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

Metastasis is responsible for 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 unexpectedly uncovered surprising fundamental insights into mechanisms of gene regulation.

Metastatic disease is the primary cause of cancer mortality but remains poorly understood at the molecular level. The Tavazoie lab studies the molecular and cellular mechanisms underlying this process. Their work has also uncovered novel roles for transfer RNAs (tRNAs) in gene regulation.

The lab employs genome-wide technologies to identify recurrent molecular alterations associated with enhanced metastatic capacity. Molecular and genetic studies in mice are used to implicate critical genes that regulate this process, with clinical association studies confirming human relevance and biochemical studies implicating signaling pathways involved. This has led to the discovery that modulation of tissue-specific sets of small non-coding RNAs (microRNAs) drives metastasis formation in distinct cancer types by altering expression levels of critical downstream genes. These genes activate pathways 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. Major efforts in the lab aim to understand how metastases initiate in end-organs, how metastatic cells reprogram surrounding host cells and metabolism, how immune-evasion occurs, and how extreme metastatic gene expression states are established. Recent work uncovered the first evidence for an inherited genetic basis for human metastasis formation—providing a powerful genetic foundation for future studies. 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.

Furthermore, by studying how rare cancer cells achieve extreme gene expression programs during metastasis formation, Tavazoie and his colleagues have revealed that modulation of specific transfer RNAs (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 deprivation 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

HONORARY SOCIETIES

National Academy of Medicine

SELECTED PUBLICATIONS

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

Ostendorf, B.N. et al. Common germline variants of the human APOE gene modulate melanoma progression and survival. *Nature Medicine* 26, 1048–1053 (2020).

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).

Goodarzi, H. et al. Modulated expression of specific tRNAs drives gene expression and cancer progression. *Cell* 165, 1416–1427 (2016).