

9.14

Class #13: Growth factors and cell survival III
-- apoptosis (programmed cell death)

Readings:

Vaux, D.L. and Korsmeyer, S.J. , "Cell death in development", *Cell* ,1999, 96: 245-254.
Fadeel, B., Orrenius, S., and Zhivotovsky, B. , "Apoptosis in human disease: A new skin for the old ceremony?", *Biochem. & Biophys. Res. Communications* ,1999,266: 699-717.

Also recommended:

Duke, R.C., Ojcius, D.M. and Young, J.D., "Cell suicide in health and disease", *Sci.Amer* (Dec. 1996, p.80-87.
Steller, H., "Mechanisms and genes of cellular suicide", *Science*, 1995 267:1445-1449.
Davies, A.M. , " The Bcl-2 family of proteins, and the regulation of neuronal survival", *Trends Neurosci*, 1995,18:355-358.

Additional references:

Song, Z., McCall., K. and Steller, H., "DCP-1, a Drosophila cell death protease essential for development", *Science* ,(24 Jan. 1997),275: 536-540.
Dubois-Dauphin, M., Frankowski, H., Tsujimoto, Y., Huarte, J., and Martinou, J. , "Neonatal motoneurons overexpressing the bcl-2 protooncogene in transgenic mice are protected from axotomy-induced cell death", *Proc. Natl. Acad. Sci. USA*, 1994, 91: 3309-3313.
Martinou, J., Dubois-Dauphin, M. , " Overexpression of Bcl-2 in transgenic mice protects neurons from naturally occurring cell death and experimental ischemia", *Neuron*, 1994, 13: 1017-1030.

Questions:

1. Contrast apoptosis and necrosis. [see also Davies]
2. What is Raff's extension of the well-known neurotrophic theory? [see also, Davies, 1st paragraph]
3. Compare ced-9 and bcl-2 by referring to the organism they were isolated from, their structure and function.
4. What are caspases, and what is their role in apoptosis? Give an example of a representative member.
5. Describe the effects of overexpressing bcl-2 in vivo in mice by generating mice in which a bcl-2 transgene is placed under the control of an exogenous promoter (i.e. a promoter which comes from a different gene) and which, for example, triggers the expression of the bcl-2 transgene specifically in neurons.
6. What is the phenotype (i.e. the visible effect) of a "knock-out" mouse carrying a null mutation in a bcl-2 family member (pick your favorite)?
7. How might overexpression of Bcl-2 in mice alter response to a traumatic brain injury? [see also: Martinou et al.]