Mitochondrial biosensor for studies of hypoxia and reperfusion damage

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The oxygen deprivation is commonly caused by insufficient blood supply (ischemia) to the brain, heart, or peripheral tissues and is one of the most important causes of serious illnesses (such as stroke, angina pectoris, heart attack, obesity, diabetes, cancer, autism, and Alzheimer's disease), disability, and mortality [1,2]. The coronary heart disease and stroke were two most common causes of death in the EU, accounting for more than 2 million deaths per year. The development of new methodology for studying hypoxia-induced mitochondrial damage will enable accelerated studies of life processes in mitochondria and will help in designing new means for better protection of cells against hypoxia-related mitochondrial dysfunction in life-threatening or debilitating neurodegenerative diseases. Previous studies of the mitochondria have focused mainly on the elucidation of the mechanism and understanding of the electron transfer process proceeding in vivo in the respiration chain. In studies of these processes, proteins present in mitochondria (among others, Cyt c) have been utilized.

In this work, we have investigated electrostatic interactions of mitochondria with a thiol-coated gold piezoelectrode using the electrochemical quartz crystal nanobalance (EQCN) technique (Fig.1) [3].

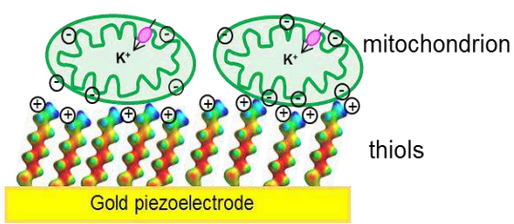

Fig.1. Scheme of the modification of a mitochondria-based quartz piezosensor.

The interactions of hemoprotein (Cyt c) and mitochondria with gold nanoparticles (AuNP) have also been investigated by measuring the bathochromic shift of the local surface plasmon (SP) and changes in the resonance elastic light scattering (RELS) intensity. Functional AuNPs have been used as nanocarriers for mitochondrial drugs modulating the biosystem sensitivity to hypoxia.

In Figure 2, the influence of different concentration of potassium ionophore valinomycin on the intensity of mitochondrial scattering is presented. After addition of 2.47 nM of valinomycin, the intensity of mitochondrial scattering was decreased ca. 23%. It indicates on the changes of mitochondrion shape and general shrinking. The effect of various drugs influencing the potassium ion-channel opening and the inner mitochondrial membrane polarization have been analyzed to elucidate mechanisms of the reduced sensitivity of some cells to hypoxia and reperfusion conditions. The RELS and fluorescence spectroscopies have been employed in the measurements [4,5].

These studies and the biosensors developed in this work enable to gain further insides into the peculiar nature of the reactive oxygen species generation and oxidative stress development under the conditions of oxygen deficit.

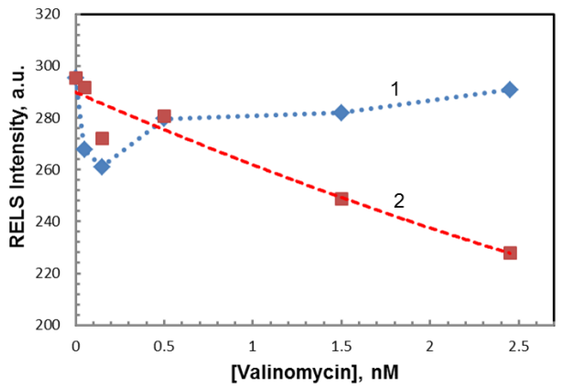

Fig. 2. Dependence of scattering intensity for mitochondrial dispersion in measurement buffer (pH = 7.22) on valinomycin concentration after injection, reaction time: (1) 1 min, (2) 5 min.

References:

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