Antibodies to a gene expressed on demethylated but not normal T cells may treat lupus flares.

Footnotes

Dept of Medicine, University of Michigan, Ann Arbor, MI

**GG-02**

**EPIGENETIC REPROGRAMMING IN NAÏVE CD4+ T CELLS FAVOURING T CELL ACTIVATION AND NON-TH1 EFFECTOR T CELL IMMUNE RESPONSE AS AN EARLY EVENT IN LUPUS FLARES**

1Patrick Coit, 2Mikhail G Dozmorov, 3Joan T Merrill, 4W Joseph McCune, 4Kathleen Maksimowicz-McKinnon, 5Jonathan D Wren, 6Amr H Sawalha.

1Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan, USA; 2Department of Biostatistics, Virginia Commonwealth University, Richmond, Virginia, USA; 3Clinical Pharmacology Program, Oklahoma Medical Research Foundation, Oklahoma City, Oklahoma, USA; 4Division of Rheumatology, Henry Ford Health System, Detroit, Michigan, USA; 5Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, Oklahoma, USA; 6Department of Biochemistry and Molecular Biology, The University of Oklahoma Health Sciences Centre, Oklahoma City, Oklahoma, USA; 7Centre for Computational Medicine and Bioinformatics, University of Michigan, Ann Arbor, Michigan, USA

#These two authors equally contributed to this work

10.1136/lupus-2016-000179.54

**Background**

Systemic lupus erythematosus is a relapsing autoimmune disease that affects multiple organ systems. T cells play an important role in the pathogenesis of lupus, however, early T cell events triggering disease flares are incompletely understood. We studied DNA methylation in naïve CD4+ T cells from lupus patients to determine if epigenetic remodelling in CD4+ T cells is an early event in lupus flares.

**Materials and methods**

A total of 74 lupus patients with disease activity ranging from 0–18 as measured by the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) were included in this study. Naïve CD4+ T cells were isolated from peripheral blood samples and DNA extracted for genome-wide methylation assessment. RNA was also extracted from a subset of patients to determine the relationship between epigenetic changes and transcriptional activity using RNA sequencing and microRNA arrays.

**Results**

We demonstrate that naïve CD4+ T cells in lupus undergo an epigenetic pro-inflammatory shift implicating effector T cell responses in lupus flare. This epigenetic landscape change occurs without expression changes of corresponding genes, and poises naïve CD4+ T cells for Th2, Th17, and Tfh immune responses, and opposes inhibitory TGF-β signalling. Bioinformatics analyses indicate that the epigenetic modulator EZH2 might be playing an important role in shifting the epigenetic landscape with increased disease activity in lupus naïve CD4+ T cells. Further, the expression of miR26a and miR101, which are sensitive to glucose availability and target EZH2, negatively correlated with disease activity in lupus patients.

**Conclusion**

An epigenetic landscape shift in naïve CD4+ T cells that favours T cell activation and non-Th1 immune responses precedes transcriptional activity and correlates with lupus activity. A role for EZH2 dysregulation in triggering lupus flares warrants further investigation. The proposed T cell epigenetic model of disease flare in lupus patients is depicted in Figure 1.

**Acknowledgements**

This work was supported by the National Institute of Allergy and Infectious Diseases of the National Institutes of Health under award number R01AI097134.

10.1136/lupus-2016-000179.55

**Background**

Signal Transduction and Activation of Transcription (STAT) transcription factors are evolutionarily ancient, mediating signals from the cytoplasm to the nucleus in eukaryotic life for the past 400 million years. The STAT protein sits quiescent in the cytoplasm until phosphorylated whereupon it dimerizes with another STAT protein. The phosphorylated STAT dimer is then transported to the nucleus and becomes a transcription factor activating or suppressing gene expression. The STAT1–STAT4...