



## Anthony Purcell

### Associate Professor

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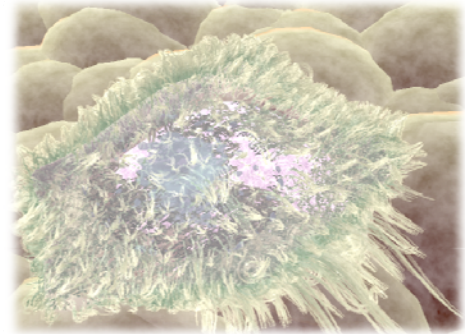
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### Research interests

My laboratory is interested in defining the targets of the immune response in infectious diseases and autoimmunity. We apply advanced techniques in structural and analytical biochemistry, proteomics, cellular immunology, molecular biology and molecular immunology to understand immunity towards self tissues, viruses and cancers.



### Techniques we use:

#### Proteomics:

**We use a number of approaches based on mass spectrometry to identify peptides presented to the immune system**

The lab has three dedicated mass spectrometers (and access to the Bio21 Institute's MS equipment)

- Two QqTOF instruments used for peptide identification and post-translational modification analysis
- One Q-TRAP mass spectrometer used for targeted protein and peptide identification and quantitation

**We use other tools of proteomics to investigate antigen expression and protein expression in disease**

- 2D gel electrophoresis
- Shotgun LC-MS/MS
- Protein-protein interaction analysis:
  - Native complex isolation and characterization by mass spectrometry
  - Surface plasmon resonance

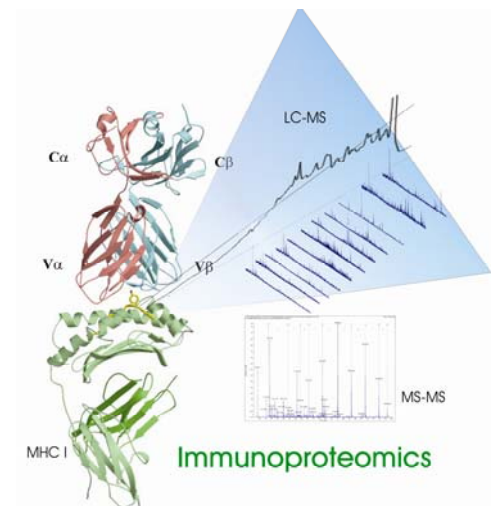
#### Cell biology and immunology

- Mammalian cell culture (from ml to L)
- T cell culture, cloning and analysis
- Proliferation and cytotoxicity assays, T cell receptor sequencing and analysis
- Animal models of disease
- Viral infection and host-virus interactions (influenza, Dengue virus, HIV, MHV)

#### Structural biology and recombinant protein technology

We use X-ray crystallography and NMR to study proteins of interest:

- T cell receptors
- MHC-peptide complexes
- Enzymes
- Toxins



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## Projects:

### Insulin misfolding and Type 1 diabetes

Insulin is the primary target of autoreactive T cells in patients with type 1 diabetes. We are investigating whether pancreatic beta cell stress and insulin misfolding contribute to the development of the disease.

### New drug targets for influenza

We are undertaking proteomic dissection of host-pathogen interactions in influenza and dengue virus infection to identify new drug targets in these dangerous human pathogens.

### HLA and autoimmunity

Our laboratory is renowned internationally for our work towards defining the immunopeptidome, ie the array of peptides presented to the immune system on the surface of antigen presenting cells. Using this holistic approach we are redefining the link between autoimmunity and HLA haplotypes. This work has relevance to several autoimmune diseases including diabetes, arthritis and multiple sclerosis, and implications for tumor immunity.

### Assembly of MHC class I molecules in the endoplasmic reticulum

MHC class I assembly involves a number of intracellular chaperones to ensure optimal peptide selection and determine the ensuing immune response towards foreign and self antigens. The aims are to (i) examine how polymorphism influences the assembly and peptide repertoire of MHC class I and class II molecules, (ii) investigate the role of chaperones and peptidases in the selection of peptide determinants, (iii) identify other components of the class I loading pathway using functional proteomics and (iv) study viral evasion molecules that subvert antigen presentation.

### Recent publications

1. Purcell AW, McCluskey J, Rossjohn J. (2007) 'More than one reason to rethink the use of peptides in vaccine design', *Nat Rev Drug Discov*, 6, 404–414.
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3. Williamson NA and Purcell AW. (2005) 'Use of proteomics to define targets of T-cell immunity', *Expert Rev Proteomics*, 2, 367–380.
4. Purcell AW, Gorman JJ. (2004) 'Immunoproteomics: Mass Spectrometry-based Methods to Study the Targets of the Immune Response', *Mol Cell Proteomics*, 3, 193–208.
5. Petersen J, Wurzbacher SJ, Williamson NA, Ramarathinam SH, Reid HH, Nair AKN, Zhao AY, Nastovska R, Rudge G, Rossjohn J, Purcell AW. (2009) 'Phosphorylated self-peptides alter Human Leukocyte Antigen Class I-restricted antigen presentation and generate tumor specific epitopes', *Proc Natl Acad Sci USA*, 106, 2776–2781.
6. Butler NS, Theodossis A, Webb AI, Nastovska R, Ramarathinam SH, Dunstone MA, Rossjohn J, Purcell AW, Perlman S. (2008) 'Prevention of cytotoxic T cell escape using a heteroclitic subdominant viral T cell determinant', *PLoS Pathog* 4, e1000186
7. Mannering SI, Pang SH, Williamson NA, Naselli G, Reynolds E, O'Brien-Simpson N, Purcell AW, Harrison LC (2009) 'The A-chain of insulin is a hot-spot for CD4+ T-cell epitopes in human type 1 diabetes', *Clin Exp Immunol*, 156, 226–231.
8. Croft NP, Purcell AW. (2010) 'Enhancing tumor vaccines: catalyzing MHC class II peptide exchange', *Expert Rev Vaccines*, 9, 129–132.
9. Theodossis A, Guillonneau C, Welland A, Ely LK, Clements CS, Williamson NA, Webb AI, Wilce JA, Mulder RJ, Dunstone MA, Doherty PC, McCluskey J, Purcell AW, Turner SJ, Rossjohn J.(2010) 'Constraints within major histocompatibility complex class I restricted peptides: presentation and consequences for T-cell recognition', *Proc Natl Acad Sci U S A*. 107, 5534–5539.
10. Safavi-Hemami H, Bulaj G, Olivera BM, Williamson NA, Purcell AW (2010) 'Identification of Conus peptidylprolyl cis-trans isomerases (PPIases) and assessment of their role in the oxidative folding of conotoxins', *J Biol Chem*, 285, 12735–12746.
11. Reed JH, Dudek NL, Osborne SE, Kaufman KM, Jackson MW, Purcell AW, Gordon TP. (2010) 'Reactivity with dichotomous determinants of Ro 60 stratifies autoantibody responses in lupus and primary Sjögren's syndrome', *Arthritis Rheum*, 62,1448–1456.
12. Burrows SR, Chen Z, Archbold JK, Tynan FE, Beddoe T, Kjer-Nielsen L, Miles JJ, Khanna R, Moss DJ, Liu YC, Gras S, Kostenko L, Brennan RM, Clements CS, Brooks AG, Purcell AW, McCluskey J, Rossjohn J. (2010) 'Hard wiring of T cell receptor specificity for the major histocompatibility complex is underpinned by TCR adaptability', *Proc Natl Acad Sci USA*, 107, 10608–10613.
13. Kulkarni KP, Ramarathinam SH, Friend J, Yeo L, Purcell AW, Perlmutter P (2010) 'Rapid microscale in-gel processing and digestion of proteins using surface acoustic waves', *Lab Chip*, 10, 1518–1520.
14. Gras S, Chen Z, Miles JJ, Liu YC, Bell MJ, Sullivan LC, Kjer-Nielsen L, Brennan RM, Burrows JM, Neller MA, Khanna R, Purcell AW, Brooks AG, McCluskey J, Rossjohn J, Burrows SR. (2010) 'Allelic polymorphism in the T cell receptor and its impact on immune responses', *J Exp Med*. In press.