Dr. Herbert and Nicole Wertheim Leadership in Healthcare and Medicine Lectureship

"Interplay of signal transduction and mitochondria in liver injury: a sab story."

Dr. Neil Kaplowitz

Professor of Physiology & Biophysics and Pharmacology & Pharmaceutical Sciences
Keck School of Medicine of USC, Division of Gastrointestinal & Liver Diseases

Date: February 6, 2015
Time: 12pm - 1pm
Venue: AHC IV 101

Biography

Neil Kaplowitz MD is Director of the USC NIDDK-sponsored Research Center for Liver Diseases. He holds two endowed chairs, the Brem Professor of Medicine and the Budnick Chair in Liver Diseases, and is Chief of the Division of Gastrointestinal and Liver Diseases. He is also Professor of Physiology & Biophysics and Pharmacology & Pharmaceutical Sciences at the Keck USC School of Medicine. Dr. Kaplowitz has received a number of honors and distinctions including election to membership in the American Society for Clinical Investigation and the Association of American Physicians. He is recipient of the Western Gastroenterology Research Prize, the William S. Middleton Award, the Solomon A. Berson Medical Alumni Achievement Award in Clinical Science from his alma mater, the Merit Award from the National Institutes of Health, the Mayo Soley Award from WSCI, the AASLD Distinguished Achievement Award, and the ALF Distinguished Scientific Achievement Award. He has served as the President of the American Association for the Study of Liver Diseases, and Vice-Chair for Research of the American Liver Foundation. He has also served as Associate Editor of leading medical and scientific journals such as Hepatology, Gastroenterology and the American Journal of Physiology. In recent years he has focused on the role of signal transduction, ER and mitochondrial stress in the pathogenesis of liver injury. He has published more than 195 peer-reviewed, scientific articles, 150 scholarly reviews and has edited ten books related to liver diseases.

Abstract

The outer membranes of mitochondria have emerged as hubs for the association of signal transduction modules with the regulation of mitochondria in the physiology and pathobiology of hepatocytes and other cell types. Mitochondria are the main source of reactive oxygen species. Thus, signaling modules are brought into close proximity to reactive oxygen species. This phenomenon is well illustrated by the MAPKinases, and specifically JNK. P-JNK binds to an outer membrane protein known as Sab (SH3BP5) which is a JNK docking protein and substrate of JNK.

When MAPK activation pathways lead to JNK activation, e.g. TNF receptor signaling, palmitate via detergent insoluble membrane, ER stress, or ROS derived by mitochondria, P-JNK binding to Sab initiates a self-amplifying process which involves intramitochondrial signaling leading to disruption of electron transport, enhanced ROS release and sustained JNK activation. Sustained JNK activation then promotes apoptosis (TNF+NF-kB inhibition, lipoapoptosis, or severe ER stress) or necrosis (acetaminophen toxicity). Knockdown or conditional knockout of Sab inhibits sustained JNK activation and cell death in all these contexts.

Co-sponsor information.

Department of Cellular Biology & Pharmacology
p.305-348-4745 | f. 305-348-1577
gregory.anderson@fiu.edu | http://medicine.fiu.edu/about-us/departments/basic-sciences/cell-biology-and-pharm/index.html

FIU Herbert Wertheim College of Medicine