Ageing is the major risk factor of various diseases including cardiovascular diseases. Chronic, sterile, low-grade inflammation observed in older organism that have been recently named "inflamm-ageing", results in accelerated development of endothelial dysfunction and large arteries stiffness. These two phenotypes; systemic endothelial dysfunction and increased stiffness of large arteries, can be measured in clinical conditions, and predict morbidity and mortality of cardiovascular diseases. Accordingly, the improvement in endothelial function and artery stiffness can have therapeutic effects. However, mechanisms involved in inflamm-ageing are not clear.

Our preliminary results suggest, for the first time, that E3L.CETP mice, representing a unique model of mild hiperlipidemia with human-like lipid profile, display inflamm-ageing and accelerated age-dependent deterioration of endothelium-dependent vascular function, that is associated with a switch from nitric oxide- to hydrogen peroxide- dependent vasodilation followed by impaired vascular mitochondrial function possibly associated with vascular metabolic reprogramming.

In the present project, we hypothesize that accelerated age-dependent dysfunctional vasculature in E3L.CETP mice might be explained by vascular metabolic reprogramming that could contribute to vascular inflamm-ageing and subsequently to persistent vascular inflammation, enhanced susceptibility of vascular wall to inflammatory insults, and to endothelial dysfunction and arterial stiffness. We aim to characterize metabolic signature of inflamm-ageing in murine models, and in particular to define the mechanisms and importance of metabolic reprogramming in the development of age-dependent endothelial dysfunction in large arteries and in coronary microcirculation, as well as in arterial stiffness. Project will be based on interdisciplinary, state-of-the art methodologies including e.g.; Magnetic Resonance Imaging – MRI to assess endothelial function *in vivo* in mice, microfluidic device to characterize *in vitro* primary endothelial cells isolated from mice, and targeted and non-targeted metabolomics to define metabolic pathways of dysfunctional endothelium and vascular wall *ex vivo*.

Given the fact, that endothelial dysfunction and arterial stiffness represent major functional markers of ageing cardiovascular system preceding cardiovascular diseases, deciphering of the mechanisms of metabolic reprogramming contributing to vascular inflamm-ageing may bring novel therapeutic opportunities.