# Propositions

belonging to the thesis

## The aging cardiovascular system: genetic and epigenetic determinants of vascular outcomes and cardiometabolic risk

1. DNA damage in endothelial cells results in loss of endothelium-derived nitric oxide which largely contributes to age-related endothelial dysfunction (this thesis).

2. A proper regulation of autophagy plays a role in cardiometabolic health in human populations (this thesis).

3. Genetic variation in the *LDLRAD4* gene, a potential regulator of transforming growth factor-β, associates with infrarenal aortic diameter (this thesis).

4. Epigenetic variation in the *AHRR* gene. a locus strongly related to the tumor-promoting effect of smoking, associates with carotid intima media thickness (this thesis).

5. DNA methylation at the *ABCG1* gene constitutes a potential mechanism through which statins increase type-2 diabetes risk (this thesis).

6. Targeting autophagy modulators has potential in the treatment and prevention of age-related diseases.

7. Despite the multiple criticisms, the era of genome-wide association studies is not over.

8. Prospective cohort studies with longitudinal measures of DNA methylation and gene expression represent the best approach to further explore the epigenetic link between exposure and outcome association.

9. Epigenetic knowledge is becoming "a social phenomenon in itself" (Landecker and Panofsky, 2013).

10. The integration of high-throughput omics technologies and high-dimensional data modeling, fed into experimental work will lead to discoveries regarding the micro-universe of the cell beyond our knowledge.

11. Support must come from a place of understanding.

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