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ARC Australian Laureate Fellow

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OTHER PROGRAM AFFILIATIONS

Cancer

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The academic research program within this laboratory is concerned with defining the key molecular interactions underlying receptor recognition events that are the primary determinants of innate and adaptive immunity.

The laboratory's research has provided an understanding of the basis of peptide, metabolite and lipid presentation, T-cell triggering, aberrant T-cell reactivity, monomorphic and polymorphic Natural Killer (NK) receptor recognition. The team's research on anti-viral immunity has provided an understanding of the factors that shape MHC-restriction (e.g. Immunity, 2003, 2016; Nature Immunol, 2005, 2007, 2015). Moreover, we have demonstrated how the pre-TCR, a receptor crucial for T-cell development, functions by autonomous dimerization (Nature, 2010). In relation to aberrant T-cell reactivity, our team has provided insight into alloreactivity (Immunity, 2009), Celiac Disease (Immunity, 2012; NSMB, 2014) and HLA-linked drug hypersensitivities (Nature, 2012, NSMB 2014). Regarding innate and innate-like recognition, the team has shed light into how Natural Killer cell receptors interact with their cognate ligands (Nature 2011; J. Exp. Med. 2008 & 2016; Nature Immunol 2013; NSMB 2017; Cell 2017). Further, we have provided fundamental insight into how T cells recognise lipid-based antigens in the context of protective and aberrant immunity (Nature, 2007; Nature Immunol 2010, 2011, 2012, 2015, 2016; Nature Comms. 2016). Most recently, our team identified the long sought after ligand for MAIT cells, namely showing that MAIT cells are activated by metabolites of vitamin B (Nature 2012, 2014; Nat Commun 2012; Nat Immunol 2016; Nat Immunol, 2017). The industrial research program of the laboratory includes a close collaboration with Janssen (one of the Pharmaceutical companies of Johnson & Johnson), for the development of new therapies to treat rheumatoid arthritis.

In Goodpasture's disease when the molecule DR15 is present it can select and instruct T cells to attack the body. But when people also have the protective DR1 molecule present these T cells are held at bay and can be overturned. Nature. 545, 243-247 (2017). [Illustrator: Vanette Tran]

T-cells becoming distracted when presented with drugs. Nature Immunology 18, 402–411 (2017). [Illustrator: Vanette Tran]

Research Projects

1. **MHC-restricted protective immunity**
2. **T-cell autoimmunity and alloreactivity**
3. **HLA-linked drug hypersensitivities**
4. **Lipid-mediated immunity**
5. **Metabolite-mediated immunity**
6. **NK cell recognition**
7. **T-cell signaling machinery**

Selected significant publications:

1. Ooi JD, Petersen J, Tan YH, Huynh M, Willett ZJ, Ramarathinam SH, Eggenhuizen PJ, Loh KL, Watson KA, Gan PY, Alikhan MA, Dudek NL, Handel A, Hudson BG, Fugger L, Power DA, Holt SG, Coates PT, Gregersen JW, Purcell AW, Holdsworth SR, La Gruta NL, Reid HH#, **Rossjohn J**# and Kitching AR#. 2017. Dominant protection from HLA-linked autoimmunity by antigen-specific regulatory T cells. *Nature* 545: 243-247
2. Birkinshaw RW, Pellicci DG, Cheng TY, Keller AN, Sandoval-Romero M, Gras S, de Jong A, Uldrich AP, Moody DB, Godfrey DI, **Rossjohn J**. 2015. alphabeta T cell antigen receptor recognition of CD1a presenting self lipid ligands. *Nat Immunol* 16: 258-66
3. Kjer-Nielsen L, Patel O, Corbett AJ, Le Nours J, Meehan B, Liu L, Bhati M, Chen Z, Kostenko L, Reantragoon R, Williamson NA, Purcell AW, Dudek NL, McConville MJ, O'Hair RA, Khairallah GN, Godfrey DI, Fairlie DP, **Rossjohn# J** & McCluskey# J. 2012. MR1 presents microbial vitamin B metabolites to MAIT cells. *Nature*. 491, 717-723.
4. Illing PT, Vivian JP, Dudek NL, Kostenko L, Chen Z, Bharadwaj M, Miles JJ, Kjer-Nielsen L, Gras S, Williamson NA, Burrows SR, Purcell AW#, **Rossjohn# J** & McCluskey# J. 2012. Immune self-reactivity triggered by drug-modified Human Leukocyte Antigen peptide repertoire. *Nature*. 486, 554-558.
5. Vivian JP, Duncan RC, Berry R, O'Connor GM, Reid HH, Beddoe T, Gras S, Saunders PM, Olshina MA, Widjaja JML, Harpur CM, Lin J, Maloveste SM, Price DA, Lafont BAP, McVicar DW, Clements CS, Brooks# AG & **Rossjohn# J**. 2011. Killer cell immunoglobulin-like receptor 3DL1-mediated recognition of human leukocyte antigen B. *Nature*. 479, 401-405.

# denotes joint senior author