Gene Variants in Multiple Melanomas

Patients with multiple primary cutaneous malignant melanomas in Norway have a significantly higher likelihood of carrying a MC1R variant and an ASIP haplotype than blood donors, according to a recently published case-control study by Helsing et al. No association with TYR and TYRP1 variants was found.


Patients with multiple primary melanomas often have a positive family history of melanoma, indicating an hereditary component of the disease mechanism. Known genetic risk factors are rare, high-penetrant germline mutations in 2 genes encoding key regulators of the cell cycle, CDKN2A and CDK4, and common, low-penetrant alleles of the pigmentation gene MC1R. More recently, single nucleotide polymorphisms (SNPs) of 3 other genes affecting melanogenesis, ASIP, TYR and TYRP1, have been linked to increased risk of melanoma in genome-wide association studies.

The study confirms that MC1R polymorphisms are relatively frequent in the Norwegian population, and even more frequent in patients with multiple primary melanomas. The variants with the highest effect appeared to be Asp84Glu and Arg151Cys, whereas Asp84Glu and Arg160Pro increased the risk of multiple primary melanomas in CDKN2A/CDK4 mutation-positive patients. Carriers of 2 RHC variants of MC1R showed the highest risk of developing melanoma. However, MC1R is a low-penetrance melanoma gene, and a clinical implication of determining the MC1R status remains to be shown.

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