PSORIASIS

FINE MAPPING AND SUBPHENOTYPING IMPLICATES ADRA1B GENE VARIANTS IN PSORIASIS SUSCEPTIBILITY IN A CHINESE POPULATION

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Introduction: A genomic region identified by Genome Wide Association Studies (GWAS) on 5q33.3 lies between and encompasses the IL12B and PTTG1 genes and contains many potential psoriasis causal variants.

Objective: To further examine the influence of potential causal variants in and around this region.

Materials and Methods: We first used the 1000 Genomes Project reference haplotypes to impute an additional 2,171 variants in the region, and then used lasso-based regression analysis to assess the independent contributions of these variants to psoriasis susceptibility, and tested lasso-selected SNPs for association with different clinical psoriasis subtypes.

Results: We first found evidence for association for 62 out of the 2,171 SNPs in this region. The most significant locus and largest number of associated SNPs were all located in ADRA1B gene, which is between the IL-12B and PTTG1 genes in the 5q33.3 region. Variants in the ADRA1B gene were the most strongly associated with the plaque psoriasis subgroup, and showed a stronger association with moderate-to-severe skin disease group and an earlier age at onset of psoriasis. Polygenic inheritance analysis showed that variants in the ADRA1B gene explain 46.5% of the heritable component of the liability to psoriasis.

Conclusions: The association of variants in the ADRA1B gene with psoriasis could explain why variants in the broader IL-12B, ADRA1B and PTTG1 gene region have been found to be associated with psoriasis previously, although more studies confirming this should be pursued.