Platelet-derived microRNAs play a pivotal role in cardiac remodeling after myocardial ischemia and reperfusion

J. Schuette1, M.C. Manke1, K. Hemmen2, B. Schoerg3, G. Ramos4, M. Pogoda5, F. Kollotzek1, P. Muenzer1, B. Pichler3, F. Lang6, B. Nieswandt7, K.G. Heinze2, M. Gawaz8, N. Casadei5, O. Borst1

1University Hospital of Tuebingen, Department of Cardiology and Cardiovascular Medicine, DFG Heisenberg Group Thrombocardiology, Tuebingen, Germany
2University of Wuerzburg, Rudolf Virchow Center for Translation and Integrative Bioimaging, Wuerzburg, Germany
3University Hospital of Tuebingen, Department of Preclinical Imaging and Radiopharmacy, Werner Siemens-Foundation, Tuebingen, Germany
4University Hospital Wuerzburg, Department of Internal Medicine I, Comprehensive Heart Failure Center, Wuerzburg, Germany
5University Hospital of Tuebingen, Institute of Medical Genetics and Applied Genomics, NGS Competence Center, Tuebingen, Germany
6University Hospital of Tuebingen, Institute of Physiology, Tuebingen, Germany
7University Hospital Wuerzburg, Rudolf Virchow Center, Institute of Experimental Biomedicine I, Wuerzburg, Germany
8University Hospital of Tuebingen, Department of Cardiology and Cardiovascular Medicine, Tuebingen, Germany

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Background: Platelets can infiltrate ischemic myocardium and are increasingly recognized as critical regulators of inflammatory processes during myocardial ischemia and reperfusion (I/R). Platelets contain a broad repertoire of miRNAs, which, under certain conditions such as myocardial ischemia, may be transferred to surrounding cells or released into the microenvironment. Recent studies could demonstrate, that platelets contribute substantially to the circulating miRNA pool holding the potential for so far undiscovered regulatory functions.

Purpose: The present study aimed to determine the role of platelet-derived miRNAs in myocardial injury and repair following myocardial I/R.

Methods and Results: Combining an in vivo model of myocardial I/R, multimodal in vivo and ex vivo imaging approaches (LSFM, PET&MRI, speckle-tracking echocardiography), in vitro immune cell migration assays and Next-generation deep sequencing analysis of platelet miRNA expression pattern in mice with a MK/platelet-specific knockout of pre-miRNA processing ribonuclease Dicer, the present study discloses a key role of platelet-derived miRNAs in the tightly regulated cellular processes orchestrating LV remodeling after myocardial I/R following transient LCA ligation. Disruption of the miRNA processing machinery in platelets by deletion of Dicer resulted in increased myocardial inflammation, impaired angiogenesis, and accelerated development of cardiac fibrosis, culminating in an increased infarct size by d7 that persisted through d28 of myocardial ischemia and reperfusion. Worsened cardiac remodeling after myocardial infarction (MI) in mice with a platelet-specific Dicer deletion (Dicer Ptf4Δ/Ptf4Δ) resulted in an increased fibrotic scar formation and distinguishably increased perfusion defect of the apical and anterolateral wall at d28 post-MI. Altogether, these observations culminated in an impaired LV function and hampered long-term cardiac recovery after experimental MI and reperfusion therapy. Treatment with the P2Y12 antagonist ticagrelor completely reversed increased myocardial damage and adverse cardiac remodeling observed in Dicer Ptf4Δ/Ptf4Δ mice.

Conclusions: The present study discloses a critical role of platelet-derived miRNA in myocardial inflammation and structural remodeling processes following myocardial ischemia and reperfusion.
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