Penn NET Center – Overview of Clinical and Basic Science Research

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Disclosures

• Bryson Katona
  • Consulting: Exact Sciences
  • Paid travel: Janssen
  • Clinical trial/study funding: Janssen, Immunovia, Epigenomics

• Heather Wachtel
  • None
Overview

• Overview of the Penn NET Center

• Pheochromocytoma/Paraganglioma (PCC/PGL)

• Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs)
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PENN NET Center Overview

NETs

- Medical Oncology
- Nuclear Medicine
- Pulmonary
- Gastroenterology
- Interventional Radiology
- Medical Genetics
- Surgery
- Cardiology
- Head and Neck Surgery
- Cancer Biology
- Pathology
- Radiation Oncology
- Endocrinology
- Nephrology

Perelman School of Medicine
University of Pennsylvania
Challenges associated with research in NETs

• Rarity and heterogeneity of NETs

• Few researchers compared to other fields

• Limited funding

• Limited/poor models for studying NETs in the lab
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  • Database and tumor collection
  • Basic science and translational laboratory research
  • Clinical studies and trials

• Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs)
IT STARTS WITH YOU
Pheochromocytoma/Paraganglioma

- Patients consented: 402
- Banked DNA samples: 335
- Tumor samples: 91
**Pheochromocytoma/Paraganglioma**

- **Patient samples**
- **Research**
- **Novel Therapies**

- *Genomic profiles and targeted therapy for malignant PCC/PGL*
  Heather Wachtel, Kate Nathanson

- *Examining modifiers for sporadic and SDHx-related PGL/PCC*
  Lauren Fishbein (UC Colorado), Kate Nathanson

- *DNA methylation in pheochromocytomas and paragangliomas*
  Prodromos Chatzikyriakou, Rebecca Oakey (Kings College, London)

- *Comparison of PASS/GAPP histopathologic scoring of PCC/PGL*
  Heather Wachtel, Lauren Fishbein (UC Colorado)


**Pheochromocytoma/Paraganglioma**

- **Patient samples**
- **Research**
- **Novel Therapies**

- **Weight changes after PCC/PGL surgery**
  - Heather Wachtel

- **Oncologic associations and penetrance in succinate dehydrogenase pathogenic variants**
  - Heather Wachtel, Kate Nathanson

- **Multi-center study of PCC/PGL identified during pregnancy**
  - Debbie Cohen, Irina Bancos (Mayo Clinic)

- **Multi-institutional study to examine current screening in SDHx pathogenic variant carriers**
  - Kate Nathanson, Lauren Fishbein (UC Colorado)

- **Enrollment in American-Australian-Asian-Adrenal Alliance (A5)**
Efficacy and Safety of High-Specific-Activity I-131 MIBG Therapy in Patients with Advanced Pheochromocytoma or Paraganglioma

Daniel A. Pryma¹, Bennett B. Chin², Richard B. Noto³, Joseph S. Dillon⁴, Stephanie Perkins⁵, Lijia Solnes⁶, Lale Kostakoglu⁷, Aldo N. Serafini⁸, Miguel H. Pampaloni⁹, Jessica Jensen¹⁰, Thomas Armor¹⁰, Tessa Lin¹⁰, Theresa White¹¹, Nancy Stambles¹⁰, Stuart Apfel¹⁰, Vincent DiPippo¹¹, Syed Mahmood¹⁰, Vivien Wong¹⁰ and Camilo Jimenez¹²
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Database and tumor collection

• GEP-NETs as of 2020
  • Patients consented in the database
    428
  • Banked blood samples
    269
  • Tumor samples
    121
Use of database information

Predictors of Recurrence and Survival in Patients With Surgically Resected Pancreatic Neuroendocrine Tumors

Rachel E. Rosenblum, MD,* Cynthia K. Harris, MD,* Kiwoon Joshua Baeg, BS,* Julie A. Starr, BS,† Lauren K. Brais, MPH,‡ Kristen M. Stashek, MD,* Stephen C. Ward, MD, PhD,§ Bryson W. Katona, MD, PhD,‡ Thomas E. Clancy, MD,¶ Juan P. Wisnivesky, MD, DrPh,* Matthew H. Kulke, MD,¶ David C. Metz, MBBCh,¶ Michelle Kang Kim, MD, PhD,¶ and Jennifer A. Chan, MD, MPH,‡

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Collaboration between Penn, Dana Farber, and Mount Sinai
Examined 501 patients with surgically resected pancreatic NETs
Use of tissue samples are critical for research

- Tissue sharing collaborations outside of Penn:
  - Dr. Juanita Merchant (University of Arizona)
  - Dr. Scott Oakes (UCSF → University of Chicago)
  - Tron corporation (Europe)

- Tissue use within Penn:
  - Dr. Xianxin Hua (Department of Cancer Biology)
  - Dr. Xiaolu Yang (Department of Cancer Biology)
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Advances in NET CAR-T therapy

- Dr. Xianxin Hua’s talk will go into this in detail!
Study of NET liver metastases

- Dr. Terence Gade’s talk will go into this in more detail

Patient Derived Xenografts (PDX)

- Tumor tissue from donor patient
- Harvested at biopsy or surgery and directly implanted into immunocompromized mice
- Expansion of tumor material from mouse to mouse (never touched plastic)

www.criver.com
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Original Article

Safety and Feasibility of Integrating Yttrium-90 Radioembolization With Capecitabine-Temozolomide for Grade 2 Liver-Dominant Metastatic Neuroendocrine Tumors

Michael C. Soulen, MD,* Diana van Houten, CRNP,* Ursina R. Teitelbaum, MD,† Nevena Damjanov, MD,† Keith A. Cengel, MD,‡ and David C. Metz, MD§

Pancreas • Volume 47, Number 8, September 2018
CapTem+Y90

- The Phase 2 trial of CapTem plus Y90 TARE for liver-dominant G2 NETS is funded and will be opening this year

- Recruitment goal is 50 patients

- 3 centers participating:
  - University of Pennsylvania
  - Roswell Park
  - Emory
RETNET Trial


Randomized Embolization Trial for NeuroEndocrine Tumor Metastases to the Liver (RETNET): study protocol for a randomized controlled trial

James X. Chen¹, E. Paul Wileyto²,³ and Michael C. Soulen¹,³,4*  

The RETNET trial is a prospective, multicenter randomized controlled trial designed to determine the optimal embolotherapy technique for NET liver metastases.
RETNET Trial

- 12 active sites
- 62 out of 130-170 patients recruited
PRRT can be administered to a diverse NET population

Baseline liver function test abnormality increases the likelihood of PRRT discontinuation
Resection Trends for Duodenal Carcinoid Tumors: A Single Center Experience

S. Kumar, N. Mahmud, R. Roses, B.W. Katona, G. G. Ginsberg, D.C. Metz

- Results support considering endoscopic resection of duodenal carcinoids less than 10 to 15 mm
- Operative resection reserved for those lesions with higher-grade, high mitotic rate, and positive resection margins after endoscopic resection
Patients with diminutive and small rectal NETs (< 2cm) are at risk of metastatic disease, especially if grade 2 or grade 3.

Tumor grade is a dominant predictor of dissemination.
• 1478 patients with PNET from the National Cancer Database (2004-2014)

• Chromogranin A levels were predictive of metastatic disease and how well patients did

• When matching chromogranin A levels, metastatic PNET patients undergoing surgery did better
Long-Acting Somatostatin Analogue Safety Monitoring Protocol for Outpatients With Neuroendocrine Tumors

JORDAN GABRIELSEN, PharmD, GIANNA GIRONA, PharmD, BONITA BENNETT, BSN, RN, and ANNA JUNG, PharmD, BCPS

Baseline (prior to initiation)
- Gallbladder US (if no prior imaging)
- CBC, complete metabolic panel, TSH, HbA1c, vitamin B12, zinc
- Stool studies for osmolality and electrolytes, Sudan stain, pancreatic elastase
- Vital signs
- Physical exam

6 months post-initiation
- Gallbladder US
- CBC, complete metabolic panel, TSH, HbA1c
- Vital signs
- Physical exam
- Evaluation of TRAEs

Annual
- Gallbladder US
- CBC, complete metabolic panel, TSH, HbA1c
- Vital signs
- Physical exam
- Evaluation of TRAEs

Other considerations
- Cardiovascular disease
  - Can consider a baseline and annual ECG and echocardiogram
- Vitamin B12
  - If normal at baseline, test every 12 months
  - If low test every 6 months
- Zinc
  - Measure every 3 months for patients with excessive fluid losses maintained on TPN
  - HbA1c/glucose
    - If normal at baseline, test annually
    - If elevated in the pre-diabetic range, test every 6 months
    - If diabetic, test every 3 months
- Diarrhea
  - If patient reports diarrhea, consider further testing (i.e., stool studies, hydrogen breath test)
Optimizing the Management of Carcinoid Syndrome to Reduce the Impact of Diarrhea

RORY RANDALL,¹ CNP, AOCNP®, BONITA BENNETT,² RN, BSN, TIFFANY VALONE,³ PA-C, MS, OT, and KIRSTEN BLUE,³ PA-C, MS

- Overview of functional NETs and treatment paradigms
- Overview of carcinoid syndrome-specific therapies
- Differential diagnosis of diarrhea in the setting of a NET
- Assessment of the impact of diarrhea on patient’s daily lives
NET Clinical Trials at Penn

• Update provided by Dr. Jennifer Eads later today
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Thank you!

- Our patients
- Co-Directors of Penn NET Center
  - Debbie Cohen
  - David Metz
- NET Center Support
  - Bonnie Bennett
- Medical Genetics
  - Katherine Nathanson
  - Staci Kallish
  - Maria Bonanni
  - Anna Raper
  - Stephanie Asher
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  - Megan Lawrence
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  - Robert Roses
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  - Paul Foley
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  - Ian Folkert
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  - Michael Soulen
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  - Jeffrey Mondschein
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  - Diana Van Houten
  - Laura Herron
  - Amanda Davis
  - Ginna Deitrick
  - Scott Trerotola
  - Deepak Sudheendra
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  - Megan Melick
- Palliative Care/Pain
  - Alyssa Wold
  - Pain management team
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  - Andrew Bellet
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  - PheoPara Alliance
  - NANETS
  - Run for the Stripes
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- Radiology
  - Jennifer Gillman
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  - Stamatoula Pilati
  - Jennifer Schroeder
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