Institute of Molecular and Cell Biology
A*STAR

SEMINAR ANNOUNCEMENT

We would like to invite you to attend this seminar hosted by Dr. John Connolly:

Date: 8 November 2018, Thursday
Time: 11:00AM – 12:00PM
Venue: Level 3, IMCB Seminar Room 3-46, Proteos, Biopolis

Speaker: Mr. Jeremy Brooks, PhD student, University of Queensland, Brisbane, Australia
Title: Deletion and anergy restrain self-reactive B cell responses in a physiological repertoire

Failure to establish B cell tolerance underlies antibody-mediated autoimmunity but our mechanistic understanding of self-reactive B cell control is incomplete. B cell receptor (BCR) transgenic models suggest that deletion and anergy are key, but the precise timing and contribution of each vary depending on the model and setting. To resolve the tolerance mechanisms active in a physiological setting, we developed a sensitive tetramer assay to monitor antigen-specific B cells within a normal repertoire. In a mouse model expressing ovalbumin (OVA) as a ubiquitous membrane-bound self-antigen (actin.mOVA), self-reactive OVA-specific B cells (OB) were partially deleted from the peripheral repertoire. Surprisingly, deletion did not occur in the bone marrow and self-reactive OB cells developed normally to a terminal mature phenotype in the spleen before deletion was apparent. Residual naïve OB cells were functionally anergic because immunization with OVA failed to elicit expansion and class-switch recombination (CSR) of OB cells. In contrast, we also show additional provision of diverse innate and T cell-mediated stimuli to B cells enabled self-reactive OB cell expansion, germinal centre recruitment and CSR. Transient IgG1 autoantibody production occurred, but affinity maturation and terminal plasma cell differentiation were impaired. Bone marrow chimeras revealed that density of self-antigen plays a key role in the stringency of B-cell tolerance. OB cell responses were unimpeded when self-antigen was expressed by less than 5% of all cells. In sum, we refine our current understanding of the role of deletion and anergy in governing B cell tolerance in a normal polyclonal repertoire.

Biography:
Jeremy received a Bachelor of Science with Class I Honours in Immunology from Griffith University in 2014. He then joined the Autoimmunity and Tolerance Laboratory as a PhD student under the supervision of Ray Steptoe at the University of Queensland. His research focuses on characterising how the immune system maintains immunological tolerance by restraining self-reactive B cells. Jeremy has presented his work at national and international meetings and has won numerous prizes including competitive travel grants, the Jian Zhou Pre-Doctoral Award, Frazer Foundation grant, and a Children's Hospital Foundation PhD project grant.