Polymorphisms in Phase I and Phase II genes and breast cancer risk and relations to persistent organic pollutant exposure: an Inuit case-control study

Mandana Ghisari[1], Hans Eiberg[2], Manhai Long[1], Eva C. Bonefeld-Jørgensen[1]

[1]Aarhus University - Center for Arctic Health, Denmark, mg@mil.au.dk; [2]University of Copenhagen- Department of Cellular and Molecular Medicine, Denmark

The incidence of breast cancer (BC) among Inuit in Greenland has considerably increased from a very low level to approximately 60% of the incidence in Denmark. Previously, we reported that persistent organic pollutants (POPs) such as perfluorinated compounds (PFCs) and polychlorinated biphenyls (PCBs) are risk factors in Breast Cancer (BC) development in Greenlandic Inuit women. Genetic polymorphisms in genes involved in xenobiotic metabolism and in oestrogen biosynthesis and metabolism might modulate the individual susceptibility to environmental carcinogens in relation to developing BC.

Aim and Methods. The present case-control study aimed to investigate the effect of polymorphisms in the genes CYP1A1, CYP1B1, COMT and CYP17, CYP19 and the BRCA1 founder mutation in relation to BC risk and to explore possible interactions between the gene polymorphisms and serum POP levels on BC risk in Greenlandic Inuit women. The study population consisted of 31 BC cases and 115 matched controls, with information on serum levels of PFCs, PCBs and organochlorine pesticides (OCPs).

Results. We found an independent association of CYP1A1 (Val) and CYP17 (A1) with BC risk. An increased BC risk was observed for women with high serum levels of PFOS and PFOA and carriers of at least: one CYP1A1 variant Val allele; one variant COMT Met allele; or the common CYP17 A1 allele.. The risk of BC was not significantly associated with exposure to PCBs and OCPs, regardless of genotype for all investigated SNPs. The frequency of the Greenlandic founder mutation in BRCA1 was as expected higher in cases than in controls.

Conclusion. The BRCA1 founder mutation and genetic polymorphisms in CYP1A1 (Val) and CYP17 (A1) can increase the BC risk among Inuit women and the risk increase with higher serum levels of PFOS and PFOA. Serum PFC levels were a consistent risk factor of BC, but inter-individual polymorphic differences might cause variations in sensitivity to the PFC/POP exposure.