ATOPIC ECZEMA/DERMATITIS

IDENTIFICATION OF TMEM232 GENE ASSOCIATED WITH ATOPIC DERMATITIS THROUGH TARGETED CAPTURE SEQUENCING AND HACAT CELLS EXPERIMENT

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Background: Atopic dermatitis(AD) is an inflammatory skin disease. The 5q22.1 region was found to be associated with AD in our previous genome-wide association study.

Objective: The aim of this study was to search for functional variation and causal gene with AD in 5q22.1 region.

Methods: The previous genotyped data of four SNPs and six deletions in 5q22.1 was enrolled from 3055 Chinese Hans AD patients and 4346 controls. The PHASE v2.1 was used for reconstructing haplotypes; PLINK 1.07 software was used for statistical analysis of haplotype frequencies; Targeted region capture sequencing was to discover gene functional variants; HaCaT cell transfection experiment was to explore gene function.

Results: The H15 haplotype (GACTGCATAGCTAAGTACA) was significantly associated with AD (P=2.72E-10, OR=0.14, 95%CI=0.07-0.28), with a frequency of 0.13% in cases and 0.95% in controls; Of observed functional region, variants of H15 haplotype on TMEM232 have statistically significant (P=7.33E-5, OR=0.33, 95%CI=0.19-0.58). The cell viability in the pCMV6-Entry-TMEM232 (TMEM232) groups was lower than in the cells transfected with pCMV6-Entry (Vect) group and cells with no DNA transfection (Con) group (all $P < 0.05$). Furthermore, after Ca2+ stimulation, TMEM232 inhibited the expression of INV and LOR compared to the Vect and Con group (all $P<0.05$). Overexpression of TMEM232 inhibits the proliferation and differentiation of HaCaT cells in vitro.

Conclusion: This study revealed the H15 haplotypes may reduce incidence of AD. TMEM232 gene may play a role in AD.