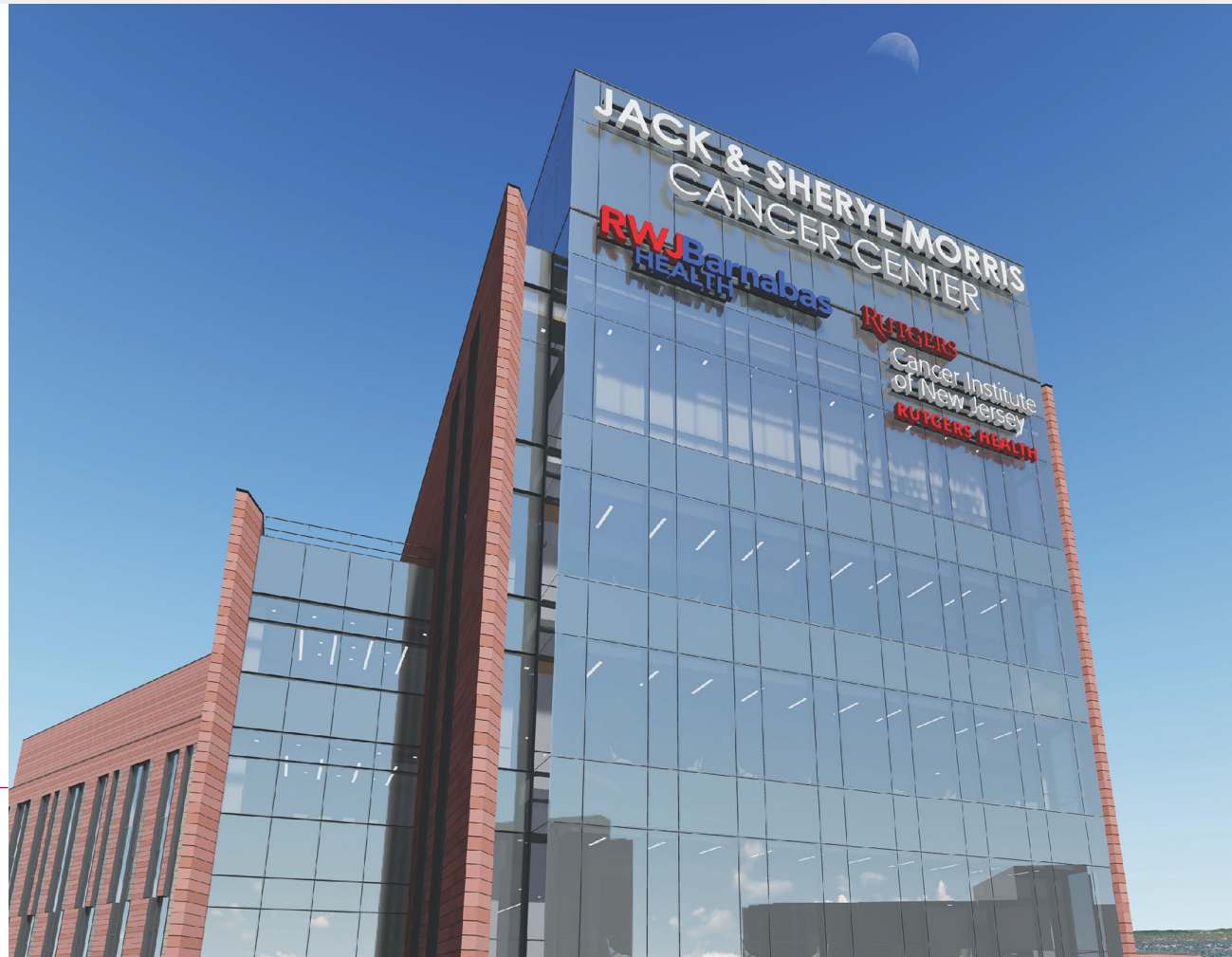


Clinical Investigations and Precision Therapeutics

Shridar Ganesan, MD, PhD
Wadih Arap, MD, PhD

April 26, 2023



RUTGERS
Cancer Institute
of New Jersey
RUTGERS HEALTH

NCI Comprehensive
Cancer Center
A Cancer Center Designated by the
National Cancer Institute



RWJ Barnabas
HEALTH

Clinical Investigations and Precision Therapeutics



Shridar Ganesan, MD, PhD

Omar Boraie Chair in Genomic Science
Chief, Molecular Oncology

- NCI R01s (2)
- NCI P01 Project
- ECOG Trials (2)
- DoD

Ganesan's Role in Program

- Liaison to DSGs/members (NB)
- Expert in Cancer Genomics



Wadih Arap, MD, PhD

Director, CINJ at University Hospital
Chief, Hematology/Oncology, RU NJMS

- NCI R01s (2)

Arap's Role in Program

- Liaison to DSGs (UH/NJMS)
- Expert in Experimental Therapeutics

Shared Program Responsibilities

- Work with clinical investigators across RWJBH to translate Center science into high impact translational and clinical research
- Mentor junior faculty
- Run CIPT Program meetings
- Encourage collaboration with other Programs
- Emphasize catchment area priorities to program members
- Work to increase diversity through recruitment and training programs
- Evaluate new members

Program Aims

AIM
1

To target **cell death and survival** pathways in cancer treatment and prevention (collaboration with CMI and CP)

AIM 1

Arap*	Long-Traynor*
Berger*	Panettieri*
Evens*	Schaar
Ganesan	Steinberg
Jabbour	Strair
Kahaleh	Suh*
Langenfeld	

*New Member

Program Aims

AIM
1

To target **cell death and survival** pathways in cancer treatment and prevention (collaboration with CMI and CP)

AIM
2

To target **DNA repair and cell cycle** checkpoint abnormalities in cancer (collaboration with GICG and CP)

AIM 2

Aleksunes	Howell
Baker*	Jabbour
Braver*	Kim*
Cole*	Mattes*
D'Ambrosio*	Omene
Foran	Parikh*
Ganesan	Salacz*
Haffty	Steinberg
Hatout*	Stephenson*
Hochster	

*New Member

Program Aims

AIM
1

To target **cell death and survival** pathways in cancer treatment and prevention (collaboration with CMI and CP)

AIM
2

To target **DNA repair and cell cycle** checkpoint abnormalities in cancer (collaboration with GICG and CP)

AIM
3

To target the **immune microenvironment** in cancer (collaboration with CMI and CP)

AIM 3

Arap*	Jabbour
Beaulieu*	Kowzun*
Einstein	Libutti
Ganesan	Mayer
George*	Nehra*
Ghoduossipour*	Omene
Gulhati*	Pierce
Haigentz*	Sarkar*
Hinrichs*	Shah*
Hochster	Stephenson*
Hou*	Weiss*

*New Member

Program Aims

- AIM 1** To target **cell death and survival** pathways in cancer treatment and prevention (collaboration with CMI and CP)
- AIM 2** To target **DNA repair and cell cycle** checkpoint abnormalities in cancer (collaboration with GICG and CP)
- AIM 3** To target the **immune microenvironment** in cancer (collaboration with CMI and CP)
- AIM 4** To investigate markers of **response and resistance to cancer therapy** (collaboration with CP, CMI and GICG)

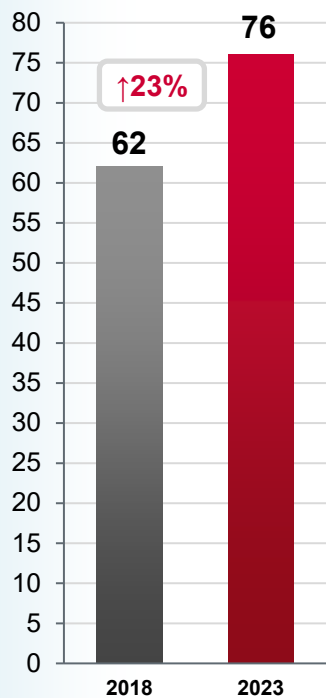
AIM 4

Agarwalla*	Girda*	Ohri*
Alexander	Goel*	Palmisiano*
Bhatla*	Haigentz*	Pierce
Boland*	Hochster	Prud'homme*🏆
Chaudhary	Imanguli*	Riedlinger
Cohen*	Kahaleh*	Roden*
Deek*	Kim*	Saraiya
Doraiswamy*	Langan*	Schleicher*
Drachtman	Leiser*	Sharma*
Eladoumikdachi*	Liu*	Toomey*
Evens	Lue*	Toppmeyer
Ganesan	Masterson	Zhang*
George*	Moerdler*	

*New Member

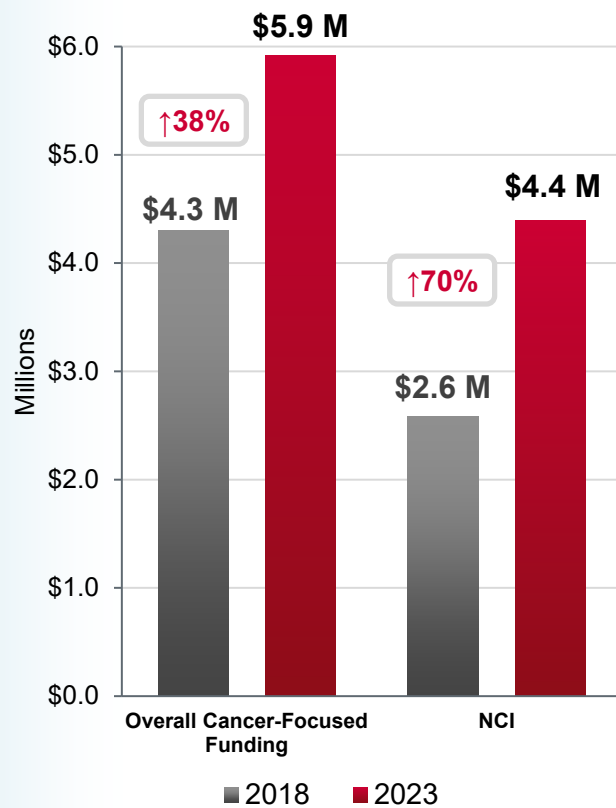
Program Membership Profile

Membership

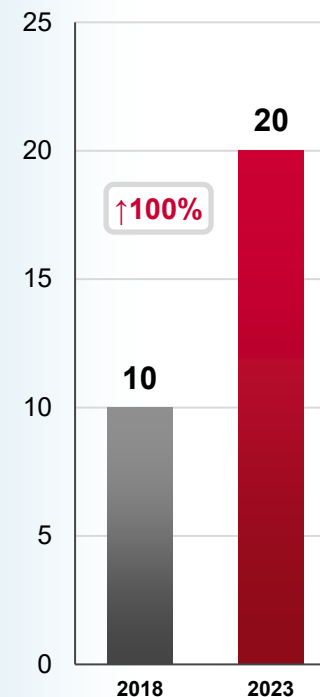


2023
22 Departments
7 Schools
2 Universities
44 New Members

Total Cancer Relevant Funding



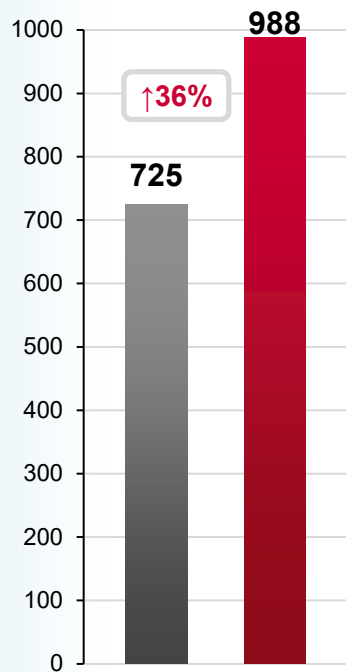
R01 Equivalents



2018: 10 PIs/PDs
2023: 15 PIs/PDs

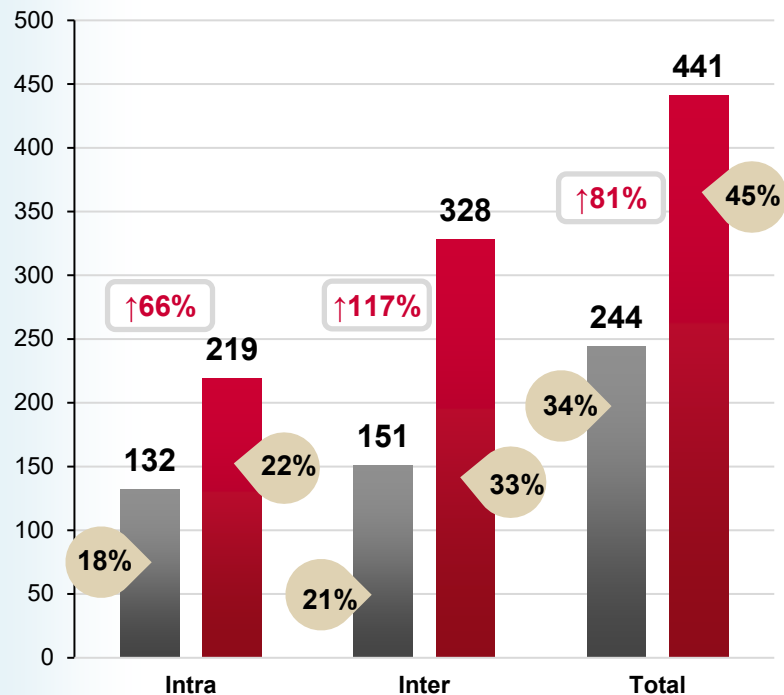
Program Productivity and Collaborations

Total Publications



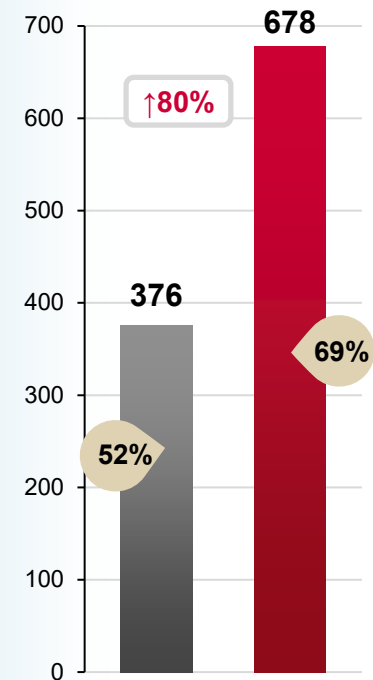
■ 2018 Submission ■ 2023 Submission

Collaborative Publications



■ 2018 Submission ■ 2023 Submission

Collaborative Publications with Other Institutions



■ 2018 Submission ■ 2023 Submission

Response to Prior Critique

Scored **Excellent to Outstanding**

Expand Precision Medicine

- Molecular Tumor Board now regularly attended by Partner institutions in Health system and trainees across Consortium
- Precision Oncology platform and MTB led to multiple high impact translational discoveries leading to grants, publications

Increase Peer Reviewed Funding

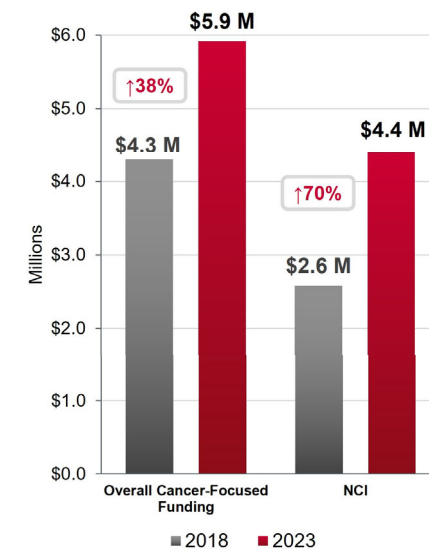
- Significantly increased cancer focused funding

Multi-project Grants

- Obtained P01 in DNA repair in collaboration with GICG
- CIPT members participated in multi-institution NCI grants (UM1, UH3)
- CIPT member is project leader on inter-institutional NET SPORE



Total Cancer Relevant Funding



Scientific Impact of Program

Novel Biomarkers of Response and Resistance

- Mutation burden in immune checkpoint therapy
- ERV as a mechanism of immunogenicity in low mutation burden cancers
- Novel mechanisms of resistance to targeted agents
- Targeting PIK3CA mutations in vascular malformations
- **Identification of truncated FGFR2 as a potent, targetable oncogenic driver in multiple cancers**

Development of new treatment approaches

- Novel BMP inhibitors
- New gene therapy vectors and ADCs
- Novel targets for immunotherapy

Investigator-Initiated Clinical trials

- Neo-adjuvant chemo-immunotherapy in locally advanced NSCLC
- Novel design of neo-adjuvant therapy for TNBC
- Cellular immunotherapy: TCR targeting HPV E7 and KKLC1
- First *in vivo* metabolic tracing studies in human pancreatic and breast cancer

Article

Truncated *FGFR2* is a clinically actionable oncogene in multiple cancers

<https://doi.org/10.1038/s41586-022-05066-5>

Received: 19 January 2021

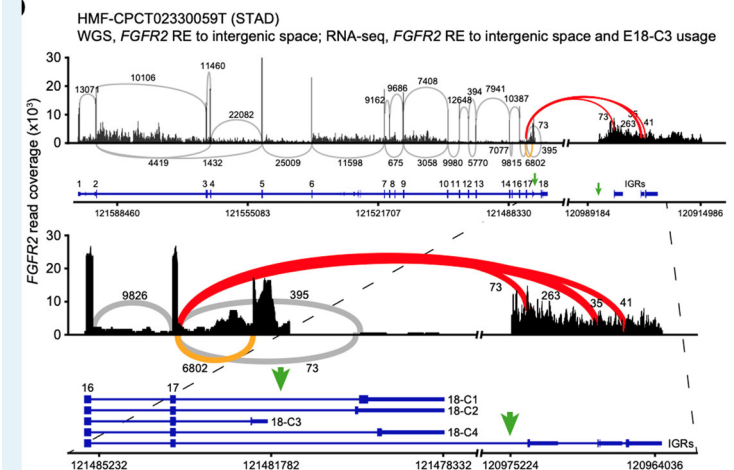
Accepted: 3 July 2022

Published online: 10 August 2022

Open access

Check for updates

Daniel Zingg^{1,2,22}, Jinhyuk Bhin^{1,2,3,22}, Julia Yemlyanenko^{1,2,22}, Sjors M. Kas^{1,2,22}, Frank Rolfs^{1,2,4}, Catrin Lutz^{1,2}, Jessica K. Lee⁵, Sjoerd Klarenbeek⁶, Ian M. Silverman⁷, Stefano Annunziato^{1,2}, Chang S. Chan^{8,9}, Sander R. Piersma⁴, Timo Eijkman^{1,2}, Madelon Badoux^{1,2}, Ewa Gogola^{1,2}, Bjorn Siteur¹⁰, Justin Sprengers¹⁰, Bim de Klein^{1,2}, Richard R. de Goeij-de Haas⁴, Gregory M. Riedlinger¹¹, Hua Ke^{8,9}, Russell Madison¹², Anne Paulien Drenth^{1,2}, Eline van der Burg^{1,2}, Eva Schut^{1,2}, Linda Henneman^{1,2,5,9}, Martine H. van Miltenburg^{1,2}, Natalie Proost^{1,2}, Huiling Zhen^{1,2}, Ellen Wientjens^{1,2}, Roebi de Bruijn^{1,2,3}, Julian R. de Ruiter^{1,2,3}, Ute Boon^{1,2}, Renske de Korte-Grimmerink^{1,2}, Bastiaan van Gerwen^{1,2}, Luis Féliz^{1,2}, Ghassan K. Abou-Alfa^{1,2,5}, Jeffrey S. Ross^{1,2,5}, Marieke van de Ven^{1,2}, Sven Rottenberg^{1,2,13,8}, Edwin Cuppen^{13,9,25}, Anne Vasilin Chessaux²¹, Siraj M. Alif, Timothy C. Burn⁷, Connie R. Jimenez⁴, Shridhar Ganesan^{8,9,21}, Lodewyk F. A. Wessels^{2,22} & Jos Jonkers^{1,2,22}



Decreasing Cognitive Toxicity of Chemotherapy in Children



Cole



Long-Traynor



Baker
(CP)



Evens

Shared Resources

- Biospecimen Repository and Histopathology Service
- Comprehensive Genomics

Grants

- NIH/NCI R01 CA240360
- NIH/NCI R01 CA220568
- NIH/NCI R01 CA182284

Publications

Williams and Cole, *JCO* 2021
Song, et al., *Blood Advances* 2020
Ladas, et al., *JCO* 2020
Brace, et al., *J Clin Exp Neuropsych* 2019

Major Discoveries

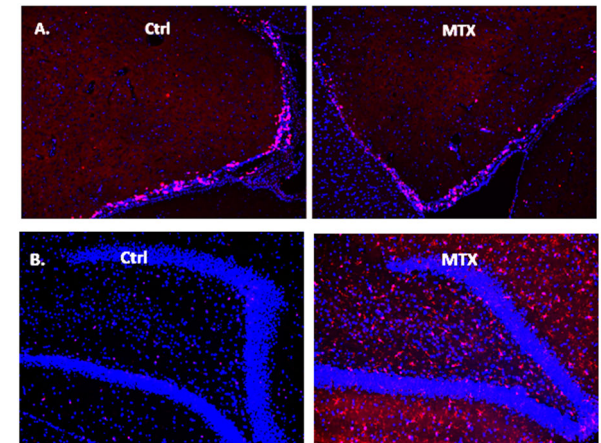
- Common genetic variants confer increased susceptibility to CRCI.
- Changes from baseline cognitive function can be detected during therapy for childhood leukemia.
- Rats treated with chemotherapy at clinically relevant doses reliably show cognitive deficits and neuropathology.
- Two interventions, memantine and antioxidants, have shown efficacy in preventing deficits in this rat model.

Ongoing Next Steps

- Clinical biomarker development
- Prospective clinical trial

Impact

Identified biomarkers that identify risk for CRCI and novel interventions for prevention



Compared to control animals, methotrexate-treated rats show decreased proliferation of neural precursors (A) and increased microglial activation, changes that persist >1 yr after the last dose of chemotherapy.

Catchment Priority

Social Determinants

Disparities Focus

Poor outcomes in Hispanic children with ALL

Rational Targeting of DNA Repair Defects in TNBC



Shared Resources

- Biomedical Informatics
- Biospecimen Repository and Histopathology Service
- Comprehensive Genomics

Grants

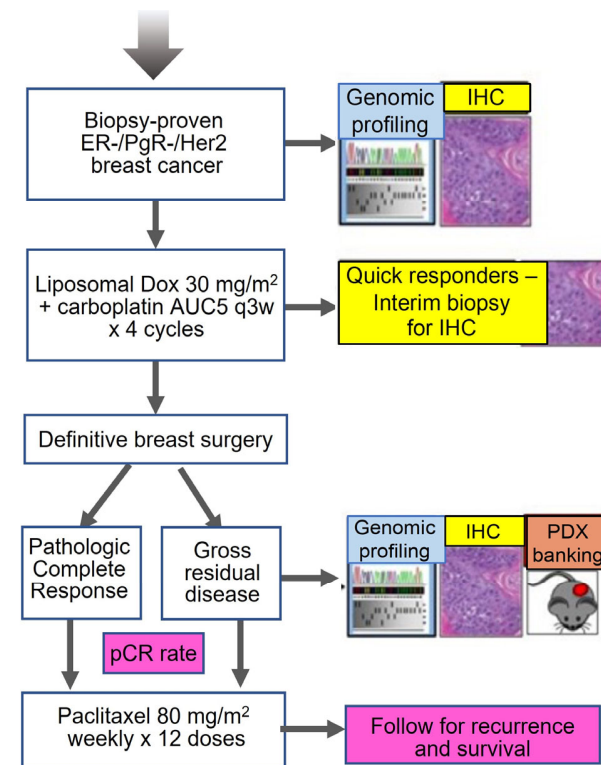
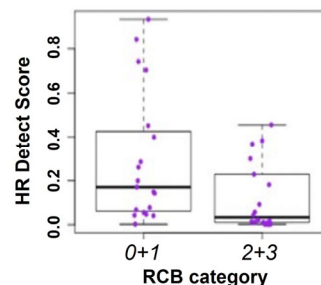
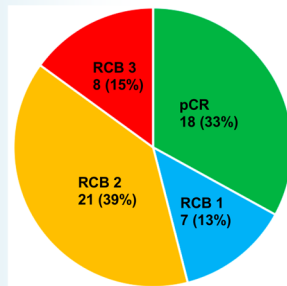
- P01 CA250957
- NJCCR Translational Award
- Pilot Funding: CETI, NJ-ACTS

Publications

- Sokol et al., *JCO Precision Onc* 2020
- Khiabnian et al., *JCO Precision Onc* 2018
- Chan et al., *Can Res Supp* 2022

Major Discoveries

- PARP inhibitors and certain classical chemotherapies are targeted agents for HRD cancers
- Methods developed to identify patterns of structural alterations that can identify HRD associated with BRCA-pathway defects
- Development of a PK-inspired regimen Doxil+Carboplatin that is effective and less toxic
- Genomic signatures of HRD associated w/response
- Epigenetic regulators are targetable in HRD deficient cancers



Impact

Rationally reducing toxicity, enhancing efficacy of chemotherapy for TNBC

Catchment Priority

Breast Cancer, Hereditary Cancer

Disparities Focus

Genomic landscape of TNBC in Black women

Clinical Translation from CMI



White (CMI)



Rabinowitz (CMI)



Hochster



Omene (COE Liaison)

Shared Resources

- Biomedical Informatics
- Biospecimen Repository and Histopathology Service
- Comprehensive Genomics

Grants

- Ludwig-Princeton Branch grant

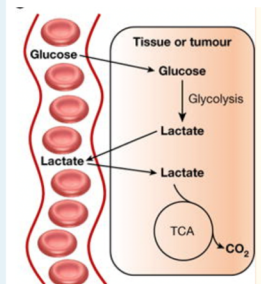
Publications

Poillet-Perez, *Nat Cancer* 2020
Nagarsheth, *Nat Medicine* 2021

Major Advances

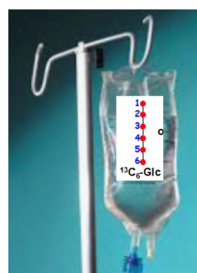
In vivo metabolic tracing of human cancer: pancreatic cancer and breast cancer

Glucose feeds tumor TCA through lactate

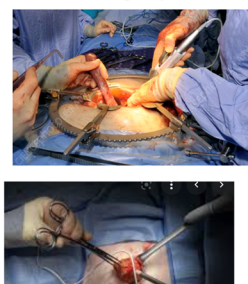


Hui et al, Nature

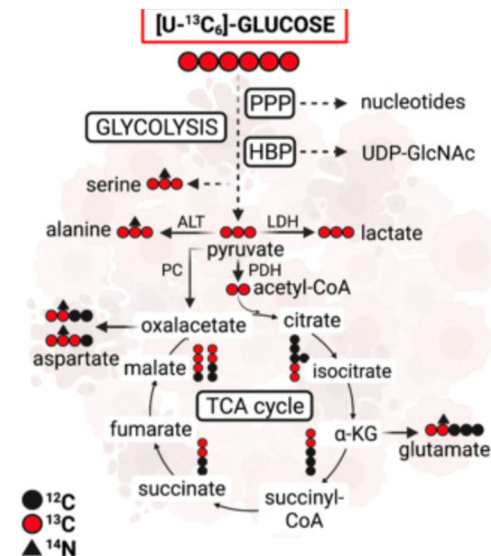
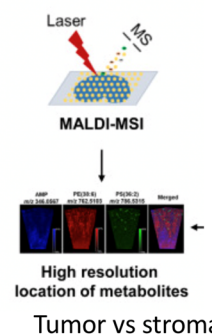
Tracer Infusion



Specimen Acquisition at Surgery



Metabolomic Analysis



Impact

In vivo metabolic analysis of human cancer; pancreas cancer metabolic labelling trial open and accruing (NCT05296421); breast cancer metabolic labelling trial registered and will open soon (NCT05736367)

Catchment Priority Breast Cancer

Truncated FGFR2: Oncogenic/Targetable in Multiple Cancers



Ganesan



Chan (GICG)



Riedlinger



Hochster

Shared Resources

- Biomedical Informatics
- Biospecimen Repository and Histopathology Service
- Comprehensive Genomics

Grants

- R01, Ganesan, C. Chan (in preparation)
- Pilot Funding: CETI

Publications

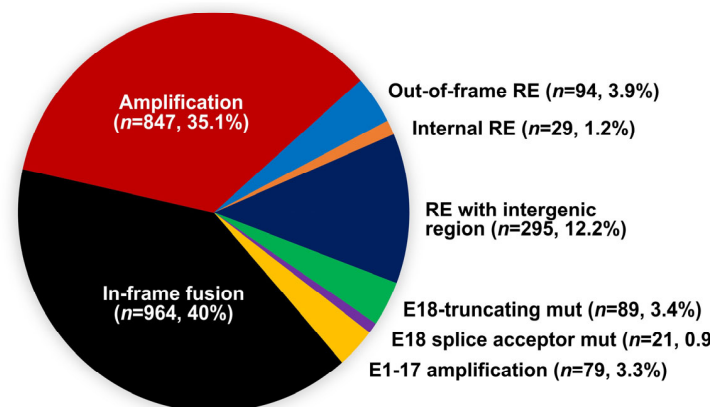
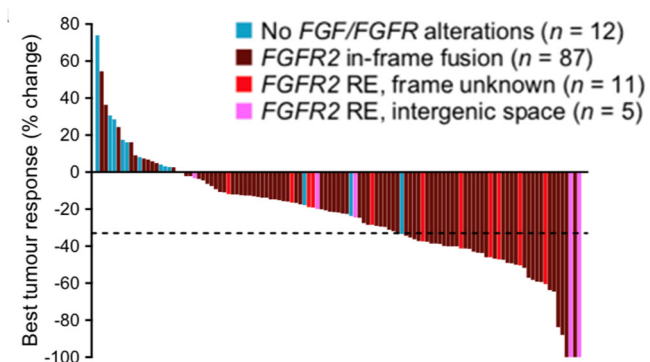
Zingg et al., *Nature* 2022

Major Discoveries

- Hybrid capture-based RNA sequencing demonstrated that out-of-frame FGFR2 rearrangements seen in tumors can generate a transcript encoding for truncated FGFR2
- Truncated FGFR2 is oncogenic in mouse models, and sensitive to FGFR2 inhibitors
- Cholangiocarcinomas with non-canonical FGFR2 alterations respond to FGFRi
- Genomic alterations that can generate truncated FGFR2 transcript are present in multiple cancer types including breast

Impact

Increases number of patients and cancer types that will benefit from FGFR-targeted therapy; **Clinical Trial in development**



Catchment Priority
Breast Cancer

Using Real World Evidence to Stratify Lymphoma

AIM
4



Evens



David
(Former CIPT)

Shared Resources

- Biostatistics

Grants

- 1R01CA262265

Publications

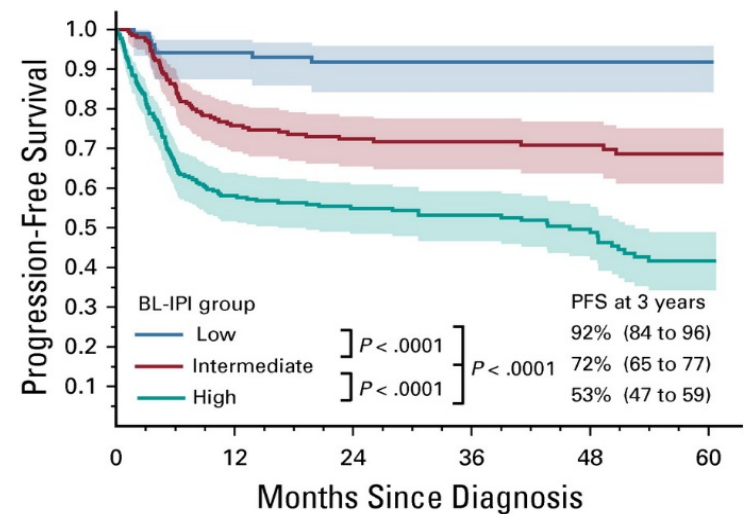
Evens et al., *Blood* 2021
Olszewski et al., *JCO* 2021
Rodday et al., *JCO* 2022
Evens et al., *Hematologica* 2022

Major Discoveries

- Largest analysis of Burkitt lymphoma completed to date (all work led by CINJ)
- New prognostic model for Burkitt derived and validated (BL-IPI)
- Pre-clinical work identified PI3 kinase as a key pathway of resistance in high-grade lymphoma
- RWE based prognostic index for Advanced Hodgkin's Lymphoma developed and validated

Impact

Identified and validated clinical prognostic indexes for Burkitt and Hodgkin's Lymphoma

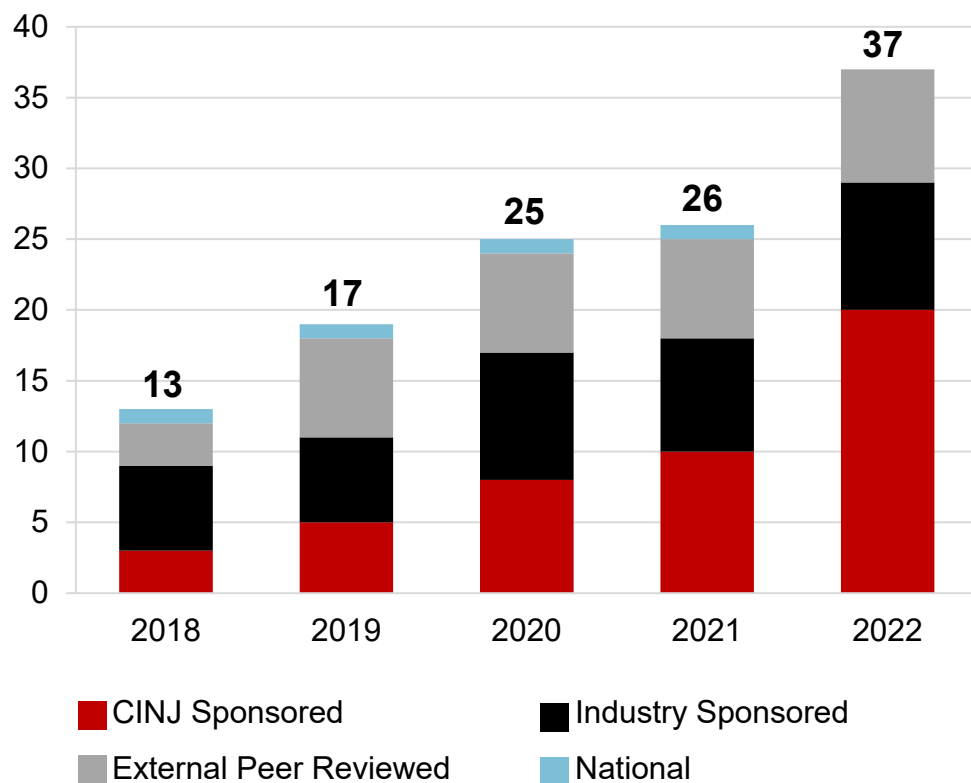


Disparities Focus

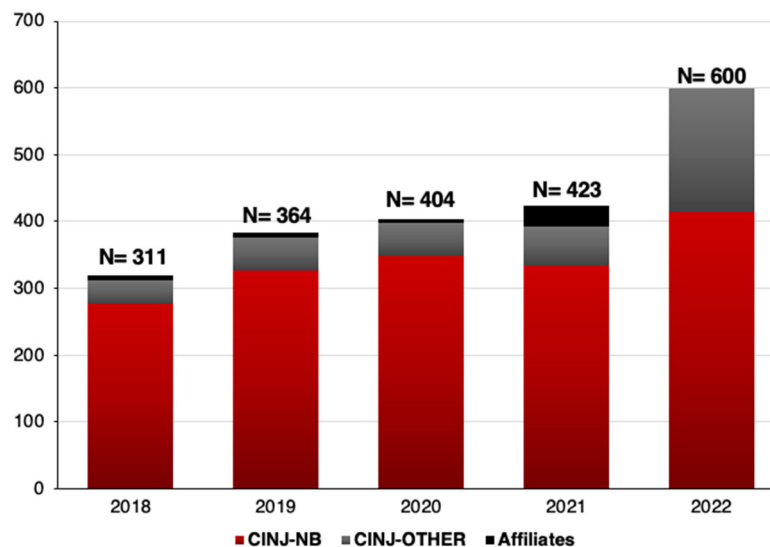
Older adults

Clinical Trial Portfolio

Number of Investigator-Initiated Trials by Funding Source



Treatment Accrual



CY2022

- **414** accruals at CINJ New Brunswick hub
- **186** accruals at other system sites

600 Total, 38% to Institutional IITs

**45% Minority Accrual
(from 37.5% in 2018)**

Research Responsive to Catchment Area



Omene
(COE Liaison)



Mattes



Ganesan



Omene



Haffty



Bandera
(CPC)



Zeinomar
(CPC)

Shared Resources

- Biomedical Informatics
- Biospecimen Repository and Histopathology

Grants

- Funded by CHECoE pilot award; Omene worked with COE to incorporate community input

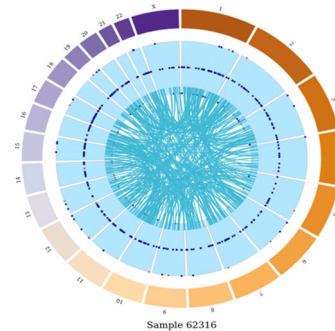
Publications

- Omene et al., *Cancer Immunol Res* 2020
Mattes et al., *Int J Radiat Oncol Biol Phys* 2022
Mattes et al., *Adv Radiat Oncol* 2021

1. Why do Black women have worse outcomes with TNBC?

PI: Omene

- What is the role of obesity and other host factors in this disparity?
- Investigate the rearrangement landscape and TME of TNBC in Black women



Obese, TNBC
Residual disease

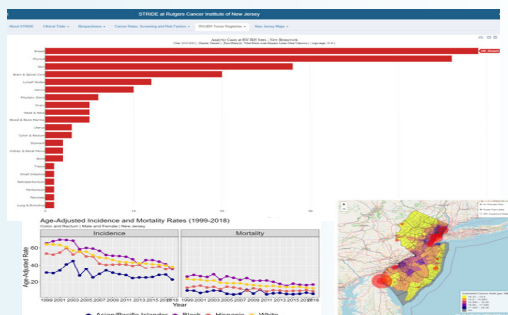
2. How can we increase diversity in Radiation Oncology?

PI: Mattes

- How do academic radiation oncology departments engage medical student populations that are under-represented in medicine?
- Need for increased outreach to under-represented populations by Radiation Oncology residency programs



Additional Examples of Catchment Area Responsiveness



Collaboration with COE

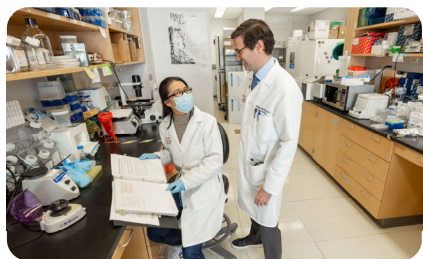
- **V Foundation Grant** (Omene) Enhancing Awareness and Participation of Black Breast Cancer Patients in Clinical Trials: Outreach and Engagement; working with community patient advocates
- **PINPOINT** (Ganesan, working with Kinney and Hudson) increasing awareness of precision oncology approaches in Black cancer patients
- **STRIDE**: Multiple CIPT investigators worked with COE to query **STRIDE dashboard** to help guide trial design and map out trial sites to best serve local populations



Bidirectional Communication with the Community

- **Dialogue with Community Cancer Action Board**
Hochster, George, Ganesan and Omene have had discussions with CCAB on clinical research, precision oncology, and clinical trial enrollment that have resulted in implemented strategies to increase enrollment of underrepresented populations
- **Interaction with Community Organizations** CIPT members Toppmeyer, Ganesan, Omene have engaged in public educational and research dialogues with local organizations (local chapters of Susan Komen, AHEPA, Hadassah) on cancer risk, screening and treatment; Community Science Café participation scheduled

Education and Training over Grant Period



Training Grants

- NCI R25 Rutgers Youth Enjoy Science
- NCI R25 Supp: Oncology Physician Training Initiative to Maximize Diversity
- T32 Environmental Toxicology
- R25 Summer Research Experience

Junior Faculty Training

- Clinical Trials in Progress
- ECI mentees CTEP



Fellowship Training in Oncology

- E.g., Medical, Surgical, Radiation

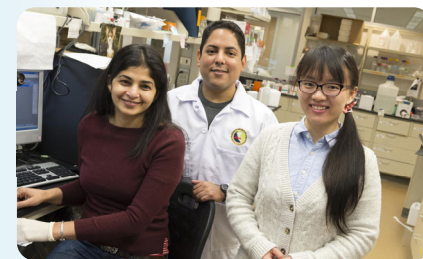
Precision Oncology: Molecular Tumor Board

- Attended by clinicians in network hospitals, nationally
- Attended by trainees: residents, fellows, Rutgers and PU undergraduates



Bioconnect/BOLD

- CIPT created training modules for middle school students
 - Virtual molecular lab
- Participate in BOLD summer program to introduce high school students to professions in cancer medicine



Graduate Students/ Postdoctoral Fellows

- 20 PostDocs, 18 GradStuds trained; ~6.8 pubs/PostDoc and 3.8 pubs/GradStud
- Academic positions
 - NYU
 - NCI
 - DFCI
- Industry positions
 - Novartis
 - Merck

Value Added: Center to Program

Development Funds

17 Pilot Awards
(CETI Awards and other RFAs)

~\$830,000

Support Services

- Office of Human Research Services
- All Shared Resources

Meetings and Retreats

- CIPT Program Meetings
- Investigator Meetings

Member Recruitment

46 Program members in current funding period

Administrative Contributions

- Grants Office
- Faculty Recruitment
- IST
- Multi-Project Application Support
- Medical Writer Services
- Specialized Research Administrative Support
- COE

PED

Helps with faculty recruitment/retention to enhance diversity

COE

Provides guidance on catchment area burden and community needs; connects members to community and Community Cancer Action Board

Value Added: Program to Center

- Key hub for translation of center science and inter-programmatic clinical collaboration
- Precision medicine efforts and MTB; platforms for education and collaborative research
- Opportunities for national validation of early phase trials through ET-CTN and Big Ten Collaborations

- **Policy Impact:**
CIPT members are part of ASCO guideline panels in somatic tumor testing, and renal cancer treatment
- **Education:**
Fellowships in Medical Oncology, Surgical Oncology, Radiation Oncology

PED

Members implementing research on how to increase diversity in training programs

COE

Responsiveness to catchment area priorities and needs: breast, colon, lung, prostate, and HPV-related cancers; disparities

Future Plans

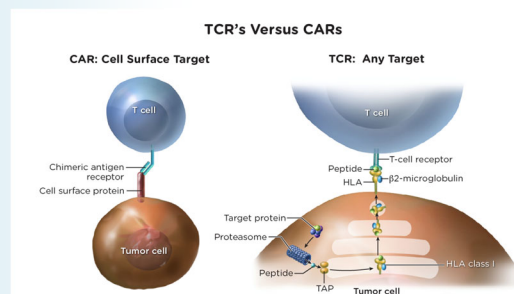
1 Expansion of Phase I Program

- RWJBarnabas Health: bring trials to patients
- First-in-human trials with Rutgers-developed compounds



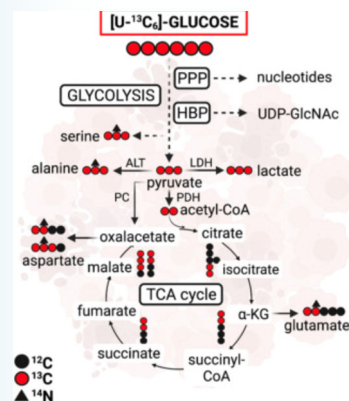
2 Development of Cellular Immunotherapy Program

- Expand repertoire of novel cellular immunotherapy agents, targeting solid and hematologic malignancies



3 Translational Studies from Ludwig-Princeton Branch

- Develop human studies geared to profile and intervene in metabolic and immunologic defects in cancer



4 Pediatric Cancer Focus

- Recruit to expand translational research in Pediatric Oncology, Supported by NJ State funds



Thank You

Q&A Segment



RUTGERS
Cancer Institute
of New Jersey
RUTGERS HEALTH

