Death is Part of Life
the Function of Apoptosis

Normal Development: deletion of excess number of neurons, interdigital web

Immune system function: clonal selection of T and B cell lineage, cytotoxic T cell attack

Tissue homeostasis: in intestinal villocryptal modeling, endometrium cyclic proliferation and deletion

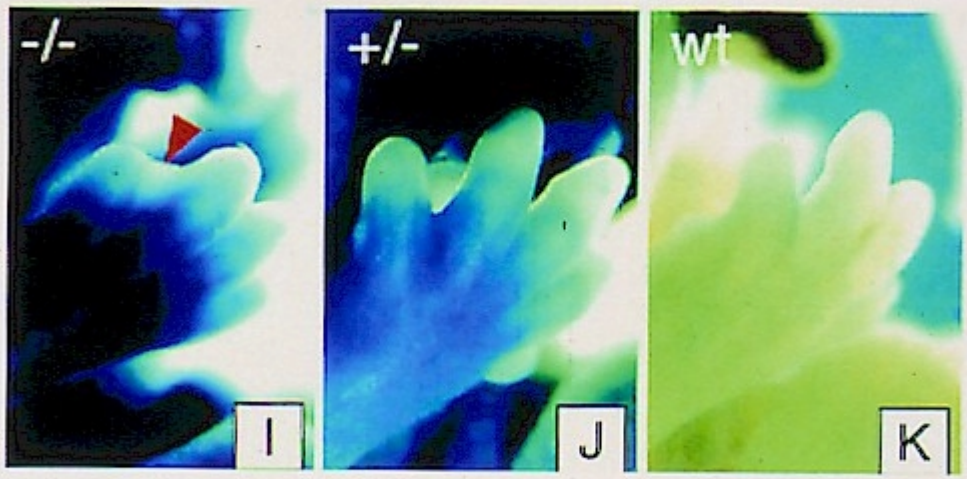
Deletion of damaged cells: sunburn cells, chemical and radiation damaged cells, viral infected cells

Hormone-dependent tissue atrophy

Caspase-9 Knock Out Mice Have Extra Brain Tissue

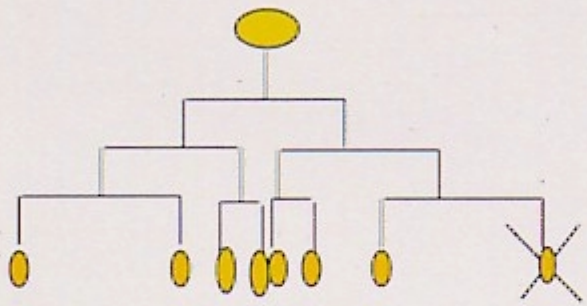
Kuida et al., Cell 94, 325; Hakem et al., Cell 94, 339.

Delayed Recession of Interdigital Web in Apaf-1 Knock Out Mice



Cecconi et al., 1998, Cell 94, 727-737.

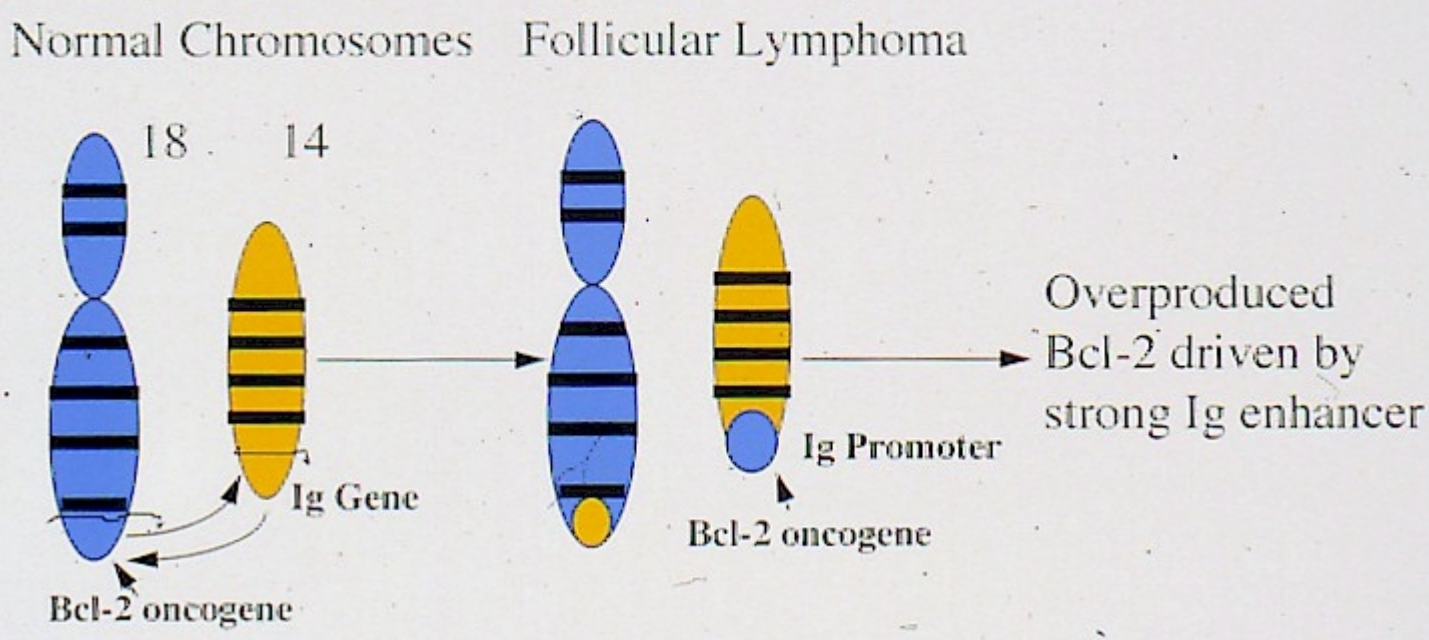
Apoptotic Pathway in C. Elegans



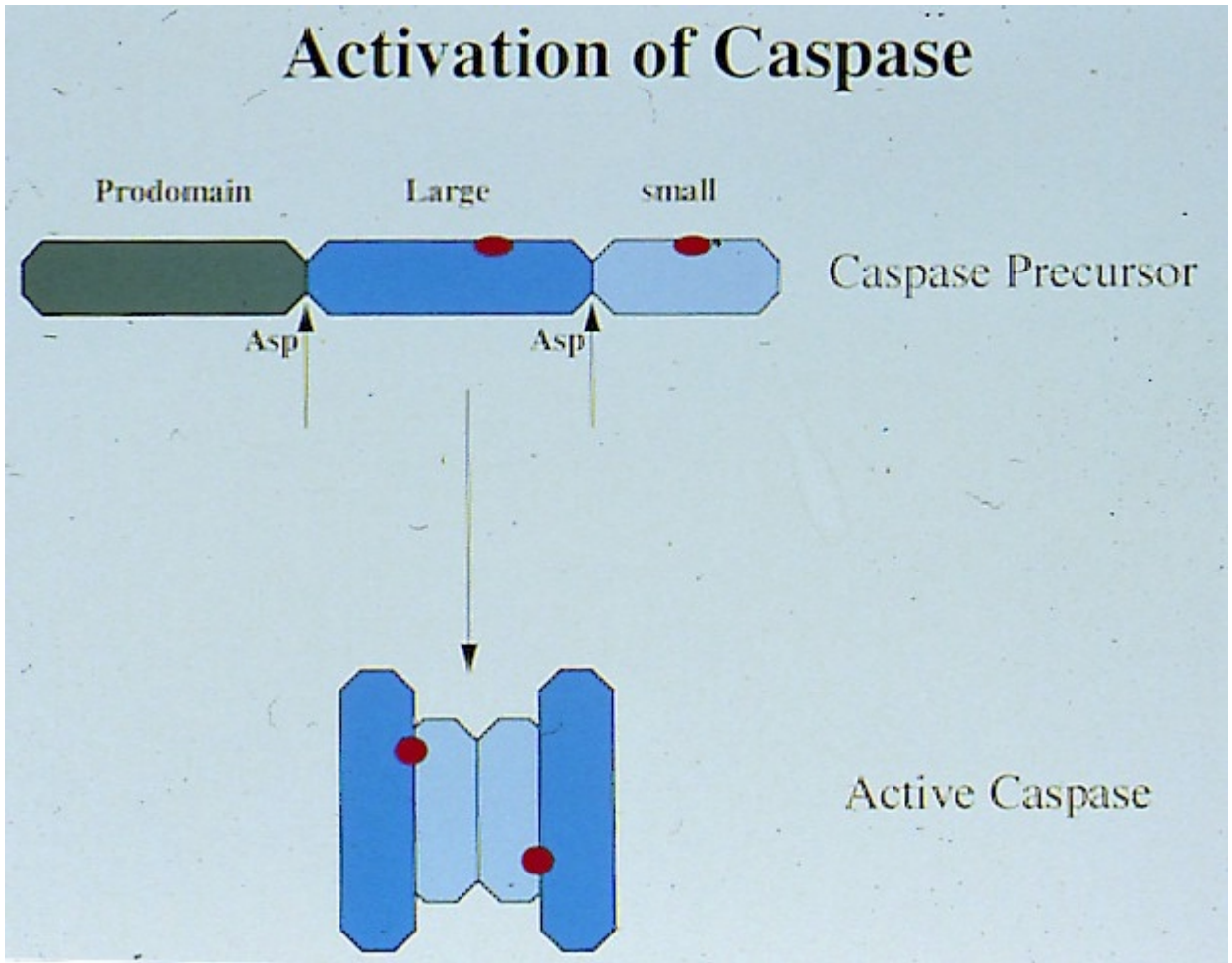
131 out of 1090 cells die during development

Egl-1 $\xrightarrow{-}$ Ced-9 $\xrightarrow{-}$ Ced-4 $\xrightarrow{+}$ Ced-3 $\xrightarrow{+}$ Apoptosis

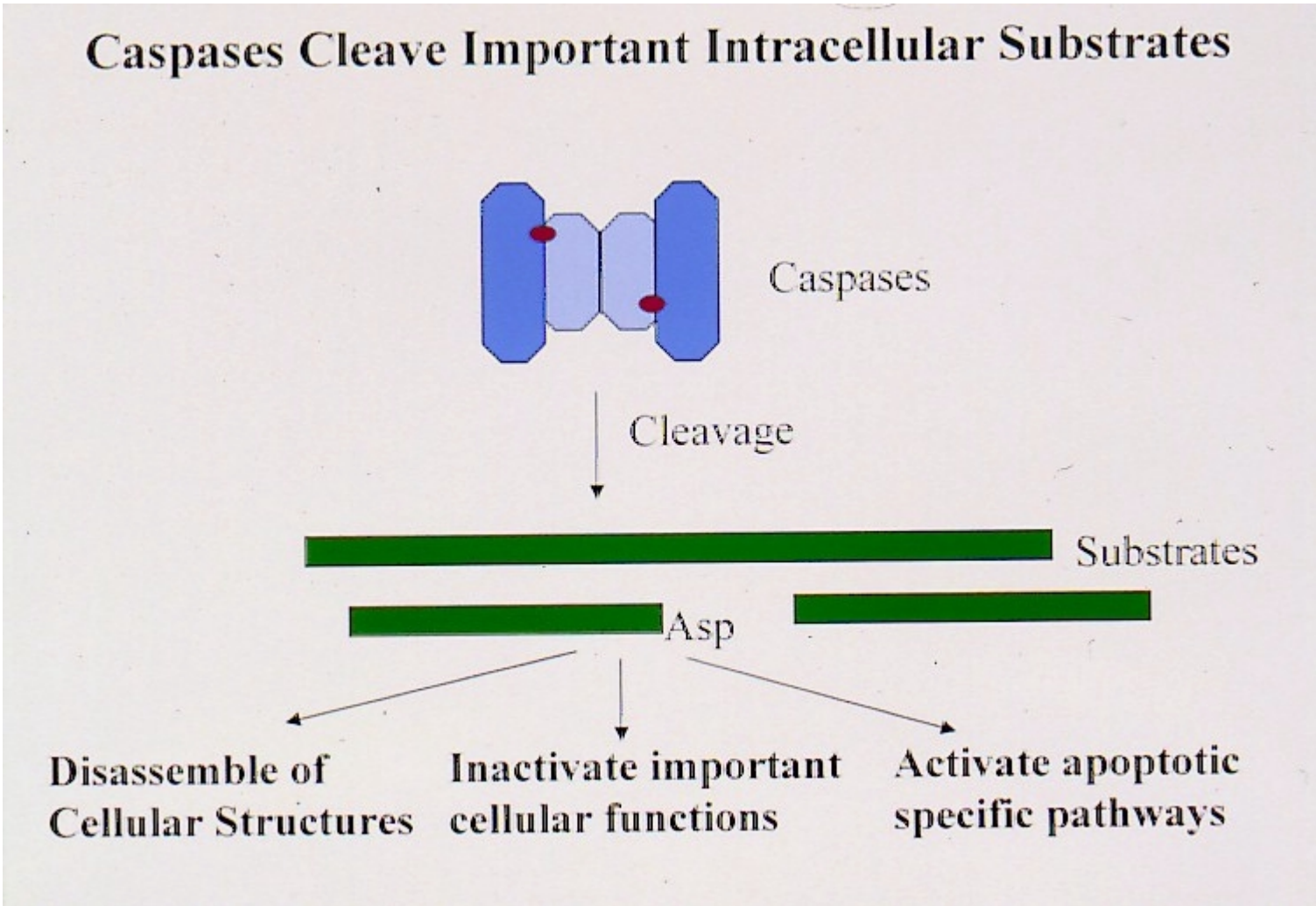
Chromosomal Translocations in Follicular Lymphoma



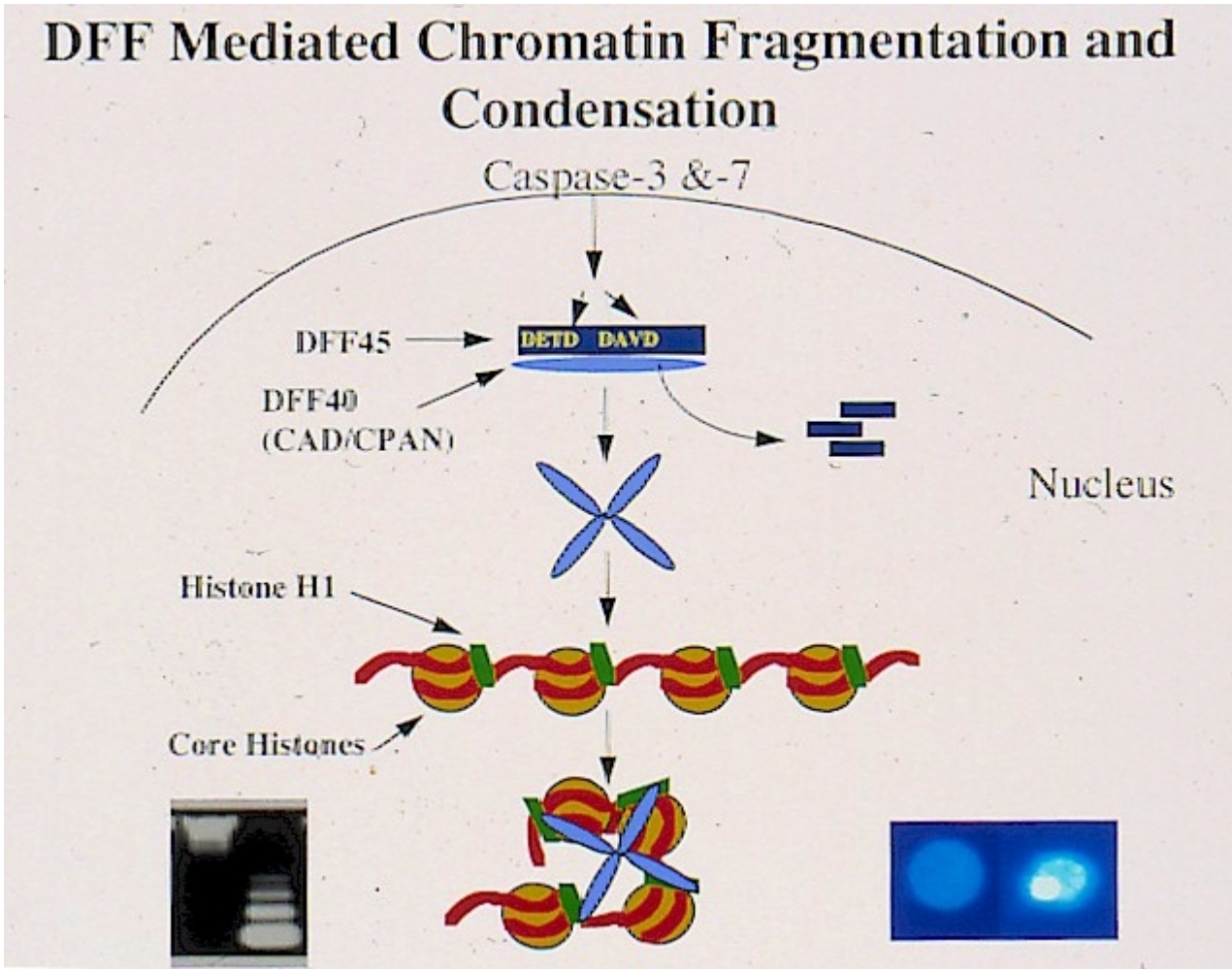
Activation of Caspase



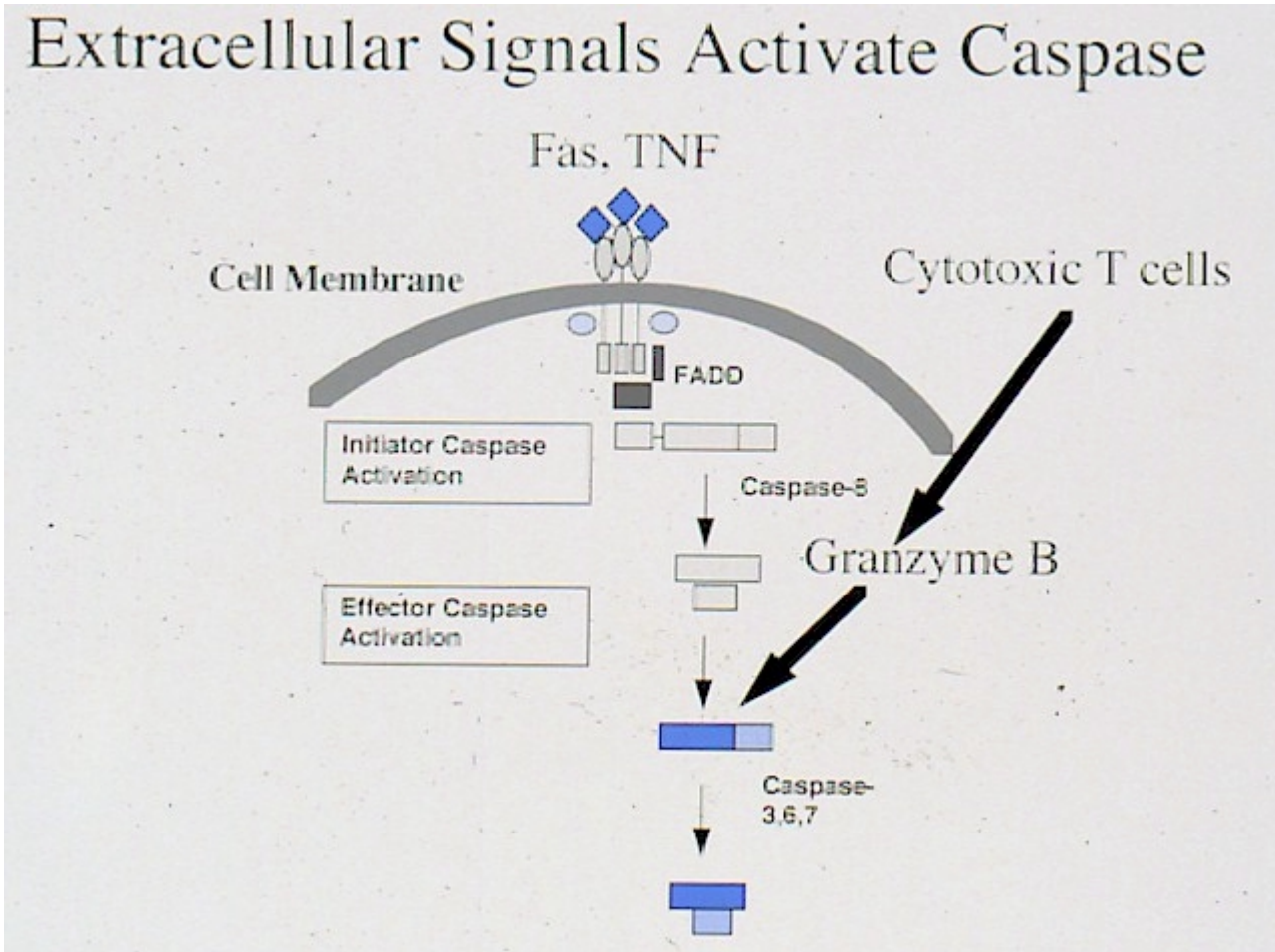
Caspases Cleave Important Intracellular Substrates

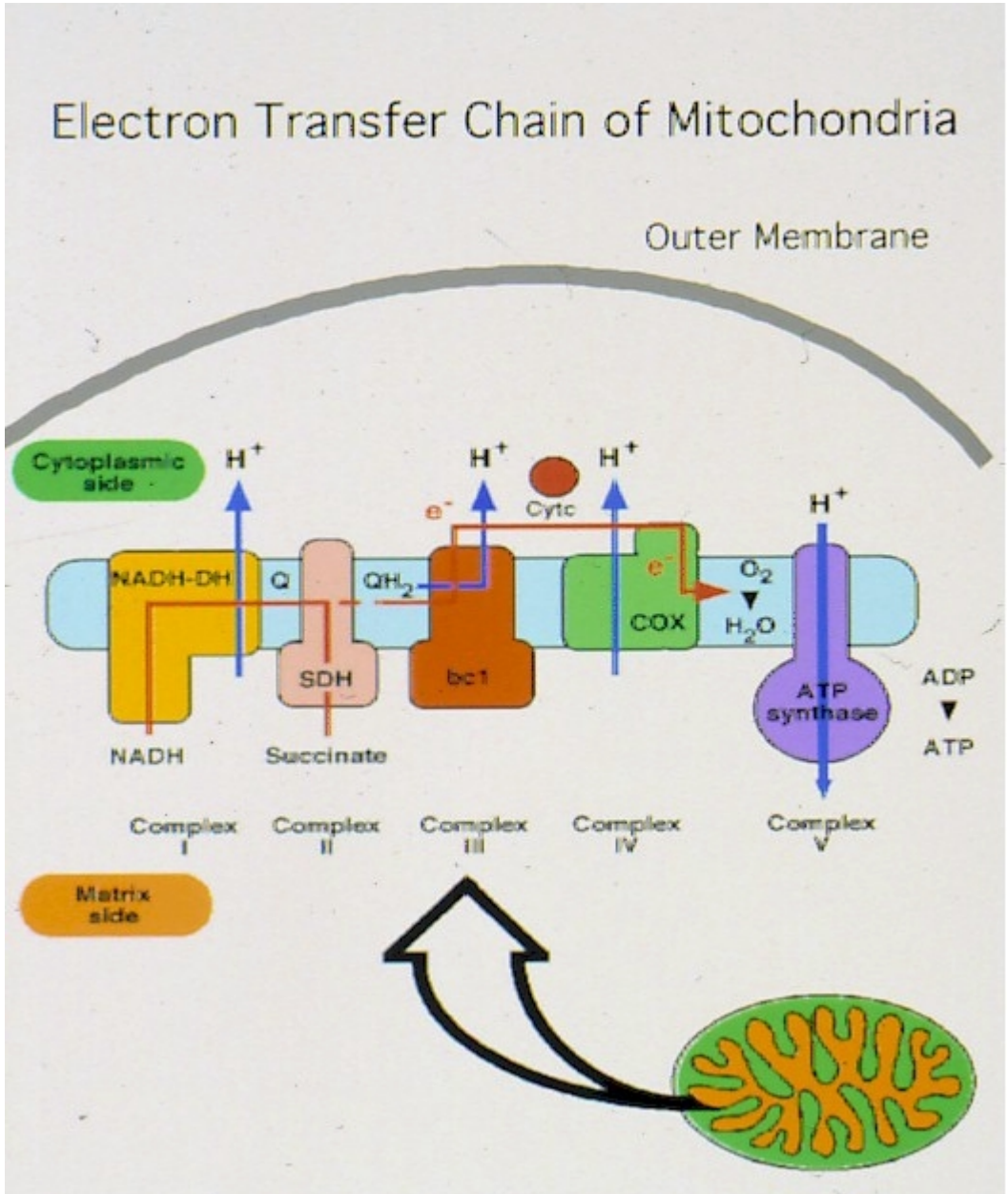


DFF Mediated Chromatin Fragmentation and Condensation



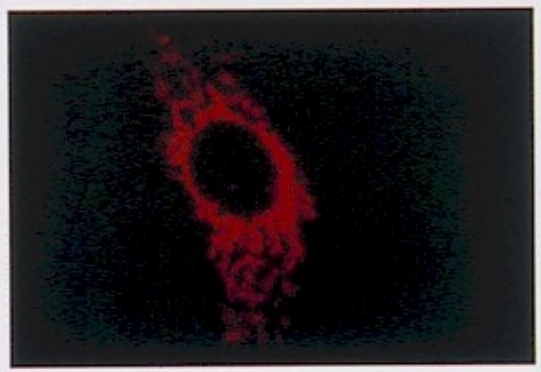
Extracellular Signals Activate Caspase




Electron Transfer Chain of Mitochondria
Outer Membrane
Cytoplasmic side
H+
H+
H+
H+
e-
Cytc
e-
NADH-DH
Q
QH2
SDH
bc1
COX
O2
H2O
ATP synthase
ADP
ATP
NADH
Succinate
Complex I
Complex II
Complex III
Complex IV
Complex V
Matrix side

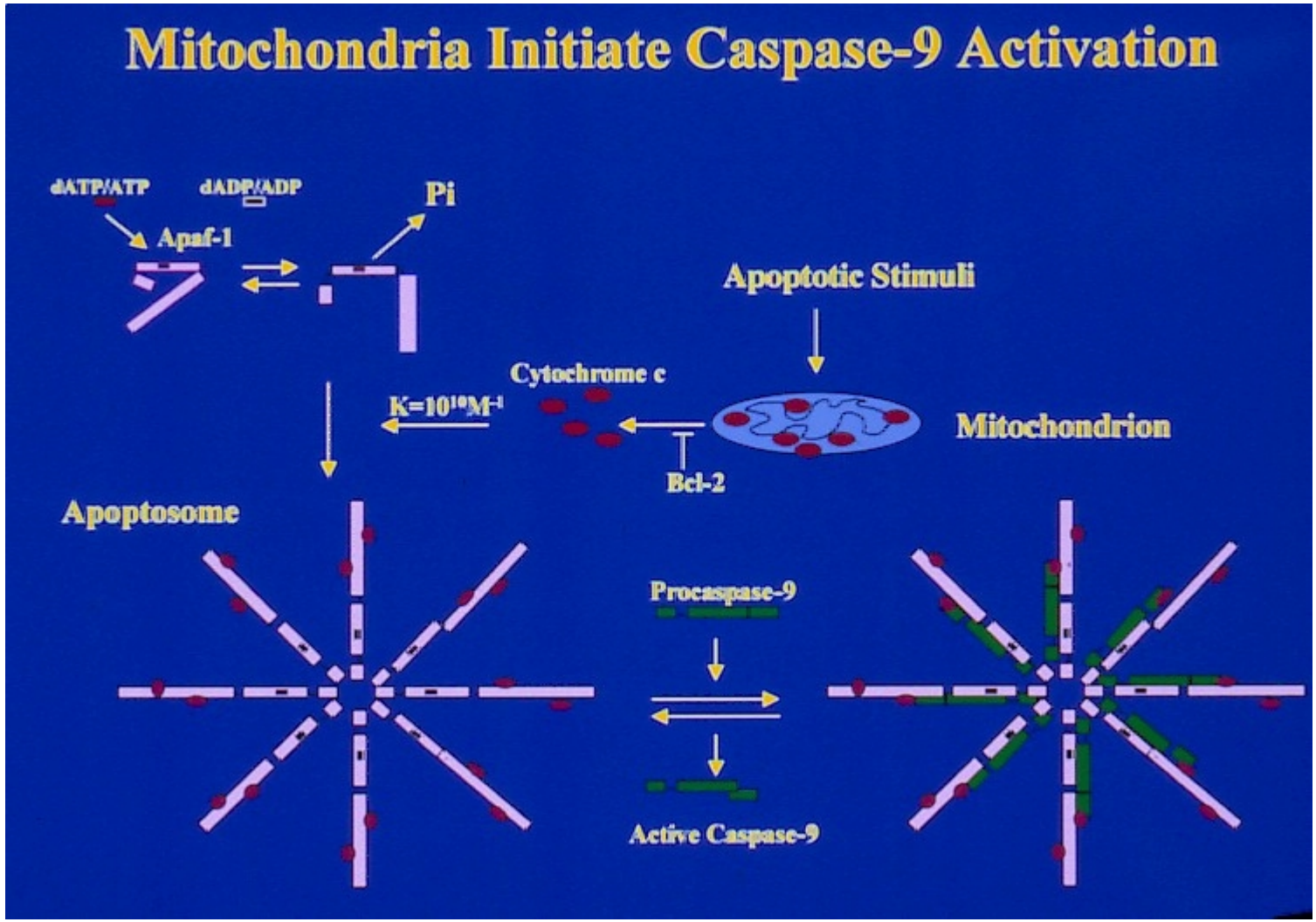
Release of Cytochrome c from Mitochondria during Apoptosis

Normal



UV-treated

Mitochondria Initiate Caspase-9 Activation



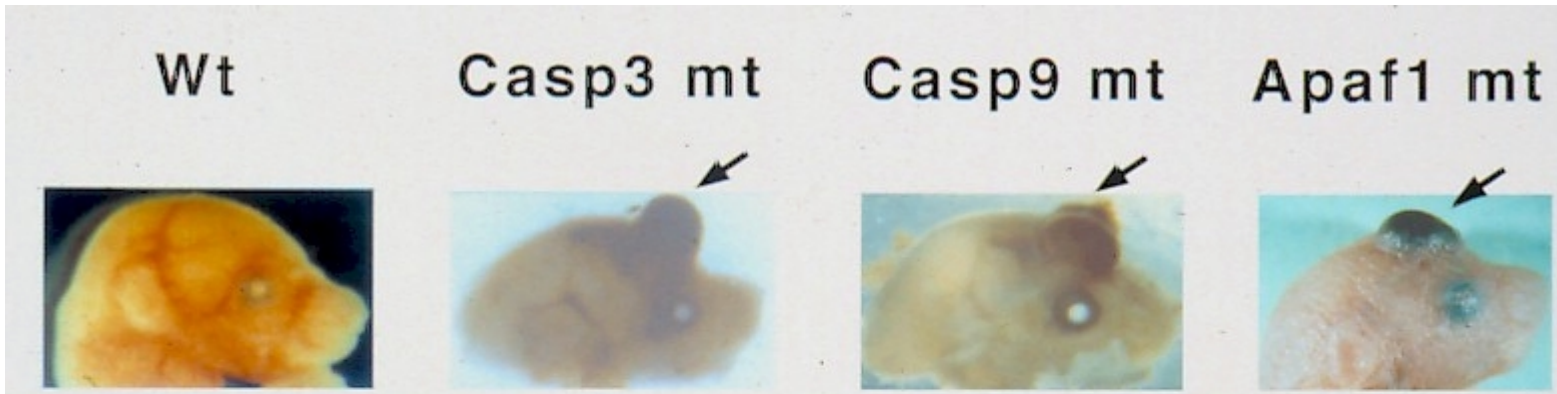
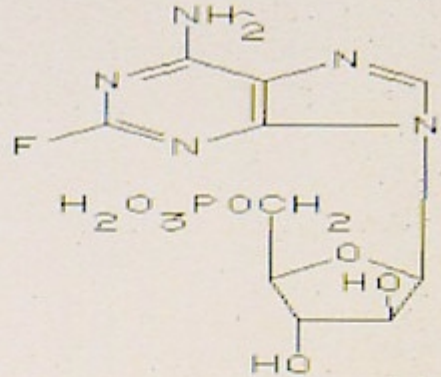


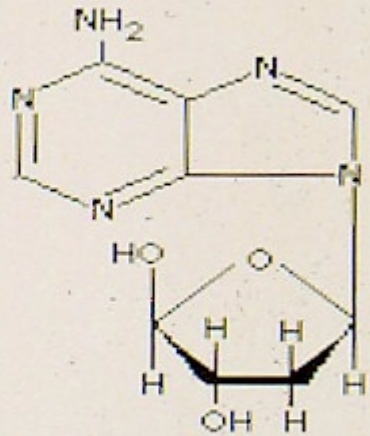
Figure 2: Brain morphology of wild type and Apaf-1, Caspase-9, and Caspase-3 mutant mice

Nucleotides that Activate Apaf-1

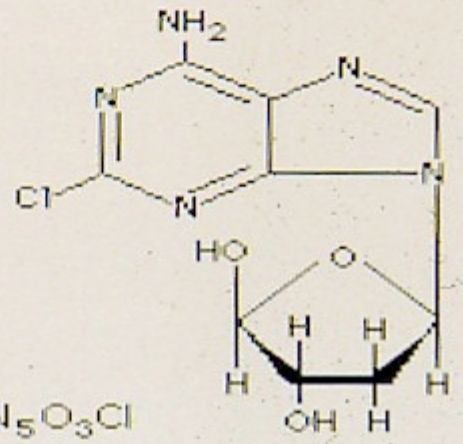
Fludarabine



dAMP



Cladribine



$C_{10}H_{12}N_5O_3Cl$