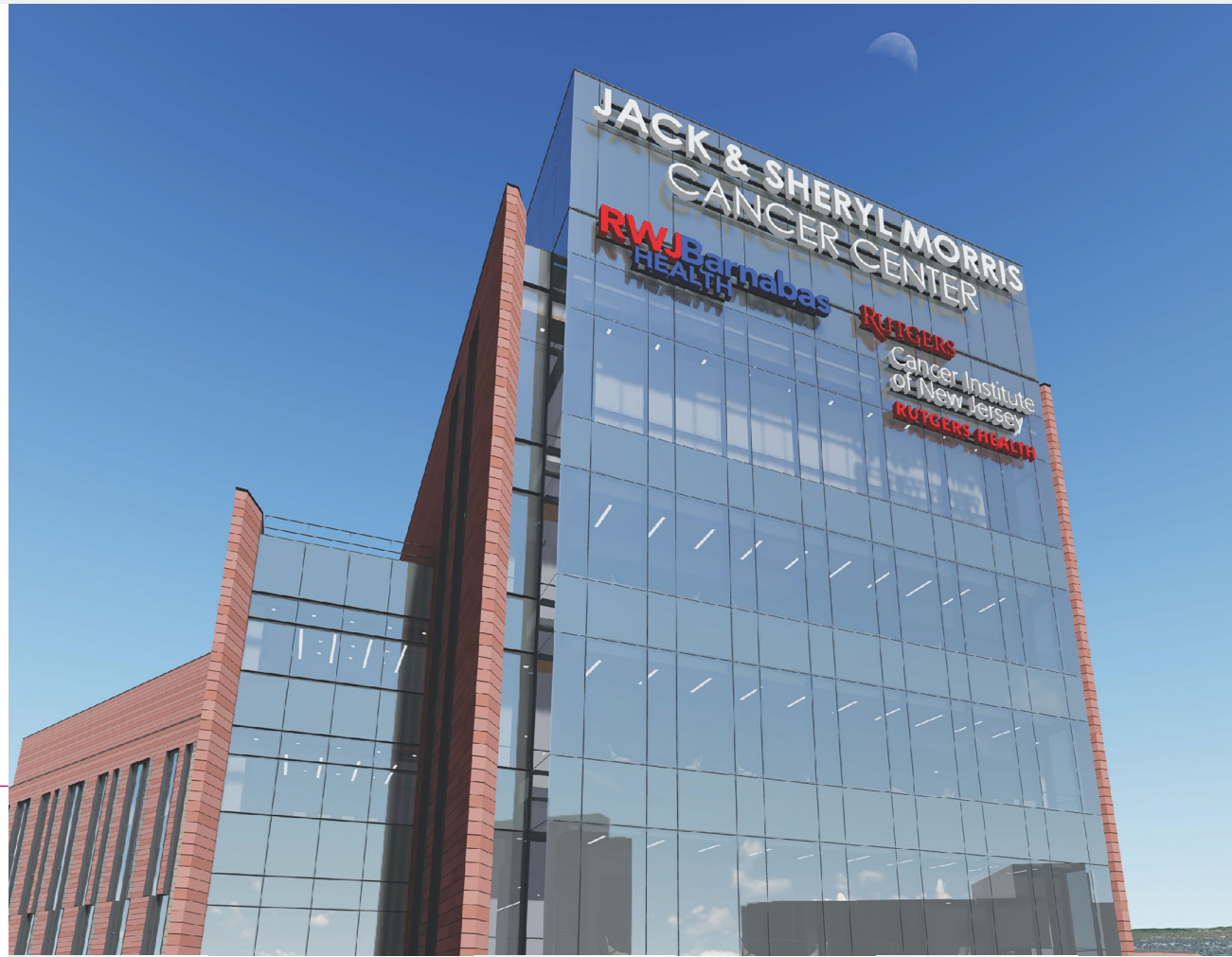


Cancer Metabolism and Immunology (CMI)

Wei-Xing Zong, PhD
Christian Hinrichs, MD

April 26, 2023

RUTGERS
Cancer Institute
of New Jersey
RUTGERS HEALTH



≡ Cancer Metabolism and Immunology



Wei-Xing Zong, PhD

John L. Colaizzi Professor
Chemical Biology

- NCI R01 (3)

Zong's Role in Program

- Expertise in Cancer Metabolism
- Co-Director of T32 Training Award



Christian Hinrichs, MD

Professor of Medicine
Chief, Cancer Immunotherapy

- NCI R00, Cancer Moonshot, and CCSG supplement

Hinrichs's Role in Program

- Expertise in Cancer Immunology
- Co-Director of Cancer Immunology and Metabolism CoE

Shared Program Responsibilities

- Organize Program meetings
- Recruit new Members and evaluate Membership
- Help new Members acquaint with colleagues
- Facilitate intra- and interprogrammatic collaborations
- Nominate researchers for New Investigator Awards

Program Aims

AIM 1

Cancer Cell Metabolism: To delineate the role of cell metabolism in the control of tumor cell growth, proliferation, and survival and to modulate metabolic pathways to improve cancer therapy

AIM 1

Anthony	Rabinowitz 
Davidson* 	Radovick
Driscoll	Sampath
El Ouaamari	Su
Glytsou*	Valvezan*
Guo G	White
Guo J	Wondisford
Jacinto	Woychik
Kiledjian	Zong

*New Member

Program Aims

AIM
1

Cancer Cell Metabolism: To delineate the role of cell metabolism in the control of tumor cell growth, proliferation, and survival and to modulate metabolic pathways to improve cancer therapy

AIM
2

Tumor-host Interactions: To identify the metabolic, physical, and immunological relationships between the tumor and host to identify new approaches to cancer therapy

AIM 2

Bhattacharya	Korennykh 
Birge	Lasfar
Blaser*	Laskin
Cao*	Mouradian*
Devenport 	Nelson 
Donia* 	Nickels
Gao	Parekkadan
Gitai 	Runnels
Gow	Schwarzbauer 
Irvine	Toettcher 
Johnson*	Wood
Kang 	

*New Member

Program Aims

AIM
1

Cancer Cell Metabolism: To delineate the role of cell metabolism in the control of tumor cell growth, proliferation, and survival and to modulate metabolic pathways to improve cancer therapy

AIM
2

Tumor-host Interactions: To identify the metabolic, physical, and immunological relationships between the tumor and host to identify new approaches to cancer therapy

AIM
3

Tumor Immunology: To discover and develop innovative immune-based cancer treatment strategies including cell and gene therapy approaches

AIM 3

Chiou*

Lattime

Denzin

Lim* 

Etchegaray*

Liu D*

Gennaro*

Payne*

Goldberg

Ploss 

Hinrichs*

Pritykin* 

Fitzgerald-

Sant'Angelo

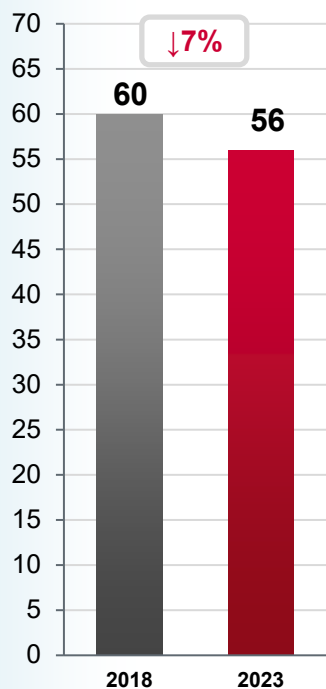
-Bocarsly

Kotenko

*New Member

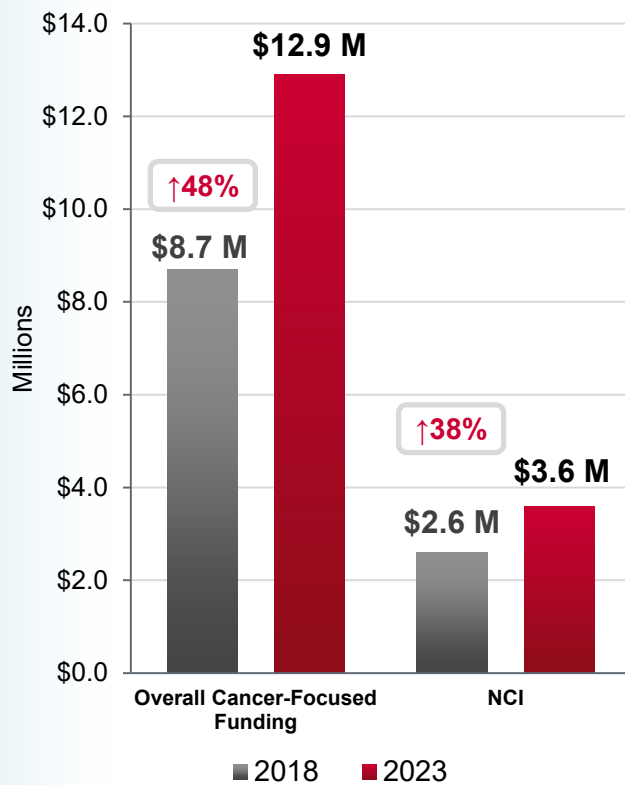
Program Membership Profile

Membership

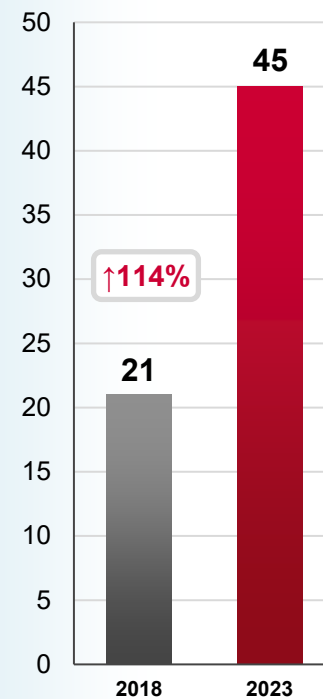


2023
26 Departments
9 Schools
3 Universities
16 New Members

Total Cancer Relevant Funding



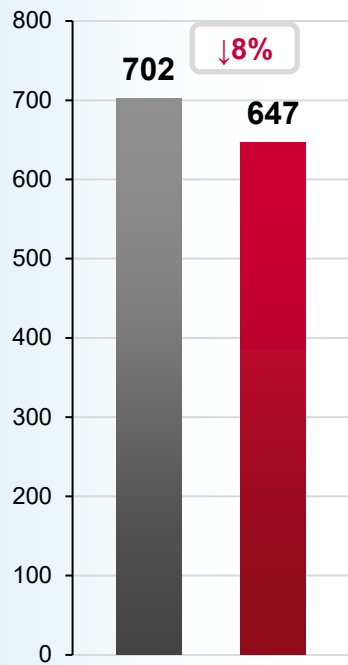
R01 Equivalents



2018: 16 PIs/PDs
2023: 31 PIs/PDs

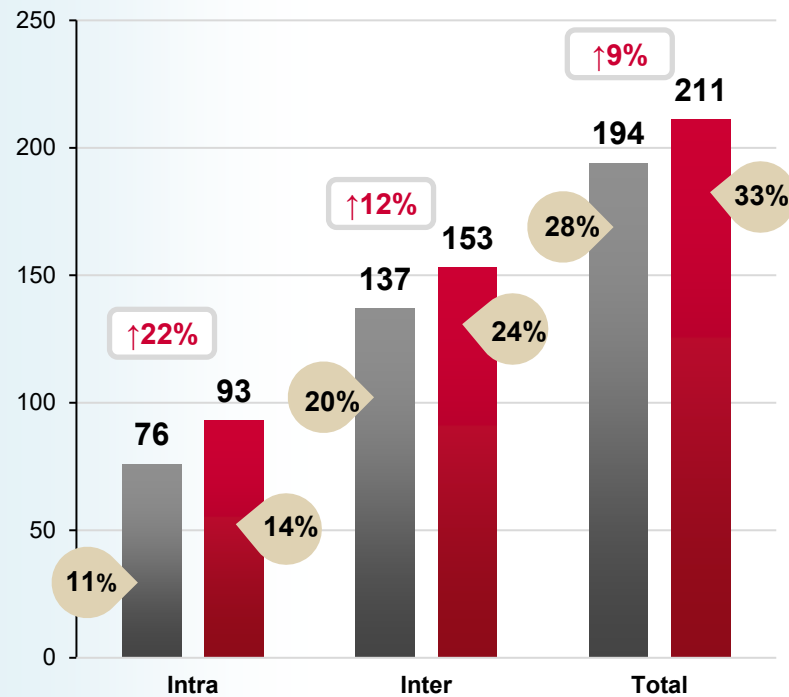
Program Productivity and Collaborations

Total Publications



■ 2018 Submission ■ 2023 Submission

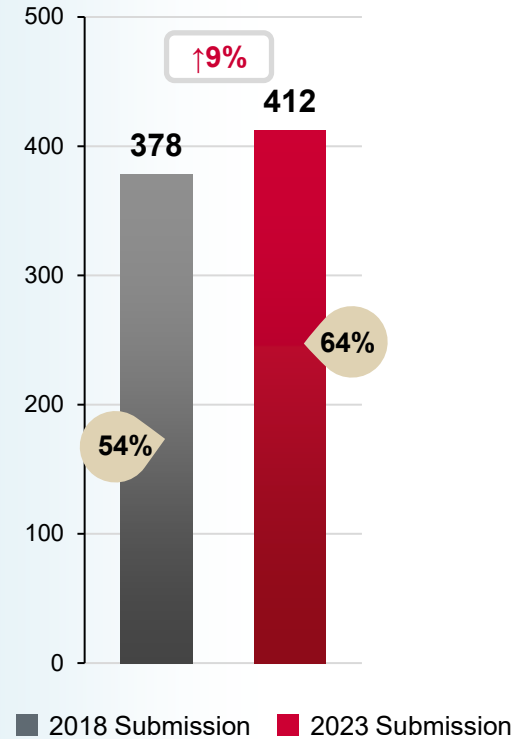
Collaborative Publications



■ 2018 Submission ■ 2023 Submission

High impact publications (IF ≥ 10): 43% (277)
Publications with citations ≥ 10: 47% (303)

Collaborative Publications with Other Institutions

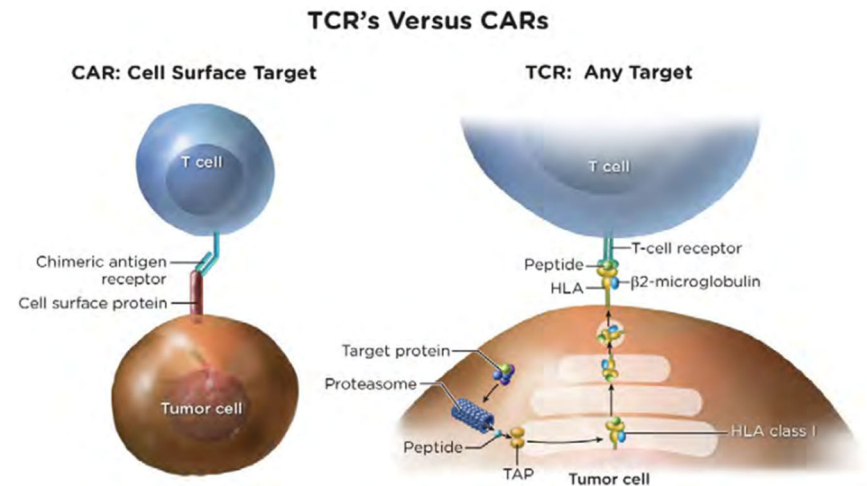


■ 2018 Submission ■ 2023 Submission

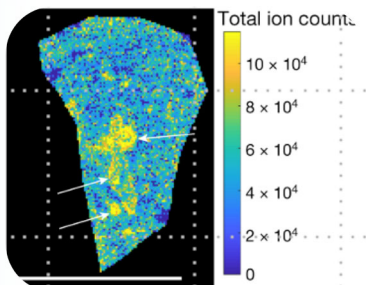
Response to Prior Critique

Scored **Excellent**

- Increased impactful work across the Program
 - Existing and new Members, new research expertise
- Increased large, collaborative grants
 - Ludwig Cancer Research Institute - Princeton Branch
 - Cancer Grand Challenge
 - Cancer Moonshot
- Developed plan for Cancer Immunology
 - Cancer Immunology and Metabolism Center of Excellence
 - Working Group, Journal Club, joint recruitments
 - Hinrichs appointed Chief of Cancer Immunotherapy and CIMCoE Co-Director
 - Additional immuno-oncology recruits
 - Process Development Laboratory, GMP Facility, Immune Monitoring/Flow Cytometry

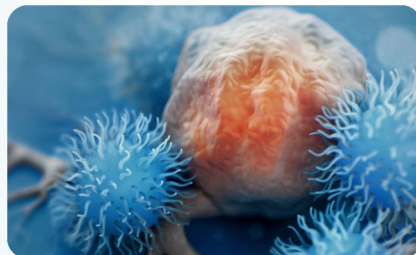


Scientific Impact of Program



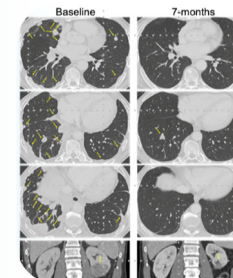
Advances in Cell Metabolism

- Quantitative metabolite imaging *in situ*
- Nitrogen metabolism in cancer development and therapeutics
- Regulation of mTOR signaling
- Nutrient scavenging (autophagy) in cancer development
- Tissue stiffness regulating autophagy and therapy-resistance
- Autophagy in metabolic diseases



Advances in Cancer Immunology

- Regulation of metastasis and stemness development
- Autophagy in immune escape
- Endocytic pathway in mucosal homeostasis and colon cancer
- Cell polarity and microenvironment tension in cancer development, metastasis, and therapy resistance
- Butyrophilin BTN3A1 regulates anti-tumor $\alpha\beta$ and $\gamma\delta$ T cells
- Inferred TCR specificity analysis identifies T cells targeting lung cancer antigens



Novel Therapeutics

- Targeting MTDH-SND1 interaction in metastatic breast cancer
- Combined ICB and T-cell therapy
- Development of CD147 CAR-T cells to treat HCC
- Metabolic profiling of PDAC patients
- E7 TCR-T cells for treatment of HPV-associated cancers
- KK-LC-1 TCR-T cells for treatment of gastric, lung, breast, and cervical cancers

Cancer Cell Metabolism



Rabinowitz



Kang



J. Guo



Davidson



Herranz (CP)

Shared Resources

- Metabolomics
- Genome Editing

Grants

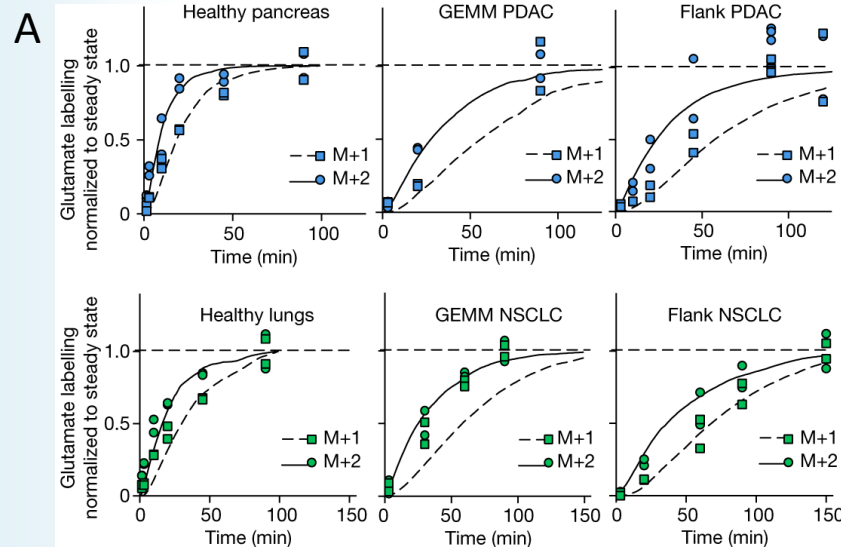
- R01CA163591
- R01CA237347
- R50CA211437
- R21CA263136
- RP-19-180-01
- Ludwig-Princeton
- RSG-19-165-01
- T32CA257957
- SU2C 3.1416
- K99CA273517

Publications

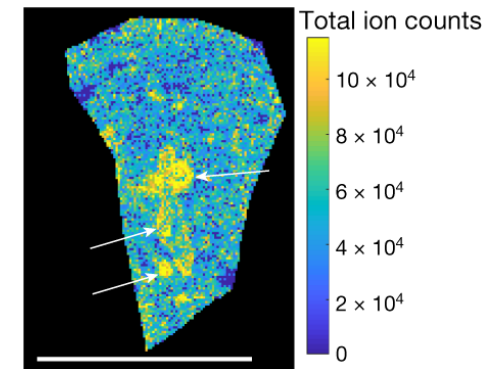
- Poillet-Perez, *Nature* 2018
- TeSlaa, *Cell Metab* 2021
- Wang, *Nat Methods* 2022
- Bartman, *Nature* 2023

Major Discoveries

- Slow TCA flux and ATP production in primary solid tumors
- Metastatic tumors adapt to faster TCA flux
- MALDI-MSI to spatially resolve metabolic activity



B



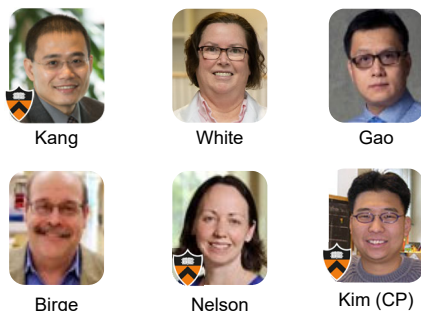
Impact

Paradigm-shifting discovery on cancer metabolism

Catchment Priority

Colon, Lung, and Breast Cancers

Tumor-host Interaction



Shared Resources

- Metabolomics
- Genome Editing
- Immune Monitoring

Grants

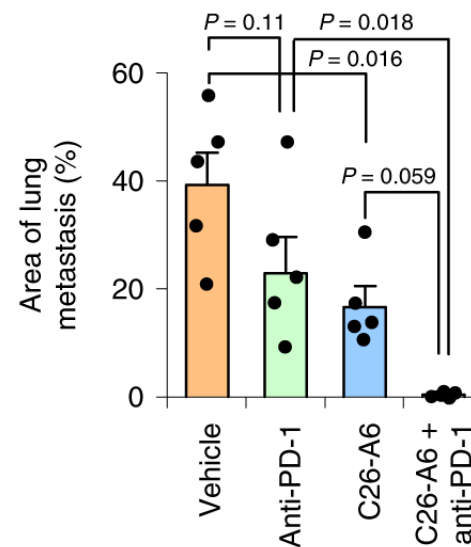
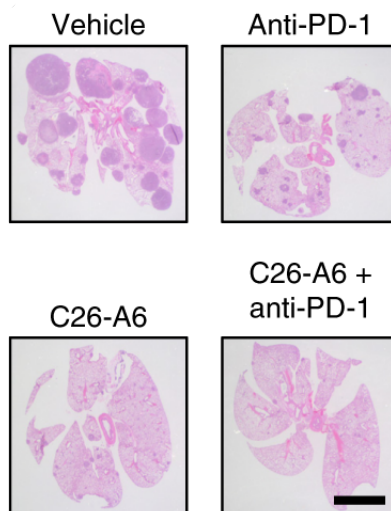
- R01CA163591
- ACS RP-19-180
- R01CA260137
- R01DK132885
- Ludwig-Princeton
- U01CA214292
- T32CA257957

Publications

- Poillet-Perez, *Nat Cancer* 2020
- Esposito, *Nat Cell Biol* 2021
- Shen, *Nat Cancer* 2022 (a)
- Shen, *Nat Cancer* 2022 (b)

Major Discoveries

- Mechanistic basis for tumor-host interaction in metastasis
- Autophagy important for immune escape and therapy resistance
- Endocytic pathway in mucosal homeostasis and colon cancer
- Apoptosis receptors in PD-L1 therapy



Impact

Basic discoveries in tumor-host interaction facilitating therapeutics

Catchment Priority

Breast Cancer, Colon Cancer, and Melanoma

Innovative Cell and Gene Therapies



Shared Resources

- Biomedical Informatics
- Immune Monitoring and Flow Cytometry
- Metabolomics
- Biospecimen Repository and Histopathology Service

Grants

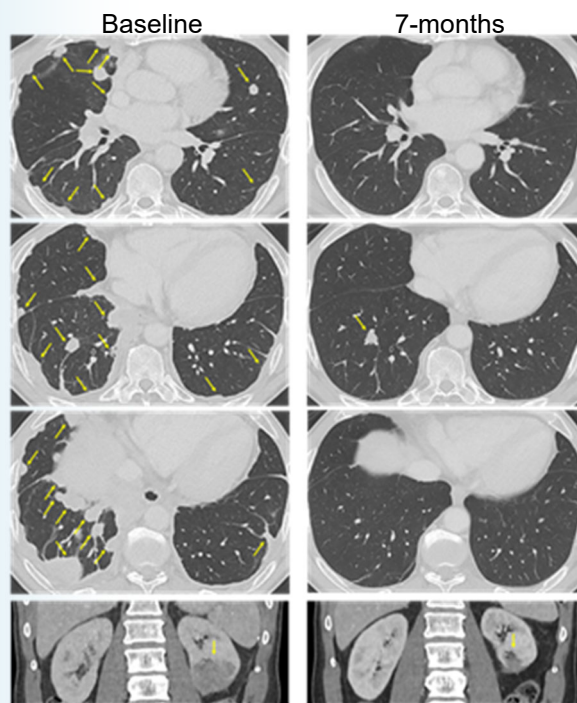
- ACS RP-19-180
- R01AT010243
- R01AI130191
- R01DK132885
- R01AI130197
- R00CA195682
- V2020-012
- 3P30CA072720-22S1

Publications

- Chiou, *Immunity*, 2021
- Nagarsheth, *Nat Med*, 2021
- Tseng, *Nat Commun* 2021
- Davies, *J Immunother Cancer* 2022

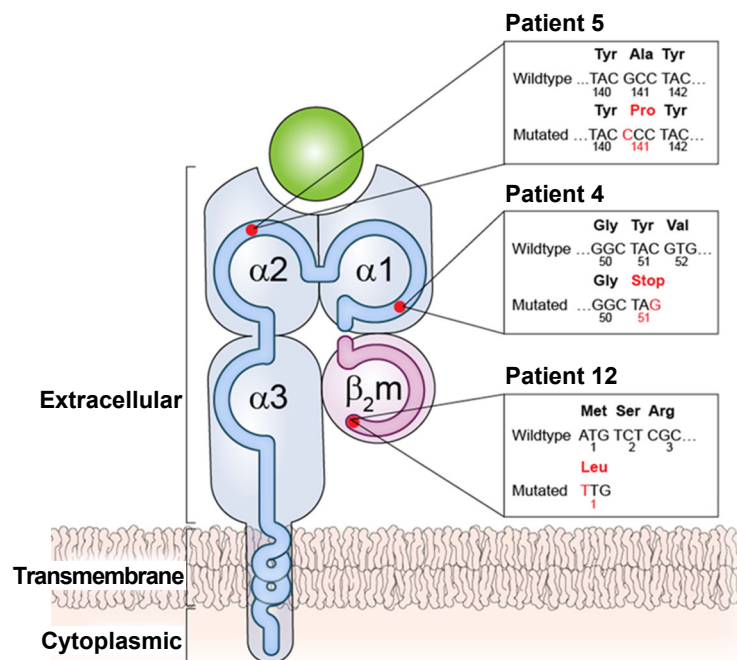
Major Discoveries

- Adoptive T-cell therapies for viral and non-viral cancers
- Inferred specificity analysis to identify TCRs targeting shared viral-cancer antigens
- Non-synergy of PD-1 blockade with T-cell therapy in solid tumors



Impact

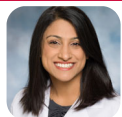
Development of a new class of highly personalized, highly targeted, potent therapeutics for a range of cancer types



Catchment Priority

Lung, Breast, HPV-related Cancers

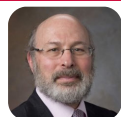
Translational Research



George
(CIPT)



Girda
(CIPT)



Hochster
(CIPT)



Hinrichs



Kim (CP)



Kang



Haigentz
(CIPT)



Riedlinger
(CIPT)



Jabbour
(CIPT)

Shared Resources

- Immune Monitoring and Flow Cytometry
- Biostatistics
- Metabolomics
- Genome Editing
- Biospecimen Repository and Histopathology Service

Grants

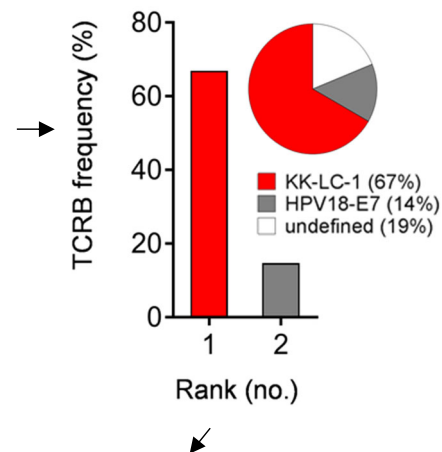
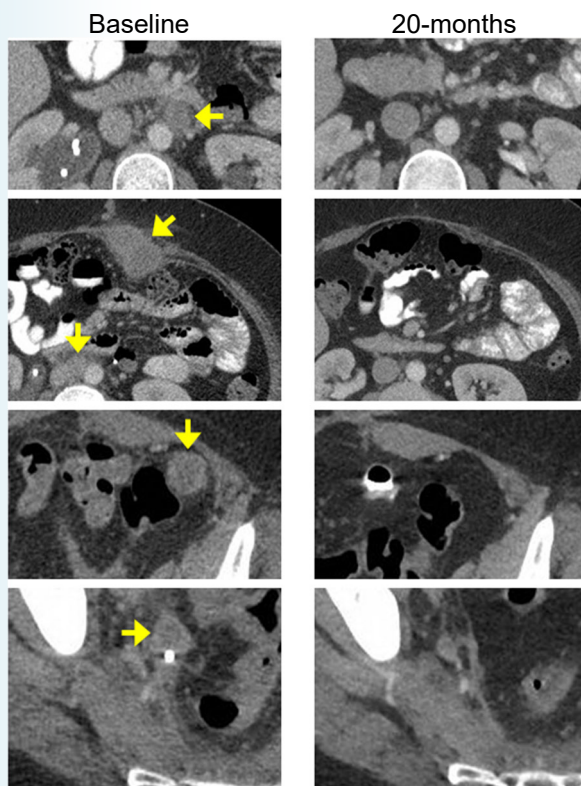
- R50CA211437
- ACS RP-19-180-01
- Komen for the Cure SAC160067
- 3P30CA072720-22S1

Publications

- Shen, *Nat Cancer* 2022 (a)
- Shen, *Nat Cancer* 2022 (b)
- Nagarsheth, *Nat Med* 2021
- Marcinkowski, *J Immunother Cancer* 2019

Major Discoveries

- Development of inhibitors of MTDH-SND1 interaction for treating metastatic breast cancer
- Initiation of KK-LC-1 TCR-T cell therapy for gastric, lung, breast, and cervix cancers
- Initiation E7 TCR-T cell therapy for HPV-associated cancers



CINJ phase I trial targeting KK-LC-1 for gastric, lung, breast, and cervix cancers.

- IIT, investigator-sponsored IND
- Process Development Laboratory, GMP, expanded Immune Monitoring, and many other distinct institutional capabilities

Research Responsive to Catchment Area



Cao
(COE Liaison)



J. Guo



Stroup
(CPC)



Pine
(former GICG)

Shared Resources

- Metabolomics
- Genome Editing
- Immune Monitoring

Grants

- R01CA237347
- K22CA190521
- ACS RSG-19-165-01
- Komen for the Cure SAC160067

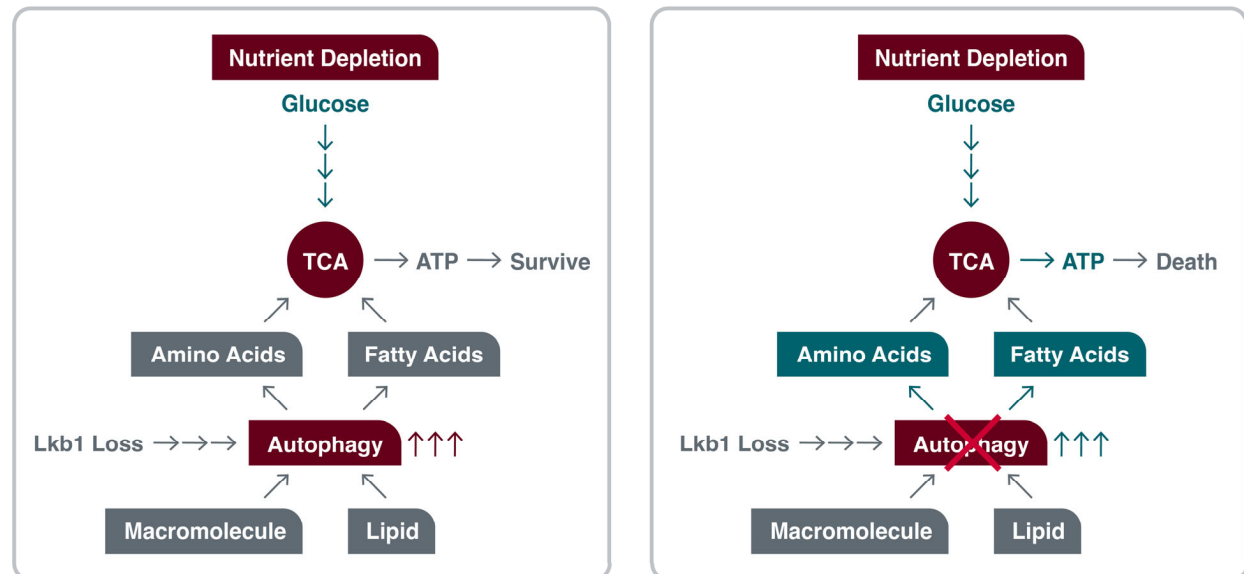
Publications

- Bhatt, *Genes Dev* 2019
- Arauz, *J Thoracic Oncol* 2020
- Esposito, *Nat Cell Biol* 2021
- Nerger, *Curr Biol* 2021

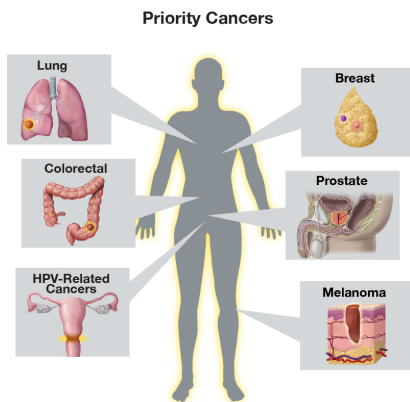
Major Discoveries

- STK11 is more prevalently mutated in NSCLC from Black patients compared to White patients
- STK11 encodes LKB1, a tumor suppressor that regulates cell metabolism
- Loss of LKB1 promotes autophagy-mediated cell growth/survival and renders tumor cells susceptible to autophagy inhibition

Metabolic Vulnerability of NSCLC

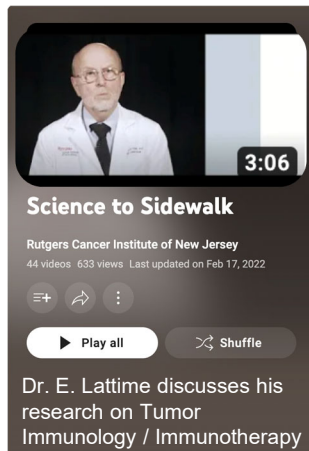


Additional Examples of Catchment Area Relevance



Catchment Area Responsive Research in the Program

- 52% publications (2021-2022) relevant to catchment area priorities
- Lung cancer: Chiou, J. Guo, Hinrichs, Lattime, White, Nelson 🏆
- Breast cancer: Kang 🏆, Wood, Lasfar, Hinrichs, Nelson 🏆
- Diabetes/obesity: Sant'Angelo, Sampath, Wondisford
- HPV, environmental factors, health disparities: Cao, Hinrichs, Laskin, Woychik, Gow, Radovick



Bidirectional Communication with the Community

- COE provides information on cancer burden, disparity, and community needs; facilitates community outreach
- Anthony, Hinrichs, and Cao presented at COE Community Science Cafés and/or CCAB meetings
- Bidirectional communication with Cao led to extending lung cancer HPV integration studies to HIV+ tumor datasets
- Bidirectional communication with Hinrichs facilitated outreach for lung, breast, and cervix cancer cell therapy trials

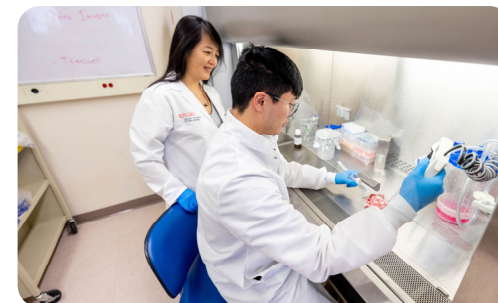
Education and Training over Grant Period

Peer-Reviewed Training Grants

- 50 NJCCR fellowships
- 1 NCATS
- 2 F30
- 1 F32
- 1 F99/K00
- 1 K99/R00
- T32 postdoc and predoc training award

Faculty Development Awards

- K99CA252602/R00CA252602 (Glytsou)
- American Cancer Society Scholar Award RSG-19-165-01 (Guo)
- V Foundation V2020-012 (Chiou)
- GO2-VAPF Young Innovator Team Awards (Guo)



Outcomes Since 2018

- **92** Postdocs hired (4 URM)
- **112** Postdocs completed training
- **4.1** Avg. Pubs as result of Training
- **6** Post CINJ NIH Funding (5.4%)
- Top Academic Positions: Fudan U, Tsinghua U, RWJMS, U California, Penn State
- Top Companies: BMS, Kayo Thera Inc.
- **102** PhD students hired (13 URG)
- **90** PhD students completed training
- **3.6** Avg Pubs as result of training: 3.6
- **2** Post CINJ NIH Funding (2.2%)
- Top Academic Positions: U California, Princeton, RWJMS, NYU Langone, U North Carolina
- Top Companies: BMS, Omnicom, Boston Consulting Group

Value Added: Center to Program

Development Funds

5 New
Investigator Awards
\$230,000

6 Pilot Awards
\$400,000

Shared Resources

- Biomedical Informatics
- Biospecimen Repository and Histopathology Service
- Biostatistics
- Comprehensive Genomics
- Genome Editing
- Immune Monitoring/Flow Cytometry
- Metabolomics

Meetings and Retreats

- Cancer Metabolism Working Group
- Cancer Immunology Working Group
- Annual Retreat
- Tri-state Metabolism Meetings

Member Recruitment

- Blaser
- Cao
- Chiou
- Davidson
- Donia
- Etchegaray
- Gennaro
- Glytsou
- Hinrichs
- Johnson
- Lim
- Liu
- Payne
- Pritykin
- Mouradian
- Valvezan

Center Administration

- Lab Services
- Grants Office
- Faculty Recruitment
- IST
- Multi-Project Application Support
- Medical Writer Services
- Philanthropic Funding Development
- Administrative Support
- Strategic Planning Facilitation
- Support for GMP Operationalization
- Workforce Development

PED

Guidance to diversify research teams

COE

Guidance on catchment area and community needs, connects members to community

Value Added: Program to Center

- **Paradigm-Shifting Science:** Research discoveries promote Center growth and advance cancer research and treatment
- **Shared Resources:** Metabolomics, Immune Monitoring/Flow Cytometry
- **Translation:** Translational research with CETI and CIPT
- **Catchment Priority Research:** Breast cancer, lung cancer, HPV-associated cancers
- **Education and Training:** T32 Postdoc Training Award (co-PIs: Zong and Kang 🏆)
- **Cancer Immunology and Metabolism Center of Excellence:** New faculty, resources, and collaborative projects

PED

URG trainees and workforce

COE

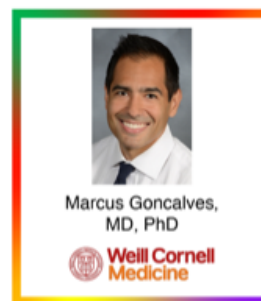
Responsiveness to catchment area priorities and needs

Cancer Grand Challenges CANCAN Team

CANcer Cachexia Action Network: CANCAN



White (CMI)



14 Investigators Across the US and UK (\$25M)



Anthony (CMI)



Davidson (CMI)

Future Directions

1 Cancer Immunology and Metabolism Research

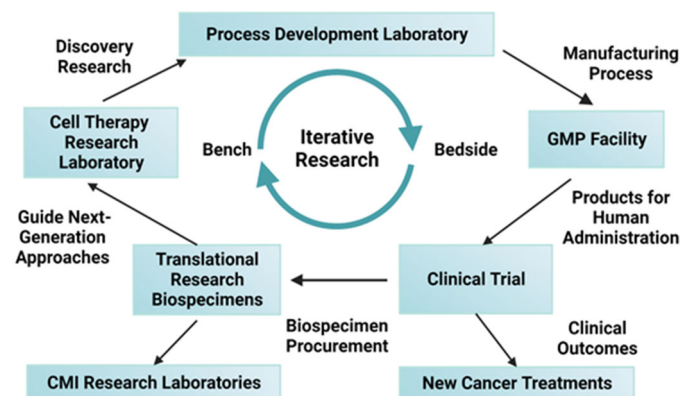
- CIMCoE and Ludwig-Princeton Branch Recruitments
- IMFC SR and Metabolomics SR Capabilities

2 Translational Research

- Novel cell and gene therapies
- Two active cell therapy IIT INDs
- **Bench to Bedside infrastructure**
- Metabolism research clinical studies

3 New Scientific Frontiers

- POLE and POLD1 hypermutation models established
- Identification of cancer cachexia mechanisms for therapeutic and dietary interventions (Ludwig-Princeton, CANCAN)
- TCR discovery for diverse cancer applications (NCI Cancer Moonshot)



Thank You

Q&A Segment



RUTGERS
Cancer Institute
of New Jersey
RUTGERS HEALTH

