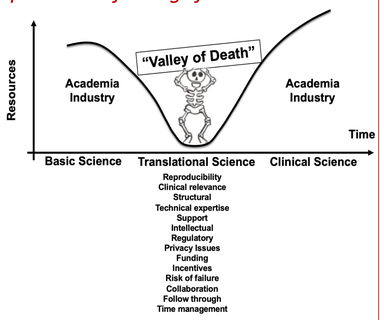
Translational Oncology (TO) Shared Resource
Director: Attila A. Seyhan, PhD

LEGORRETA CANCER CENTER
BROWN UNIVERSITY

*The "**Valley of Death**" where most preclinical findings find their demise*



Translational Research bridges the "Valley of Death" by translating early discoveries &clinical observations into clinically impactful innovative research to create novel treatments, medical procedures, preventions, & diagnostics.

Translational Research & TRDGs

- Bench-to-Bedside Interdependence
- Centered on collaborative, synergistsic scientific efforts
- Resource intensive, necessitating efficiency
- Basic & clinical science, therapeutic innovation, technology focus, practical, real-world application with clinical impact
- Integrates complex systems, non-linear thinking, iterative learning, collaborative, & team-centered

Overview

Translational research involves human subjects research in clinical trials as well as population research. More broadly, it involves the use of human tissues as well as preclinical studies that accelerate biomarker discovery, therapeutics, or device advancement in the clinic. The Translational Oncology Shared Resource advises investigators on study design leading to translational clinical protocols.

Key Services & Users

- For prioritized studies:
  - Interact with disease teams to facilitate innovative trials
  - Clinical protocol preparation.
  - NIH NCI, Industry or Foundation grant submissions to secure funding for the research.
  - Manuscript preparation for publication in high-impact journals.
  - Initiation & management of project & working groups for cross-disciplinary collaborations across the LCC Cancer Biology, Cancer Therapeutics, & Pop-Sci programs.

User Profile

Total Users: ~354 TRDG members across 11 TRDGS
Cancer Center Members Users: ~150
Members with Peer-Reviewed Funding: xxx (xx%)
Number of Programs: 3 (Cancer Biology, Cancer Therapeutics, Population Sciences)

Key Personnel

- Attila Seyhan, PhD, Technical Director
- E-mail: Attila_Seyhan@brown.edu

Translational Research Disease Groups

Description: Translational research involves human subjects research in clinical trials as well as population research. More broadly, it involves the use of human tissues as well as preclinical studies that accelerate biomarker discovery, therapeutics, or device advancement to the clinic.

Goals:

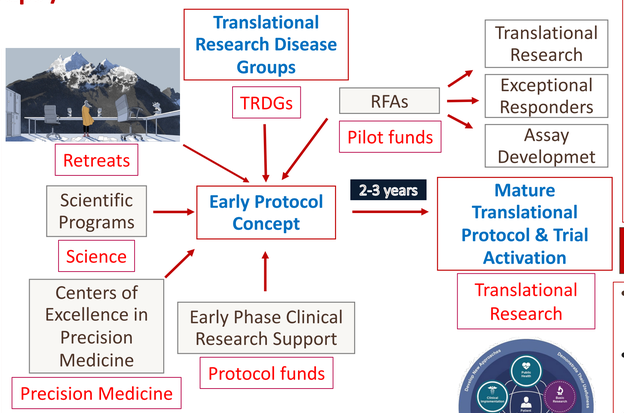
- Advise investigators on study design leading to translational clinical protocols (2-3 years from concept to innovative clinical protocol development & trial activation).
- For prioritized studies, provide support for the clinical protocol preparation as well as NIH, Industry, or Foundation grant submissions to secure funding for the research.
- Support & nurture innovative new ideas, concepts, directions, & opportunities from our research & literature into actionable Translational Research.
- Foster intra- & inter-programmatic collaborations among TRDG members, & others.
- Identify working groups in specific areas that may benefit from project development.

Infrastructure of Translational Research

Translational Research Disease Groups / (# members)

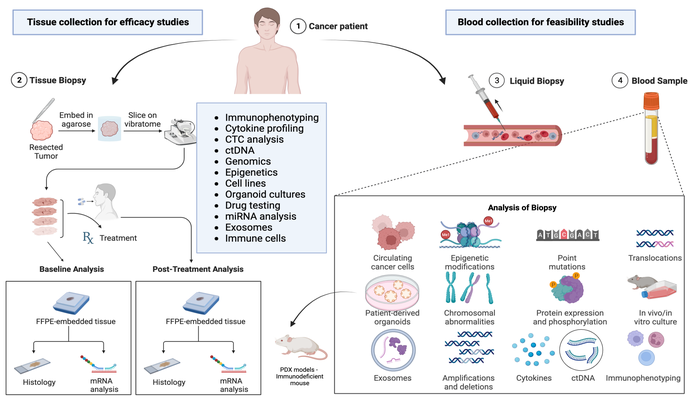
- Breast Cancer (42)
- Central Nervous System Cancer (37)
- Endocrine Cancer (19)
- Gastrointestinal Cancer (40)
- Genitourinary Cancer (30)
- Gynecological Cancer (38)
- Head & Neck Cancer (24)
- Hematological Malignancies (38)
- Sarcoma (26 members)
- Skin cancer & Melanoma (27)
- Thoracic Malignancies (34)

TRDGs Facilitate Translational Research



Tissue & blood collection for feasibility studies

Examples of Process & Functionality of TRDGs



Examples of Key Awards

Three Lifespan physicians & Brown U faculty, *Sheldon Holderm MD, PhD*, *Hina Khan, MD*, & *Emily Hsu, MD* are recipients of the Robert A. Winn Diversity in Clinical Trials Career Development Award, funded by Bristol Myers Squibb Foundation. These awards aim to increase the diversity of clinical trial volunteers, promote community engagement, & better understanding of clinical trial benefits.

Examples of Translational Impact

Winner of CuresWithinReach Award
"Repurposing the prostate cancer drug degarelix to treat bladder cancer"
Sheldon Holder, MD, PhD
Brown University

Awardee of NIH & White House's 'Cancer Moonshot Scholars' program
"Multifunctional Nanoparticle Platform to Prevent Alcohol-Associated HCC Development"
Jyothi Menon, PhD
U. of Rhode Island

Examples of Key Clinical Impact

- ***BrUOG 387:*** *TAS-116 Plus Palbociclib in Breast and Rb-null Cancer (NCT05655598). (El-Deiry W.S.)* **Status:** Recruiting
- ***BrUOG 379:*** *Phase Ib/II Trial ONC201 + Nivolumab in MSS mCRC (379) (NCT03791398) (El-Deiry).* **Status:** Completed enrollment (Lack of toxicity) **(**Bristol Myers Squibb IIT, **$1.0M**)
- ***BrUOG 392:*** *Phase I First-in-Human Investigator-Initiated Dose Escalation and Cohort Expansion Study of Oral ONC212 in Patients with Advanced Pancreatic Cancer and Other Treatment Refractory Solid Tumors (*El-Deiry, W.S.*).* **Status:** Noy yet recruiting (Warren Alpert Found, **$3.4M**)
- ***BrUOG 395:*** *ONC201, Temozolomide and Radiation For Newly Diagnosed Glioblastoma: A Phase Ib Window of Opportunity Study: BrUOG 395* (El-Deiry, W.S.). **Status:** Protocol in development.
- ***BrUOG 434:*** *Prospective Sarcoma Biospecimen Bank, Registry, and New Preclinical Therapeutics Protocol* (El-Deiry, W.S.) **Status:** Protocol in development.

Examples of Key Translational Publications

- *BrUOG 387: Phase Ib investigator-initiated trial of a heat shock protein 90 inhibitor (HSP90i) combined with a CDK4/6i in advanced breast cancer progressing on CDK4/6i.* W.S. El-Deiry et al., J. of Clin. Oncology, 2023.
- *Anti-cancer efficacy including Rb-deficient tumors and VHL-independent HIF1α proteasomal destabilization by dual targeting of CDK1 or CDK4/6 and HSP90.* Zhao S, … El-Deiry W.S. Sci Rep. 2021 Oct 22;11(1):20871.
- *Synergistic anti-tumor activity, reduced pERK, and immuno-stimulatory cytokine profiles with 5-FU or ONC212 plus KRAS G12D inhibitor MRTX1133 in CRC and pancreatic cancer cells independent of G12D mutation.* Tajiknia V,…EL-Deiry, W.S. 2023, bioRxiv.
- *ONC212 is a Novel Mitocan Acting Synergistically with Glycolysis Inhibition in Pancreatic Cancer.* Ferrarini I, … El-Deiry WS. Mol Cancer Ther.
- *Synergistic combination therapy with ONC201/TIC10, Enzalutamide and Darolutamide in castration-resistant prostate cancer.* JL Wu, ... El-Deiry WS. Cancer Research, 2023.
- *Preclinical combination of ONC201 with radiotherapy and Temozolomide in a GBM mouse orthotopic model results in reduced tumor burden and prolonged survival.* Zhou L… El-Deiry W.S. Can. Res., 2023.
- *TRAIL agonists rescue mice from radiation-induced lung injury.* Strandberg, J., … El-Deiry, W.S. bioRxiv 2023.
- *Chi3l1 Is a Modulator of Glioma Stem Cell States and a Therapeutic Target in Glioblastoma.* Guetta-Terrier C, …, Elias JA, Tapinos N. Cancer Res. 2023.
- *MDM2 inhibition in combination with imipridone ONC201 treatment as a synergistic combination in solid tumors.* George A, et al. Cancer Res. 2023;83(suppl 7):551.

Examples of Key Grants

- Warren Alpert Foundation, **$3.4M**, PI: W. El-Deiry
- Bristol Myers Squibb IIT, **$1.0M**, PI: W. El-Deiry

Future Plans

- Continue interacting with disease teams to facilitate innovative trials.
- Continue TRDG efforts and increase the user base.
- Continue ongoing development of clinical translational protocols.
- Nurture inter- and intra-programmatic and cross-disciplinary translational collaborations.
- Promote and support multi-investigator group efforts, and increase grant submissions, and publications.
- Interact with other Shared resources.
- Continue supporting yearly translational RFAs.
- Increase funded translational projects via NIH, NCI, ASCO, industry, & philanthropic funding.
- Support efforts in targeting NCI for funding.