Transitioning to Research Independence: Perspective from a Current R01 and Former K99/R00 Awardee

Shaneda Warren Andersen, PhD
Assistant Professor
Population Health Sciences, University of Wisconsin-Madison
NCI Transition Career Development Workshop

Postdoctoral Research Fellow, Vanderbilt University Medical Center

SCHOOL OF MEDICINE
VANDERBILT UNIVERSITY

- **Molecular and Genetic Epidemiology of Cancer (MAGEC) Training Program**
  - NCI R25 Training program
  - Attracted to:
    - Opportunity to work with successful, thoughtful mentors
    - Data & collaboration opportunities
    - Formal training in topics that interested me: genetic epidemiology, molecular epidemiology, cancer epidemiology, big data, cohort analysis

Postdoctoral Research Fellow, Vanderbilt University Medical Center

SCHOOL OF MEDICINE
VANDERBILT UNIVERSITY

- **K99/R00 funded by NIH/NCI**
  - Association between vitamin D and colorectal cancer risk in diverse populations
  - This award supported my transition to research independence

The K99 Award Supported:

- **Protected time as a postdoctoral fellow**
  - Effort towards research project specific to my interests
- **Experience with grants management**
- **Negotiation of Independent Position**
  - Discussed the types of items negotiable in the process of obtaining a first independent position
    - Salary & Unrestricted funds
    - Less known: access to staff, especially administrative or statistical support, travel funds, protected time, etc

The R00 Award Supported:

- **Protected time as an Assistant Professor to get my research underway**

- **(more) Experience with grants management**

- **Important Funding for my research:**
  - Data collection, Analyses, Travel to meetings, and Staff →
    - Leading to publications & results which supported my R01 application to NIH

PI: Shaneda Warren Andersen
Assistant Professor of Population Health Sciences

My current research program used molecular epidemiologic methods to investigate the relations between race, genetic variation, and molecular attributes of tumors in association with cancer risk and survivorship.

I am particularly interested in achieving health equity in colorectal cancer for vulnerable subpopulations who are less likely to undergo colorectal cancer screening: African Americans, individuals of low socioeconomic status, and adults under age 50.

Warren Andersen Research Group

Epidemiologic research program focused on cancer risk and survivorship.

Lab Members

Lauren Giurini
Graduate Student

Tom Lawler
PhD
Cancer Researcher

Zoe Walts
Graduate Student

Megan Agnew
Graduate Student

Subset of my Roles as related to NIH/NCI Support

Tenure-track Assistant Professor of Population Health Sciences

- **PI** of epidemiologic program of cancer risk and survivorship

- **Co-Investigator** within the CEECR Coordinating Center

Faculty Director of a Shared Resource within University of Wisconsin Carbone Cancer Center:

Survey of the Health of Wisconsin (SHOW)

Other NIH/NCI Career Support: Grant Review

- **Early Career Reviewer Program: Cancer Biomarkers Study Section**
  - https://public.csr.nih.gov/ForReviewers/BecomeAReviewer/ECR
  - Improve grant writing through reviewing grants
  - Hear from experts in the field

- **More recently:**
  - NIH/NCI: Cancer and Hematologic Disorders Study Section (x3)
  - NIH/NCI: P50 Specialized Programs of Research Excellence (SPORE) Study Section (x2)
  - NIH/NCI: Special Emphasis Panel – Clinical and Translational Cancer Research
  - Colorectal Cancer Alliance (x2)

Perspective:

- **Say yes to opportunities especially writing or working with collaborators who are doing interesting work**
  - Not yet/no to opportunities that are not clearly aligned with your career goals

- **Be consistent → Your early career work can be the foundation for your career**

Opportunities and Challenges of Transitioning to Research Independence for PhD-trained K Awardees

Sigrid Carlsson, MD PhD MPH
Assistant Attending Epidemiologist
Director of Clinical Research, Josie Robertson Surgery Center
Memorial Sloan Kettering Cancer Center, New York, USA

Associate Professor, Department of Urology
Sahlgrenska Academy at Gothenburg University, Sweden

Adjunct Senior Lecturer, Lund University, Sweden

Memorial Sloan Kettering Cancer Center

Former K22 awardee 2018

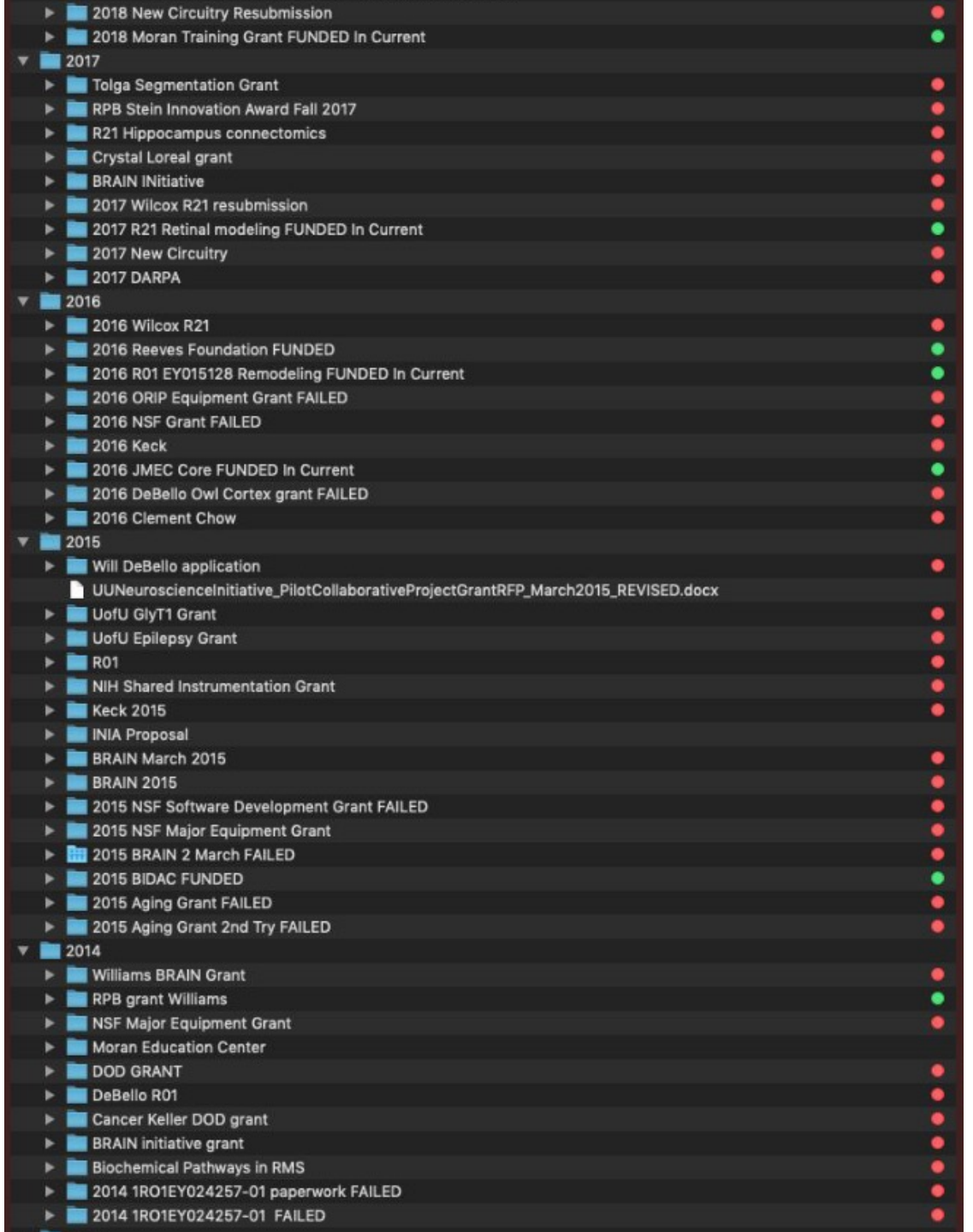
Notice of Award (NoA)

Memorial Sloan Kettering Cancer Center

GOLDEN BUZZER

Lavender Darcangelo AGT 2023

Normalizing the experience



Take home messages

- Very few proposals get funded on the first try! Keep hopeful and do your best while waiting
- It's okay to throw away good ideas!
- Learn the grant writing blueprint
- Take courses! Talk to your peers!
- Reviewers: good or bad?
- The best way to deal with reviewers? Capitulate!
- Your success will depend on how well you can handle criticism. Let go of your ego!
- Red ink is a love language. Really!
- Diverse teams are more successful
- We are the actions we repeat. Success is therefore not an act but a habit
- Who says "I can't"? Nobody! You're not a quitter!
- Keep on! (D train)

T H A N K Y O U

Memorial Sloan Kettering Cancer Center

Photo: MSK

Opportunities and Challenges of Transitioning to Research Independence K22/K00

Thales Papagiannakopoulos, Ph.D.

Associate Professor
Department of Pathology
Perlmutter Cancer Center
NYU School of Medicine

papagt01@nyumc.org

My Background

Integrating Complex Genetic, Environmental and Physiologic Factors

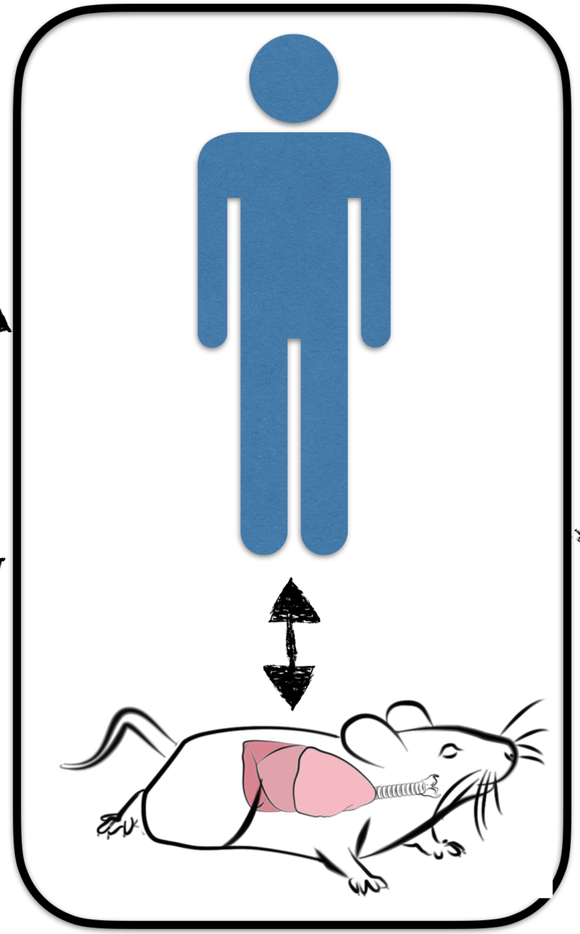
Physiology

Papagiannakopoulos et al. Cell Met.,2016
Masri et al. Cell, 2016

Environmental Factors

Diets

LeBoeuf et al, Cell Met., 2019



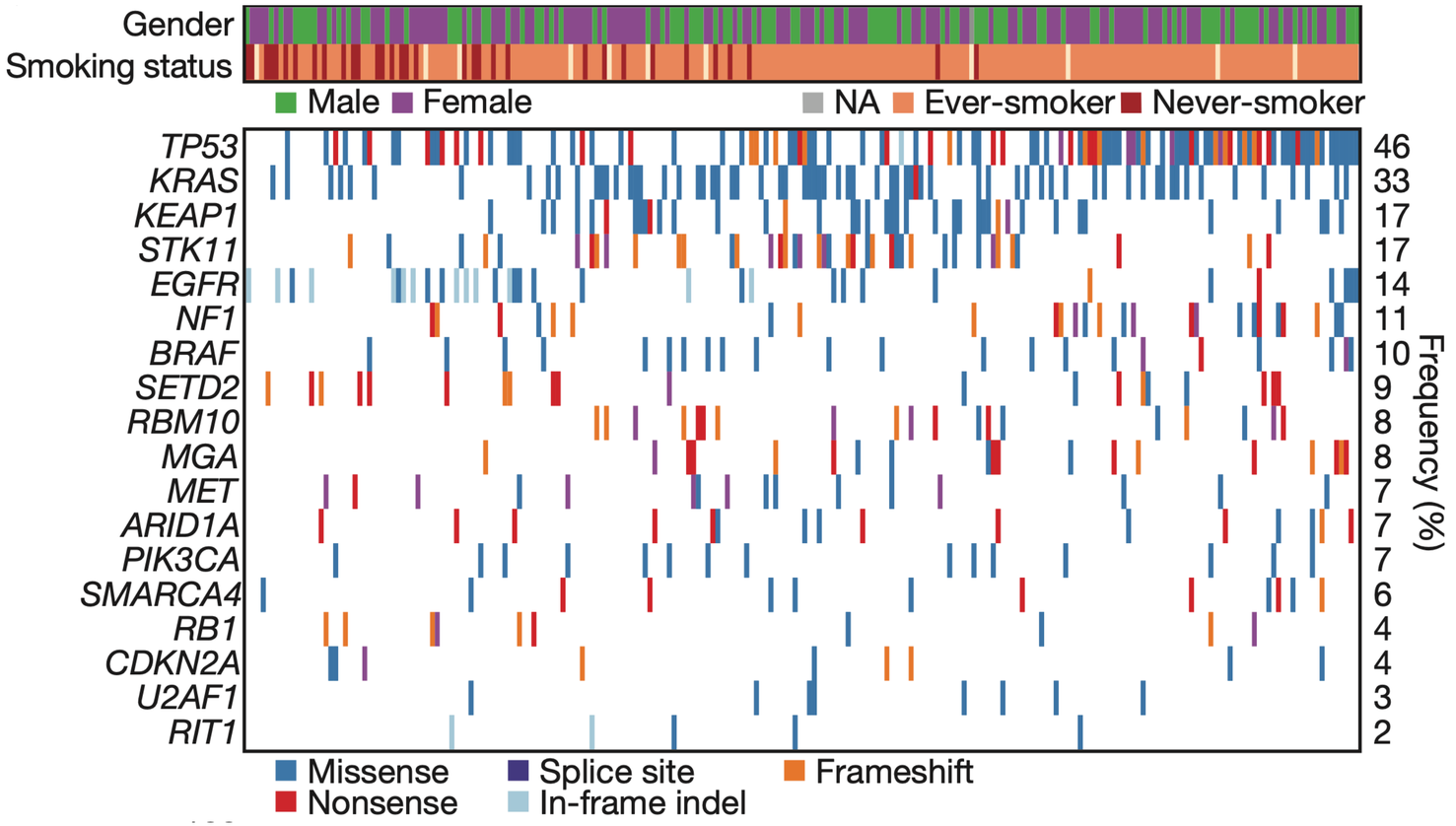
Tumor Progression

Tumor Microenvironment & Immune Respones

Tumor Metabolism & Systemic Physiology

2010-2015:
Postdoc Jacks
Lab at MIT

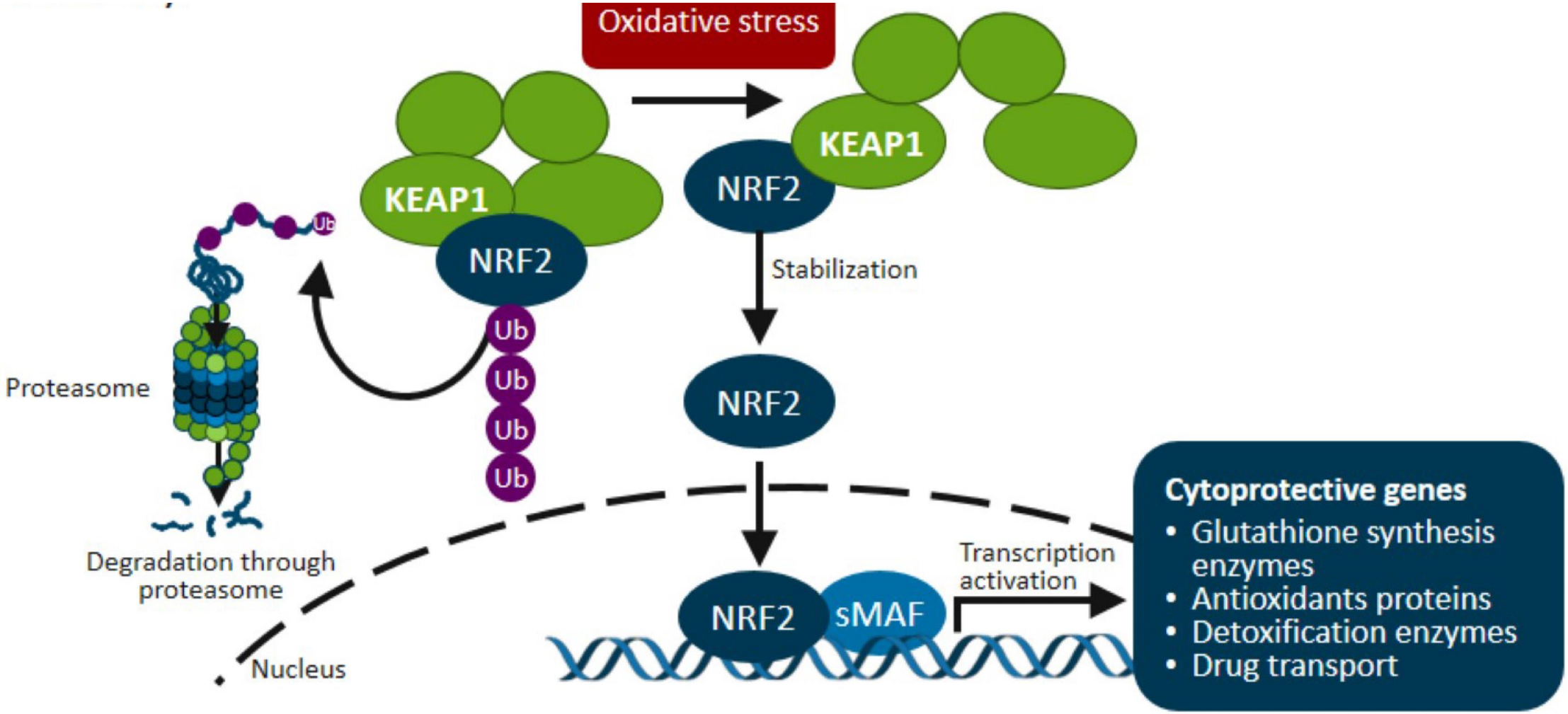
Lung Adenocarcinoma: What are the differences between genetic subtypes?



Genetic subtypes may define:

- Different mechanisms of progression
- Histological differences
- Differential responses to standard of care (e.g. immunotherapy)
- Sensitivity to new therapeutic approaches

Loss of function mutations in *KEAP1* lead to NRF2 antioxidant activation



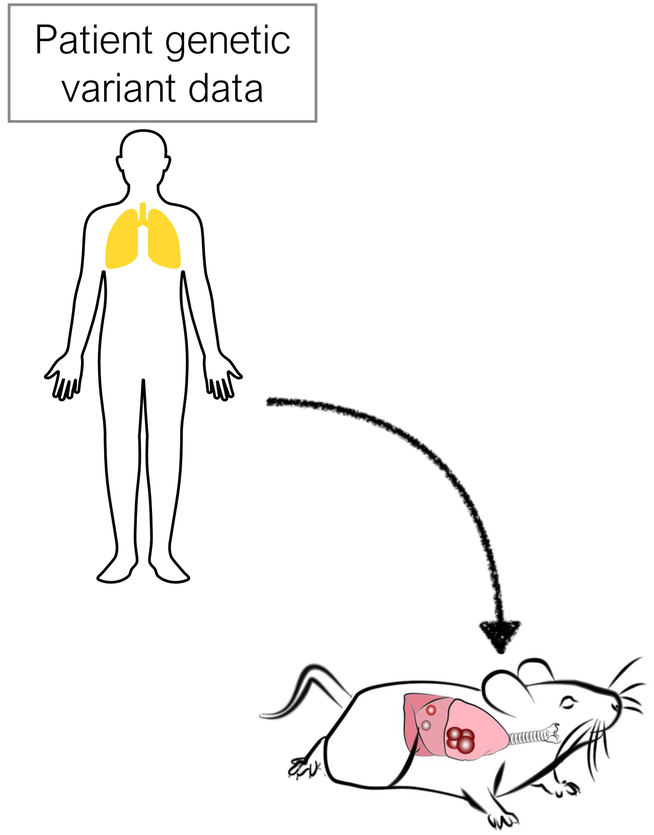
2010-2015: Postdoc Jacks Lab at MIT

2015-2020: Assistant Professor NYU

2016-2019: K22 - Elucidating the role of the Nrf2 anti-oxidant pathway in lung adenocarcinoma

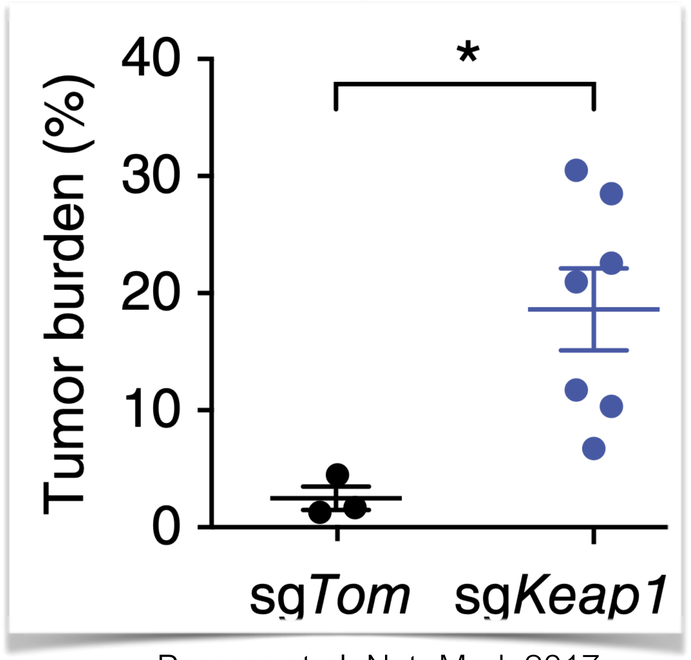
2020-current: Professor Associate NYU

Strategy - CRISPR/Cas9-based precision medicine platform

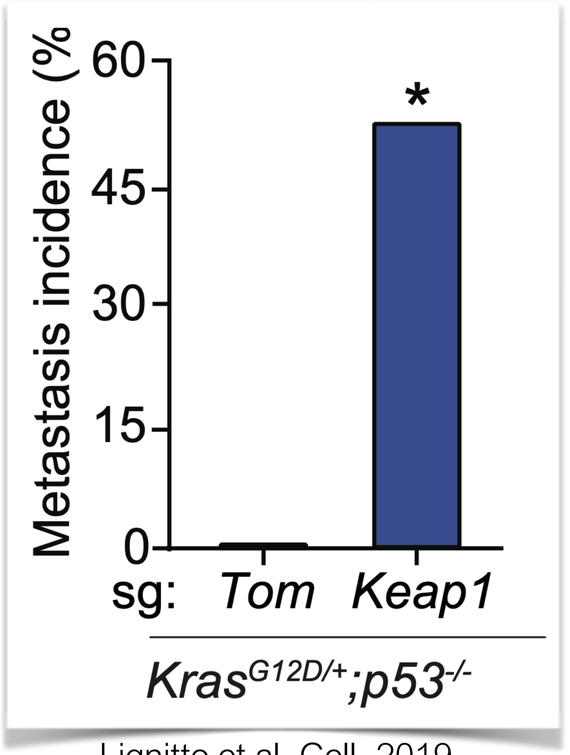


Rapid CRISPR-based modeling of mutations in mouse models

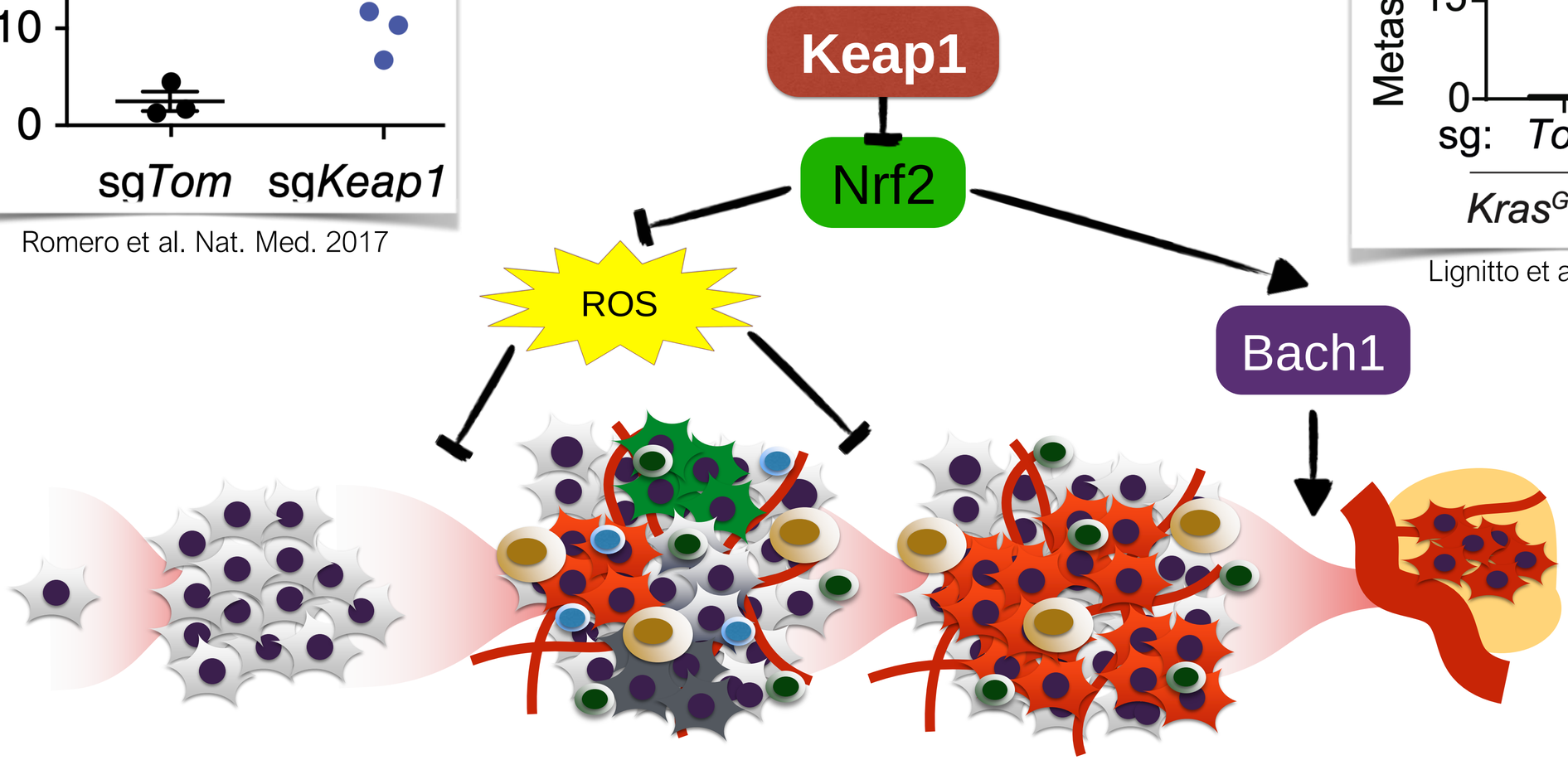
Keap1 mutations promote tumorigenesis at multiple stages



Romero et al. Nat. Med. 2017

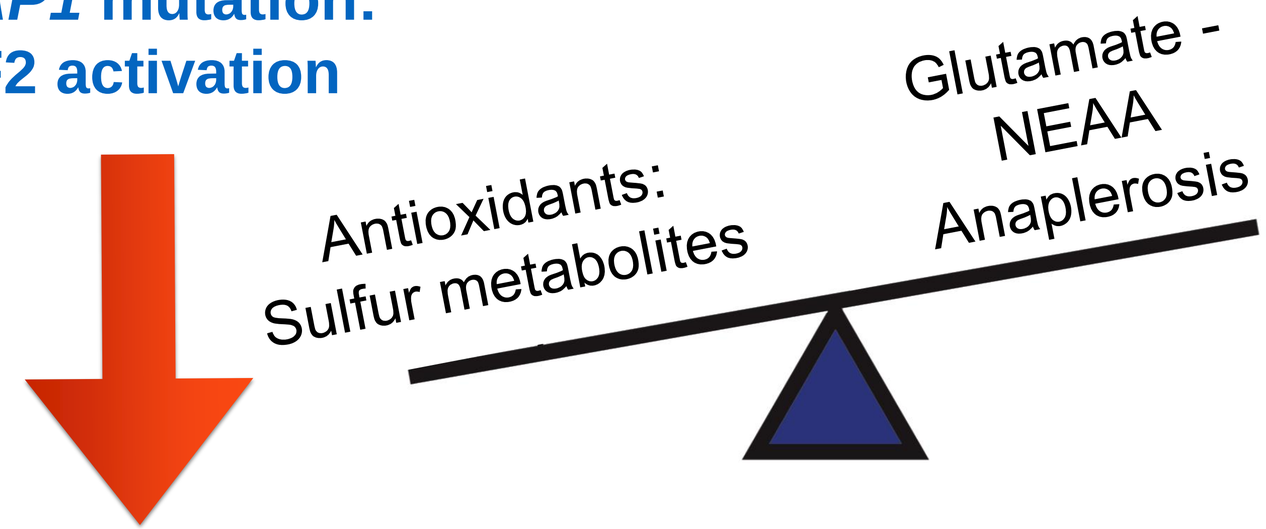


Lignitto et al. Cell. 2019



Are there druggable imbalances that arise in *KEAP1* mutant tumors?

***KEAP1* mutation:**
NRF2 activation



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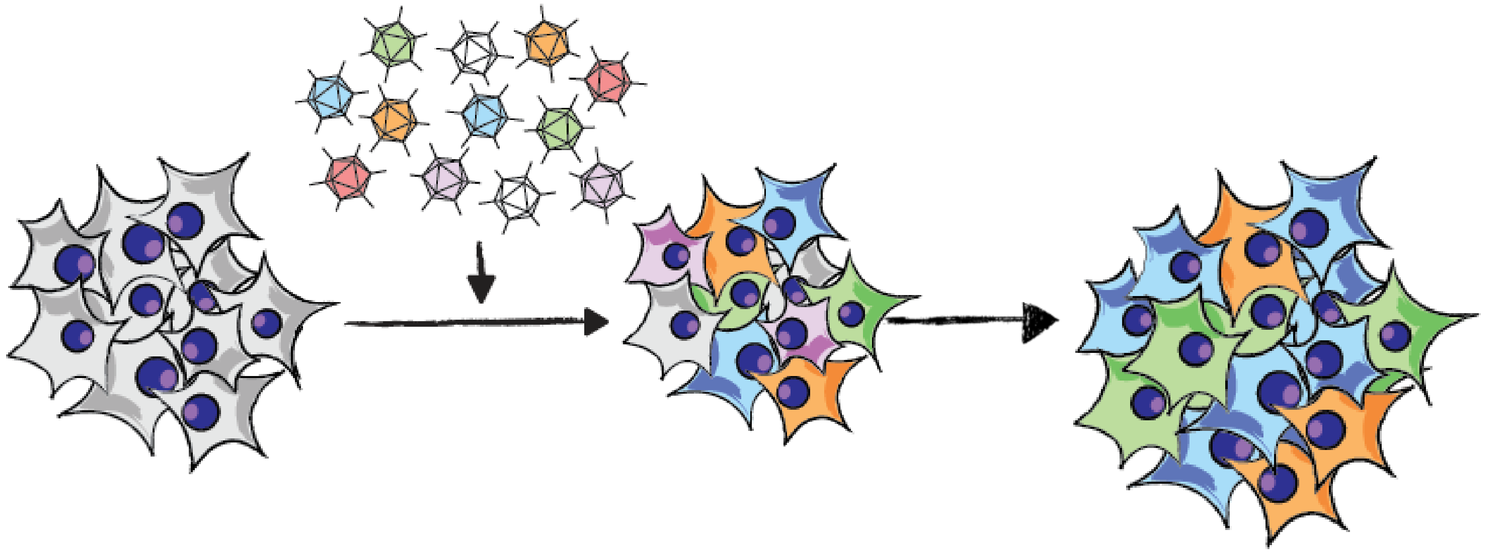
2018-2021: ACS - Characterizing the role of serine uptake in KRAS-driven lung cancer

2018-2025: R37 - Identifying metabolic dependencies in genetic subtypes of KRAS-driven lung cancer

2018-2023: R01 - Uncovering Genotype Specific Vulnerabilities in KRAS Mutant Lung Cancer

CRISPR screens to identify synthetic lethal targets in *KEAP1* mutant tumors

Metabolism focused CRISPR/Cas9 libraries



Glutamine Metabolism
Romero et al., Nature Medicine, 2017
Sayin et al., Elife, 2017

Non-essential Amino acids
LeBoeuf et al., Cell Metabolism, 2019

Heme Synthesis
Wu et al., In preparation

Pentose Phosphate Pathway
Ding et al., Science Advances, 2021

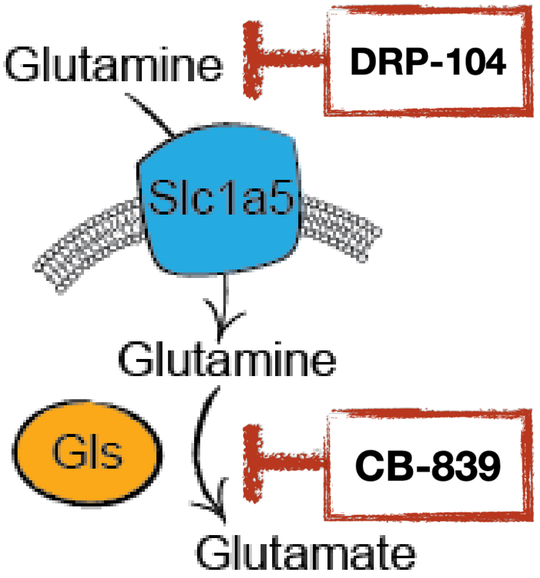
Phase 2 clinical trials with agents targeting glutamine metabolism in *KEAP1* mu

CTEP-NCI trial

NCT03872427 - Testing Whether Cancers With Specific Mutations Respond Better to Glutaminase Inhibitor, CB-839 HCl, Anti-Cancer Treatment, BeGIN Study

Dracen Sponsored Trial

NCT04471415 - First-in-human Study of DRP-104 as Single Agent and in Combination With Atezolizumab in Patients With Advanced Solid Tumors



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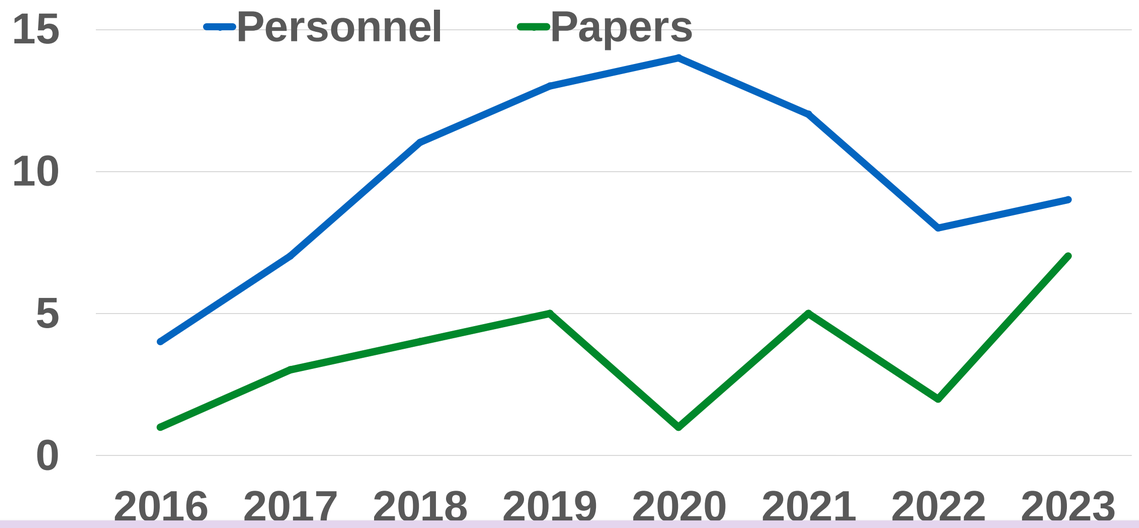
2018-2023: R01 - Uncovering Genotype Specific Vulnerabilities in KRAS Mutant Lung Cancer

2023-2028: R01 - Therapeutic potential of a novel glutamine antagonist in KEAP1 mutant lung cancer

2024-2029: R01 - Novel approaches to target KEAP1 mutant tumors



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2015-2020: Assistant Professor NYU

2020-current: Professor Associate NYU

2022-current: Director of Graduate Program

2016-2019: K22

2018-2021: ACS

2018-2025: R37

2018-2023: R01

2023-2028: R01

2024-2029: R01

Mentor for F99/K00 postdoctoral Fellow

Mentor for two F30 Awardees

Ad-Hoc Reviewer in Multiple NCI review panels including K99/R00

Acknowledgements

papagt01@nyumc.org

PapaG Lab
Ali Rashidfahrokki
Ray Pillai
Katherine Wu
Jozef Bossowski
Makiko Hayashi
Michael Cross
Sahith Rajalingam

Alumni
Volkan Sayin
Sarah LeBoeuf
Hongyu Ding
Warren Wu
Simranjit Singh
Filio Karakousi
Anastasia Zavitsanou
Luiz Gustavo Dubois
Dimitris Karagiannis
Doug Biancur
Betül Güzelhan
Yue Peng
Burcu Karadal
Annie Huang
Jennifer Sahni

Collaborators:
Sergei Koralov (NYU)
Kwok Wong (NYU)
Dan Littman (NYU)
Shohei Koide (NYU)
Andre Moreira (NYU)
Harvey Pass (NYU)
Charles Rudin (MSKCC)
Francisco Sanchez-Rivera (MIT)
Kivanc Birsoy (Rockefeller)
Kuan-Lin Huang (Mt. Sinai)
Scott Lowe (MSKCC)

NIH NATIONAL CANCER INSTITUTE

thalesplab.com
@ThalesPapaG

My pathway from K22 award to promote diversity to R37 MERIT Award

My background:

- BS Biology + MSc Biochemistry (UNal Colombia); PhD Cell Biology UTMB (Galveston, TX)
  Studied antiapoptotic molecules in SCI
- Postdoctoral Fellow Tulane/University of Colorado 2007-2013
  *Studied antiapoptotic molecules in cancer, breast cancer, hormones. O*btained DOD BCRP postdoctoral fellowship

K22 to promote diversity: Key for my transition to independence.

Why did I apply?

- I needed to develop a project not overlapping with mentors as they were young faculty, and I could not take my postdoc project with me.
- I identified a research gap in hormone biology, brain biology and brain metastases in BC. Merging neuroscience and cancer research to study the tumor microenvironment was novel and exciting area of research.
- I did not train with mentors well known in the metastases or neuro oncology community.

My pathway from K22 award to promote diversity to R37 MERIT Award

How did I prepare my K22 application:

- Found external mentors willing to provide training in the novel aspects of BM research (Pat Steeg, NCI).
- Obtained approval from DOD BCRP grant to use some funds for preliminary data.
- *Applied in 5th year of postdoc. Funded on first submission (2013).*

K22 award opened many doors:

- Paid 100% of my salary so I could have protected time to consolidate my research project.
- Incentivized my institution to keep me in the payroll while I consolidated my research ☺
- Provided research funding that was key to pursue preliminary experiments to make a competitive R01 application.

My pathway from K22 award to promote diversity to R37 MERIT Award

K22 award alone was not sufficient to get me tenure-track assistant professor positions:

- It took me almost 3 years of job applications (~2 years into K22) and obtaining an additional DoD BCRP award to get competitive job offers.
- I obtained offers from two institutions. Remained at UC and started tenure track position at UC in 2016.

K22 funded research (2013) led to R37 MERIT award (2018):

- It took a lot of additional research to the proposed studies in the K22 to write a competitive R01 application.
- I submitted R01 application twice (~40% percentile in the same SS). Grant scored 3% in a different SS in first submission. (*Chose your SS wisely, try others if your app is not well received in one*)

My pathway from K22 award to promote diversity to R37 MERIT Award

What things I did that helped my transition to independence and successful R01s:

- I invested in grant writing course (intensive ones) … great applications are lost in bad grantsmanship.
- **Do solid science.** Rigor of your research weights heavily in SS and will impact your reputation over time. *Solid science does not need to be in a CNS paper*.
- Get multiple mentors and be a good mentee: *do what you say you are going to do when you say you are going to do it.*
- Invest in learning project management, leadership skills. Your research is as good as your team.