of family members and improved therapy for patients and families.

Acknowledgements Childhood Arthritis and Rheumatology Research Alliance (CARRA) Small Grant, McLaughlin Centre, University of Toronto.

### Innate Immunity

**II-01 TLR9-DEFICIENCY EXACERBATES AUTOIMMUNE DISEASE IN MODELS OF SLE AND CUTANEOUS LUPUS THROUGH B CELL INDEPENDENT MECHANISMS**

1. Kerstin Nundel, 2Anette Christ, 3Punvi Mande, 4Wei-Che Ko, 5John E Harris, 2Eicke Latz, 1Ann Marshak-Rothstein*. 1Department of Medicine, University of Massachusetts School of Medicine, Worcester, Massachusetts, USA; 2Institute of Innate Immunity, University Hospital Bonn, University of Bonn, Bonn, Germany; 3Department of Dermatology, University of Massachusetts School of Medicine, Worcester, Massachusetts, USA

10.1136/lupus-2018-lsm.100

**Background** TLR9 appears to play both a protective and a disease-promoting role in animal models of SLE. Even though TLR9 is required for the production of anti-dsDNA and anti-nucleosome autoantibodies, TLR9-deficient autoimmune-prone mice invariably develop more severe disease than their TLR9-sufficient counterparts. Molecular mechanisms that account for this paradoxical function of TLR9 have mainly been explored in cell lines to a large extent. We have focused on competition between TLR7 and TLR9 for binding to Unc93B1 and the ability to access to the appropriate signaling compartment. Our own in vitro comparison of bone marrow derived macrophages and bone marrow derived dendritic cells, obtained from TLR9-sufficient versus TLR9-deficient mice and stimulated with TLR7 ligands, suggested that the impact of TLR9-deficiency might be highly cell type specific, and led us to focus on primary cells obtained from animal models of systemic autoimmunity.

**Methods** We initially used pristane-injected BALB/c mice as a model of SLE, and found that TLR9-deficiency let to exacerbated renal disease and the accumulation of an unusual myeloid subset in the kidneys of these mice. We have directly examined the contribution of TLR9-deficient and TLR7-sufficient cells in these mice using a mixed bone marrow chimera strategy. We have also developed an inducible rapid onset model of cutaneous lupus that depends on the injection of OVA-specific T cells into mice that express an OVA fusion protein on class II+cells; here, TLR9-deficient mice and TLR9-deficient and TLR7-sufficient recipients develop cutaneous lesions with many of the features of discoid lupus within 4 weeks of T cell injection. Cells isolated from the kidneys of the BALB/c pristane mice and the skin of the cutaneous lupus mice have been further characterized by flow cytometry and gene expression.

**Results** These studies have identified a myeloid subset present at sites of inflammation and in normal peripheral blood that appears to be uniquely impacted by the loss of TLR9. Functional properties of these cells will be discussed.

**Conclusions** TLR9 deficiency impacts very specific myeloid subsets apart from its effects on B cell development and differentiation.

Acknowledgements This project has been supported by the Lupus Research Alliance and NIAMS.