LSU HealthNewOrleans
HEALTH SCIENCES CENTER

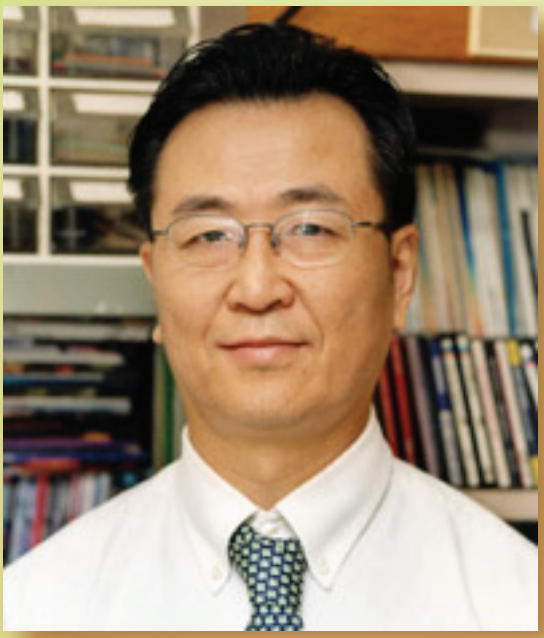
School of Medicine

Neuroscience Center of Excellence

Special Seminar

in Neuroscience sponsored by

G.N.O.S.N.
Greater New Orleans Society for Neuroscience
a chapter of the Society for Neuroscience



Cell Death, Autophagy and Lysosomes in Brain Cells: Roles of Zinc and Metallothionein-3

Jae Y. Koh, M.D., Ph.D.
Department of Neurology,
University of Ulsan, College of Medicine
Seoul, Korea

Change in Venue

4:00 p.m.
Thursday
October 18, 2012

Lion's Eye Building
8th Floor
Conference Room

more info: zdavis@lsuhsc.edu

Over the last two decades, a number of investigators have presented evidence that cellular zinc dyshomeostasis may contribute to brain cell death. In this presentation, I am going to show that oxidative injury to neurons and astrocytes causes cell death at least in part through lysosomal damage that is triggered by zinc dyshomeostasis. In addition, I am going to present evidence that increases in intracellular free zinc levels are required for activation of autophagy in these cells. Also, while attempting to search for the zinc source in brain cells, we found that metallothionein-3 (MT3) plays a key role in lysosomal functions; its absence caused, 1) reduced oxidative cell death, 2) reduced zinc dyshomeostasis, but 3) defects in autophagy and lysosomal functions. Zn-MT3 played a key role in actin-mediated c-abl signaling in astrocyte, which in turn regulates lysosomal functions. Considering that MT3 levels are reduced in AD and that MT3 plays a role in autophagic degradation, we sought to examine whether Aβ metabolism was altered in MT3-null astrocytes. In MT3 null astrocytes, clathrin-dependent endocytosis and distribution of early endosomes were altered, which changes were replicated by cytochalasin-D, an inhibitor of actin polymerization. Secondly, Aβ uptake was reduced and delayed in MT3-null astrocytes. Hence, it may be that the down-regulated MT3 seen in AD may contribute to reduced turnover of Aβ by astrocytes.

layout&design e.d. guillot NCE 092812