Dronedarone promotes cardiac repair after a heart attack

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An article published in *Experimental Biology and Medicine* reports that the antiarrhythmic drug, dronedarone, promotes cardiac repair after a heart attack. The study, led by Dr. Uwe Lendeckel, Professor for

Medical Biochemistry and Molecular Biology at the University Medicine Greifswald, provides mechanistic explanations for the reduced infarct size that has been observed in response to dronedarone treatment in numerous animal models.

Acute myocardial infarction, or heart attack, is the leading cause of death in the western world. Disability may develop in surviving patients due to the remaining dysfunction of the myocardial microcirculation or heart injury. Therapies that promote microvascular recovery and stabilize the infarct scar are predicted to improve the long-term outcome for patients. Data from large clinical studies show that dronedarone, an antiarrhythmic drug used to treat atrial fibrillation (AF), reduces cardiovascular mortality, hospitalization, and the incidence of myocardial infarction in patients with AF. Studies in animal models indicate that dronedarone improves microvascular function and reduces infarct size. Identification of the molecular targets and pathways regulated by dronedarone may lead to the development of improved therapies for patients.

In the current study, Dr. Lendeckel and colleagues used an integrated "omics" approach to identify the molecular mechanisms that underlie dronedarone-mediated effects on infarcted, border-zone or healthy tissue in a porcine model of ischemia/reperfusion myocardial infarction. The effects of dronedarone on gene expression were greatest in the infarct border zone. Furthermore, the major dronedarone-regulated targets were matricellular proteins associated with tissue remodeling and cell movement. Co-author Dr. Carmen Wolke, University Medicine Greifswald, said: "It was surprising to see that dronedarone' s effects on mRNA profiles were almost exclusively confined to the border zone. In the infarct area, dronedarone, although less effective, still showed partial impact on gene expression." Dr. Christian Scharf, head of the research laboratory, Department of Otorhinolaryngology, Head and Neck Surgery, University Medicine Greifswald, emphasizes: "The

identification of the molecular targets, pathways, and signaling hubs that underlie the previously observed effects of dronedarone might well be employed in future therapeutic strategies." Dr. Lendeckel added: "To what extent dronedarone can improve cardiac functionality in the long term, remains to be assessed in future studies. Most importantly, there are no experimental hints that dronedarone per se has direct harmful effects after induced myocardial infarction in ventricular tissue."

Dr. Steven R. Goodman, Editor-in-Chief of *Experimental Biology & Medicine*, said "Lendeckel and colleagues have utilized transcriptomics, proteomics, interactomics and an integrated "omics" analysis to demonstrate, in a pig model, the impact of dronodarone on key proteins involved in post-infarction cardiac healing and remodeling primarily in the infarction border zone. Their elegant studies should help in the design of future therapeutic strategies".

More information: Ravi K Chilukoti et al. Integration of "omics" techniques: Dronedarone affects cardiac remodeling in the infarction border zone, *Experimental Biology and Medicine* (2018). DOI: 10.1177/1535370218788517

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