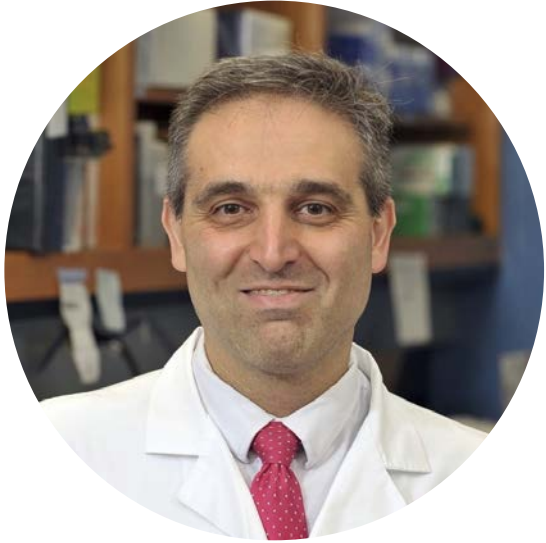


# TIMOTHY A. JOHNSON MEDICAL SCHOLAR LECTURE SERIES

Presented by the Fralin Biomedical Research Institute at VTC and the Virginia Tech Carilion School of Medicine



**HOSSEIN ARDEHALI, M.D., Ph.D.**

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## *In Person Lecture: Novel Iron Sensing Mechanisms and Role of Hexokinase Mitochondrial Binding in the Development of HFpEF*

In the first part of his talk, Dr. Ardehali will talk about novel mechanisms of iron sensing. All living cells require a minimal iron threshold to sustain anabolic metabolism. However, the mechanisms by which cells sense iron to regulate anabolic processes are unclear. Here, Dr. Ardehali and his lab report a universal eukaryotic pathway for iron sensing in which molecular iron is required to sustain active histone demethylation and maintain the expression of critical components of the pro-anabolic mTORC1 pathway. Specifically, they identify the iron-binding histone-demethylase KDM3B as an intrinsic iron sensor that regulates mTORC1 activity by demethylating H3K9me<sup>2</sup> at enhancers of a high-affinity leucine transporter and RAPTOR. By directly suppressing leucine availability and RAPTOR levels, iron deficiency supersedes other nutrient inputs into mTORC1. In the second part, Dr. Ardehali will talk about mechanism of heart failure with preserved ejection fraction (HFpEF), which is a common cause of morbidity and mortality worldwide, but its underlying pathophysiology is not well-understood and treatment options are limited. Hexokinase-1 (HK1) mitochondrial-binding and protein O-GlcNAcylation are both altered in conditions with risk factors for HFpEF. Here Dr. Ardehali and his team report a novel mouse model of HFpEF and show that HK1 mitochondrial-binding in endothelial cells (EC) is critical for the development of HFpEF. The researchers demonstrate increased mitochondrial dislocation of HK1 in ECs from HFpEF mice.

FRIDAY, SEPT. 22, at 1 p.m.

Room M203, 2 Riverside Circle.

Watch via Zoom at <https://fralinbiomed.info/MedScholar-Join>,

Or at <https://fbri.vtc.vt.edu/events/live-webcast.html>

