

# Precision Medicine for mNETs: Update on Organoid Research

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9<sup>th</sup> Annual Focus on Neuroendocrine Tumor

6 March 2020



Penn IR

**PIGI LAB**

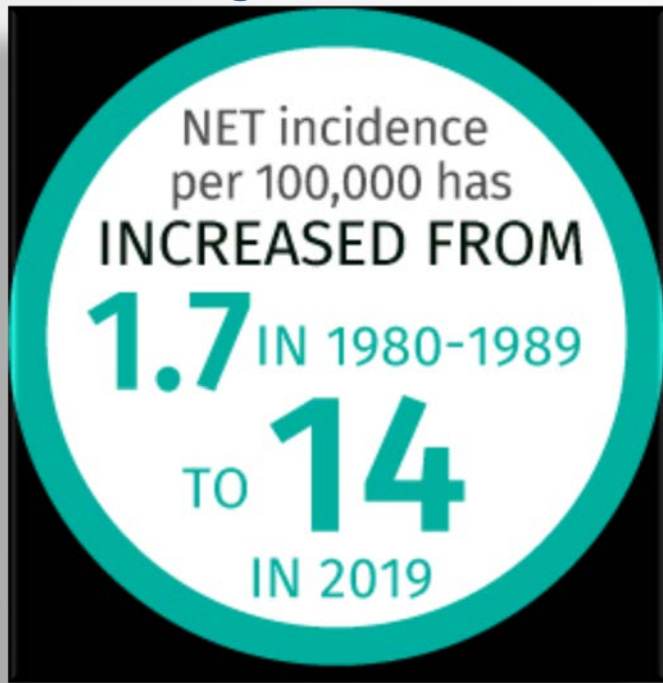
Penn Image-Guided Interventions Laboratory

# ■ DISCLOSURES

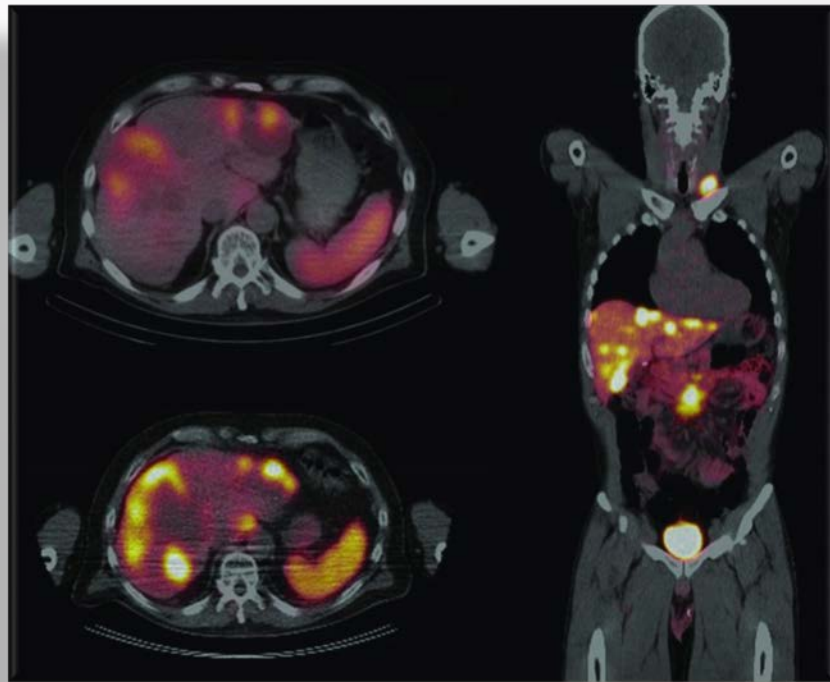
- Trisalus Life Sciences- Scientific Advisory Board
- Grant Funding
  - NIH
  - Veterans Administration
  - Society of Interventional Oncology
  - Society of Interventional Radiology
  - RSNA

# NETs: A GROWING HEALTH PROBLEM

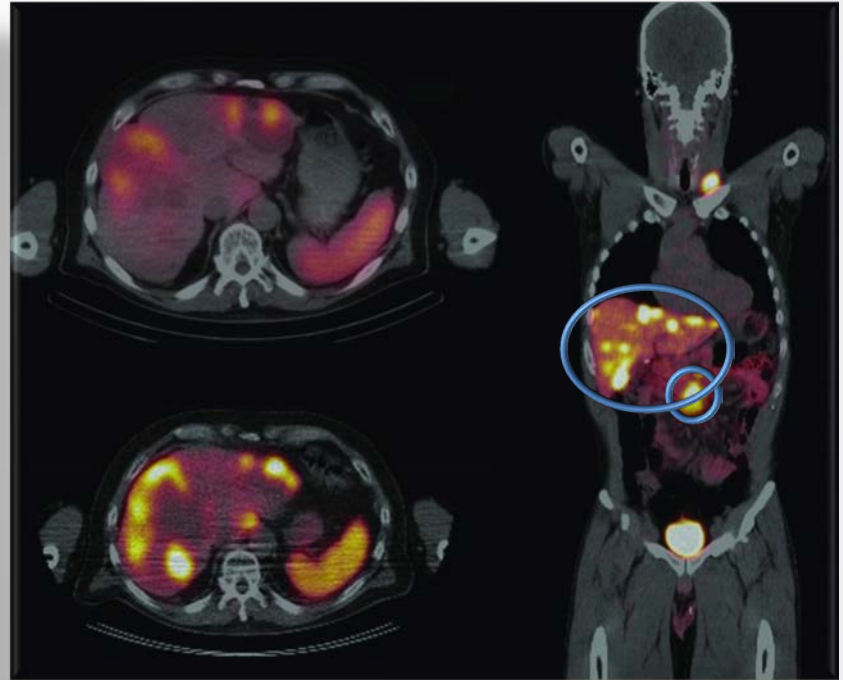
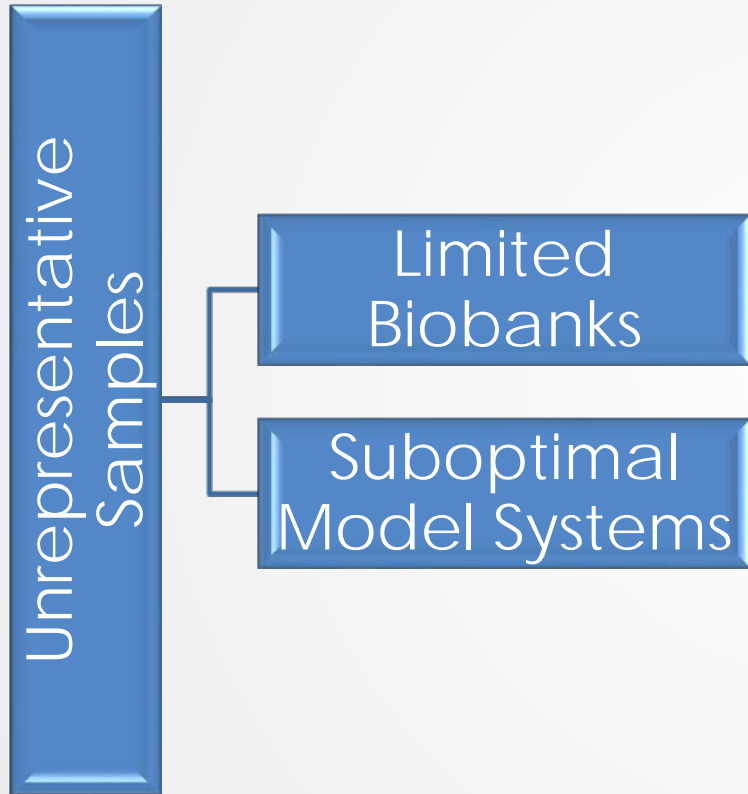
## Increasing Incidence of NET



## Metastatic Disease is Common



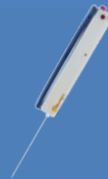
# THERAPEUTIC TARGETING OF mNETs: CHALLENGES



# Penn mNET Biopsy Protocol



**Observational Clinical Trial:**  
Biopsy of Liver mNETs at time of TAE/TACE



Genetic  
Sequencing

Genome  
Mapping

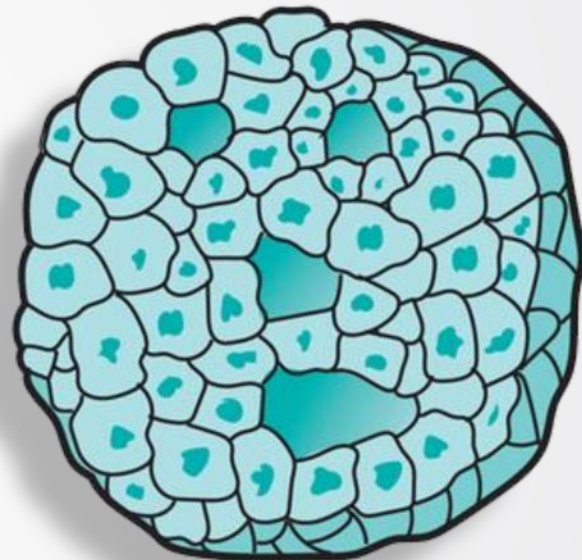
Metabolomic  
Profiling

Model  
Generation

# MODEL GENERATION: ORGANOIDS

## Tumor Organoids Provide Unique Cancer Models

- Self-organizing 3D structures grown *in vitro*
- Recapitulate the architecture and function of the parent human tumor
- Diverse applications
  - Study of representative cancer biology
  - Precision medicine
    - Identify optimal therapy for each patient



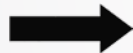
Schematic of Tumor Organoid

# mNET ORGANOID CREATION: CHALLENGES

mNET  
Patient



Biopsy

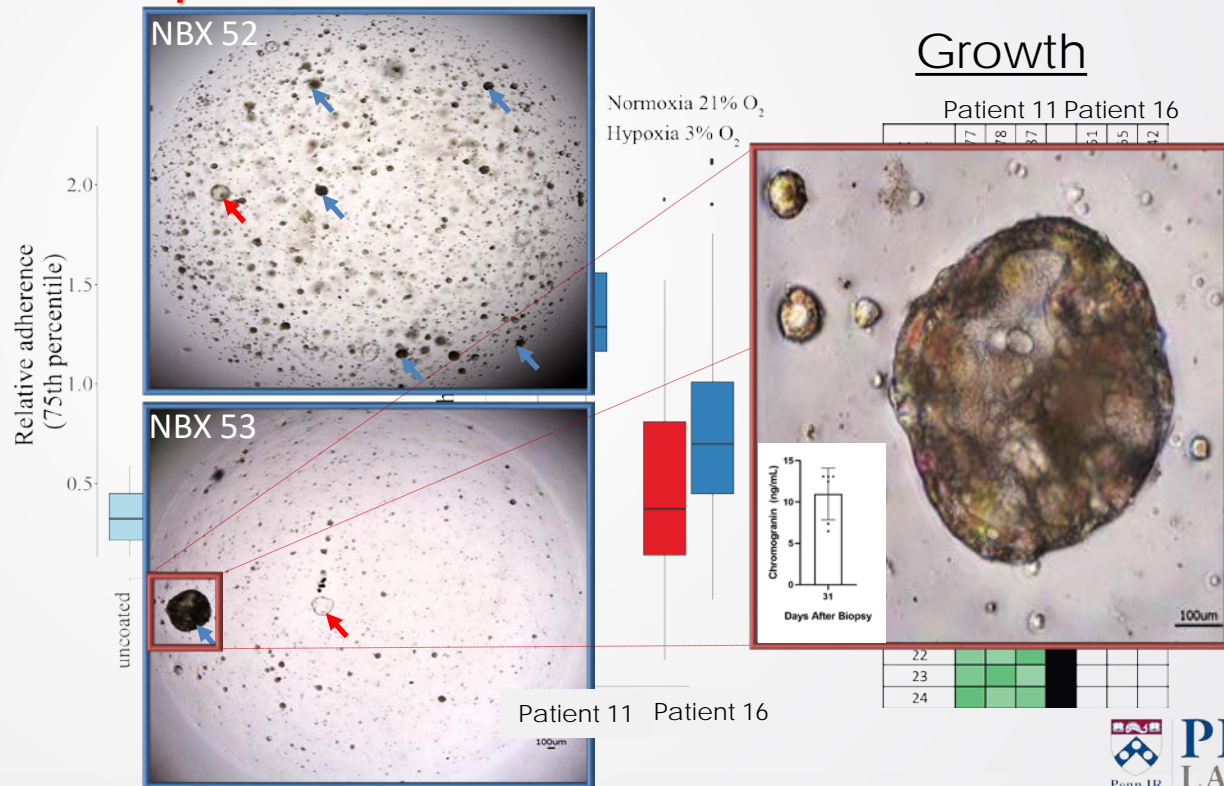


Methods for organoid generation from mNET biopsy samples are not well established

mNET  
Patient



## Biopsy

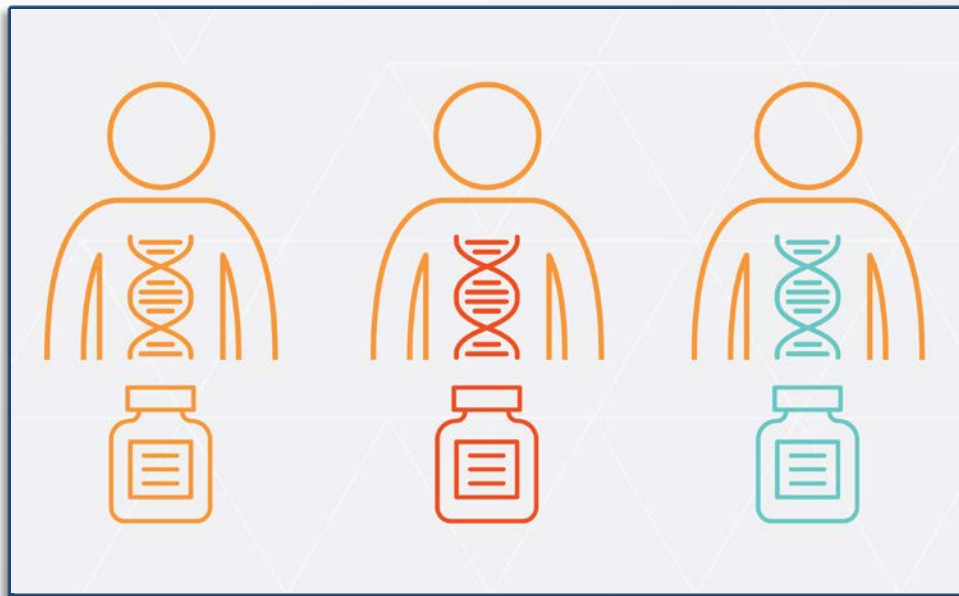


# PRECISION MEDICINE

Personalized therapy against specific vulnerabilities in each patient's cancer

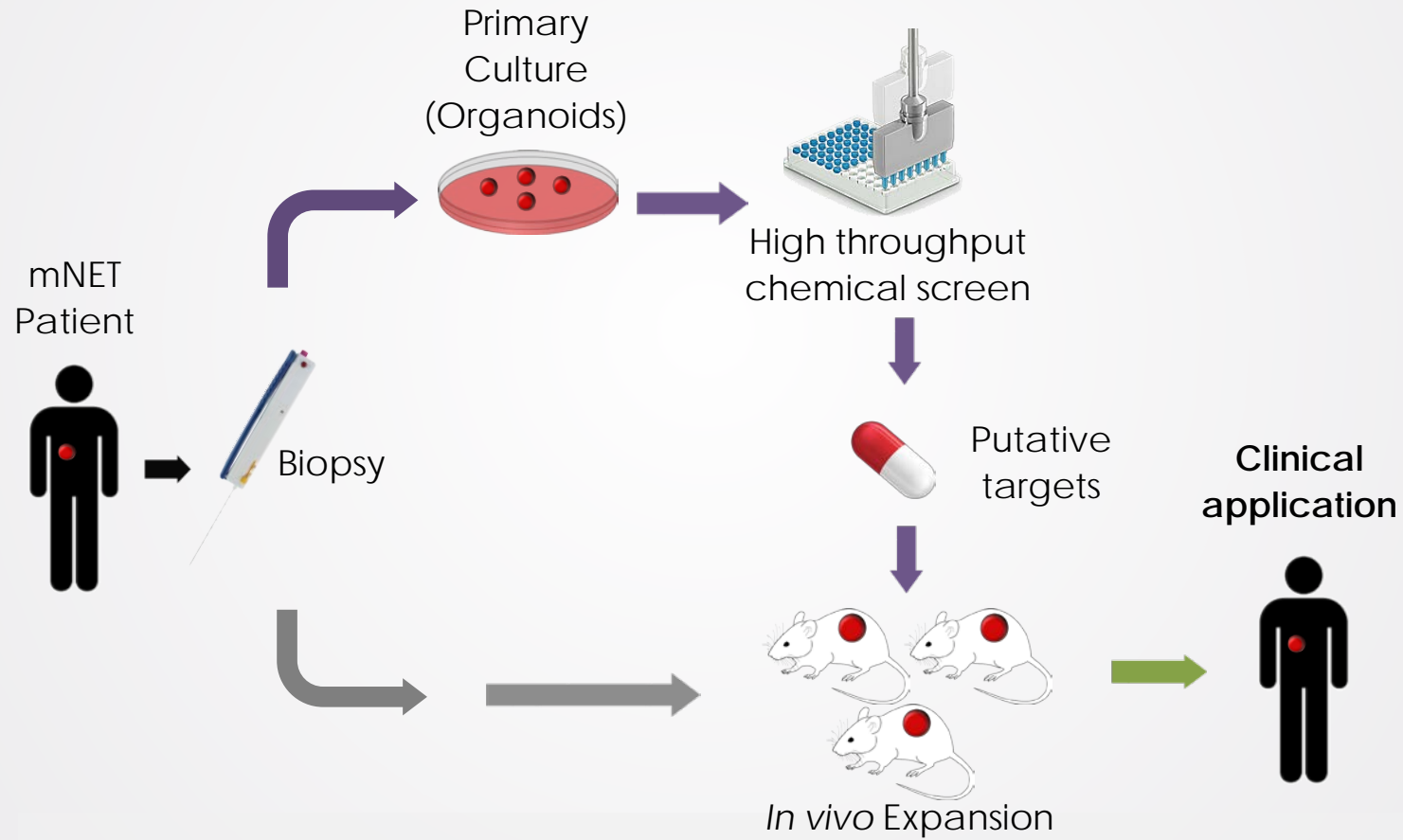
## Key Components

- Consistent acquisition of tissue samples
- Safety & compatibility with current clinical workflow
- Robust patient-derived models (organoids)



*The right drug for the right patient*

# PARADIGM

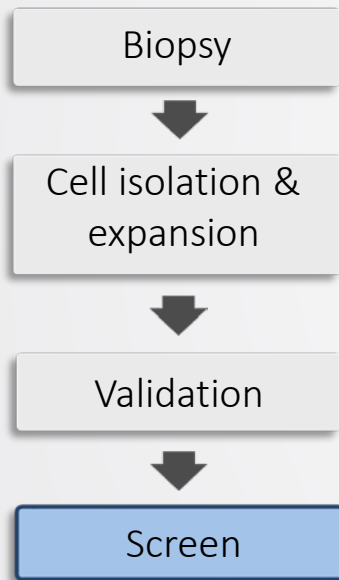


# Precision Medicine: Patients 17 & 20

## 44 Hits that overlap

**15 Hits unique to Patient 17 (M898)**

**8 Hits unique to Patient 20 (M2842)**



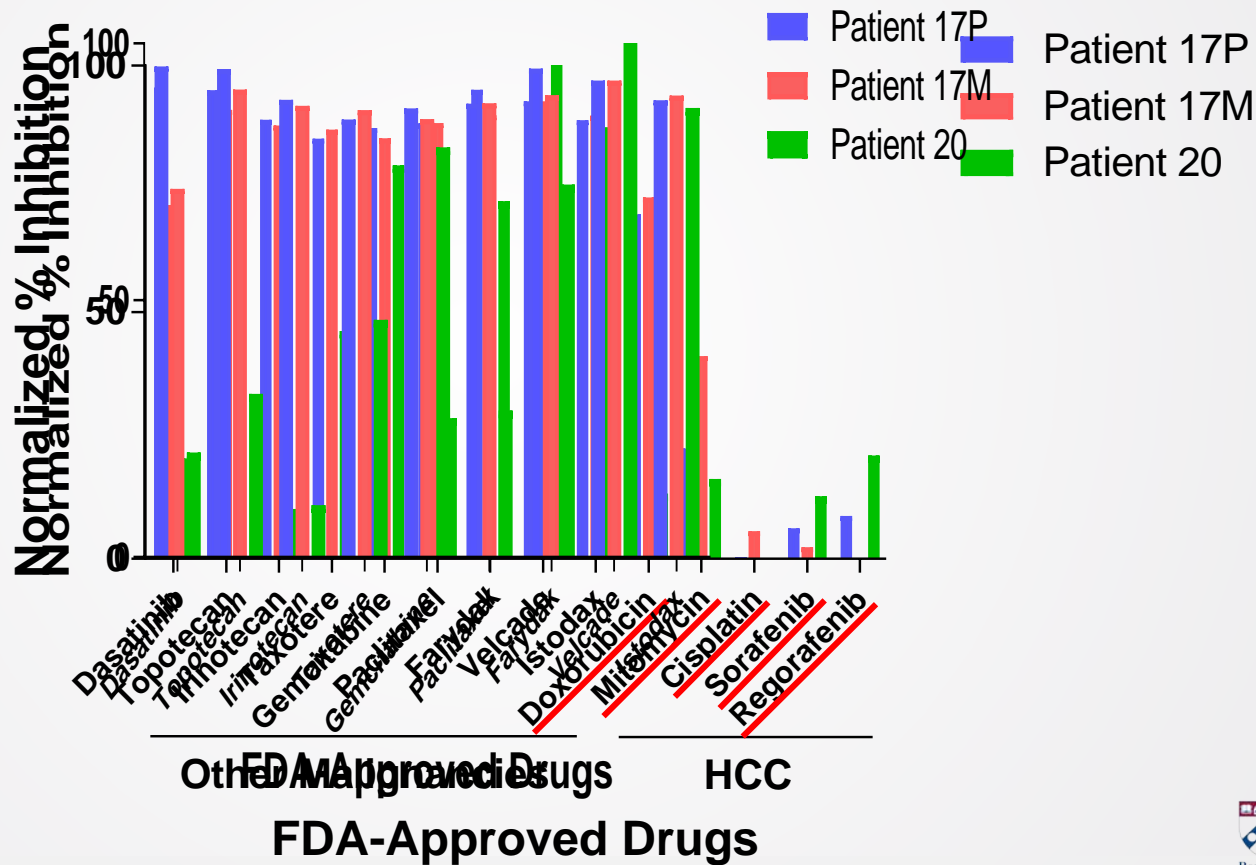
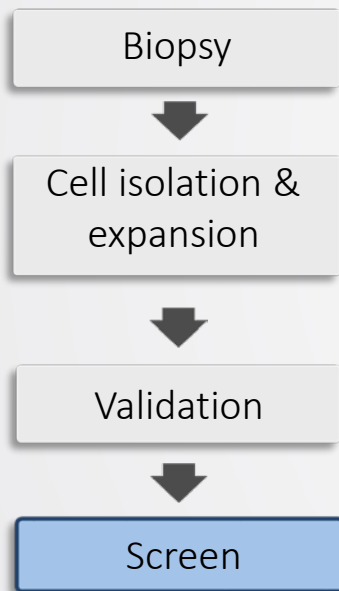
Product Name	Class	Catalog No.	Targets
PHA-793887	kinase	S1487	CDK
Celecoxib	cancer	S1261	COX
PP121	kinase	S2622	DNA-PK, PD
I-BET151 (GSK120151A)	epigenetic	S2789	Epigenetic
GW9508	cancer	S8014	GPR
Atorvastatin Calcium	metabolis	S2077	HMG-CoA
BI-847325		S7843	MEK
Pimasertib (AS-703026)	kinase	S1475	MEK
Cephalomannine	other	S2408	Others
Elaiophylin	microbiok	S1448	Others
Apigenin	metabolis	S2262	P450 (e.g.
VS-5584 (SB2343)		S7016	PI3K
EHop-016	kinase	S7319	Rac
Dasatinib Monohydrate		S7782	Src
QNZ (EVP4593)	cancer	S4902	TNF-alpha

Patient 17M

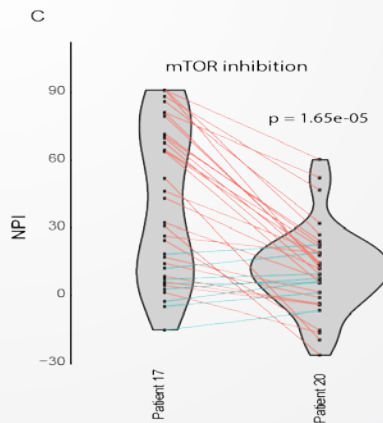
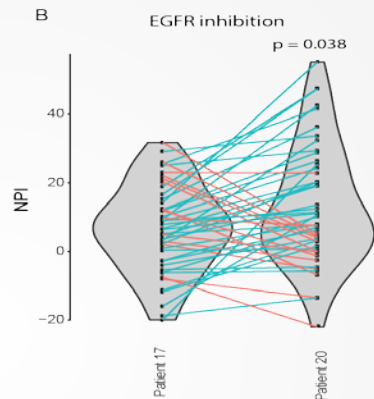
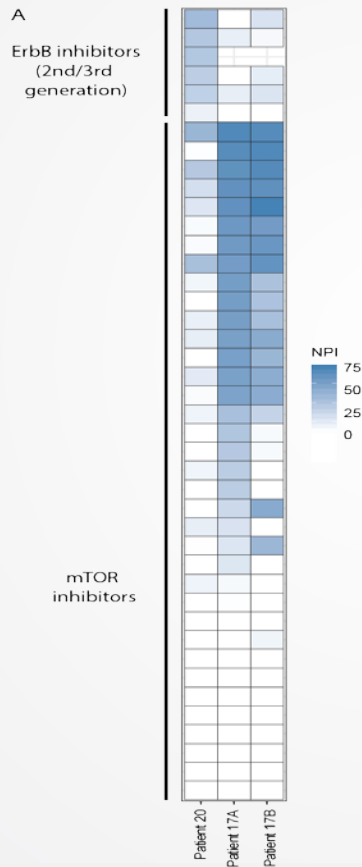
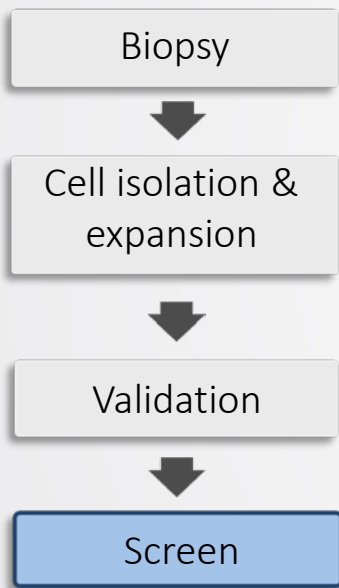
Product Name	Class	Catalog No.	Targets
Oligomycin A	IonCh	S1478	ATPase
Gemcitabine	cancer	S1714	Autophagy,DNA/RNA Synthesis
GZD824	kinase	S7194	Bcr-Abl
Dinacilicb (S127935)	kinase	S72768	IGF1R
Gemcitabine (S1714)	cancer	S1714	DNA/RNA Synthesis
Panobinostat (LBH589)	epigenetic	S1030	HDAC

Product Name	Class	Catalog No.	Targets
Deguelin		S8132	Akt
KPT-276	HIF	S7251	CRM1
Poziotinib (HM781-36B)	HSP (e.g. HSP90)	S7358	EGFR
Mitoxeresib (ABBV-075)	HSP (e.g. HSP90)	S8400	Epigenetic
17-AAG (Tanespimycin)	Kineasin	S1141	HSP (e.g. HSP90)
BMS-707035	Microtubule Associated	S1366	Integrase
BAY 1217389	Microtubule Associated	S8215	Kinesin
NMS-873	Microtubule Associated	S7285	p97
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# Precision Medicine: Patients 17 & 20



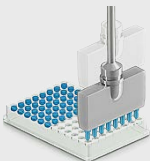
# Precision Medicine: Patients 17 & 20



# SUMMARY



- Feasible to establish mNET organoid cultures from needle biopsy samples



- Drug screening enables identification of existing, FDA-approved drugs on a patient-by-patient basis



Foundation for precision medicine approach to mNET

# FUTURE DIRECTIONS: DEVELOPMENT FOR CLINICAL IMPLEMENTATION

- 1 Optimize culture of, and validate, *in vitro* (organoid) & *in vivo* models

# FUTURE DIRECTIONS: DEVELOPMENT FOR CLINICAL IMPLEMENTATION

- 1 Optimize culture of, and validate, *in vitro* (organoid) models
- 2 Leverage models for precision medicine paradigm for patients with mNETs

# ACKNOWLEDGEMENTS

## Patient Volunteers

### PIGI Lab

Penn IR

Dan Ackerman

Kelley Weinfurtnr

Michael Soulen

Greg Nadolski

Stephen Hunt

James Chen

## Stem Cell & Xenograft Core

Tony Secreto

Josh Glover

## HT Screening Core

Sara Cherry

David Schultz

## Funding



## Philanthropy

Rick Mainwaring