mgr inż. Monika Pichla **Rzeszów, 08.04.2021**

Dissertation title: Assessment of potential drugs in vitro against age-related diseases

Supervisor: prof. dr hab. Izabela Sadowska-Bartosz

ABSTRACT

The doctoral dissertation consists of four articles published in the *Oxidative Medicine and Cellular Longevity, Molecules* and *Analytical Biochemistry*, that focus on (i) the review of contemporary trends in the use of nanoparticles as therapeutics for neurodegenerative diseases, (ii) the assessment of the neuroprotective properties of nitroxide-containing redox nanoparticles (NRNPs); and (iii) a validation of methods used to determine the biological properties of the selected nanoparticles.

Cells of the SH-SY5Y cell line were treated with 6-hydroxydopamine (6-OHDA) – as one of the most common neurotoxins used to induce a model of Parkinson's disease. Based on our research, it was shown that the neuroprotective nature of NRNPs and their ability to cross the blood-brain barrier was superior in relation to nitroxides *per se*. In accordance with the obtained results, 6-OHDA toxicity mostly depends on damaging the mitochondria, which can lead to depolarization of the inner mitochondrial membrane, a decrease in the mitochondrial mass and a decrease in ATP levels.

Among an array of tested compounds, two of them: the NRNP1 – a copolymer based on poly(styrene-co-malein anhydride) and NRNP2/NRNP ^{pH} – a pH-sensitive radical-containing nanoparticle that was designed and developed using a self-assembling amphiphilic block copolymer (PEG-*b*-PCTEMPO) composed of a hydrophilic poly(ethylene glycol) (PEG) segment and a hydrophobic poly(chloromethylstyrene) (PCMS) segment in which the chloromethyl groups were converted to 2,2,6,6-tetramethylpiperidinyloxys (TEMPOs), protected mitochondria from the damage of reactive oxygen species, after exposure to 6-OHDA, so the that we were able to confirm the protective properties of NRNPs.

Moreover, both nitroxides and NRNPs can alter the redox balance of cells through the oxidation of intracellular antioxidants. The results indicate that both NRNPs and nitroxides *per se* increase the oxidation rate of the three most popular fluorescent probes used for the reactive oxygen species measurement, therefore the interpretation of the results obtained using these probes should be approached with particular care.

Nonetheless, *in vitro* studies are only an introduction to understanding the properties of NRNPs and more detailed information about their properties might be provided by *in vivo* studies.