Medical University of Graz

Impact of Inflammation on Atherosclerosis Progression after Myocardial Infarction (VASC HEALTH Consortium)

Summary

Peter Rainer, Division of Cardiology and Center of Medical Research, Medical University of Graz

Supervisor:	PD Dr. Peter Rainer
Availability:	This position is available.
Offered by:	Medical University of Graz
Application deadline:	Applications are accepted between August 03, 2022 00:00 and September 20, 2022 23:59 (Europe/Zurich)

Description

Background:

Atherosclerosis of the coronary arteries leads to ischemic heart disease and heart failure. In addition to conventional risk factors, inflammation contributes to atherosclerosis progression and plaque rupture, causing atherothrombosis and myocardial infarction (MI). Systemic inflammation post-MI accelerates atherosclerosis progression by immune cell recruitment and activation. Subsequent events often occur early after MI, and anti-inflammatory therapies may prevent recurrent cardiovascular events. cGAS-STING is an innate immune sensor for DNA and strongly expressed in atherosclerotic plaques.

This PhD position is advertised within the frame of the new Med Uni Graz Research Flagship on Healthy Vascular Aging VASC HEALTH with joint supervision and ample cooperation possibilities.

Hypothesis and Objectives:

Hypothesis: Selective small molecule STING inhibition attenuates atherosclerosis acceleration in the critical time window post-MI and attenuates disease progression and prevents secondary events.

Objectives: Establish mouse model of post-MI atherosclerosis progression. Characterize atherosclerotic disease with and w/o selective STING inhibition. Characterize heart failure remodeling. Validate implicated pathways and immune cells in human patient cells and samples.

Methodology:

We will induce MI in an atherosclerotic mouse model model, induce myocardial infarction, and measure post-MI atherosclerosis progression (plaque area, composition, immune cell content, and cellular phenotype (flow cytometry, scRNAseq) with and without selective STING inhibition. In addition, we will phenotype myocardial remodeling and heart failure phenotype (echocardiography, histology, gene expression). We will use human cells and tissues to validate findings in patients (blood cells, endothelial cells, plaques).

References:

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