Biotinylated boronic acid derivative as a tool for targetable detection of oxidants in cancer cells

Oxidative stress is a phenomenon indicating the excessive production of reactive oxygen and nitrogen species (**RONS**) in cells of living organisms. Reactive forms of oxygen and nitrogen, such as hydrogen peroxide (H_2O_2), hypochlorous acid (HOCl) and peroxynitrite ($ONOO^-$), are created continuously throughout the life of all living cells. And although in the case of their low concentration they are necessary for the functioning of the body, when their production increases excessively they cause a significant havoc in organism. **RONS** have also positive effects on the body. Their participation in cell signalling and its defence against pathogens should definitely be mentioned. On the other hand, excessive production of **RONS** can cause destructive changes in the genetic material, proteins and lipids, which has a direct impact on the occurrence of diseases, including neoplastic diseases (multiple myeloma, lung cancer) and neurodegenerative diseases (multiple sclerosis, Alzheimer's disease). Therefore, in order to understand the impact of **RONS** on the cells, it is necessary to create tools (so-called probes or chemosensors) that can detect them in the organism. Basing on the probe response, we are able to determine the condition of individual cells and even distinguish cells with a potentially cancerous nature.

To this type of chemosensors we can include boronic acid derivatives, which react with, among others, H_2O_2, HOCl and $ONOO^-$ creating markers manifesting, for example, fluorescent properties (emission of light with lower energy with irradiation of light with higher energy). By applying the proper techniques, we can detect the specific-markers that are formed during oxidation of probe. On the Internet it is possible to find video showing the application of such compounds (https://youtu.be/Ve6kmq64eRA). Unfortunately, after years of research, these compounds are still not perfect. One of the shortcomings of these chemosensors is the lack of simultaneous targeting of cancer cells and their mitochondria (cellular organelles partially responsible for the production of **RONS**).

During this project an attempt will be made to resolve this problem. Experiments will be made to synthesize and to characterize a novel boronate probe overcoming previous problems. The usage of biotin and a positive charge located in the chemosensor structure will result in preferential transport into the mitochondria of cancer cells. The idea of the operation is presented in **Figure 1**.

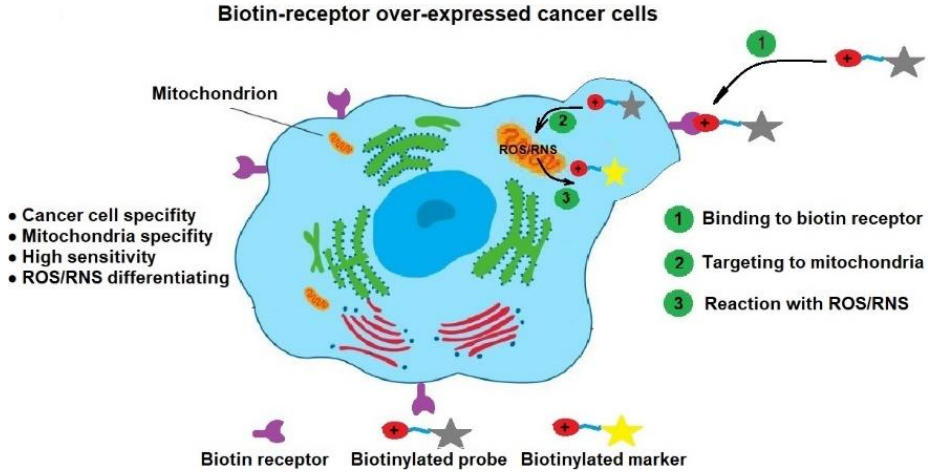

Fig. 1 The general idea of operation used in proposed biotinylated boronate-based probe.

This type of solution is highly innovative. The obtained compound will probably be the first boronate probe of this type in the world! Additionally, we plan to obtain the probe deprived of biotin fragment, but with a positive charge. This control chemosensor will target to the mitochondria, but without discrimination between normal and cancer cells. The designed tools will allow to understand the cellular microenvironment and to determine which and in what quantities **RONS** are formed in both healthy and diseased cells.