UNIVERSITÀ DEGLI STUDI DI PADOVA

PROJECT

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1) Project title

Development of molecular diagnostic systems for health, nutrition and well-being prediction to slow down the aging process

2)Abstract (max 500 words)

In a scenario of increasing life expectancy worldwide, it is mandatory to identify the characteristics of a healthy aging phenotype. Furthermore, the biological age is not that indicated on the identity card but is written on the DNA. Growing indications have shown that telomere length (TL) and age-correlated DNA methylation changes in certain CpG loci (DNAmAge) are early hallmarks of biological aging, and may be primary indicators of cellular dysfunction and in age-related disorders. TL, the non-coding DNA sequences that cap chromosomes and shorten at each cell division, measures mitotic or replicative cellular aging. DNA methylation age (DNAmAge) is an emerging epigenetic marker of non-mitotic cellular aging, assessed through the analysis of methylation at a specific subset of cytosine-guanine dyads (CpG), which showed a strong correlation with the chronological age. We recently automated the method proposed by Zbieć-Piekarska et al. to increase the efficiency and rapidity, maintaining high prediction accuracy. The development of these biomarkers has led to the definition of an "epigenetic clock" theory of aging; the difference between DNAmAge and chronological age defined as "age acceleration" (AgeAcc) is indicative of altered biological functions and elevated risk for morbidity and mortality.

The project aims to verify in a population undergoing aging (i.e., age 45-55) how much the genetic variants that predispose to active aging, slow down biological aging.

To this end, it will be analyzed how much the indicators of biological age (TL and DNAmAge) differ from the chronological age in the population characterized by genetic variants related to active aging.

The variants considered concern the response to stress and oxidative damage (Catalase, GPX, SOD), some signaling pathways related to the mechanisms of nutrition, growth and energy reserve (FOXO3A, IGF-1, BDNF, LMNA), factors responsible for correct activation of enzymes and pro-inflammatory molecules, in response to environmental or pathogenic factors such as bacteria or viruses (IFNG, IL6, IL1b, NLRP1, NLP3, MEFV), immune factors involved in immunosenescence and neurodegeneration (IFN-gamma, IL-6, TNFSF15, PSORS1C1, APOE, FOXO3A) and factors involved in the maintenance of the skeletal and muscular system, associated with sarcopenia, osteoporosis and joint problems (e.g. ACE, ACTN3, VDR, FTO, NOS3, COL1A1, ESR1, HIF1A, IL6, TNFA, IGF2, MMP1, MMP3, VEGFA).

In addition to the objective of producing reliable results of the analyzed variants, with this activity we want to prototype the procedure for producing personalized reports, with an integrated and simplified

description of the set of identified variants.