

Impact of Inflammation on Disease Progression and Extracellular Matrix Remodeling in Failing Hearts

Summary

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Supervisor: PD Dr. Peter Rainer
Availability: This position is available.
Offered by: Medical University of Graz
Application deadline: Applications are accepted between August 14, 2020 00:00 and October 10, 2020 23:59 (Europe/Zurich)

Description

Background:

Cardiovascular disease (CVD) causes tremendous disease burden world-wide. CVD, regardless of its etiology, often converges towards heart failure, a constantly progressing clinical syndrome with high mortality. Loss of myocardial contractile function and development of fibrosis are hallmarks of heart failure and largely irreversible. Recently, we began to understand that inflammatory phenomena – both innate and adaptive – are important contributors to disease progression although underlying mechanisms are hardly defined. Modern methods now enable us to study these processes in unprecedented detail.

Hypothesis and Objectives:

Hypothesis: Inflammation drives disease progression in heart failure and/or repair after injury.

Objective: Characterize inflammation in early and late stages of heart failure and study the interplay of inflammatory cells with cardiac resident cells (myocytes, fibroblasts, vascular cells) in order to understand underlying molecular pathophysiology and devise potential therapeutic targets.

Methodology:

Preclinical murine in vivo heart failure models including genetic manipulation and phenotyping (pressure overload hypertrophy and failure, ischemia, echocardiography, histology, molecular biology). In vitro signaling studies (primary culture and cell lines, loss and gain of function). Flow cytometry, bulk and single cell RNAseq. Validation in human tissues and cells.

References:

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- Van Linthout S, Tschöpe C. Inflammation - Cause or Consequence of Heart Failure or Both?. *Curr Heart Fail Rep.* 2017;14(4):251-265. doi:10.1007/s11897-017-0337-9
- Bacmeister L, Schwarzl M, Warnke S, et al. Inflammation and fibrosis in murine models of heart failure. *Basic Res Cardiol.* 2019;114(3):19. Published 2019 Mar 18. doi:10.1007/s00395-019-0722-5
- Vagnozzi RJ, Maillat M, Sargent MA, et al. An acute immune response underlies the benefit of cardiac stem cell therapy. *Nature.* 2020;577(7790):405-409. doi:10.1038/s41586-019-1802-2



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