MELANOMA AND MELANOCYTIC NAEVI

CUTANEOUS MELANOMA AND INTERLEUKIN 1 RECEPTOR ANTAGONIST (IL-1RA) GENE (IL-1RN) VARIABLE NUMBER OF TANDEM REPEATS (VNTR) POLYMORPHISM IN NORTHEAST ITALY.

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Introduction: Interleukin-1 (IL-1) mediated inflammation is proposed to contribute to the development and progression of some cancers including melanoma. Notably, interleukin 1 receptor antagonist (IL-1RA) seems to have effects on tumor survival and progression.

Objective: The association of IL-1RA gene (IL-1RN) intron 2 variable number tandem repeat (VNTR) polymorphism (rs2234663) with cutaneous melanoma was investigated.

Materials and Methods: We analyzed 133 cutaneous melanoma cases (72 non-metastatic melanoma patients, plus 61 metastatic melanoma patients), and 382 matching healthy controls from Northeast Italy. IL-1RN-VNTR polymorphism was determined by DNA fragment length analysis after polymerase chain reaction amplification. According to number of 86-bp repeats five different IL-1RN alleles were identified.

Results: IL-1RN-VNTR 1/2 genotype was more frequent among cutaneous melanomas (43.6%) than among controls (29.6%) (P=0.003) and the group of all heterozygous genotypes containing the one allele 2 and one long allele (2/L) had OR= 1.66, P=0.002. Conversely, IL-1RN-VNTR 1/1 genotype was less frequent among melanomas (45.9%) than among healthy controls (57.9%) (P=0.017). No significant findings were found comparing metastatic (MetM) versus non-metastatic melanoma (NMetM) patients.

Conclusions: We first showed that carriage of the 1/1 IL-1RN-VNTR genotype was protective, whereas 1/2 was risky for melanomas versus healthy controls. IL-1RN alleles may modulate IL-1RA levels. IL-1RA by binding to IL-1 receptor 1 (IL-1R1) is a potent competitive inhibitor of the proinflammatory cytokines IL-1α and IL-1β thus having anti-inflammatory roles. Results suggest how exploring biological effects of IL-1RN gene polymorphism may lead to new understanding and possibly may indicate new strategies in personalized prevention of melanoma.