URLS for online links
Swiss-Prot
http://us.expasy.org/sprot/
BAD
http://us.expasy.org/cgi-bin/niceprot.pl?Q92934
BAK
http://us.expasy.org/cgi-bin/niceprot.pl?Q16611
BIM
http://us.expasy.org/cgi-bin/niceprot.pl?O43521

Entrez:
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene
BAX
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene&cmd=Retrieve&dopt=Graphics&list_uids=581

BACTERIAL PATHOGENESIS

Cheating death

Obligate intracellular pathogens, such as *Chlamydia*, reside and replicate in the relative safety of cytoplasmic vesicles. But infected cells often burst this cytoplasmic bubble by committing altruistic suicide through the induction of apoptosis. Now, a recent study in the *Journal of Experimental Medicine* shows that *Chlamydia* can inhibit this programmed cell death by eliminating pro-apoptotic proteins.

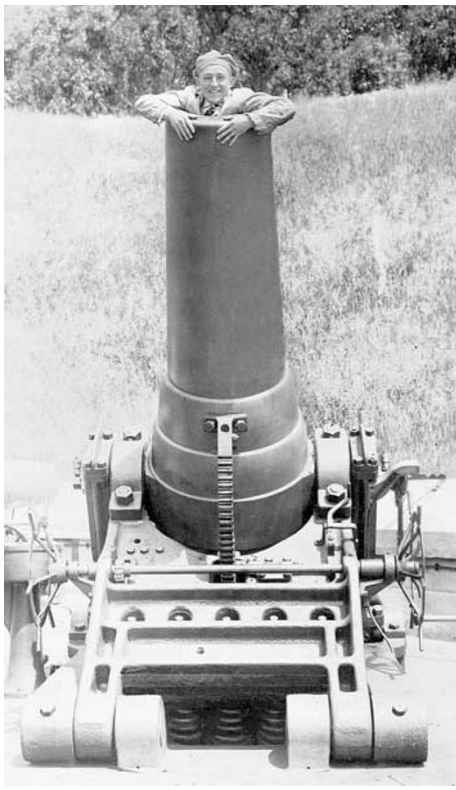
To investigate the molecular mechanisms used by *Chlamydia* to modulate apoptosis, Georg Häcker and colleagues exposed both *Chlamydia*-infected and uninfected human cells to UV irradiation. UV irradiation activates pro-apoptotic proteins such as BIM, which in turn activates BAX and BAK. The pathway culminates with the release of cytochrome *c* from the mitochondria and the induction of the deadly caspase cascade.

As expected, cells that had been infected with *Chlamydia* were protected against UV-induced apoptosis. Importantly, cytochrome *c* was retained in the mitochondria in these cells, in contrast to control cells, which showed cytosolic staining with anti-cytochrome-*c* antibodies. Infected cells had normal amounts of BAX/BAK protein — the mediators of cytochrome-*c* release — but the level of activated protein was reduced.

So, Fischer *et al.* turned their attention to the BH3-only protein BIM, and made the startling discovery that, despite normal expression of BIM mRNA, the protein had "almost completely disappeared from *Chlamydia*-infected cells". The same was true for two other BH3-only proteins, PUMA and BAD, and experiments using a proteolytic inhibitor implicated the proteosome as the agent of destruction.

In normal cells, BIM is protected from activation by sequestration to the cytoskeleton, and disruption of cellular architecture by intracellular infection might release the protein and induce apoptosis. By destroying BIM, *Chlamydia* prevents host-cell death, thereby ensuring its own survival.

Shannon Amoils



References and links

ORIGINAL RESEARCH PAPER Fischer, S. F. *et al. Chlamydia* inhibit host cell apoptosis by degradation of proapoptotic BH3-only proteins. *J. Exp. Med.* **200**, 905–916 (2004)
FURTHER READING Byrne, G. I. & Ojcius D. M. *Chlamydia* and apoptosis: life and death decisions of an intracellular pathogen. *Nature Rev. Microbiol.* **2**, 802–808 (2004)