Aging is a major risk factor for developing disease, but **chronological age is only a rough measure of the aging** process. The biological age of an organism can be higher or lower than its chronological age. Accelerated or decelerated aging processes are then observed, respectively. However, biological aging is a very complex process that is not easily captured by a single diagnostic test. A breakthrough in this regard has been the development of **epigenetic clocks** based on DNA methylation analysis, which show a strong correlation with the risk of developing many diseases and mortality. Importantly, **biological aging is a modifiable process**. Although there is much research in the literature supporting the impact of lifestyle on the rate of epigenetic aging, and it is suggested that epigenetic clocks may be groundbreaking tools for monitoring health in response to specific treatments or health-promoting activities, more work is needed before methods can be implemented, particularly in the area of **interventional research**.

The project aims to investigate the effects of **dietary or supplemental omega-3 fatty acids**, as well as **aerobic-resistance** training, on epigenetic aging and a range of other health biomarkers in intervention groups. The planned interventions aim to slow aging processes by **targeting inflammation**, which is considered a hallmark of aging. The literature points to the beneficial role of omega-3 fatty acids and physical activity in health and in the fight against chronic inflammation. The proportions of individual fatty acids in the body determine the tendency to inflammation, and the use of omega-3 fatty acids makes it possible to reverse inflammation and lipotoxicity. Moreover, the role of omega-3 fatty acids in the context of biological rejuvenation may be much broader and include, among others: beneficial effect on brain function and improvement of adaptation to physical exercise. However, the importance of omega-3 fatty acids for different target groups and in slowing down epigenetic aging processes has not yet been well studied. An additional goal of the project is to **compare the response of different epigenetic clocks to the interventions** used and thus assess their usefulness for future clinical implementation.

Two interventions will be conducted in two independent groups of subjects. The **first 12-week intervention** will be conducted in a group of 100 people (including 25 controls) with **metabolic syndrome (MetS)**, a cluster of comorbid conditions that increase the risk of developing chronic diseases. Diet and lifestyle modification are considered the primary treatment for MetS. Therefore, the intervention will include the use of an anti-inflammatory diet with a controlled proportion of fatty acids and a low glycemic index. The diet developed will also use the latest knowledge on the impact of dietary habits on epigenetic aging, and the diet will be partially combined with aerobic-resistance training. As part of **the second 8-week intervention**, a group of 80 physically active people (including 20 people from the control group and 20 people receiving placebo) will be subjected to two rounds of omega-3 fatty acid supplementation. The intervention will use innovative assumptions, high doses of omega-3 acids of different types and origins.

The project will collect **genetic and epigenetic data on a genome-wide scale**. An innovative element of the project will be the use of different epigenetic clocks to **measure the success of the intervention**. Biological age as determined by different epigenetic clocks and a number of other epigenetic biomarkers (e.g. epigenetic BMI, risk of developing diabetes, physical fitness indicators) will be compared between specific time points and between study participants and controls. The impact of the intervention on **epigenetic age, health and other functional parameters** will be assessed. The effect of single nucleotide polymorphisms (SNPs) on the efficacy of the intervention will also be investigated. In addition, the impact of the intervention on body composition, lipid profile, adipokines and inflammatory markers will be measured in the MetS group. In the physically active subjects, the peroxidation-antioxidant balance, neuromuscular functions and cognitive functions will also be monitored.

The study will provide new data on the impact of dietary or supplemental omega-3 fatty acids on epigenetic aging. The results of the project should be helpful in the future to **develop non-invasive methods to support the treatment of people with metabolic syndrome** and reduce the risk of developing chronic diseases. The intervention should result in reduced epigenetic ageing, weight loss, reduction of systemic inflammation and insulin resistance in a group of MetS. Improvements in neuromuscular conduction and cognitive function in physically active individuals should also be achieved. In addition, the identification of methylation markers responsive to intervention will contribute to **a better understanding of the mechanisms underlying aging and treatment options**. The project aims to **promote a healthy lifestyle** and seek interventions that **improve the quality of life of an aging society**.