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XRCC1 and *XPD* genetic polymorphisms, smoking and breast cancer risk in a Finnish case-control study

Katja Metsola[1], Vesa Kataja[2], Pia Sillanpää[1], Päivi Siivola[1], Liisa Heikinheimo[1], Matti Eskelinen[3], Veli-Matti Kosma[4,5], Matti Uusitupa[6] and Ari Hirvonen[1]

[1]Department of Industrial Hygiene and Toxicology, Finnish Institute of Occupational Health, Helsinki, Finland
[2]Department of Oncology, Kuopio University Hospital, Kuopio, Finland
[3]Department of Surgery, Kuopio University Hospital, Kuopio, Finland
[4]Department of Clinical Pathology, Kuopio University Hospital, Kuopio, Finland
[5]Department of Pathology and Forensic Medicine, University of Kuopio, Kuopio, Finland
[6]Department of Clinical Nutrition, University of Kuopio, Kuopio, Finland

Corresponding author: Katja Metsola, katja.metsola@ttl.fi

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Abstract

Introduction It has been suggested that individuals with reduced DNA repair capacities might have increased susceptibility to environmentally induced cancer. In this study, we evaluated if polymorphisms in DNA repair genes *XRCC1* (*Arg280His*, *Arg399Gln*) and *XPD* (*Lys751Gln*) modify individual breast cancer risk, with emphasis on tobacco smoking.

Methods The study population consisted of 483 incident breast cancer cases and 482 population controls of Finnish Caucasian origin. The genotypes were determined by PCR-RFLP-based methods. Odds ratio (OR) and confidence intervals (CIs) were calculated by unconditional logistic regression analyses.

Results No statistically significant overall effect in the breast cancer risk was seen for any of the studied polymorphisms. However, a significant increase in breast cancer risk was seen among ever smoking women if they carried at least one *XRCC1-399 Gln* allele (OR 2.33, 95% CI 1.30–4.19, p_{int} 0.025) or *XPD-751 Gln/Gln* genotype (OR 2.52, 95% CI 1.27–5.03, p_{int} 0.011) compared to smoking women not carrying these genotypes. The risks were found to be confined to women smoking at least five pack-years; the respective ORs were 4.14 (95% CI 1.66–10.3) and 4.41 (95% CI 1.62–12.0). Moreover, a significant trend of increasing risk with increasing number of the putative at-risk genotypes (p for trend 0.042) was seen. Women with at least two at-risk genotypes had an OR of 1.54 (95% CI 1.00–2.41) compared to women with no at-risk genotypes. Even higher estimates were seen for ever actively smoking women with at least two at-risk genotypes.

Conclusion Our results do not indicate a major role for *XRCC1* and *XPD* polymorphisms in breast cancer susceptibility, but suggest that they may modify the risk especially among smoking women.

Introduction

Breast cancer is the most common female cancer among western societies and its incidence increases constantly. Hormonal factors like early age at menarche, later age at menopause, later age at first full term pregnancy, and hormone replacement therapy are known to be the main risk factors for sporadic breast cancer [1,2]. Also, alcohol appears to contribute to the increased risk for this malignancy, whereas the results concerning smoking are inconsistent [3-6]. The inconsistencies might be due to several factors. For instance, cigarette smoke increases the production of reactive oxygen species (ROS) and contains chemical carcinogens capable of forming DNA adducts [7], both implicated in carcinogenesis. On the other hand, tobacco smoke has been suggested to have an anti-estrogenic and, therefore, anti-carcinogenic effect [8]. It has also been suggested that the genetic background might modify the association between tobacco smoke and breast cancer [4].

BER = base excision repair; bp = base pair; CI = confidence interval; NER, nucleotide excision repair; OR = odds ratio; PARP = poly(ADP-ribose)polymerase; PCR = polymerase chain reaction; RFLP = restriction fragment length polymorphism; ROS = reactive oxygen species.