

S001 The association of sequence variants in DNA repair and cell cycle genes with cancer risk: genotype/phenotype correlations

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DNA repair systems maintain the integrity of the human genome and cell cycle checkpoints are a critical component of the cellular response to DNA damage. Thus the presence of variants in genes involved in these pathways which modulate their activity might impact on cancer risk. Many molecular epidemiological studies have studied the association between variants, and in particular single nucleotide polymorphisms (SNPs), and cancer risk. For instance *ATM* SNPs have been associated with increased risk of breast, prostate, leukaemia, colon and early onset lung cancer and *OGG1* SNPs and the intron 3 16-bp repeat in *TP53* with an increased risk of lung cancer. In contrast the variant allele of the rare *CHEK2* missense variant (rs17879961) was significantly associated with a *lower* incidence of lung and upper aero-digestive cancers. Interestingly for some variants a strong-gene environment interaction has also been noted, for instance a greater absolute risk reduction of lung and upper aero-digestive cancers in smokers than in non-smokers carrying the I157T *CHEK2* variant and an interaction between *TP53* intron 3 16-bp repeats and multiple X-ray exposures and lung cancer risk. The challenge is now to understand the molecular mechanisms underlying these associations.