UNIVERSITÀ DEGLI STUDI DI PADOVA

PROJECT

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1) Project title

Modulation of biological aging: the effect of pharmacological and complementary intervention.

2) Abstract (max 500 words)

Aging is a complex process characterized by a progressive deterioration of physiological integrity and of the body's ability to respond appropriately to internal and external stressors. While chronological aging reflects the passage of time and is the same for all of us, biological aging doesn't get on at the same pace. Biological aging results from the accumulation of a wide variety of molecular, cellular and organs' damage over time from ambient exposure. This leads to a gradual decrease in physical and mental capacity, a growing risk of disease, and ultimately, death. There is considerable population variation in the rate at which people visibly age as well as become impaired by age-related frailty and disease. Measurement of this biological aging may allow pre-emptive targeted health-promoting interventions, perhaps in a personalized and disease-specific fashion. It would also aid in testing interventions that attempt to modulate the aging process. Our previous findings, on telomere length (TL) and age-dependent methylation changes in certain CpG loci (DNAmAge) supports the hypothesis of the benefits of intensive relaxing practices, which influence two key molecular mechanisms involved in cellular aging, and could represent a novel and inexpensive preventive strategy for stress- and age-related diseases.

The aim of the PhD project is to explore strategies that slowdown biological age in order to extend healthy years of life.

Biological aging will be studied by exploring mitotic and non-mitotic pathways, using TL and DNAmAge. We will delve into the effect of an epigenetic diet, physical activity and epigenetic drugs.

To this aim we will build a complete and detailed definition of 'epigenetic diet'. Nutrients and other food components can in fact modify DNA methylation patterns to modulate biological functions that influence health and aging. Some vitamins and flavanols are able to modify DNA methylation and this could be useful for healthy aging. Also, alkaline water seems to be able to help by slowing down biological aging and reverse aging process. Alkaline water daily intake was found to influence telomerase activity, ROS concentration and other molecular mechanisms accountable for biological aging. Furthermore we will investigate the influence of physical activity compared to relaxing training. We envisage that strong physical activity could increase aging, instead relaxing training could slow down aging. The populations under study will be subjects exposed to work-related stress and university staff participating in mindfulness and physical activity courses.

Finally we will study the effect of different epigenetic drugs, most of these are DNA Methyltransferases (DNMT) inhibitors, like hydralazine, azacytidine and decitabine. In particular, we will investigate the effect of epigenetic drug on DNAmAge organs rejuvenation. In collaboration with the kidney

transplantation center we will analyze the DNA methylation process and the potential DNAmAge reversal during normothermic perfusion and after treatment with DNMT inhibitors of discarded kidneys.