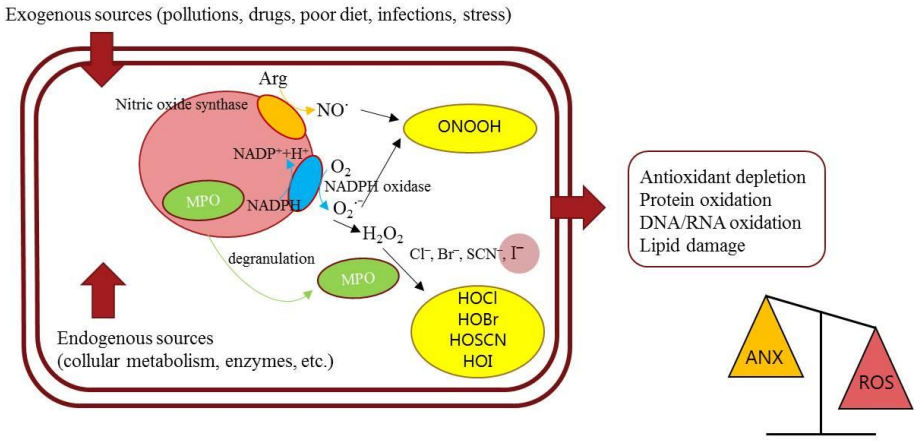
Two faces of iodide in oxidative stress– Marta Ignasiak-Kciuk

The aim of this project is to analyze and understand the reactions between amino acids, peptides, proteins and oxidizing iodine species, as well as ICN and I_2CN formed during oxidative stress in cells and characterization of biomarker of iodine-induced modifications important in cell damage. We assume that the presence of iodide anions can cause both, protective and damaging effect on biologically important proteins. An additional goal of the project is to define modifications formed in proteins during sensitized photo-oxidation in the presence and absence of oxygen and to demonstrate the possible effect of iodide on these processes. Results obtained in this project will be used in creation of analytical method for scanning biomaterials for the presence of iodine-induced modifications of proteins.

Living cells possess a number of defense mechanisms against pathogens (bacteria, viruses). One of them is the production of oxidizing agents by enzymes family called peroxidases. These enzymes catalyze the conversion of halide ions X^- (chloride, bromide or iodide) as well as SCN^- into their hypohalous acids HOX using hydrogen peroxide H_2O_2. However, uncontrolled production of oxidants due to a disturbance of peroxidase can lead to serious damage to biologically important molecules, such as proteins, nucleic acids, lipids and sugars. This can result in so-called **oxidative stress** described in literature as effect of HOCl and HOBr action. However, living cells contain also iodide, an essential element for the functioning of living organisms, whose deficiency or excess leads to serious diseases of the thyroid gland, in both humans and animals.

Due to the presence of iodide anions I^- in cells, it is interesting to identify the effect of various concentrations of iodide on the processes occurring during oxidative stress (eg. formation of hypoiodous acid HOI as one of the reactive forms of iodine). However, there are only few works on the oxidation of the peptides and proteins by HOI/I_2 system, as well as on activity of iodine cyanide ICN, formed by peroxidase in the presence of iodide anions and thiocyanate anions SCN^-. Reference literature focuses mostly on the mechanism of tyrosine iodination, the process necessary in the formation of thyroid hormone, and toxicity of ICN towards pathogens.

In order to fully illustrate this processes kinetic measurements of reactions rate will be performed. It will allow determining the speed of the reactions taking place between the oxidative iodine species and proteins. Knowledge on kinetics of the reaction is crucial in understanding the mechanisms in living cells, where damage to the protein does not depend exclusively on amount of oxidant, but also on reaction rate. Kinetic studies will be performed using the stopped-flow spectroscopy and chromatographic techniques with competitive kinetic assay. Stable products and modification will be analyzed using analytical methods, such as liquid chromatography and mass spectrometry, as well as biochemical methods such as western blot, ELISA and gel electrophoresis. Potential impact of modifications on structure and functionality of protein will be examined (especially for extracellular matrix proteins). The results will allow for the understanding of cellular processes during oxidative stress, as well as the influence of iodide ions on protein damage. Obtained results will fill gaps in scientific literature on oxidative stress, as well as it will solve the dispute concerning addition of iodine to food products.



Scheme 1. Scheme representing the formation of oxidative stress in living cells.