Commentary

Should we expect novel biomarkers of myocardial infarction?

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Recent studies have revealed important roles for microRNAs (miRNAs) in cardiovascular disease, including acute myocardial infarction (AMI). miRNAs are small, 20–25 nucleotides long, non-coding RNA molecules, which inhibit gene expression by promoting mRNA degradation or preventing translation (1,2). Although the biological functions of miRNAs are not fully understood, numerous studies have shown that some miRNAs have unique expression profiles in certain tissues or cell types (3). Recent discoveries have revealed the existence of freely circulating, stably expressed miRNAs in human blood cells or plasma/serum (4,5). The circulating miRNAs have been shown to be sensitive and informative biomarkers in the diagnosis of cardiovascular diseases. The article by Yao and colleagues (6) describes circulating miRNA-122-5p as a potential novel biomarker for diagnosis of acute myocardial infarction. In that study, the authors investigated the level of miRNA-122-5p by quantitative real-time PCR (RT-qPCR) and found that its expression was up-regulated at 4, 8, 12, and 24 h in AMI patients compared to non-AMI controls, and displayed similar trends to the cTnI concentrations. A high correlation was observed between the circulating miR-122-5p and cTnI concentrations. The receiver operating characteristic (ROC) curve analysis showed that miRNA-122-5p in plasma had considerable diagnostic accuracy for AMI with an area under curve (AUC) of 0.855. The results suggest that miRNA-122-5p could leak from cardiac myocytes into the circulation during the early stages of AMI.

This circulating miR-122-5p could be a useful biomarker for the diagnosis of AMI. Furthermore, miRNA expression analysis, particularly when combined with clinical parameters, such as cTnI concentrations, provides better understanding of the changes that occur in the myocardium and determine the potential role of extracellular miRNA-122-5p as a paracrine signaling molecule. The authors took into account that the small sample size was a major limitation of the study.

The authors do not state how they found out that this miR-122-5p might be elevated in AMI—until now it was mainly linked with liver injury (7). However, some papers showing upregulation of miR-122 (miR-122 and miR-122-5p are originating from the same hairpin, see e.g., https://www.exiqon.com/mirsearch) in AMI have also been published (8,9). Of note, the study by Li *et al.* (9) was performed using miRNA microarrays representing 1,205 human miRNAs and the results were validated on a large group of patients (two independent cohorts of 111 and 428 patients). Therefore, we have another replication showing increase in miR-122-5p expression in patients with AMI.

Interestingly, numerous studies have indicated that heart-specific miRNAs could be released into the circulation during AMI, making them potentially useful in aiding diagnosis or guiding therapy in acute coronary syndrome (10). Such miRNAs can easily be detected in the circulation and serve as potential biomarkers for cardiovascular diseases. For instance, Gidlöf *et al.* (11) found that the plasma level of some cardiac-associated miRNAs, such as miRNA-1, miRNA-133a, miRNA-208b, and miRNA-499-5p significantly increased in STEMI patients. D'Alessandra *et al.* (12) have reported that in an acute hind-limb ischemia, unlike in AMI, plasma levels of miRNA-1, miRNA-133a, miRNA-133b, and miRNA-499-5p did not increase, indicating that they are ideal biomarkers for AMI. Ai *et al.* (13) showed that circulating miRNA-1 level was significantly higher in AMI patients compared with non-AMI group and the level returned to normal on discharge following medication. Corsten *et al.* (14) evaluated plasma levels of heart-associated

miRNAs (miR-1, miR-133a, miR-208b, and miR-499), fibrosis-associated miRNAs (miRNA-21 and miRNA-29b), and leukocyte-associated miRNAs (miRNA-146, miRNA-155, and miRNA-223) in patients with various cardiac damage including AMI, viral myocarditis, diastolic dysfunction, and acute HF. miR-208b and miRNA-499 were found to be significantly elevated in AMI patients compared to healthy controls. The ROC curve analysis revealed a good diagnostic value of miRNA-208b and miRNA-499 as biomarkers for AMI.

Circulating miRNA-122-5p could broaden our understanding of the role of miRNAs in the pathogenesis of acute coronary syndromes and, if confirmed, it could become a novel biomarker for AMI. We need publications on large cohorts of patients with clinical follow-up, to see if expression of miR-122-5p gives us additional predictive value to clinical data and classical biomarkers. The real revolution is just behind the doorstep—first attempts are currently being made to use miR antagonists for the treatment of patients: now those with hepatitis C, but a novel field in cardiology is opening up (15).

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Footnote

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