The body's cells are constantly exposed to the negative effects of external factors such as pathogens or toxic metabolites. So, there must be a protection mechanism in place to allow them to survive. One such mechanism is the production of type I interferons, which are proteins belonging to the class of cytokines that protect cells from viral infection. Type I interferons activate the production of many proteins in cells, which are designed to prevent the multiplication of the virus and limit its destructive effects. The only question is, what if the **type 1 interferon response (INF-1) is activated but in the absence of interferon production?** It may seem surprising, but this is exactly what we observe **in mice deficient in heme oxygenase 1** (Hmox1). Heme oxygenase 1 is an enzyme that breaks down heme into biliverdin, iron and CO, but our recent research shows that it may also be potentially involved in replication and DNA repair. Thus, the question arises whether Hmox1 can affect INF-1 and what is the mechanism behind it?

In order to understand the process observed in an animal model, we want to use an in vitro model that will be stable lines of iPS cells (induced pluripotent stem cells), obtained by means of molecular biology tools, with different Hmox1 variants. Using this cellular model, we want to test three potential pathways of INF-1 activation with the following research objectives: i) To investigate whether Hmox1 influences the type I interferon response induced by **oxidative stress and inflammation**, ii) To check whether Hmox1 affects the type I interferon response induced by **hemolytic stress**, iii) To investigate whether the type I interferon response results from **genotoxic stress** in Hmox1 deficient cells.

By focusing on these three stress variants for cells, we will verify the impact of: i) oxidative stress and the resulting inflammation, which can mobilize cells by specialized proteins (including TNFα), ii) hemolytic stress resulting from hemolysis (decay) of erythrocytes, which may increase the pool of toxic free heme, iii) genotoxic stress, resulting from DNA damage and disturbed DNA replication. All three of these cellular stresses can activate the same interferon type I response genes - the question is which stress?