ABSTRACT NUMBER: 68

Epigenetic and Expression Analysis of Ankylosing Spondylitis Association Loci Point to Key Cell Types Driving Disease

Zhixiu Li[1], Katelin Haynes[2], Gethin P. Thomas[3], Tony J. Kenna[1], Paul Leo[1] and Matthew A. Brown[1], [1]Translational Genomics Group, Institute of Health and Biomedical Innovation, Queensland University of Technology, Translational Research Institute, Brisbane, Australia, Brisbane, Australia, [2]University of Queensland Diamantina Institute, Brisbane, Australia, Brisbane, Australia, [3]Research Office, Charles Sturt University, Wagga, Australia, Wagga, Australia

Meeting: 2016 ACR/ARHP Annual Meeting

Date of first publication: September 28, 2016

Keywords: Ankylosing spondylitis (AS), Disease susceptibility, epigenetics and microbiome, Gene Expression

SESSION INFORMATION

Date: Sunday, November 13, 2016

Session Type: ACR Poster Session A

Session Title: Genetics, Genomics and Proteomics - Poster I

Session Time: 9:00AM-11:00AM

Background/Purpose: Susceptibility to ankylosing spondylitis (AS) is primarily genetic; thus far 113 susceptibility variants for AS have been identified. However, most of the AS associated SNPs do not directly affect protein-coding genes. Studies of disease- and trait-associated SNPs suggest they may act by affecting gene regulatory regions in specific cell types or tissues. Therefore, identifying the AS relevant cell types is crucial for further mechanistic studies.

Methods: We applied several bioinformatics methods to utilize epigenetic, gene and protein expression information to identify the primary relevant cell types through which genetic variants associated with AS operate. In total, there are 113 AS associated loci; 39 of them show genome-wide significance in AS-only analyses, whereas the remainder are genome-wide significant in analyses leveraging pleiotrophy with other related diseases (Crohn's disease (CD), psoriasis, primary sclerosing cholangitis (PSC) and ulcerative colitis (UC))[1].

Results: AS-associated SNPs are disproportionately found in regions bearing epigenetic marks indicating transcriptional activity found in immune cell types including monocytes, CD4+ and CD8+ T cells, NK cells, regulatory T cells, and B cells. Gene expression studies showed enrichment of AS associated loci in genes specifically expressed in monocytes and NK cells while protein expression study shows protein products of AS associated loci were significantly enriched in CD8+ T cells. Epigenetic analyses also showed evidence that AS-associated signals operate in gut cell types including in mucosa from the small intestine, sigmoid colon and rectum. These findings particularly relate to pleiotropic loci also associated with IBD, psoriasis, and PSC.

Conclusion: These findings highlight the role of key immune cell types in the mechanism by which genetic associations with AS drive the disease, as well as providing further evidence for the involvement of the gut in the pathogenesis of AS. [1]Ellinghaus D. at al, Nature Genetics 2016

Disclosure: Z. Li, None; **K. Haynes**, None; **G. P. Thomas**, None; **T. J. Kenna**, None; **P. Leo**, None; **M. A. Brown**, None.