EPIDEMIOLOGY

# GENETIC VARIANTS IN INTERLEUKIN 2 SIGNALING PATHWAY PREDICT MELANOMA-SPECIFIC SURVIVAL IN TWO PATIENT COHORT GWAS STUDIES

*Wei Dai* [1]

*Fourth Military Medical University, Dermatology Department, Xi'an, China* [1]

The translation of basic findings concerning interleukin 2 (IL-2) signaling pathway had a profound impact on the development of cancer immunotherapy. In the present study, we comprehensively assessed associations of 9944 common single-nucleotide polymorphisms (SNPs) in 83 genes of the IL-2 signaling pathway with cutaneous melanoma disease-specific survival (CMSS). The dataset from a published genome-wide association study (GWAS) by The University of Texas M.D. Anderson Cancer Center was used as the discovery set, and the identified significant SNPs were validated by another dataset from a GWAS from the Nurses' Health Study and Health Professionals Follow-up Study. We found eight noteworthy SNPs associated with CMSS in both studies after multiple comparison correction by using the Bayesian false-discovery probability method. By performing functional prediction, linkage disequilibrium analysis, and stepwise Cox regression selection, we identified four independent SNPs (i.e., SYK rs158688 A>G, CSNK2A1 rs2734228 A>G, CCND3 rs9369324 G>A and FYN rs35552830 T>A) that predicted CMSS, with an allelic hazards ratio of 1.53 (95% confidence interval=1.21-1.94, P=4.21×10-4), 1.44 (1.13-1.84, P=0.003), 1.47 (1.16-1.87, P=0.001) and 0.55 (0.38-0.81, P=0.002), respectively. Finally, the SYK rs158688 variant GG genotype and the CSNK2A1 rs2734228 GG genotype were found to be associated with a significantly decreased mRNA expression level of corresponding genes. These SNPs may be potential markers for CM prognosis, if validated by additional larger and mechanistic studies.