An investigation into the novel SLE-associated gene CXorf21

Leonardo Jones¹,α, Christopher A. Odhams¹, Amy L. Roberts¹, Deborah S. Cunninghame Graham¹, Timothy J. Vyse¹

¹King’s College London, United Kingdom

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Introduction: Systemic lupus erythematosus (SLE) is a complex genetic, autoimmune disease, that displays a 9 : 1 female gender bias and has a relatively unknown aetiology. In a recent SLE genome-wide association study (GWAS) a novel locus containing CXorf21 was found to be associated with the disease. Evidence that CXorf21, a gene with relatively unknown structure and function, escapes X-chromosome inactivation, makes it an interesting candidate for further investigation.

Methods: A conditional association analysis based on rs887369 (the most associated SNP in the CXorf21 locus) was run to investigate the GWAS association signal. This signal was then refined, with the use of Haploview, to a set of candidate causal SNPs. An epigenetic analysis followed, to functionally annotate the selected variants.

Results: A single GWAS association signal was located in the region ChrX 30,501,000-30,651,000, containing CXorf21. Statistical prioritisation refined the associated variants within this locus, to a set of five candidate causal SNPs, which co-localised with the epigenetic modification H3K36me3 in innate immune cell lines.

Conclusions: This study identified five candidate causal SNPs as responsible for the association signal in the CXorf21 locus. The co-localisation of these SNPs with H3K36me3 (an epigenetic modification believed to activate gene transcription) in innate immune system cell lines provides some clues about their function. However, further work should investigate the biological effects of these SNPs to determine the risk allele function.