Abstract

Single cell gel electrophoresis or comet assay combined with enzymes of excision repair is a method for measuring DNA strand breaks and oxidative damage. Using this approach we analysed ineffective hematopoiesis in patients with low-risk MDS. Refractory anemia (RA) exhibited a higher DNA instability in bone marrow cells when compared to controls and the extent of DNA fragmentation correlated with cytopenia. No similar relationship was observed in RA with ring sideroblasts (RARS), although the levels of DNA breaks markedly exceeded even the values detected in RA. Both groups of patients also showed high levels of oxidative damage to DNA. However, there was no clear relationship to the levels of serum ferritin, cytopenia or associated inflammation. This suggested that the oxidative DNA damage *per se* is not responsible for extensive apoptosis in low-risk MDS. In any case, it undoubtedly contributes to genome instability and disease progression.

The second part of thesis was aimed to the impact of air pollution and genetic polymorphisms on oxidative damage to DNA, lipids and proteins of city bus drivers and garagemen. Both groups exhibited a higher level of DNA breaks and oxidative damage to proteins than the controls, while an increased level of lipid peroxidation was detected only in bus drivers. The incidence of oxidized DNA lesions correlated with exposure to benzene. The carriers of at least one variant *hOGG1 (Cys)* allele tended to higher DNA oxidative damage than those with the wild genotype, while *XPD23 (Gln/Gln)* homozygotes were more susceptible to the induction of DNA strand breaks. Oxidative damage to lipids and proteins was associated with exposure to carcinogenic polycyclic aromatic hydrocarbons. Advanced age and high levels of LDL cholesterol increased the risk of lipid peroxidation while the high levels of vitamin C had protective effect.

In the last part of thesis, the biological effects of several superparamagnetic iron oxide nanoparticles (SPIONs) were tested using human bone marrow stem cells from two donors. Regardless of their surface coating, all types of SPIONs induced high levels of DNA damage and long term oxidative stress in cells from both donors. In contrast, the standard tests on cell viability and cell death demonstrated harmful effects of nanoparticles only in cells from one donor. Hence, the absence of acute toxic effects does not warrant the safety of nanoparticles for biomedical applications.