

The Way to longevity - Effects of resveratrol or/and nanodiamonds on sirtuin activity in *Acheta domesticus*

Is a glass of wine able to prolong life? If so, how is it possible? In literature, there are numerous reports on the potential health benefits associated with its components. Red wine, specifically when examining its chemical composition, contains notable antioxidants in the form of polyphenols and flavonoids. Among the polyphenols, resveratrol (RV) found in red grapes (*Vitis vinifera*) appears to draw attention. Based on available research, it has demonstrated high efficacy as an antioxidant, helping to combat the harmful effects of free radicals in the body, which contribute to oxidative stress and aging processes. Additionally, it may support healthy vascular function, regulate cholesterol levels, reduce inflammation, and impact other risk factors related to cardiovascular diseases. Furthermore, it influences metabolism by activating sirtuins (SIRT), which can regulate energy homeostasis, fat oxidation, and glucose utilization.

Sirtuins are commonly referred to as "longevity enzymes" due to their involvement in genome protection through the regulation of DNA repair processes and cell defense against endogenous and exogenous damage. They function as key controllers of the inflammatory response and metabolic regulation, thereby supporting protection against neurodegenerative diseases. Since the first ground-breaking discovery of sirtuins nearly 60 years ago (as of 2023), researchers continue to search for promising activators that can safely stimulate and modify their activity. While there is considerable research suggesting the role of sirtuins in longevity and aging processes, it is important to note that intensive studies are still ongoing in this field to better understand the precise mechanisms of action and their therapeutic potential. This raises the question of what effect nanoparticles and their effective activator, such as resveratrol, may have?

Nanoparticles, due to the increasing interest in innovative materials and growing demand, find applications in interdisciplinary sciences. Particularly intriguing are nanodiamonds (NDs), which are small carbon particles at the nanoscale level. They have the potential to function as drug carriers, including the delivery of biologically active substances (possibly even RV to enhance sirtuin activity). The potential benefits of NDs caught our attention, and therefore, the project aims to investigate the effects of NDs and/or RV on sirtuin activity. Assuming the presence of synergy between NDs and RV, potentially better effects of sirtuin activation and their impact on processes related to longevity and aging can be expected. In our preliminary studies carried out on a model organism, the cricket - *Acheta domesticus*, we observed significant differences in sirtuin activity [ng/min/mg] between the control group and the selected line, as we possess a unique line of this cricket species selected for longevity. Additionally, the RV-treated group from the longevity-selected line exhibited higher SIRT activity and survival compared to the wild-type line. Therefore, in the project, we aim to attempt a detailed explanation of the effects of NDs and/or RV on sirtuin activity. Having the unique line of this cricket selected for longevity enables us to investigate the differences within the same species after exposure to RV, NDs, and NDs+RV. We will determine the extent of DNA damage by detecting the phosphorylation state of ATM and histone H2A.X using flow cytometry analysis. We will examine the activity of specific sirtuins using fluorometric assays and the activity of selected antioxidant enzymes (catalase, superoxide dismutase, and lipid peroxidation) in the tested groups. The data obtained in the project will be discussed in the context of stress theory, aging, and DNA damage.

Currently, it seems that the journey towards understanding the mechanisms and factors influencing sirtuin activity is progressing slowly towards the distant goal of extending life. Therefore, the essence lies in assembling a comprehensive map by integrating (still) fragmented data into a coherent whole. This may bring us closer to understanding the essence of this process and identify new supplementary points that complement existing knowledge. The results of this project will contribute to taking action to create a complete puzzle, although it still requires further exploration and guidance to ensure the correct direction in understanding the aging process. The unique cricket line will serve as a steppingstone towards humans and provide opportunities to determine where the way to longevity begins.