

REPROGRAM

H O R I Z O N 2 0 2 0 R E S E A R C H P R O G R A M

Targeting epigenetic REPROGRamming of innate immune cells in Atherosclerosis Management and other chronic inflammatory diseases

In this project, entitled REPROGRAM, it is proposed that trained immunity is an important pathway promoting an activated state of innate immune cells. Hence, modulation of the trained immunity pathway offers an attractive strategy to effectively attenuate the chronic inflammatory state in atherosclerosis as well as other chronic inflammatory diseases. The key scientific and technological concepts and objectives are defined as follows:

1. To unravel the molecular mechanisms through which systemic risk factors for cardiovascular diseases elicit trained immunity of innate immune cells, focussing on monocytes, macrophages and hematopoietic stem and progenitor cells.
2. To assess the relevance of trained immunity as a common mechanism for the development of disease-specific pathophysiology, and its role in the development of co-morbidities in both women and men.
3. To investigate the role of trained immunity in atherosclerotic cardiovascular diseases and chronic inflammatory diseases.
4. To evaluate whether modulation of trained immunity will lead to a reduction of the pro-inflammatory state both in atherosclerosis and chronic inflammatory diseases, offering innovative immune-modulatory therapeutic strategies.

To achieve these ambitious objectives, REPROGRAM will rely on translational research to identify common disease mechanisms important for innovation in the development of evidence-based treatments. REPROGRAM will evaluate the impact of trained immunity using *in vitro*, *ex vivo* and *in vivo* studies, combining preclinical and clinical (cohort) studies, and demonstrate the relevance and therapeutic potential of modulating trained immunity in cardiovascular diseases as well as chronic inflammatory diseases in general.