ABSTRACT

Sporadic colorectal cancer (CRC) is a common disease with complex aetiology and diverse molecular phenotypes. Failure of DNA repair systems is one of the leading determinants of cancer onset and development. The efficiency of these systems and susceptibility to cancer can be affected by genotype variations, including common single nucleotide polymorphisms (SNPs).

In this work, an association between SNPs and haplotypes of DNA mismatch repair (MMR) genes, SNPs and their combinations in other DNA repair genes, and a risk of sporadic CRC was investigated in a hospital-based case-control study. As result of our study, certain MMR SNPs and haplotypes altered CRC risk, as demonstrated for the first time in the Czech population. Individual SNPs in DNA repair genes seem to have a limited effect on CRC risk, with possible modification by age or smoking. Several of the associations observed were site-specific, confirming the molecular heterogeneity of CRC.

DNA repair capacity varies significantly between individuals, between different tissues of the same organism, and also between malignant and normal cells. To assess the background level of this variability, the association between SNPs in DNA repair genes and the individual DNA repair capacity in healthy individuals was investigated. Several polymorphisms in base-excision repair genes and their binary combinations affected either irradiation-specific DNA repair or oxidative DNA repair rates; smoking and occupational status play an important role.

Air pollution negatively affects acute and chronic morbidity, including cancer. The analysis of the polymorphisms in metabolizing gene *EPHX1* was a part of the research on relationships between occupational exposure to carcinogenic polycyclic aromatic hydrocarbons, chromosomal aberrations (CA), DNA adducts, and DNA polymorphisms. The *EPHX1* diplotype affected the frequency of CA, suggesting a protective role in metabolism of environmental carcinogens.