Scientific background and prior contributions of our group

The infiltration and activation of immune cells at sites of injury is a prominent feature of virtually all types of acute cardiovascular diseases. Their impact on cardiac repair processes and disease progression, however, have long been viewed as contradictory as immune cell subtypes such as macrophages drive both inflammatory and reparative activities. Recent paradigm shifting studies in murine models of acute and chronic cardiovascular diseases determined a very heterogeneous and dynamic composition of the cardioimmunological network, which is offering an explanation for this paradox of cardiac inflammation. More importantly, these findings may help to design selective immunomodulatory strategies to either augment intrinsic repair or suppress excessive immune–inflammatory responses. Certainly, the identity of signals and mechanisms that coordinate the recruitment and activity of distinct immune cell subpopulations at sites of myocardial damage mostly remains elusive.
We have recently reported that cardiomyocytes allocated within the border zone of infarcted regions direct sustained macrophage accumulation to the site of experimental myocardial injury via the rapid but transient release of a novel secretory protein termed Regenerating islet-derived protein 3 beta (Reg3β). Moreover, a genetic deficiency of Reg3β was shown to be required for formation of granulation tissue and revascularization of the infarcted area to maintain the hearts function and structural integrity.

Description of the project

The major aim of this project is to specify the mechanism(s) by which Reg3β and other members of the Reg protein family promote the formation of venous and lymphatic vascular structures within ischemic regions. Single cell transcriptome analysis of cardiac tissue derived leukocytes from WT and Reg gene deficient mice will be employed to identify potential candidates promoting revascularization of the infarcted heart. The establishment of light sheet microscopic imaging and dynamic characterization of vascular structures within the period of cardiac remodeling constitutes the second pillar of this project. Finally, underlying mechanisms of this presumed intercellular interaction will be studied more in depth by molecular biological, flow cytometric and protein biochemical analytical tools that are routinely used by our group.

Project–related references by our group

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