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Hematopoietic stem cells (HSCs) are exceptional – they give rise to all blood cells and in the same time can self-renew, hence the stem cell pool can be maintained lifelong. Their characteristic feature is a quiescence – very rare proliferation and low metabolic activity. Therefore their DNA is protected from the risk of damage. On the other hand, the quiescent cells cannot use the most effective repair mechanisms – they can run them only after the cell cycle activation.

In our earlier research we found that heme oxygenase-1 (HO-1), which usually is an antioxidative cytoplasmic enzyme, behaves distinctly in HSCs – it localizes to the nucleus, where it possibly interacts with other proteins, influencing their function. It seems that among its partners can also be the proteins involved in DNA repair.

We already know that if HSCs do not have HO-1, they have more DNA breaks, proliferate faster and age faster. We suppose that HO-1 deficiency leads to increased proliferation and, in consequence, to increased oxidative stress and DNA damage. One can expect that this should also be associated with more effective DNA repair. We suppose, however, that lack of HO-1 impairs function of DNA proteins responsible for joining the DNA breaks. The aim of our project is verification of those suppositions. **We want to understand the influence of HO-1 on DNA damage, and its role in DNA repair mechanisms and maintaining the genome fidelity.**

Experiments will be performed in HSCs and their downstream progenitors, isolated from the bone marrow of typical and HO-1 deficient mice. Cells will be cultured in vitro or transplanted to typical mice. We will analyze number of DNA breaks, expression of genes associated with DNA repair, localization of DNA repair proteins, presence of mutations, and repopulation potential of HSCs with and without HO-1 (or with modified HO-1 – only nuclear, only cytoplasmic or enzymatically inactive form).

Project should allow to understand better the mechanisms protecting blood forming cells from DNA injury and mutations.