A MITOCHONDRIA-INITIATED APOPTOTIC PATHWAY

Xiaodong Wang

Howard Hughes Medical Institute, Department of Biochemistry, University of Texas
Southwestern Medical School, 5323 Harry Heines Boulevard, Dallas, Texas 75235-9038
xwang@biochem.swmed.edu

Emerging evidences indicate that in mammalian cells, mitochondria are not only metabolic centers that provide energy and other essential molecules to sustain life, but also key regulatory centers for cell death. When cells are insulted by apoptotic stimuli, mitochondrial homeostasis is interrupted resulting in releasing of proteins that normally reside in the intermembrane space of mitochondria. The roles of two such proteins in apoptosis have been defined in molecular details. One protein is cytochrome c that normally functions in electron transfer chain in mitochondria. The release of cytochrome c into the cytosol triggers a chain of molecular events mediated by Apaf-1 protein that causes the activation of intracellular protease, caspases. Another novel protein, Smac, is also released from mitochondria to cytosol similar to cytochrome c and functions in apoptosis by removing the inhibitory activities of IAPs, a family of proteins that attenuate apoptosis by inhibiting the activity of caspases.

In this meeting, I will discuss the detailed biochemical mechanism how these proteins interact with each other to determine the life and death of cells.