

Portelli, Michael A., Bennett, Neil D., Hankinson, Jenny, Ntalla, Ioanna, Henry, Amanda, Billington, Charlotte K., Shaw, Dominick, Pogson, Zara E.K., Fogarty, Andrew, McKeever, Tricia, Jonker, Leon, Singapuri, Amisha, Heaney, Liam, Mansur, Adel, Thomson, Neil C., Chaudhuri, Rekha, Holloway, John, Lockett, Gabrielle, Howarth, Peter, Niven, Rob, Tobin, Martin D., Wain, Louise, Hall, Ian P., Brightling, Chris E., Simpson, Angela and Sayers, Ian (2016) Determining the contribution of IL33 and IL1RL1 polymorphisms to clinical and immunological features of asthma. *American Journal of Respiratory and Critical Care Medicine*, 193 . A2922.

Downloaded from: <http://insight.cumbria.ac.uk/id/eprint/3097/>

Usage of any items from the University of Cumbria's institutional repository 'Insight' must conform to the following fair usage guidelines.

Any item and its associated metadata held in the University of Cumbria's institutional repository Insight (unless stated otherwise on the metadata record) may be copied, displayed or performed, and stored in line with the JISC fair dealing guidelines (available [here](#)) for educational and not-for-profit activities

provided that

- the authors, title and full bibliographic details of the item are cited clearly when any part of the work is referred to verbally or in the written form
 - a hyperlink/URL to the original Insight record of that item is included in any citations of the work
- the content is not changed in any way
- all files required for usage of the item are kept together with the main item file.

You may not

- sell any part of an item
- refer to any part of an item without citation
- amend any item or contextualise it in a way that will impugn the creator's reputation
- remove or alter the copyright statement on an item.

The full policy can be found [here](#).

Alternatively contact the University of Cumbria Repository Editor by emailing insight@cumbria.ac.uk.

Determining The Contribution Of IL33 And IL1RL1 Polymorphisms To Clinical And Immunological Features Of Asthma

M. A. Portelli¹, N. D. Bennett², J. Hankinson³, I. Ntalla², A. Henry¹, C. K. Billington¹, D. Shaw¹, Z. E.K. Pogson¹, A. Fogarty¹, T. McKeever¹, L. Jonker⁴, A. Singapuri², L. Heaney⁵, A. Mansur⁶, N. C. Thomson⁷, R. Chaudhuri⁷, J. Holloway⁸, G. Lockett⁸, P. Howarth⁸, R. Niven³, M. D. Tobin², L. V. Wain², I. P. Hall¹, C. E. Brightling², A. Simpson³, I. Sayers¹

¹University of Nottingham, Nottingham, United Kingdom, ²University of Leicester, Leicester, United Kingdom, ³University of Manchester, Manchester, United Kingdom, ⁴North Cumbria University Hospitals NHS Trust, Carlisle, United Kingdom, ⁵Queen's University of Belfast, Belfast, United Kingdom, ⁶Birmingham Heartlands Hospital, Birmingham, United Kingdom, ⁷University of Glasgow, Glasgow, United Kingdom, ⁸University of Southampton, Southampton, United Kingdom

Corresponding author's email: michael.portelli@nottingham.ac.uk

Rationale: *IL33* (9p24.1) and the *IL33* receptor (*IL1RL1*, 2q12) have been reproducibly identified as asthma susceptibility genes. However, the variants driving genetic associations are not yet fully defined. Using a population based birth cohort of 1059 children (Manchester Asthma and Allergy Study-(MAAS)) and 2536 adults with asthma (Genetics of Asthma Severity and Phenotypes - (GASP)) cohort we aimed to define genetic variants associated with clinical and immunological features of asthma.

Methods: MAAS samples were genotyped using the Illumina 610 Quad array and imputed using 1000G reference panel. GASP samples were genotyped using two custom designed Affymetrix arrays (UK BiLEVE/UK Biobank array). Datasets were quality controlled for gender mismatches, outliers and relatedness. Data was generated for the *IL33/IL1RL1* regions consisting of the genes and surrounding regions (chr9:5715785–6757983 & chr2:102427961–103468497) on the following traits: asthma diagnosis (MAAS), atopy, FEV₁ (GASP) and FEV₁/FVC (MAAS and GASP) as well as total blood eosinophil counts and serum total IgE levels (GASP). Variables for blood eosinophils and total IgE were log10 transformed. Analysis was carried out in PLINK using linear or logistic regression modelling including appropriate covariates for each trait.

Results: In the MAAS cohort, we replicated the association of the *IL33* locus with asthma diagnosis, identifying potentially two independent novel signals in that locus (rs10975398; $P=1.70E-05$; $B=-1.519$; $MAF=0.32$ and rs2890697; $P=1.10E-04$; $B=-1.573$; $MAF=0.43$). This association survived a Bonferroni correction for multiple testing. Although not surviving correction, an association was also identified for atopy in the *IL1RL1* locus for MAAS ($P=1.08E-04$; $MAF=0.48$). In GASP we identified modest associations not in known LD with published loci (P -value range: $5.00E-02$ – $7.60E-04$) for FEV₁, FEV₁/FVC, atopy, blood eosinophils and total IgE in both the *IL33* and *IL1RL1* loci.

Multiple SNPs presented nominal association ($P<0.01$) with more than one trait such as atopy & total IgE, providing supporting evidence for association.

Conclusion: We replicated the association of *IL33* region SNPs with asthma diagnosis in MAAS, highlighting the role of this locus in childhood asthma. Although trait association signals did not survive correction for multiple testing, nominal association across multiple phenotypes in GASP provides suggestive evidence of the role of the *IL33/IL1RL1* genetic polymorphisms in determining clinical and immunological features of asthma.

*Drs Bennett, Hankinson and Portelli contributed equally to this study

This abstract is funded by: Asthma UK, AirPROM, University of Nottingham, MRC, NIHR

Am J Respir Crit Care Med 193;2016:A2922

Internet address: www.atsjournals.org

Online Abstracts Issue