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OTHER PROGRAM AFFILIATIONS

Cancer

Development and Stem Cells

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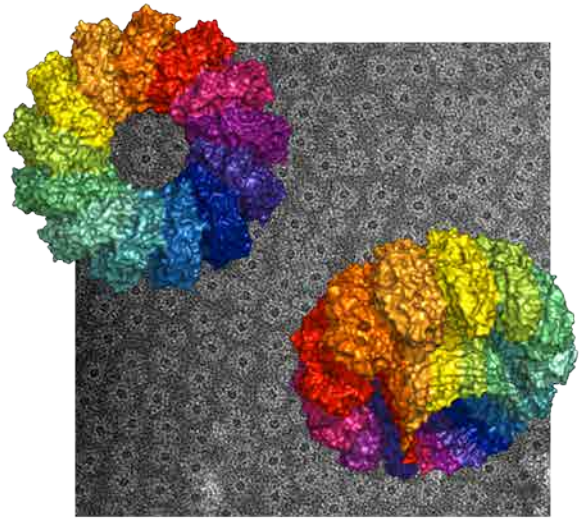
Pore forming toxins (PFTs) are fascinating proteins have the ability to breach cell membranes by forming pores in the lipid bilayer. These pores can be either lytic to the target cell, e.g. by osmotic flux, or the pores can mediate the translocation of proteins (typically toxins) into the cytoplasm of the target cell. They are found in all kingdoms of life, especially pathogenic bacteria. Our research looks at the structure and evolution of pore forming toxins such as the MAC, fungal toxins and aerolysin.

Our research also explores the role of pore forming proteins in animal development, their development to target and kill cancer cells.

Research Projects

1. **Electron Microscopy of immune system proteins**
2. **Enhancing the activity of antibiotics using the MAC (collaboration with Prof Li, Pharmacy)**
3. **Mapping the evolution of the MACPF/CDC superfamily of pore forming proteins**



Pleurotolysin, a hole punching protein from the carnivorous oyster mushroom. The background is the negative stain TEM image. The rainbow object is the model based on single particle cryo-electron microscopy.

Selected significant publications:

1. Dudkina NV, Spicer BA, Reboul CF, Conroy PJ, Lukoyanova N, Elmlund H, Law RH, Ekkel SM, Kondos SC, Goode RJ, Ramm G, Whisstock JC, Saibil HR, **Dunstone MA**. 2016. Structure of the poly-C9 component of the complement membrane attack complex. *Nat Commun* (7):10588

2. Lukoyanova N, Kondos SC, Farabella I, Law RH, Reboul CF, Caradoc-Davies TT, Spicer BA, Kleifeld O, Traore DA, Ekkel SM, Voskoboinik I, Trapani JA, Hatfaludi T, Oliver K, Hotze EM, Tweten RK, Whisstock JC, Topf M, Saibil HR, **Dunstone MA**. 2015. Conformational changes during pore formation by the perforin-related protein pleurotolysin. *PLoS Biol*. 13(2):e1002049

3. Reboul CF, Whisstock JC, **Dunstone MA**. 2014. A new model for pore formation by cholesterol-dependent cytolysins. *PLoS Comput Biol*. 10(8):e1003791.

4. Reboul CF, Mahmood K, Whisstock JC, **Dunstone MA**. 2012. Predicting giant transmembrane β-barrel architecture. *Bioinformatics*. 28(10):1299-302.

5. Rosado CJ, Buckle AM, Law RH, Butcher RE, Kan WT, Bird CH, Ung K, Browne KA, Baran K, Bashtannyk-Puhalovich TA, Faux NG, Wong W, Porter CJ, Pike RN, Ellisdon AM, Pearce MC, Bottomley SP, Emsley J, Smith AI, Rossjohn J, Hartland EL, Voskoboinik I, Trapani JA, Bird PI, **Dunstone MA**, Whisstock JC. 2007. A common fold mediates vertebrate defense and bacterial attack. *Science*. 317(5844):1548-51