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LT20

Hosted by Dr Low Boon Chuan

ALL ARE WELCOME!

Cofilin, actin cytoskeleton and apoptosis

Apoptosis acts to eliminate redundant or excess cells during development. Mitochondria play a pivotal role in the transduction of apoptotic signals, by releasing proapoptotic proteins such as cytochrome c that in turn initiate caspase activation cascade. Using proteomic approach we observed that cofilin, an actin binding protein, was translocated into mitochondria in response to apoptotic stimuli prior to cytochrome c release. Silencing of cofilin expression by small interfering RNA (siRNA) blocks cytochrome c release and renders cells resistant to apoptosis. Cofilin can be inactivated and dissociated from actin by phosphorylation at Ser 3 residue. Cofilin translocation depends on the phosphorylation status of cofilin with only dephosphorylated cofilin translocating into mitochondria. The cofilin^{S3D} mutant that harbors substitution of Ser3 with Asp and mimics the phosphorylated form of cofilin blocks its translocation and delays the onset of apoptosis, whereas targeted expression of cofilin in mitochondria strongly induces apoptosis. The apoptosis inducing ability of cofilin, but not its mitochondrial localization, was dependent on the functional actin-binding domain. Our data suggest that cofilin plays an important role in transducing apoptotic signals to mitochondria and reveal a novel mechanism of actin cytoskeleton in apoptosis regulation.



Department of Biological Sciences
Seminar Announcement