CENTER FOR DERMAL RESEARCH
SEMINAR SERIES REMOTE

The Center for Dermal Research Welcomes

Bishr Omary, Rutgers University and Rutgers Health

"Diseases of the Intermediate Filaments Cytoskeleton: From Pathogenesis to Drug Discovery"

Monday, April 22, 2024 at 5:30pm EST Remote

Dr. M. Bishr Omary is Henry Rutgers Professor of Biomedical Sciences at Rutgers University, and Senior Vice Chancellor for Academic Affairs and Research for Rutgers Health. He completed his PhD training at the University of California San Diego (UCSD), then his medical degree at the University of Miami, followed by internal medicine residency at UC Irvine and gastroenterology fellowship at UCSD. He then spent 19 years at Stanford University including serving as Chief of Gastroenterology and Hepatology, then 11 years at the University of Michigan including serving as chair of the department of molecular and integrative physiology then executive vice dean for research at the medical school before moving to Rutgers in 2019. His laboratory currently studies the pathogenesis and therapeutic approaches to rare diseases that cause liver and skin damage, and a urea cycle enzyme nonenzymatic functions and utility as a biomarker of liver injury.

Abstract

Intermediate filament proteins (IFs) make up one of the three major cytoskeletal protein families that are found in most cells of higher eukaryotes. Cytoplasmic IFs are expressed in a cell specific manner; for example, specific keratins are expressed in different epithelial cells, desmin in myocytes, neurofilaments in neurons, while lamins are the IFs in nuclei. The selective cell and tissue expression of IFs has made them widely used biomarkers of tissues and human disease. Mutations in genes encoding these proteins cause or predispose to >80 mostly rare human diseases that include skin, neuronal, muscle, metabolic, and liver disorders. To date, no treatment is available for these diseases except for the management of some of their complications such as diabetes.

IFs serve key mechanical and nonmechanical functions in cells, with the major mechanical function being protection of cells from fragility and cell death. The major regulators of IF function are posttranslational (PTMs) modifications and interaction with their associated proteins, with phosphorylation being the best studied PTM. Our laboratory has focused on studying the function, regulation, and disease association of IFs, including the development of potential therapies. We have used high throughput drug screening to identify compounds that protect from the detrimental consequences of disease-relevant keratin mutations. Some of these compounds are being formulated for potential testing in patients with the blistering skin disease epidermolysis bullosa simplex.

References: (i) Omary MB, Coulombe PA, McLean WHI. (2004). Intermediate filament proteins and their associated diseases. N Engl J Med 351:2087-2100; (ii) Rietscher K, Jahnke H-G, Lin EW, Has C, Omary MB, Magin TM. (2022). Kinase inhibition prevents epithelial damage in epidermolysis bullosa simplex via keratin and cell contact stabilization. J Invest Dermatol 142:3282-3293; (iii) Li P, Rietscher K, Jopp H, Magin TM, Omary MB. (2023). Posttranslational modifications of keratins and their associated protein as therapeutic targets in keratin diseases. Curr Opin Cell Biol 85:102264.

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