Chapt. 18. Cell death

- Overview:
  - 2 types of cell death:
    - Necrosis:
      - Origin of name.
      - Result of trauma, starvation etc.
      - Very messy process, compartments mix, components (often toxic) are released into the surrounding tissue.

- Overview:
  - 2 types of cell death:
    - Apoptosis:
      - Origin of name
      - Very regulated process. Seems designed by evolution to be the least disruptive way to eliminate cells.
      - Normally common and benign.
      - Important in development.
      - Also safety role to prevent tumors.

A physical comparison of these two processes.
(Fig. 18-20)

Necrosis Apoptosis
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• Things that can lead to apoptosis.
  - Apoptosis is often the result of loss of chemical signals (growth factors)
  - Apoptosis can also be in response to signals generated elsewhere in the organism.
  - Lastly, Apoptosis can be the result of certain types of cellular damage. It is thought to play a safety role in tumor prevention. For example DNA damage often initiates apoptosis before the cell can become tumorogenic.

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• Apoptosis is a normal (and continuous) process:
  - Some dramatic examples:

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• The mechanism -- a protease cascade.

(A) procaspase activation

(A) procaspase activation
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• Apoptosis activates nucleases as well as proteases.

• Thus the cell is chewed up from the inside out in a regulated manner.
Progeria: premature aging

Characterized by:
- Premature aging
- Atherosclerosis
- Heart Failure
- Loss of Hair

Caused by:
- Break down of Nuclear Lamin A

Progeric Cells Can Be Reversed - A Profound Discovery

- Reversal of the cellular phenotype in the premature aging disease Hutchinson-Gilford progeria syndrome
Progeric Cells Can Be Reversed - A Profound Discovery

• Over expression of normal lamin A does not correct instabilities in mutant cells.
• Addition of abnormal protein into normal cells produced the abnormalities.
• HOWEVER, inhibiting the splicing of the aberrant mutated gene results in production of normal lamin A and elimination of abnormally spliced forms of lamin A.

Most importantly

• One week after correcting the splicing defect, the mutant lamin A protein had been eliminated and more than 90% of progeria cells were restored to normal; visually, the nuclei lost their wrinkles and lobes and returned to a natural ellipsoid shape, and the expression of other nuclear proteins was also restored to normal levels. According to the authors, "It's amazing that we could take a cell that looked about ready to die, and a few days later it was healthy and ready to divide again."
• http://www.targethealth.com/ontarget/2005/03142005.htm