

## **Xeroderma pigmentosum genes and melanoma risk.**

Katarzyna Paszkowska-Szczur,

<sup>1</sup>Department of Genetics and Pathology, International Hereditary Cancer Center, Pomeranian Medical University, Szczecin, Poland

*Xeroderma pigmentosum* is a rare autosomal recessive disease that is associated with a severe deficiency in nucleotide excision repair. The presence of a distinct the nucleotide excision repair (NER) mutation signature in melanoma suggests that perturbations in this critical repair process are likely to be involved with disease risk. We hypothesized that persons with polymorphic NER gene(s) are likely to have reduced NER activity and are consequently at an increased risk of melanoma development. We assessed the association between 94 SNPs within seven XP genes (XPA–XPG) and the melanoma risk in the Polish population. We genotyped 714 unselected melanoma patients and 1,841 healthy adults to determine if there were any polymorphisms differentially represented in the disease group. We found that a significantly decreased risk of melanoma was associated with the Xeroderma pigmentosum complementation (XPC) rs2228000\_CT genotype (OR=0.15;  $p < 0.001$ ) and the rs2228000\_TT genotype (OR=0.11;  $p < 0.001$ ) compared to the reference genotype. Haplotype analysis within XPC revealed the rs2228001\_A1G1475A\_G1G2061A\_A1rs2228000\_T1rs3731062\_C haplotype (OR=0.26;  $p < 0.05$ ) was associated with a significantly decreased disease risk. The haplotype analysis within the Xeroderma pigmentosum group D (XPD) showed a modest association between two haplotypes and a decrease in melanoma risk. There were no major differences between the prevalence of the XP polymorphisms among young or older patients with melanoma. Linkage disequilibrium of XPC: rs2228001, G1475A, G2061A, rs2228000 and rs3731062 was found. The data from our study support the notion that only XPC and XPD genes are associated with melanoma susceptibility.