Myocardial infarction is pathologically defined as myocardial cell death due to prolonged ischemia, which is the most severe manifestation of coronary artery disease. A sudden rupture of plaque and formation of thrombus leads to acute myocardial infarction. Once the oxygen supply is occluded, the onset of myocardial infarction is initiated as little as 20 min after and the complete myocardial cell necrosis happens in a few hours. Prolonged ischemia leads to the loss of heart contractility due to the poor proliferation capability of the myocardial cell. The timely revascularization of the occluded artery is the key for myocardial infarction therapy. However, these treatments only reduce the severity of coronary artery disease, rather than restoration of the contractility of the infarcted heart. Therefore, novel therapeutic strategies to reduce the myocardial cell death and/or stimulate heart regeneration are highly desirable for the future.

Cardiac cell death plays a critical role in the pathogenesis of myocardial infarction, due to the terminal differentiation and loss of regenerative ability of cardiomyocytes. Myocardial infarction usually involves three main types of cell death process including apoptosis, necrosis, and autophagy. MicroRNAs are defined as single-stranded non-coding RNAs with around 22 nucleotides. Cardiac cell death processes are regulated by a variety of molecules, among which microRNAs have shown outstanding regulatory functions. Recently, a large body of research has emphasized the importance of microRNAs in regulating apoptosis, necrosis, and autophagy in cardiomyocytes, which play a decisive role in myocardial infarction. Nevertheless, more regulatory pathways and the link between different pathways of microRNAs regulating cardiac cell death need to be clarified urgently.

The significance of microRNAs in regulating myocardial infarction has been well emphasized by multiple studies. Several microRNAs are downregulated/upregulated depending on the type of myocardial injury. The significant changes in their expression pattern upon myocardial infarction highlights their contribution in regulation of pathogenesis of myocardial infarction.

The regenerative capacity largely declines within seven days after birth and remains very low in the adult heart. Thus, the activation of endogenous heart regeneration and the triggering of cardiomyocytes renewal could provide new clues for the therapy to treat myocardial infarction. Different approaches have been proposed to regenerate new cardiomyocytes: (I) to promote resident cardiomyocytes proliferation by inducing them to re-enter the cell cycle; (II) to activate endogenous stem cells or progenitors such as cardiac stem cells differentiation; (III) to stimulate endogenous regeneration through direct reprogramming from cardiac fibroblasts into cardiomyocytes. It has been demonstrated that microRNAs are critical regulators of these processes and exhibit as potential new therapeutic targets for myocardial infarction.

Circulating microRNAs in the blood have recently emerged as potential biomarkers for the diagnosis or prognosis of myocardial infarction due to their stability and specificity in plasma. A large body of studies explored the fact that microRNAs are leaked from the heart into the circulation after myocardial injury, during which their expression is elevated and dynamic. Circulating microRNAs are stable and can be easily quantified by real-time PCR assay. Among these abundant microRNAs in the heart, four cardiac-enriched microRNAs (miR-208, miR-499, miR-1, and miR-133) are consistently found to be increased in the plasma of acute myocardial infarction patients. Although the potential value of microRNAs as biomarkers has been established in small-scale studies, it is difficult to validate them in large cohorts of patients with myocardial infarction. In addition, the methods of microRNAs detection need to be optimized. The standardized assays for the detection of microRNAs in patients may reduce the inconsistency and microRNAs may become potential biomarkers for diagnosis of myocardial infarction patients. More prospective studies are underway to assess the diagnostic value of microRNAs as biomarkers. The sensitivity and specificity of circulating microRNAs have an attractive prognostic value in response to myocardial infarction, and relevant research is being designed and carried out.

Accumulating evidence reveals that microRNAs function as pro- or anti-myocardial infarction factors through their influence on myocardial cell death and cardiomyocyte regeneration pathways. So far, significant progress has been made to unveil the microRNAs-regulated signaling pathways of myocardial infarction, which has improved our understanding of heart pathogenesis.

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