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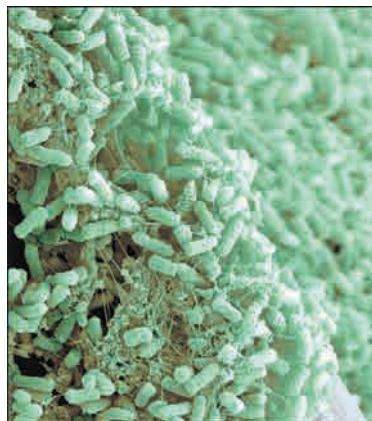
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WEB <http://lithgow-lab.med.monash.edu/index.php/research>

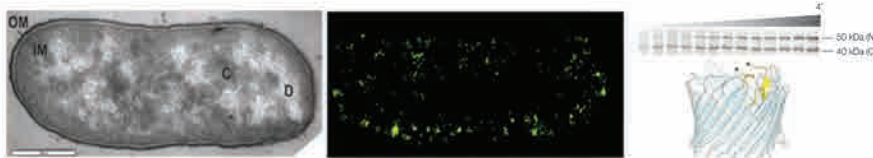
Bacterial pathogens depend on surface exposed proteins to mediate cell-cell contact, biofilm formation and immune evasion. As a result, the process of cell surface protein assembly is an Achilles's heel for bacterial pathogens, and one that we are working to attack. The first stage in this work is to understand in molecular detail how bacterial outer membrane proteins are assembled. We mapped the evolution and topological features of the outer membrane protein assembly machinery, solved the structure of its key catalyst, BamA, and have developed new assays to measure its activity in outer membrane protein assembly. We discovered the TAM, and showed how it assists BamA in the assembly of outer membrane proteins. Using super-resolution microscopy and cryo-electron microscopy we image bacterial cells for nanoscale details of the bacterial cell surface. We are currently developing high-throughput genetic screens to better understand the factors that enable the regulation, and spread, of antibiotic resistance in bacterial pathogens.

Research Projects

1. Mechanism of outer membrane protein assembly in bacterial pathogens
2. Nanoscale imaging of the bacterial cellscape
3. Bacterial cell biology and the spread of antibiotic resistance
4. Regulation of outer membrane protein assembly in bacterial pathogens (Collaboration with Professor Richard Strugnell (Melbourne Uni.), Professor Gordon Dougan (Wellcome Trust Sanger Institute))



Bacteria colonizing a biomedical device.



Super-resolution imaging of bacterial cell surface protein assembly.

Selected significant publications:

1. Shiota T, Imai K, Qiu J, Hewitt VL, Tan K, Shen HH, Sakiyama N, Fukasawa Y, Hayat S, Kamiya M, Elofsson A, Tomii K, Horton P, Wiedemann N, Pfanner N, **Lithgow T**, Endo T. 2015. Molecular architecture of the active mitochondrial protein gate. *Science* 349:1544-1548
2. Shen HH, Leyton DL, Shiota T, Belousoff MJ, Noinaj N, Lu J, Holt SA, Tan K, Selkrig J, Webb CT, Buchanan SK, Martin LL, **Lithgow T**. 2014. Reconstitution of a nanomachine driving the assembly of proteins into bacterial outer membranes. *Nat Commun.* 5:5078
3. Leyton DL, Johnson MD, Thapa R, Huysmans GH, Dunstan RA, Celik N, Shen HH, Loo D, Belousoff MJ, Purcell AW, Henderson IR, Beddoe T, Rossjohn J, Martin LL, Strugnell RA, **Lithgow T**. 2014. A mortise-tenon joint in the transmembrane domain modulates autotransporter assembly into bacterial outer membranes. *Nat Commun.* 5:4239
4. Dunstan RA, Heinz E, Wijeyewickrema LC, Pike RN, Purcell AW, Evans TJ, Praszkiel J, Robins-Browne RM, Strugnell RA, Korotkov KV, **Lithgow T**. 2013. Assembly of the type II secretion system such as found in *Vibrio cholerae* depends on the novel Pilotin AspS. *PLoS Pathog.* 9(1):e100311
5. Selkrig J, Mosbahi K, Webb CT, Belousoff MJ, Perry AJ, Wells TJ, Morris F, Leyton DL, Totsika M, Phan MD, Celik N, Kelly M, Oates C, Hartland EL, Robins-Browne RM, Ramarathnam SH, Purcell AW, Schembri MA, Strugnell RA, Henderson IR, Walker D, **Lithgow T**. 2012. Discovery of an archetypal protein transport system in bacterial outer membranes. *Nat Struct Mol Biol.* 19:506-510