Translational Research

Shridar Ganesan, 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

RUTGERS

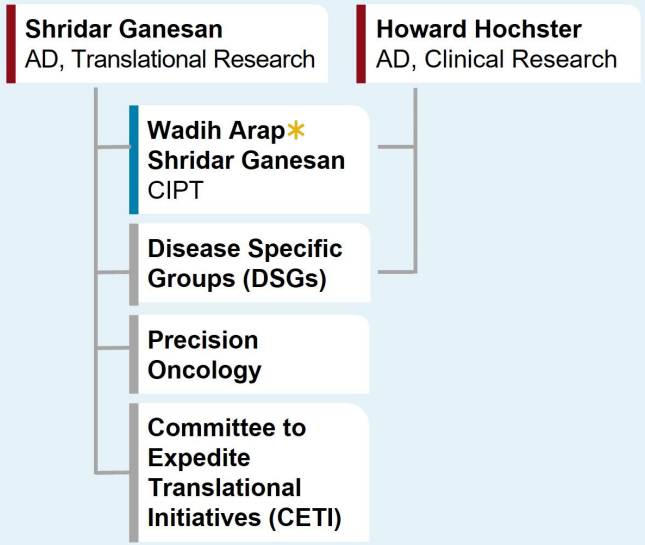
PRINCETON UNIVERSITY

RWJBarnabas HEALTH

Associate Director for Translational Research

Shridar Ganesan, MD, PhD

Omar Boraie Chair in Genomic Science
Chief, Molecular Oncology
Rutgers University



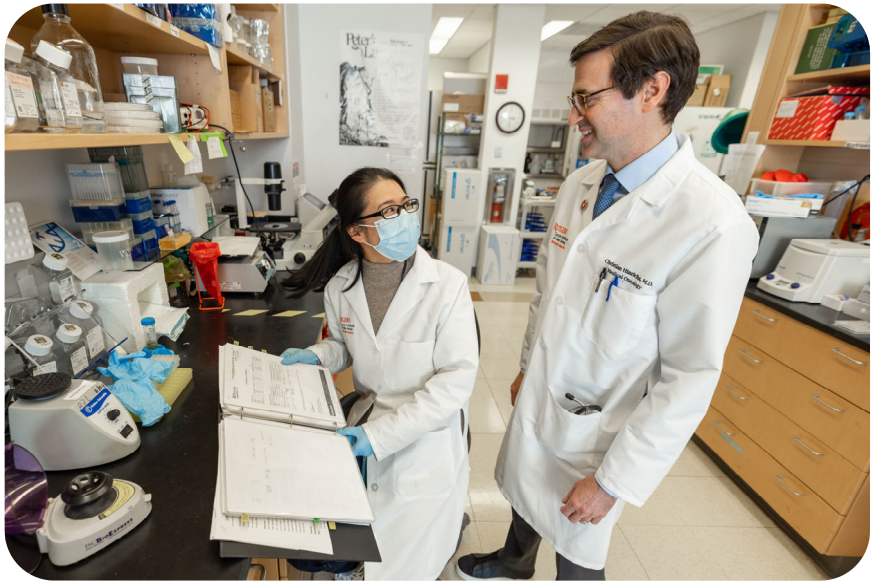
*New Incumbent

Mission:

- Promote transition of basic science discoveries across the Consortium into clinical/translational studies
- Promote translation of important clinical findings into novel basic research projects
- Foster interprogrammatic collaborations
- Provide mentorship and support to junior faculty
- Maintain/expand clinical and translational research infrastructure

Tools to Promote Translation

- Committee to Expedite Translational Initiatives (CETI): Pilot funding
- Rutgers NIH Grant: Research Evaluation and Commercialization Hub (REACH): Pilot funding and Rutgers Office for Research support for commercialization
- Precision Oncology Platform: Pilot Funding/CETI



Committee to Expedite Translational Initiatives (CETI)

Membership

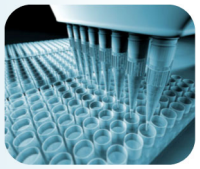
- Co-Chairs
  - AD Translational Research (Ganesan)
  - Chief, Cancer Biology (Pasqualini)
- Associate Directors
  - Clinical Research (Hochster)
  - Basic Research (Shen)
  - Population Science/Community Outreach (Kinney)
- Deputy Director (White)
- Program Leaders

Process

- Quarterly meetings
- Program Leaders nominate projects ready for translation into clinical trials
- Most promising project PIs
  - Present at CIPT translational meeting
  - Apply for Pilot Funding ($100 K/year for 1-3 projects)
- Pilot Project applications reviewed by CETI and *ad hoc* external reviewers annually

Criteria For Prioritizing Translational Projects

Concept generated by peer-reviewed research of a Center Member



Stage of development of therapeutic intervention or diagnostic assay

Addresses cancer burden in Catchment Area

Availability of appropriate patient population, biospecimens

Potential for clinical impact

Potential for peer-reviewed funding for trial or correlative studies

Funded Pilot Project: CIPT

Weiss
Clinical
Investigator
(CIPT)

Sarkar
Basic
Scientist
(CIPT)

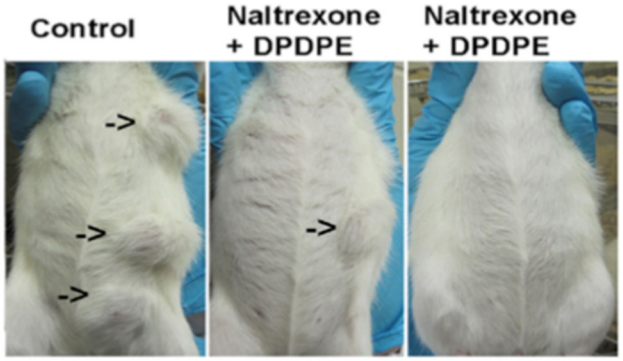
Funding
R01CA208632
(Sarkar)

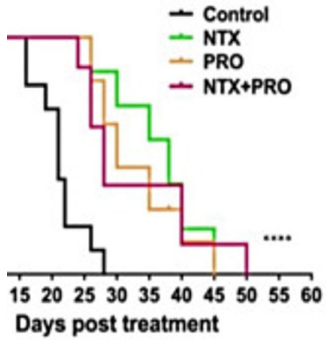
Characterization of tumor and immune responses to anti-PD1 mono and combination with naltrexone, propranolol and immunotherapy

Hypothesis: NK activity can be effectively suppressed by B-adrenergic and Mu-opioid signaling and contributes to immunosuppressive tumor microenvironments

Aims: Test effect of inhibiting B-adrenergic and Mu-opioid signaling using propranolol and naltrexone on response to anti-PD1 therapy in two validated preclinical syngeneic xenograft models of cancer (CTEP consultation)

Status: Preclinical data generated to support IIT (Weiss) **IIT supported by Clinical Trial Award**





Impact
Novel approach to increase efficacy of immune checkpoint blockade

Catchment Priority
Melanoma, Breast

Selected Translational Awards

Biomarker discovery from FFPE RNA sequencing for precision oncology therapeutic intervention

$60,000
to C Chan (GICG)
and Ganesan (CIPT)

- *Nature* 2022, IIT in preparation, R01 in preparation

Choices About Genetic Testing and Learning Your Risk with Smart Technology

$50,000
to Kinney (CPC) and Foran (CIPT)

- NCI R01: Addressing Genomic Disparities in Cancer Survivors (PI Kinney)
- Clinical trial to increase guideline based genetic testing rates in Black cancer patients

Dissecting the antileukemic potential of IRS-17 (novel anti-folate)

$75,000
to Herranz(GICG)
and Gitai (PU)

- Preclinical validation of efficacy of novel anti-folates

Targeting hepatocellular carcinoma carrying Hepatitis B virus integration in KMT2B

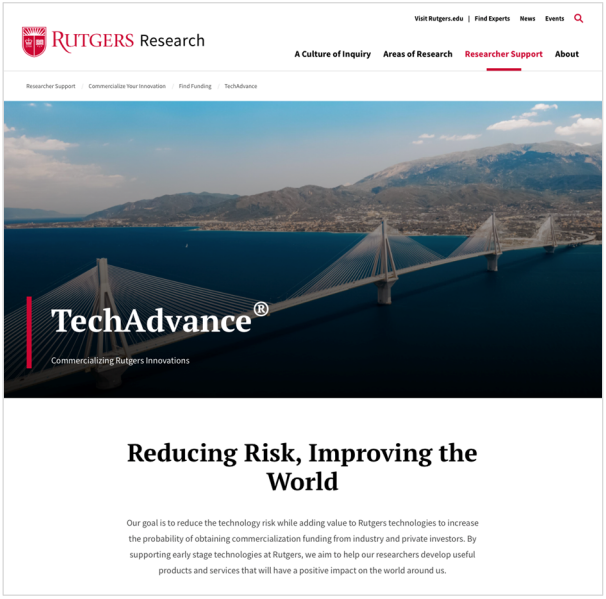
$75,000
to Cao (CMI)

- Novel therapeutic vulnerability in HBV-associated HCC
- NCI RO1

Rutgers: NIH REACH Grant ($4 M)

RUTGERS OPTIMIZES INNOVATION
HealthAdvance

- **Support commercialization** of key research findings from Rutgers investigators
  - Combined with RU TechAdvance Program
- **Rigorous peer-review** evaluation of proposals
- Selected projects are **supported financially and administratively** by Rutgers Office for Research



LIF to Protect GI Stem Cells from XRT/Chemo

Hu
(GICG)

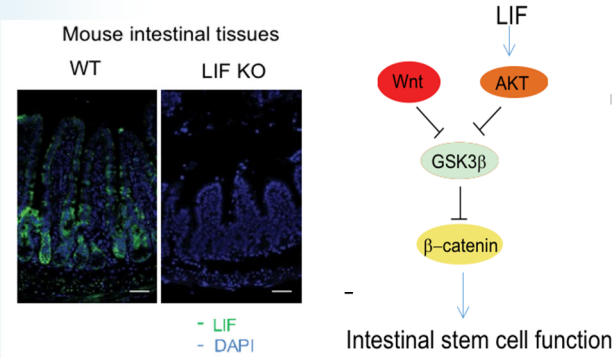
Strair
(CIPT)

Provisional Patent
LIF Therapy for Inducing Intestinal Epithelial Cell Regeneration

REACH (RU Tech Advance) Grant
Application of leukemia inhibitory factor in prevention and treatment of radiation/ chemo-induced gut syndrome
Jan 2020 - July 2021

Publications
Wang et al., *Blood* 2022
Wang et al., *Cell Death Dis* 2020

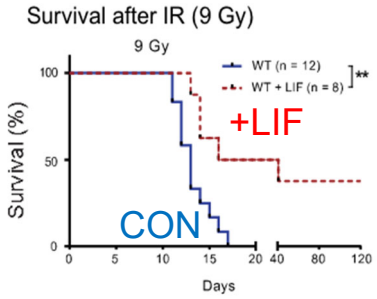
LIF required for intestinal stem cell health

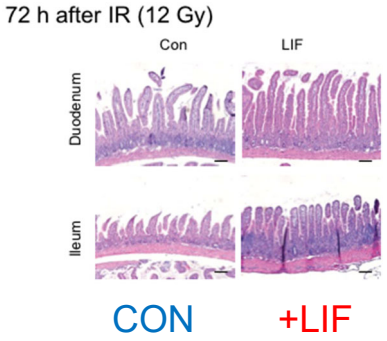


Clinical Protocol in preparation examining role of LIF in GI-GVHD (CETI)

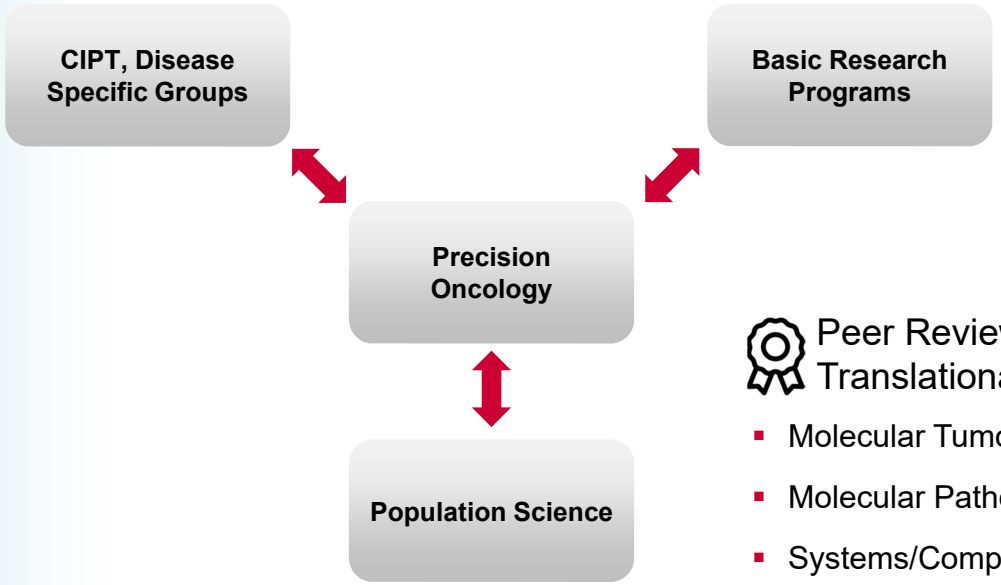
Impact
Development of novel approach to reduce gut toxicity of cancer therapy

LIF protects mice from GI toxicity of lethal irradiation



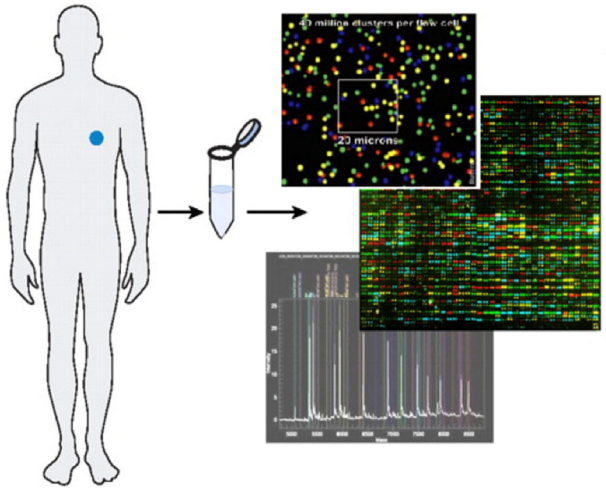


Precision Oncology: Engine for Discovery



Peer Reviewed Pilot Translational Awards

- Molecular Tumor Board
- Molecular Pathology
- Systems/Computational Biology



MacConaill LE, Garraway LA
JCO 2010;28:5219-5228

Endogenous Retroviruses as Biomarker of Response to Immune Checkpoint Therapy


Ganesan (CIPT)


Riedlinger (CIPT)

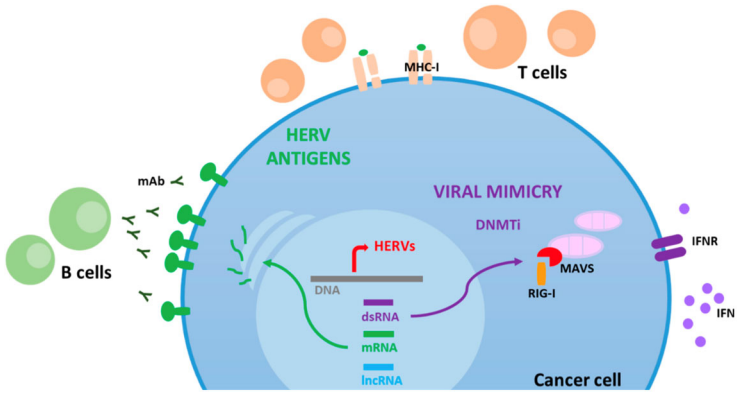

Bhanot (GICG)

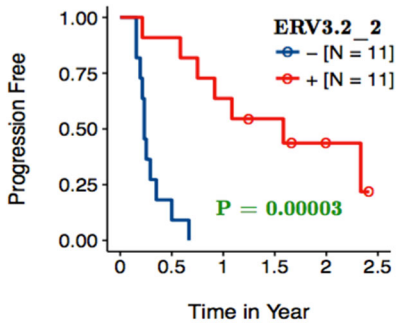
Provisional Patent
ERV as biomarker of response to Immunotherapy in cancer

Grants
- DoD: KC180159
- ORIEN NOVA

Publications
Panda et al., *JCI Insight* 2018
Smith et al., *JCI* 2018
DeCuba et al., *JCI Insight* 2020

- Certain low mutation burden cancers have excellent responses to ICB
- ERV expression is associated w/ T-cell infiltrate and IC expression in ccRCC
- ERV expression associated w/ response to ICB in ccRCC (Bhanot, Ganesan)





Impact
Novel biomarker to identify low mutation burden cancers that will respond to immune checkpoint blockade

Biotech Startups Based on Center Science

VESCOR THERAPEUTICS LLC	**White** (CMI) Identify novel modulators of the autophagy pathway as cancer therapeutics; partnership with IACS at MDA and Deerfield
MBRACE THERAPEUTICS	**Pasqualini** (CP), **Arap** (CIPT) Platform technology for developing Antibody-Drug Conjugates using phase display to identify targets and a novel site-directed conjugation strategy to deliver payloads; Venture funded
KAYO THERA	**Kang** (CMI) Targeting key pathways in cancer metastasis and growth; seed-funded; optimizing lead compounds for first in human studies
MITO BIOPHARMA	**Jin** (CP): Targeting mitochondrial metabolism for cancer and metabolic syndromes; seed funding from Mega Hill
PhageNova Bio	**Pasqualini** (CP), **Arap** (CIPT) Developing hybrid bacteriophage adeno-associated virus vector for cancer therapy and vaccine development; seed funding, working on IND

Examples of CINJ Translational Pipeline

CETI / TA	REACH	Discovery	Pre-IND	Phase 1	Phase 2+	GICG	CP	CMI	CIPT	Catchment
		Mito Uncouplers					■			
✓	✓	BMP inhibitors					■	■	■	$
		MTDH1 inhibitors					■	■		
✓		New Anti-Folates					■	■		
	✓	PAN-TAM/GAS6 Kinase Inhibitors						■		
		KayoThera / ALDH1i					■	■	■	
		Targeted AAVP / PhageNova Bio				■	■		■	
		MBRC-101-001 & MBRC-102-001 / MBrace Therapeutics				■	■		■	
	✓	LIF for GVHD				■			■	
		TCR: KLK						■	■	$
✓		Microbiome intervention for chemo						■	■	$
✓		FGFR2i for truncated FGFR2 (in prep)				■			■	
✓		Propanolol / naltrexone to enhance response to PD-1 Ab						■	■	$
		Pembrolizumab for DDRd cancers				■			■	
		BAMM Trial; Autophagy Inhibitor						■	■	$
✓		Carboplatin / LipoDOX for TNBC				■			■	$

Future Directions

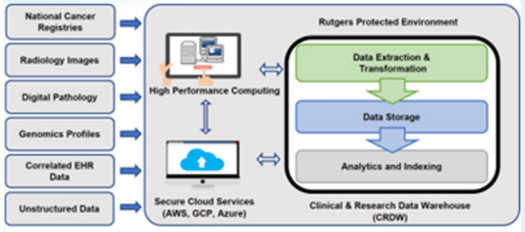
1. Expand cellular immunotherapy platforms (working with Cancer Immunology and Metabolism CoE)

2. Expand infrastructure for *in vivo* metabolic studies in human cancer with Ludwig-Princeton Branch

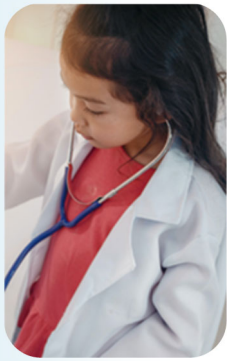
LUDWIG CANCER RESEARCH

Princeton

3. Expand Precision Oncology Platform/ MTB/CRDW to partner hospitals



4. Expand Translation in Pediatric Oncology



Thank You

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