Cell death

Major types

Apoptosis: appropriate, programmed Necrosis: inappropriate, accidental Autophagy: self-digestion

Classification of cell death



<u>APOPTOSIS</u>

What is it?

Why is it important?

How is it controlled?

What is its role in age-related disease?

<u>APOPTOSIS</u>

Programmed cell death

Orderly cellular self destruction

Process: as crucial for survival of multi-cellular organisms as cell division

Forms of cell death

Necrosis	Apoptosis	Mitotic catastrophe
Passive	Active	Passive
Pathological	Physiological or pathological	Pathological
Swelling, lysis	Condensation, cross-linking	Swelling, lysis
Dissipates	Phagocytosed	Dissipates
Inflammation	No inflammation	Inflammation
Externally induced	Internally or externally induced	Internally induced

<u>APOPTOSIS</u>

Evolutionarily conserved

•Occurs in all animals studies (plants too!)

•Stages and genes conserved from nematodes and flies to humans



STAGES OF APOPTOSIS

Genetically controlled: Caenorhabditis elegans Soil nematode (worm)



C. Elegans genes == mammalian genes

Cells are balanced between life and death



APOPTOSIS: important in embryogenesis

Morphogenesis (eliminates excess cells):



Selection (eliminates non-functional cells):



APOPTOSIS: important in embryogenesis

Immunity (eliminates dangerous cells):



Organ size (eliminates excess cells):



APOPTOSIS: important in adults

Tissue remodeling (eliminates cells no longer needed):



APOPTOSIS: important in adults

Tissue remodeling (eliminates cells no longer needed):



Steroid immunosuppressants: kill lymphocytes by apoptosis

Lymphocytes poised to die by apoptosis

APOPTOSIS: important in adults

Maintains organ size and function:



Cells lost by apoptosis are replaced by cell division

(remember limited replicative potential of cells)

APOPTOSIS: control



APOPTOSIS: control



APOPTOSIS: control



Induction and Regulation of Apoptosis



APOPTOSIS: Role in Disease

TOO MUCH: Tissue atrophy

Neurodegeneration Thin skin etc

TOO LITTLE: Hyperplasia

Cancer Athersclerosis etc

<u>APOPTOSIS: Role in Disease</u> Neurodegeneration

Neurons are post-mitotic (cannot replace themselves)

Neuronal death caused by loss of proper connections, loss of proper growth factors (e.g. NGF), damage (especially oxidative damage)

Neuronal dysfunction or damage results in loss of synapses (synaptosis; reversible) apopsosis (irreversible)

> PARKINSON'S DISEASE ALZHEIMER'S DISEASE HUNTINGTON'S DISEASE etc.

<u>APOPTOSIS: Role in Disease</u> Cancer

Apoptosis eliminates damaged cells (damage => mutations => cancer

Tumor suppressor p53 controls senescence and apoptosis responses to damage

Most cancer cells defective in apoptotic response

High levels of anti-apoptotic proteins or Low levels of pro-apoptotic proteins ===> CANCER

APOPTOSIS: Role in Disease AGING

Aging --> both too much and too little apoptosis (evidence for both)

Too much (accumulated oxidative damage?) ---> tissue degeneration

Too little (defective sensors, signals? ---> dysfunctional cells accumulate hyperplasia (precancerous lesions)