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SENIOR ATTENDING PHYSICIAN • LEON HESS PROFESSOR, ELIZABETH AND VINCENT MEYER LABORATORY OF SYSTEMS CANCER BIOLOGY

Metastasis is a fascinating biological process that causes most cancer deaths. The Tavazoie laboratory employs a systems biology approach that integrates molecular, genetic, cellular, organismal, and clinical observations to discover and characterize key molecular regulators of metastasis, with the goal of developing new therapeutics for its prevention and treatment. This work has also uncovered surprising fundamental insights into mechanisms of gene regulation.

Metastatic disease causes most cancer deaths but remains poorly understood at the molecular level. The Tavazoie lab studies the molecular and cellular mechanisms underlying this process.

How do rare cancer cells initiate metastases in end-organs? How do metastatic cells reprogram surrounding host cells' gene expression and metabolic states? How do cells evade the immune system? How are extreme metastatic gene expression states that enable all of this established? The lab tackles these questions by first employing genome-wide technologies to identify recurrent molecular alterations associated with metastasis. Molecular and genetic studies in mice identify critical genes that regulate this process, with clinical association studies confirming human relevance and biochemical studies implicating molecular pathways involved. This has led to the discovery that modulation of tissue-specific sets of non-coding RNAs drive metastasis formation in distinct cancer types by altering expression levels of critical downstream genes that alter the cellular, metabolic, or matrix composition of the metastatic microenvironment. Such changes to the microenvironment enhance the survival, immune-evasive, and invasive capacity of cancer cells. These studies have uncovered the first evidence for an inherited genetic basis for human metastasis formation—providing a powerful genetic foundation for uncovering the genetic basis of metastasis by various cancer types and providing a genetic link between metastasis and Alzheimer's disease, which the lab is studying. Scientists in the lab have applied these insights toward the development of two first-in-class metastasis-targeting therapeutics, which have been advanced into national clinical trials. Their long-term goal is to develop broadly curative metastasis-preventive regimens for common cancers.

By studying how rare cancer cells achieve extreme gene expression programs during metastasis formation, Tavazoie and his colleagues have revealed that modulation of specific tRNAs is a gene regulatory process that alters the expression of specific downstream proteins in a codon-dependent manner to causally drive cancer progression. This has led to the delineation of specific tRNA-driven pathways as well as demonstration that restriction of specific amino acids can govern codon-dependent translation of specific genes. Such tRNA modulation responses have been observed in a variety of cells and systems and are increasingly recognized as a key mode of gene regulation.

EDUCATION

A.B. in molecular and cell biology, 1995
University of California, Berkeley

M.D., 2003
Harvard Medical School

Ph.D. in neuroscience, 2003
Harvard University

MEDICAL TRAINING

Internship in internal medicine, 2003–2004
Residency in internal medicine, 2004–2005
Brigham and Women's Hospital/Harvard Medical School

Fellowship in medical oncology, 2005–2008
Memorial Sloan Kettering Cancer Center

POSTDOC

Harvard Medical School, 2004–2005

POSITIONS

Assistant Professor, 2009–2015
Associate Professor, 2015–2018
Professor, 2018–
Director, Black Family Center for Research on Human Cancer Metastasis, 2018–
The Rockefeller University

Senior Attending Physician, 2009–
The Rockefeller University Hospital

AWARDS

NIH Director's New Innovator Award, 2009

Rita Allen Foundation Scholar, 2009

Era of Hope Scholar, Department of Defense, 2010

The Rockefeller University Distinguished Teaching Award, 2013

Pershing Square Sohn Prize, 2015

Emerging Leader in Health and Medicine, National Academy of Medicine, 2018

President, American Society of Clinical Investigation, 2022

National Cancer Institute Outstanding Investigator Award, 2022

Chan-Zuckerberg Investigator Award, 2024

HONORARY SOCIETIES

National Academy of Medicine

SELECTED PUBLICATIONS

Mei, W. et al. A commonly inherited human PCSK9 germline variant drives breast cancer metastasis via LRP1 receptor. *Cell* 188, 371–389 (2025).

Padmanaban, V. et al. Neuronal Substance P drives metastasis through an extracellular RNA-TLR7 axis. *Nature* 63, 207–215 (2024).

Ostendorf, B.N. et al. Common human genetic variants of APOE impact COVID-19 mortality. *Nature* 611, 346–351 (2022).

Tavora, B. et al. Tumoural activation of TLR3-SLIT2 axis in endothelium drives metastasis. *Nature* 586, 299–304 (2020).

Tavazoie, M.F. et al. LXR/ApoE activation restricts innate immune suppression in cancer. *Cell* 172, 825–840 (2018).