Heme is an important cofactor necessary for a proper function of numerous proteins, including hemoglobin or cytochromes. Free heme can be, however, toxic to the cells due to induction of oxidative stress, first of all harmful to the cell membranes. Thus, free heme must be tightly controlled. Such function is fulfilled, among others, by heme oxygenases (Hmox1 i Hmox2), that degrade the prooxidative heme to biliverdin, iron and carbon monoxide. Hmox1 is induced in response to stress and can be found both in cytoplasm and nucleus. Cytoplasmic Hmox2 is constitutively active and is located to the cytoplasm. The role of nuclear Hmox1 is still unknown.

We suppose that hem may play another role, affecting directly the nucleic acids through binding to G-quadruplexes (G4). There are atypical structures formed by the guanine-rich sequences in RNA or DNA, which may disturb DNA replication or affect gene expression. Their recognizing and unfolding is carried out by a set of specialized proteins. We found that lack of the nuclear Hmox1 is associated with accumulation of G4 structures in cells and with upregulation of genes responsible for G4 resolving. Moreover, we demonstrated that **Hmox1 protein localizes close to G4 structures.** Numerous physicochemical studies have demonstrated that G4-folds, formed by oligonucleotides in buffers, are stabilized by heme. Such interaction has never been analyzed in biological systems. **We hypothesize that heme can be an endogenous stabilizer of G4 and that Hmox1 facilitates the destabilization and resolving of G4 structures due to the removal of heme. We suppose that Hmox1 may constitute a part of G4 processing complex.** The aim of our proposal is to verify this hypothesis.

We will answer four questions: i) what is a role of Hmox1 and Hmox2 in controlling the cytoplasmic and nuclear free heme pool; ii) do heme oxygenases prevent the accumulation of G-quadruplexes; iii) is Hmox1 required for proper DNA replication and maintaining genome stability, the processes that are impaired by unresolved G-quadruplexes; iv) how to obtain subcellular resolution and direct detection of G4 in cells. Answers to these questions can point to the neglected mechanism of heme toxicity and overlooked function of Hmox1.