Summary

Genome instability represents one of the leading forces driving the onset and development of cancer. It arises as a consequence of the combined effect of DNA damage and errors made by the DNA repair system. In many cancers, DNA damage tolerance and DNA repair pathways are disrupted or deregulated, thereby promoting cancer progression. DNA repair also appears to play a substantial role in cancer therapy response. This Dissertation Thesis was performed in response to several unclear and unresolved issues of the role of DNA damage and DNA repair in cancer pathogenesis.

The aim of the Thesis was to search for potential novel biomarkers and confirmation of the validity of already existing biomarkers related to DNA damage and DNA repair, which may be associated with cancer susceptibility and patient's clinical outcome. We also explored the biological basis of different biomarkers and their associations.

The major outcomes of this Thesis are: **1)** The elevated chromosomal aberrations (CAs) in peripheral blood lymphocytes (PBLs) may serve as a biomarker of cancer susceptibility and partially affects patients' clinical outcome. While telomere shortening contributes to the formation of CAs in PBLs only in healthy individuals, less efficient DNA double- strand break repair in PBLs is associated with telomere shortening only in cancer patients. **2)** Several genetic variants in DNA repair genes and their gene-gene interactions have been discovered that modulated the levels of CAs in PBLs. In genome-wide associations studies, several new genetic variants associated with CA frequency in PBLs were also indicated. **3)** The associations of several genetic variants in DNA repair genes with cancer susceptibility and patient's clinical outcome have been identified. The importance of studying DNA repair at a functional level, directly in tumour and non-malignant tissue, has been pointed out to reveal its potential predictive and prognostic value.

In conclusion, this Dissertation Thesis suggested and/or verified several potential candidate biomarkers associated with cancer susceptibility and patients' clinical outcome for further use in population monitoring and clinical use. However, additional studies on larger independent populations and performing functional tests are needed to replicate our findings and unravel the biological mechanisms behind.