Lecture 16 Apoptosis

Apoptosis is form of programmed cell death. Apoptosis eliminates cells that are abnormal, misplaced, nonfunction, or potentially dangerous. It a natural part of organism devlopment and maintenance. For example, tissue/organ homeostasis(live size), metamorphosis (tadopole to frog), tissue sculpting (mouse paw), immune cell apoptsis (short-lived neutrophils).

During apotosis, cells undergo morphological changes: **Characteristics of apoptosis**

- Cell shrinkage and chromatin condensation
- PS flipping to outside
- DNA fragmentation
- Nuclear membrane disruption
- Cytoskeleton collapses
- Cell surface blebs(水泡)---apoptotic bodies

It is difference between apoptosis and necrosis. For apoptsis, cells die clean and tidy(为了有序而清理). Necrosis is cauesed by acute insults(无法有序而混乱)

II. Methods to identify apoptosis cell

Annexin V staining： PS is flipped to outer leaflet of plasma membrane and can be detected by annexin V (protein)-conjugate fluorscent dye.

Cell cycle distribution, DNA fragmentation

Terminal dUTP Nick End Labelling (TUNEL). 3' Terminal deoxynucleotidyl transferase catalyzes dUTP addition on fragmented DNA, dUTP is subsequently labeled with fluorescence dye.

Western blot for apoptosis maker (Caspase 3, PARP, etc) cleaved PARP, cleaved caspase-3. Cytochrome translocation

Brief History- leading to the Nobel Prize in 2002

Sydeny Brenner estabished *C. elegans* as a novel experimental model organism. Because *C. elegans* is transported, scientists can observe cell division, differentiation and organ development under microsocpe.

John Sulston: Cell death is part of the normal differentiation process

Robert Horvitz discovered and characterized key genes controlling cell death in *C. elegans*.

Xiaodong Wangs' work revealed a key role(caspase-3 via apoptosome) for the mitochondria in programmed cell death.

IV:Players and mechanis

4.1 Caspases

Apoptosis depends on an intracellular protolytic cascade. Signal-mediated cascading activation of apoptosis.

4.2 Activation cascade:

1. Apoptotic signal triggers, 2) Adaptor com

The amplifying caspase cascade: the point-of-no-return. Here is 3 categories of human caspases.

4.3 Death receptor trigger the extrinsic pathway of apoptosis.

4.4 The intrinsic or mitochondria apoptosis activation pathway

Interactors & interactions

UV-light induced DNA damage trigger release mitochondria cytochrome c