

































• Production of oxygen radicals







## "Megachannel" (MPT) opening is

- Triggered by: matrix Ca<sup>2+</sup>
- Stimulated by:
  - Oxidants
  - Depolarisation
  - Inorganic phosphate
- Inhibited by:
  - Protons (low matrix pH)
  - Magnesium ions
  - ATP and ADP
  - Cyclosporin A















## BH3-only proteins couple apoptosis to various signalling pathways:

- Lack of external survival signals:
  - JNK kinase induces expression of BH3-only protein Bim
- DNA damage:
  - The p53 protein induces expression of BH3-only proteins Puma and Noxa
- The BH3-only protein **Bid** links extrinsic and intrinsic apoptotic pathways











## Signaling pathways dependent on proteolysis

- Proteolytic modification is an irreversible switch
- Not only death, but also development
- ...regulated proteolysis controls activity of latent gene regulatory proteins, e.g.:
  - Notch/Delta
  - -Wnt/β-catenin
  - -NF-kappaB







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![](_page_19_Figure_1.jpeg)

![](_page_20_Figure_0.jpeg)

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