Tobacco smoking, genes involved in the metabolism of xenobiotics and breast cancer risk

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Purpose: Tobacco smoking and xenobiotics metabolism pathway (XMP) genes involved in the metabolism of carcinogen compounds contained in tobacco smoke are suspected to play a role in breast cancer (BC) risk (1,2). We have studied interactions between active or passive smoking and XMP genes in BC among 1125 cases of BC and 1172 population controls with lifelong data on smoking habits and valid genotyping data obtained from a dedicated chip.

Experimental Design: The associations of BC with active/passive smoking and with 585 SNPs in 68 XMP genes, as well as interactions between genes and exposure to tobacco smoke were explored using the Adaptive Rank Truncated Product (ARTP) (3,4) method. This approach allows investigating the role of genes (seen as a set of SNPs) and of the pathway (seen as a set of genes) in disease occurrence, and to gain in statistical power as compared to a SNP by SNP approach.

Results: We reported an increased risk of BC among current smokers in postmenopausal women (OR=1.46 [1.00-2.14]) and among never smokers exposed to secondhand smoke for long duration (>20 years) (OR=1.45 [1.01- 2.09]. Genetic variation in genes of the XMP pathway was significantly associated with premenopausal BC risk (PARTP=0.008). We also observed significant interactions between XMP and smoking status / passive smoking duration, particularly via the CYP3A43, COMT, AKR1Cs and UGT1As genes.

Conclusion: The hypothesis that active and passive smoking increase BC risk (5) is reinforced by our findings of an interaction with XMP genes. Further studies are needed to clarify the role of these genes in breast cancer.

References: