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OTHER PROGRAM AFFILIATIONS



Development and Stem Cells



Neuroscience

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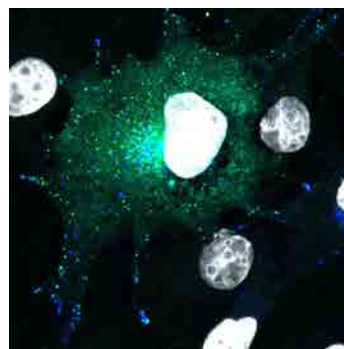
WEB med.monash.edu/biochem/bird-proteases-serpins.html

A. Proteases in immune defence. Cytotoxic lymphocytes kill infected or cancer cells by releasing proteases (granzymes) which enter the target cell via the pore-forming protein, perforin (Fig). Granzyme B kills cells due to its ability to activate caspases, and is one of the most cytotoxic proteases known. Other granzymes, and related proteases such as cathepsin G, activate cytokine signalling.

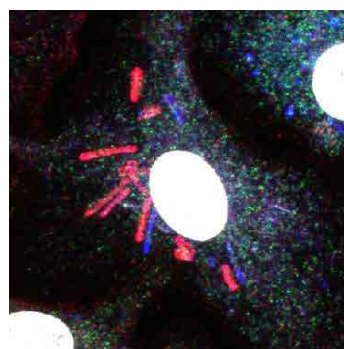
B. Regulation of proteases by serpins. Serpins trap and inactivate proteases. Some intracellular serpins protect cells against their own proteases e.g. Serpinb9 protects cytotoxic lymphocytes against granzyme B. Serpin deficiency or misfolding results in blood clots, immune dysfunction, lung and liver disease, cancer or dementia. SerpinA1 misfolding leads to liver and lung disease. We have shown that Serpinb6 deficiency causes inner ear degeneration and hearing loss.

C. Perforin-like molecules in immunity.

MPEG1 is an ancient protein related to perforin, and it is found in phagocytes of organisms ranging from sponges to humans. Its molecular role is entirely unknown, but it is suggested to perforate phagocytosed microbes.



Distribution of MPEG1 in the endolysosomal system.



Phagocytosed bacteria within a mouse macrophage.

Research Projects

1. Cathepsin G
2. Serpins and cell death
3. MPEG1

Selected significant publications:

1. Prakash MD, Munoz MA, Jain R, Tong PL, Koskinen A, Regner M, Kleinfeld O, Ho B, Olson M, Turner SJ, Mrass P, Weninger W & **Bird PI**. 2014. Granzyme B promotes cytotoxic lymphocyte transmigration via basement membrane remodeling. *Immunity* 41:960-72.
2. Bird CH, Christensen ME, Mangan MSJ, Prakash MD, Sedelies KA, Smyth MJ, Harper I, Waterhouse NJ & **Bird PI**. 2014. The granzyme B-serpinb9 axis controls the fate of lymphocytes after lysosomal stress. *Cell Death Differ.* 21: 876-887
3. Teoh SS, Vieusseux J, Prakash M, Berkowicz S, Luu J, Bird CH, Law RH, Rosado C, Price JT, Whisstock JC & **Bird PI**. 2014. Maspin is not required for embryonic development or tumour suppression. *Nat Commun.* 5:3164.
4. Tan J, Kaiserman D & **Bird PI**. 2013. Absence of Serpinb6a causes sensorineural hearing loss with multiple histopathologies in the mouse inner ear. *Am J Pathol.* 183, 49-59.
5. Rizzitelli A, Meuter S, Ramos JV, Bird CH, Mintern JD, Mangan MSJ, Villadangos J & **Bird PI**. 2012. Serpinb9 (Spi6)-deficient mice are impaired in dendritic cell-mediated antigen cross-presentation. *Immunol Cell Biol.* 90:841-51.