XRCC1, *GSTM1* EN *EPHX1* POLYMORFISMEN ZIJN PREDICTIEF VOOR MICRONUCLEUSFREQUENTIES IN MENSELIJKE POPULATIES :

resultaten van een 'pooled analysis' van de gegevens van het Human MicroNucleus project.

Synthesis

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The aim of this study was to perform a pooled analysis to assess the predictivity of genetic polymorphisms involved in metabolism (*GSTM1, GSTT1, GSTP1, EPHX1, CYP2E1*) and DNA repair (*hOGG1, XRCC1, XRCC3*) for the spontaneous background frequencies of micronuclei (MN) in the general population and for MN induced *in vivo* by occupational exposure to mutagens. These data should provide a scientific basis for the interpretation of MN variation at individual level based on genetic information. This information will also be helpful for donor selection in *in vitro* genotoxicity assays to ensure that susceptible genotypes are included in the test and for closer follow-up of workers exposed to mutagens who may be, as a result of their genetic make-up, at increased risk of genome damage.

We have collected data from 861 subjects (655 men and 206 women) made available by 7 laboratories. We analysed all data by Poisson regression for the relationships between genetic polymorphisms and MN frequencies obtained with the *ex vivo/in vitro* cytokinesis-block micronucleus test in human lymphocytes.

We showed that the polymorphisms for $EPHX1^{113}$, $EPHX1^{139}$, *GSTM1* and $XRCC1^{399}$ have a significant influence on MN frequencies in binucleated lymphocytes. In control individuals, the presence of either variant allele for *EPHX1* (*His* at codon 113 or *Arg* at codon 139) is associated with increased MN frequencies. In exposed individuals, we found that *GSTM1 null* individuals had lower MN values than *GSTM1 wild type* individuals. Individuals with the *Arg/Gln* $XRCC1^{399}$ genotype had higher MN frequencies than *wild type Arg/Arg* individuals. These observations were confirmed in the total populations.

These genetic polymorphisms can therefore be recommended as useful information to understand unexpectedly high frequencies of MN at the individual level following exposure to mutagens whose impact may be expected to be dependent on these enzymes.