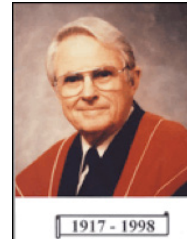




a place of mind
THE UNIVERSITY OF BRITISH COLUMBIA



Faculty of Medicine
Department of Cellular and Physiological Sciences

THE 15TH D. HAROLD COPP LECTURE

4:00 PM, TUESDAY, APRIL 16TH, 2019 LSC 2

Gökhan S. Hotamışlıgil, MD, PhD

Harvard TH Chan School of Public Health

James S. Simmons Professor of Genetics and Metabolism
Director, Sabri Ülker Center for Nutrient, Genetic Metabolic Research
Department of Genetics and Complex Diseases

- 2004 *TUBITAK Science Award*
- 2007 *Outstanding Scientific Accomplishment Award, ADA*
- 2010 *Wertheimer Award, ASA*
- 2013 *Koç Foundation Science Award*
- 2014 *Danone International Prize for Nutrition*
- 2015 *Roy O. Greep Award for Outstanding Research, Endocrine Society*
- 2018 *EASD-Novo Nordisk Foundation Diabetes Prize*



Metabolic Biology of the Endoplasmic Reticulum in Health and Disease

Proper coordination of cellular metabolism and its integration with immune response is paramount to function of cells, organs, and organisms. The endoplasmic reticulum is the main site for protein and lipid synthesis, trafficking, and the storage of cellular calcium. Work in our group over the past two decades demonstrated that ER also plays a significant role in adaptation to metabolic fluctuations, adaptation to metabolic challenges, and their integration to immune response. This important "integrated metabolic response" is disrupted by metabolic stress of chronic metabolic diseases such as obesity and diabetes in animal models and humans. Restoration of the ER adaptive folding responses by genetic or chemical means improve metabolic homeostasis in preclinical models and humans. Therefore, understanding the compositional, structural, and functional regulation of the ER and the mechanisms giving rise to its dysfunction remain critical areas of investigation and carry important translational opportunities. In recent studies, we have discovered alteration in structural organization and architecture of the organelle and identified adaptive responses that emanate from the ER during metabolic stress in physiological or pathological contexts. Here, I will present emerging evidence integrating metaflammation to endoplasmic reticulum and mitochondria function and regulation of interactions between organelles during metabolic fluctuations. I will also present our most recent observations on a novel pathway mediated by the NRF family of ER bound transcription factors, which orchestrates previously unknown countermeasures against metabolic stress to preserve ER integrity and metabolic health. Finally, how these molecular mechanisms may be exploited to understand chronic inflammatory diseases and leveraged to design novel and effective preventive and therapeutic strategies will be discussed.

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