage tracing studies in genetic mouse models and demonstrated that the splanchnic mesenchyme is the fetal origin of pancreatic CAFs (Han et al, *Nat Commun*, 2023). Dr. Han has been continuously funded during her postdoctoral training and transition to faculty (NCI T32, NCI F32, American Cancer Society Postdoctoral Fellowship and NCI K99/R00).

Dr. Han started her independent laboratory as a tenure-track Assistant Professor in the Biochemistry and Molecular Biology Department at the Medical University of South Carolina in Aug 2024. The Han laboratory investigates the persistence of the splanchnic molecular programs in pancreatic CAFs. In the long term, the Han laboratory aims to integrate developmental biology and cancer biology to develop innovative perspectives and to discover fundamental principles governing these similar but distinct life stages. Besides the NCI R00 award, the Han laboratory is currently supported by the American Cancer Society Institutional Research Grant and MUSC Digestive Disease Research Center Pilot Award.

Persistence of the fetal splanchnic program in pancreatic cancer associated fibroblasts

The pancreas is composed of the epithelial and mesenchymal cells. While mesenchymal fibroblasts are a minor component of the normal pancreas, fibroblast population expands drastically during tumorigenesis. In pancreatic ductal adenocarcinoma (PDAC), cancer associated fibroblasts (CAFs) play critical and complex roles in the tumor microenvironment. This study sought to define the origin, heterogeneity and function of pancreatic cancer associated fibroblasts. Recently we performed a series of lineage tracing studies in genetically engineered mouse models. This identified the splanchnic mesenchyme (a tissue layer adjacent to the developing fetal pancreatic epithelium) as the fetal origin of the adult pancreatic resident fibroblasts and pancreatic CAFs. Single cell transcriptomic analysis indicated persistent and dynamic gene expressions along the pancreatic mesenchymal trajectory during development, homeostasis, precancer and cancer. Intriguingly, we found that two splanchnic transcription factors, GATA6 and FOXF1, are expressed in only subsets of adult pancreatic fibroblasts in temporally and spatially distinct patterns. Similar patterns were observed in both mouse models and human patient samples. To determine the roles of GATA6 and FOXF1 in fibroblasts during tumorigenesis, we constructed dual DNA recombinase mouse genetic models, targeting Gata6 and Foxf1 in parallel. DNA recombinase FlpO directs expression of an oncogene Kras (G12D mutation) and loss of a tumor suppressor p53 in pancreatic epithelial cells to induce spontaneous tumor formation in the pancreas, recapitulating pancreatic cancer pathology in human patients. DNA recombinase Cre deletes Gata6 or Foxf1 specifically in fibroblasts. Fibroblast specific Gata6 deletion resulted in more aggressive tumor formation in the pancreas, altered gene expressions in CAFs and exacerbated

immune suppression. Fibroblast specific Foxf1 deletion resulted in more collagen content and altered collagen peptide compositions in the pancreas. This suggests critical and unique roles of GATA6 and FOXF1 in CAFs regulating the pancreatic tumor microenvironment and cancer progression. In summary, this study delineated a continuous cell trajectory of the mesenchymal lineage in the pancreas across different life stages. Additionally, this study demonstrates the persistent and selective gene expressions along the mesenchymal trajectory. Selective persistence of two fetal transcription factors, GATA6 and FOXF1, identifies novel CAF heterogeneity at the molecular and functional levels regulating the tumor microenvironment and cancer progression. These novel mechanisms shed light in complex CAF heterogeneity and provide novel targets to fine-tune the microenvironment to control cancer.

Jason Pitarresi, PhD

Assistant Professor

University of Massachusetts Chan Medical School

Dr. Jason R. Pitarresi is an Assistant Professor in the Division of Hematology-Oncology at the University of Massachusetts Chan Medical School. His lab studies how tumor cell plasticity alters tumor host interactions in pancreatic cancer, with a focus on cancer cachexia, metastasis, and immunosuppression. His work has revealed that tumor-derived factors facilitate adipose tissue wasting in pancreatic ductal adenocarcinoma by turning off *de novo* lipogenesis (DNL) in adipocytes, priming them to undergo cachectic wasting.

Pancreatic cancer cachexia is mediated by PTHrP-driven disruption of adipose de novo lipogenesis

We have used mouse models to determine that the pro-cachectic tumor-derived factor PTHrP is upregulated in pancreatic ductal adenocarcinoma. Genetic deletion or pharmacological inhibition of PTHrP reduces cachexia phenotypes in highly cachectic pancreatic cancer lines and overexpression of PTHrP induces cachexia in non-cachectic clones, demonstrating that PTHrP is both necessary and sufficient to drive cachexia. Disruption of tumor-adipose crosstalk by deletion of *Pth1r*, the cognate receptor for PTHrP, specifically in adipocytes blocked cachexia induction, suggesting direct tumor cell to adipocyte pathways that facilitate wasting. Mechanistically, we find that PTHrP blocks fatty acid synthesis in adipose tissue by potently downregulating the *de novo* lipogenesis (DNL) pathway, and we are developing tools to understand more deeply the role of DNL in cachectic adipose tissue wasting. Finally, we can block cachectic adipose tissue wasting by inhibiting PTHrP directly, or through DNL restoration therapy in adipose tissue with the PPARγ agonist Rosiglitazone. Collectively, this data identifies the PTHrP-PTH1R-DNL signaling axis as a novel regulator of pancreatic cancer-associated cachexia.

Kamiya Mehla, PhD

Associate Professor

University of Oklahoma Health Campus

I did my Ph.D. at the Institute of Genomics and Integrative Biology, Delhi, in 2012. I did my postdoctoral training under the mentorship of Dr. Michael A. Hollingsworth at the University of Nebraska Medical Center (UNMC). During my postdoctoral training, I gained expertise in tumor immunology and immunotherapy. In parallel, I gained expertise in studying metabolic alterations of tumor cells in pancreatic cancer. In 2018, I transitioned to my independent position at UNMC. Later, in 2022, I joined the Department of Oncology Science at OUHC as an associate professor. My investigations currently focus on deciphering novel tumor-immune cell crosstalk at primary tumors and at distant systemic sites, including muscle. My lab has shown the metabolic competition between immune cells and pancreatic tumor cells in the tumor microenvironment. We also demonstrated the contribution of tumor-conditioned macrophages to muscle wasting in pancreatic cancer.

Novel Regulators of Muscle Wasting in Cancer Cachexia

Pancreatic ductal adenocarcinoma (PDAC) displays a poor prognosis, contributing to approximately 460,000 deaths annually worldwide. Cachexia, characterized by significant weight loss, reduced muscle efficiency and impaired function, poor appetite, affects approximately 70% of PDAC patients and is one of the primary contributors to reduced tolerance to chemotherapy. Cachexia imparts a poor quality of life and accelerates mortality in PDAC patients. To date, multiple targeted therapeutic strategies have been employed to limit muscle wasting in cancer patients but have met with moderate success. Thus, the present study focused on identifying novel regulators of muscle wasting observed in cachexia. Our study focused on two distinct organs, skeletal muscle and cardiac tissue, to study cachexia-associated wasting in pancreatic tumor-bearing hosts. For the skeletal muscle model, we assessed the published dataset from multiple studies. We identified Peptidase inhibitor 16 (Pi16) as a common denominator that is significantly downregulated in skeletal muscle in tumor-bearing hosts compared to healthy subjects. This data was further validated in the gastrocnemius muscle of the orthotopic and genetically engineered mouse models of pancreatic cancer. Similarly, we observed a notable alteration of Pi16 expression in the cardiac tissue of tumor-bearing mice. In our orthotopic model, we observed decreased cardiac function and increased inflammation in the cardiac tissue (left ventricle) of tumor-bearing mice, as reflected in the neutrophil and macrophage populations. In our study, we subsequently show that IL-1α regulates Pi16 expression via the NF-κB-YY1 axis. Restoration of Pi16 in skeletal muscle rescues wasting and modulates the skeletal muscle immune signatures. We also noted that Pi16 inhibits cathepsin S activity and, in turn, regulates the migration of Gr-1+ granulocytes via Cathepsin S inhibition. Overall, our study is the first to demonstrate the role of Pi16 in reversing pancreatic cancer-induced muscle wasting, opening new avenues for the development of Pi16-targeted therapies to treat PDAC cancer cachexia.

Jie Wu, PhD

Professor & Stephenson Endowed Chair in Cancer Translational Research

University of Oklahoma Health Campus

Dr. Wu is a professor in the Department of Pathology and the Peggy and Charles Stephenson Endowed Chair in Cancer Translational Research at the University of Oklahoma Health Sciences Center. His laboratory conducts research in cancer biology and therapy focusing on protein tyrosine kinases and phosphatases. Dr. Wu received his undergraduate and graduate education in Xiamen University and the Shanghai Institute of Cell Biology in Chinese Academy of Sciences. He obtained his Ph.D. in Biochemistry from the University of Kansas Medical Center. During postdoctoral research at the Memorial Sloan-Kettering Cancer Center and University of Virginia, Dr. Wu made seminal contributions in delineating the MAP Kinase pathway. Dr. Wu established his independent laboratory at the H. Lee Moffitt Cancer Center and Research Institute in Tampa, Florida, where he was a Senior Member and a tenured Professor prior to relocating his lab to Oklahoma. Dr. Wu has published over 90 original research papers in addition to review articles and book chapters. His research projects at OUHSC have been supported by NCI, PHF, and OCAST grants.

Mitigating Cancer-associated Anorexia and Cachexia with Selpercatinib

The growth differentiation factor-15 (GDF15) has been identified as a mediator of cancer-associated anorexia and cachexia. GDF15 acts by binding to the RET co-receptor GFRAL located in the AP/NTS areas of hindbrain to activate the RET protein tyrosine kinase. Selpercatinib is a selective RET kinase inhibitor used to treat RET-altered cancers. Because GDF15 controls anorexia through regulating RET kinase activity in the hindbrain, and a side effect of selpercatinib treatment in RET-altered cancer patients is weight gain, we hypothesized that selpercatinib could suppress the GDF15-mediated cancer-associated anorexia and cachexia. HT1080 and KLN206 are human and mouse cancer cells that express high levels of GDF15. Mice bearing HT1080 and KLN206 xenograft tumors had reduced food consumption, loss of body weight, loss of adipose tissues, and reduced skeletal muscle strength and mass. Selpercatinib treatment alleviates HT1080 and KLN206 xenograft tumor-induced anorexia and cachexia phenotypes. Immunofluorescence staining analysis indicated that tumor-bearing mice had increased active $GFRAL^{+}$ neurons in the AP/NTS regions, which were suppressed by selpercatinib. Histological and immunohistological analyses showed skeletal muscle atrophy in tumor-bearing, cachectic mice. Selpercatinib significantly lessened the tumor-induced skeletal muscle loss. Transcriptomic, qRT-PCR, and immunoblot analyses of skeletal muscle from HT1080 xenograft tumor experiment showed that tumor-bearing mice had elevated skeletal muscle wasting genes including Trim63/MuRF1, Fbxo32/Atrogin1, Crebrf, Chac1, and reduced skeletal muscle cell differentiation genes such as Myod1, Cyp26b1, Mamstr, Adra1a. Selpercatinib treatment suppressed expression of skeletal muscle wasting genes and increased expression of skeletal muscle differentiation genes. These results suggest that selpercatinib can mitigate cancer-associated anorexia and cachexia in animal models and may be repurposed to treat anorexia and cachexia in cancer patients.

SESSION V

OK SYMPOSIUM ON PANCREATIC CANCER CACHEXIA

SATURDAY, MAY 16, 2026

SESSION 5

Moderators: Barish Edil, MD, FACS and Kamiya Mehla, PhD

8:30 am – 8:50 am	Plenary Speaker: **Lei Zheng, MD, PhD** *Macrophages: a major player in the inflammation, metabolism, and antitumor immune response in pancreatic cancer*
8:50 am – 9:10 am	**Ram V. Roy, PhD** *UBAP2 acts as scaffolds between RAC and WAVE in the regulation of membrane ruffling*
9:10 am – 9:30 am	**Wei R. Chen, PhD** *Nano-photo-immunotherapy for pancreatic cancer*
9:30 am – 9:50 am	Coffee Break

PLENARY

Lei Zheng, MD, PhD

Professor and Director

UT Health San Antonio – Mays Cancer Center

Dr. Lei Zheng is Executive Director of the Mays Cancer Center, home to the UT Health San Antonio M.D. Anderson Cancer Center and the Vice President for Oncology for the University of Texas Health San Antonio, the Mays Family Foundation Distinguished University Presidential Chair of Oncology and Professor with Tenure in the Department of Medicine in the Joe R. and Teresa Lozano Long School of Medicine (LSOM).

In the last 15 years, Dr. Zheng has been Assistant/Associate/Full Professor of Oncology and Surgery at the Johns Hopkins University School of Medicine. He served as Associate Cancer Center Director for Precision Medicine and Assistant Cancer Center Director for Translational Research and overseed the precision medicine research and practice in cancer diseases for the Cancer Center. He was also Director for the Multidisciplinary Gastrointestinal Cancer Laboratories Program and Director of the Pancreatic Cancer Precision Medicine Center of Excellence. Dr. Zheng's clinical work is focused on multidisciplinary management for pancreatic cancer, bile duct cancer, colorectal cancer liver metastases, and gastric cancer. Dr. Zheng's primary laboratory research focus is on the identification of new targets and strategy for pancreatic cancer immunotherapies by dissecting tumor microenvironment of pancreatic cancer.

Macrophages: a major player in the inflammation, metabolism, and antitumor immune response in pancreatic cancer

The resistance of pancreatic ductal adenocarcinoma (PDAC) to immune checkpoint inhibitors (ICIs) is attributed to the immune-quiescent and -suppressive tumor microenvironment (TME). we examined PDAC vaccine or radiation therapy (RT) as T cell priming mechanisms together with a dual antagonist of CCR2 and CCR5 (CCR2/5i), in combination with αPD-1 as new treatment strategies. The combination of RT, anti-PD-1 antibody, and CCR2/5i enhanced intratumoral effector and memory T cell infiltration but suppressed regulatory T cell, M2-like tumor–associated macrophage, and myeloid-derived suppressive cell infiltration. Adding RT to PDAC vaccine and anti-PD-1 antibody shortens the distances from PD-1+CD8+ T cells to tumor cells and to PD-L1+ myeloid cells, which portends prolonged survival. These findings have guided the design of next radioimmunotherapy studies by targeting M2-like TAM in PDACs. Both exogenous M1-like and M2-like macrophages promote metastasis in a mouse model of PDAC while such a role of M1-like macrophages is dependent on DNA methylation. Our results suggest that PDAC cells are able to reprogram M1-like macrophages metabolically and functionally through a GARP-dependent and DNA methylation-mediated mechanism to adopt a pro-cancerous fate.

Ram Vinrod Roy, PhD

Research Assistant Professor

OU Health Campus

I completed my Master's degree from Indian Institute of Technology Kharagpur and later earned my Ph.D. from National University of Singapore. Currently, I am working on pancreatic cancer research in the group of Dr. Priyabrata Mukherjee, where I help foster collaboration between nanotechnology and biology research groups to advance innovative approaches for pancreatic cancer diagnosis and therapy.

UBAP2 acts as scaffolds between RAC and WAVE in the regulation of membrane ruffling

Macropinocytosis enables pancreatic ductal adenocarcinoma (PDAC) cells to acquire nutrients in metabolically stressed environments. Here, we identify UBAP2, a ubiquitin-associated binding protein, as a key regulator of macropinocytosis via membrane ruffling. UBAP2 is highly expressed in PDAC cells, and its depletion significantly reduces macropinocytosis across multiple PDAC lines, including AsPC1, PANC1, and BxPC3. UBAP2 localizes to membrane ruffles and co-localizes with active RAC. In addition, loss of UBAP2 reduces RAC-GTP levels even following EGF stimulation, indicating that UBAP2 is required to sustain RAC activation. Mechanistically, UBAP2 interacts with RAC, WAVE2, and the ARP2/3 complex-core components of the actin remodeling machinery. The plasmid construct expressing full-length UBAP2 promotes interactions with WAVE2, RAC, and the ARP2/3 complex; however, deletion of the UBA domain abolishes these associations, indicating that the UBA domain is essential for mediator binding. Upon EGF stimulation, assembly of these components is enhanced in the presence of intact UBAP2 but is lost when the UBA domain is deleted. Notably, similar results are observed in cells overexpressing RACQ6LL, although RAC promotes WAVE2-ARP2/3 complex formation, this interaction is markedly attenuated in the absence of UBAP2. Collectively, these findings establish UBAP2 as a critical scaffold that integrates RAC signaling with actin cytoskeletal remodeling and macropinocytosis in pancreatic ductal adenocarcinoma, thereby linking nutrient uptake to dynamic cytoskeletal regulation.

Wei Chen, PhD

Professor and Chair, Biomedical Engineering

University of Oklahoma Health Campus

Dr. Wei R. Chen received his BS degree in physics from Shandong University, Jinan, China, in 1982. He received his PhD degree in theoretical high-energy particle physics from the University of Oregon in 1988. He changed his research from physics to cancer research in early 1990s. Currently, he is Stephenson Endowed Chair, Professor, and Director of the Stephenson School of Biomedical Engineering at the University of Oklahoma. Dr. Chen focuses on novel cancer therapies. His group developed localized ablative immunotherapy for metastatic cancers with promising outcomes in pre-clinical studies and preliminary clinical trials. He also focuses on immunologically modified nanoplatform for cancer treatment using nano-photo-immuno effects. He has published 200+ peer-reviewed articles (with an h-index of 63). He has been awarded 12 US patents and multiple international patents. Dr. Chen has received more than $12 million in funding from state and federal agencies, foundations, as well as from industrial sponsors. He was elected as a SPIE (International Society of Optics and Photonics) Fellow in 2007, an AIMBE (American Institute for Medical and Biomedical Engineering) Fellow in 2022, and a Senior Member of the National Academy of Inventors. He received the 2008 US Professor of the Year award and the 2011-2012 US Fulbright Lecturing/Research Award. He also won the Medal for Excellence in Teaching from the Oklahoma Foundation for Excellence in 2011 and the SPIE Educator Award in 2012.

Nano-photo-immunotherapy for pancreatic cancer

A unique localized ablative immunotherapy (LAIT) using the combination of nano-photo-immuno effects was developed for the treatment of metastatic cancers. Here, graphene oxide (GO) is utilized as both a light-absorbing agent for photothermal therapy (PTT) and a nanocarrier for the delivery of a novel immunostimulant, N-dihydrogalactochitosan (GC). This work aims to integrate local laser irradiation, immunotherapy, and nanomedicine using GO/GC + PTT. We report the therapeutic efficacy of the novel treatment modality and elicited immune responses on a highly aggressive and poorly immunogenic pancreatic tumor model in mice. Treatment led to primary tumor ablation, and 80% of mice remained tumor-free 100 days post-treatment. Additionally, elicited anti-tumor immunological responses were observed via the activation of pro-inflammatory anti-tumor pathways locally and systematically. Prolonged survival following tumor rechallenge gives evidence that GO/GC-treated mice developed long-term immune memory and resisted tumor recurrence. This and future work will lay the foundation for future clinical applications of this novel therapy in cancer treatment and vaccination.

SESSION VI

OK SYMPOSIUM ON PANCREATIC CANCER CACHEXIA

SATURDAY, MAY 16, 2026

SESSION 6

Moderators: Lu Han, PhD and Jingxuan Yang, PhD

9:50 am – 10:10 am	Plenary Speaker: **Christine Chio, PhD** *An Iron-Methionine Redox Axis Drives Adipose Remodeling in Pancreatic Cancer Cachexia*
10:10 am – 10:30 am	**Pankaj Singh, PhD** *Talk Title TBD*
10:30 am – 10:50 am	**Alex Arreola, PhD Candidate** *Tumor-Immune-Neural Circuit Disrupts Energy Homeostasis in Cancer Cachexia*

Christine Chio, PhD

Assistant Professor of Genetics & Development

Columbia University Irving Medical Center

Christine Chio, PhD, is an Assistant Professor of Genetics and Development at Columbia University Irving Medical Center, where she is a member of the Institute for Cancer Genetics and the Herbert Irving Comprehensive Cancer Center. Her laboratory studies how redox signaling shapes cancer metabolism, disease progression, and tumor-host interactions, using pancreatic ductal adenocarcinoma as a primary model system. Her work is based on the premise that reactive oxygen species are not merely damaging byproducts of metabolism, but can also function as signaling molecules through reversible modifications of specific amino acid residues within proteins. By investigating how these redox-dependent mechanisms regulate processes such as protein synthesis, metabolic reprogramming, metastasis, and systemic metabolic dysfunction, her research aims to uncover new therapeutic opportunities for pancreatic cancer and other KRAS-driven malignancies.

An Iron-Methionine Redox Axis Drives Adipose Remodeling in Pancreatic Cancer Cachexia

Cancer cachexia is a multifactorial wasting syndrome that contributes substantially to morbidity and mortality in pancreatic ductal adenocarcinoma (PDA), yet the mechanisms by which tumors drive systemic tissue remodeling remain incompletely understood. We find that white adipose tissue in PDA exhibits marked iron accumulation, identifying iron dysregulation as a prominent feature of cachexia-associated adipose remodeling. Building on this observation, we identify methionine sulfoxide reductase A (MSRA), an enzyme that repairs oxidized methionine residues in proteins, as a critical mediator of adipose dysfunction and systemic wasting. Mechanistically, iron stabilizes and activates MSRA, thereby coupling adipose iron accumulation to methionine redox regulation. MSRA, in turn, remodels the methionine redox proteome to promote adipose tissue reprogramming and cachexia. Using genetic and functional approaches, we show that *MsrA* is required for adipose remodeling and for the full development of cachexia in mouse models of pancreatic cancer. These findings define an iron-methionine redox axis as a previously unrecognized mechanism of tumor-host metabolic crosstalk and nominate this pathway as a potential therapeutic vulnerability in cancer cachexia.

Pankaj Singh, PhD

Professor and Chair, Dept of Oncology Sci

OU Health Campus

Alex Arreola, PhD Candidate

Graduate Student

University of Oklahoma Health Campus

Alex Arreola is an NCI F99/K00 Fellow and a member of the Min Li Lab at the University of Oklahoma Health Campus (OUHC). He is a PhD Candidate in the Pathology Graduate Program whose dissertation research has focused on understanding molecular drivers of pancreatic cancer-associated cachexia. Prior to OUHC, he obtained a Bachelor of Science in Microbiology and Cell & Molecular Biology from Oklahoma State University. Under the mentorship of Dr. Li, Alex has spent the past four years investigating how crosstalk between the pancreatic tumor–immune microenvironment and the nervous system drives cancer cachexia. During this time, he has led and contributed to multiple cachexia-related studies published in leading academic journals.

Alex is also a passionate educator and mentor. He recently completed the OU Graduate College's year-long Preparing Future Faculty Program, where he developed and applied pedagogical principles in the undergraduate classroom. He also currently serves as a near-peer mentor in the Learning and Achievement in Biomedical Sciences T32 program.

Upon graduating in the fall of 2026, Alex will expand his research on cancer-associated cachexia at the University of Chicago, under the mentorship of Dr. Kay Macleod in the Ben May Department for Cancer Research. Here, his postdoctoral research will focus on understanding how the altered metabolic status of hepatocytes shapes the liver's immune landscape during cancer cachexia. Alex's long-term vision is to lead an academic research program focused on understanding the role of host systems in driving cancer cachexia and other cancer-associated sequela.

Tumor-immune-neural circuit disrupts energy homeostasis in cancer cachexia

A debilitating feature of many cancers is the onset of cachexia. Cancer cachexia is a multifactorial syndrome characterized by systemic metabolic dysfunction and tissue wasting. It drastically affects quality of life and is a leading contributor to cancer-related mortality. An understanding of cancer cachexia's multi-organ etiology remains limited. Growth and Differentiation Factor 15 (GDF15) is a promising neural-acting target for cancer cachexia, but the underlying mechanism of its upregulation in the tumor remains unclear. This study aimed to elucidate the cellular and molecular drivers of tumor-associated GDF15 upregulation in order to advance the mechanistic understanding of cancer cachexia biology and to identify potential therapeutic targets. Orthotopic pancreatic tumor models were used to evaluate cachexia progression in Gdf15-deficient mice. Body composition was evaluated using quantitative magnetic resonance and tissue dissection. RNA sequencing was used to identify the cellular sources of GDF15 in the tumor. Molecular signaling pathways were evaluated by qPCR, ELISA, and immunohistochemistry. Mice were monitored using a metabolic and behavioral phenotyping system. Therapeutic interventions targeting GDF15, its upregulation, and its signaling complex were also employed. Gdf15-deficient mice were protected from appetite, muscle, and fat loss and showed improved metabolic and behavioral status. Single-cell RNA sequencing analysis revealed macrophages as the primary source of GDF15, which was upregulated by cancer cell-derived CSF1.

Activating the GFRAL-RET complex in the hindbrain, GDF15 promoted β-adrenergic signaling in the tumor microenvironment. Further, this enhanced the cachectic capacity of cancer cells by potentiating CSF1 upregulation. Targeting this feedforward loop via GDF15-neutralizing antibody, anti-CSF1R antibody, or Selpercatinib (RET inhibitor) attenuated cachexia and anorexia in tumor-bearing mice.

We revealed a non-cell-autonomous circuit whereby tumor cells stimulate macrophage-derived GDF15 via CSF1 and engage the nervous system to drive cachexia. Furthermore, we demonstrated that GDF15 induces sympathetic activity in the tumor microenvironment, forming a feedforward loop. This work highlights the interplay between the tumor, immune, and nervous systems as a promising therapeutic target for cancer cachexia.

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