

Animals' lifespan have been long of interest of evolutionary biologists. Many attempts have been done to explain, which factors influence the rate of organisms' aging and, as a result, make their lifespan shorter. Proposed at the beginning of the last century (i) 'rate of living hypothesis' and (ii) 'free-radical hypothesis' predict that lifespan can be negatively correlated with metabolism rate. The first hypothesis assumes that a higher metabolism rate causes a faster decline of available energy resources, and in consequence leads to faster death, while the second hypothesis links a higher rate of energy expenditure with a higher tissue damage caused by reactive oxygen species (ROS) production. Both hypothesis suggest that individuals with a low metabolism rate should live longer, however the assumptions of either of the hypotheses weren't fully confirmed by experimental results.

On the other hand, it has been documented many times that aging causes decline of numerous vital functions, including an adaptive immune response. In biology, this process is referred as an immunosenescence. The most important lymphatic organ responsible for mounting an adaptive immune response is thymus. Thymus tissue pose a specific architecture where the final stages of T-cell maturation take place. T-lymphocytes, the crucial cells for mounting of an adaptive immune response, have to be immunocompetent to recognize a wide spectrum of unknown antigens. Interestingly, thymus undergoes the age-dependent involution process (size reduction), which seems to be connected with decline of T-lymphocytes production rate and their maturation, and in consequence, a weaker an adaptive arm of immunity in older individuals. It is also worth to mention that mounting of an adaptive immune response is connected with essential metabolic costs. Therefore, it cannot be ruled out that changes in thymus tissue architecture and its functional parameters (expressed as the number of mature T-cells and their contribution to development of an adaptive immune response) correlate with individual metabolism rate.

The aim of the project is the test of the correlation between individual metabolism rate and lifespan. As a proxy of this relationship I will apply rate of changes in thymus architecture and its functional parameters observed along with thymus involution process. If changes in thymus structure really affect an individual's ability to mount of an adaptive immune response, than comparison these changes may be crucial in explaining of the direction of the link between rate of metabolism and lifespan.

The best model to test the above correlation are unique lines of laboratory mice artificially selected for high (H-BMR) and low (L-BMR) basal metabolism rate (BMR). Both line types differ in basal metabolism rate at level up to 50%. What is the most important, selected mice differ with respect to other traits contributed to the problem posed in the project. Namely, mice from the L-BMR line type have a bigger thymus mass, while their counterparts form the H-BMR line type maintain a higher amount of leucocytes in blood and build stronger an adaptive immune response against KLH antigen (a protein derived from the giant keyhole limpet *Megatoura crenulata*). Therefore, an experimental induction of thymus architecture-dependent an adaptive immune response in this animal model may let to answer the following questions: (i) whether an immunosenescence will progress in a similar rate within both line types (while the initial between line type difference in thymus tissue structure and function will be maintained or (ii) whether an immunosenescence will be strictly dependent on line type affiliation, and mice from the H-BMR line type will reduce thymus mass (and its functional parameters like the number of mature T-cells and anti-KLH IgM antibodies production) more than their counterparts with low BMR.

Results of my project will contribute to detect how the between line type difference in metabolism rate can influence the age-dependent changes in thymus structure and its outcomes. Results of my research will shed a new light to inconsistency of the relationship between metabolism rate and lifespan. In a broader context, findings of my project can add to better understanding of mechanisms driving thymus involution and may be applicable into biomedical studies.