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microRNAs FOR CARDIAC REGENERATION THROUGH INDUCTION OF CARDIAC MYOCYTE PROLIFERATION

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Summary: the present invention relates to the area of biotechnology for drug development in the field of cardiac diseases. In particular, the present invention discloses a set of human microRNAs and their use as medicaments to induce cardiac regeneration for the treatment of cardiac diseases associated with a loss of cardiomyocytes, e.g. myocardial infarction, cardiomyopathy of ischemic and non-ischemic origin, myocarditis and heart failure.

In addition, the invention discloses a method for screening biological and pharmaceutically active compounds for their ability to increase the proliferation of cardiomyocytes.

Background of the invention: there is a strong need to find effective ways of treating cardiovascular diseases, in particular those associated with a loss of cardiomyocytes such as myocardial infarction, cardiomyopathy of ischemic and non-ischemic origin, myocarditis and heart failure. These conditions collectively represent the major cause of morbidity and mortality worldwide. These disorders are largely due to the incapacity of the heart to regenerate in adult life after having suffered insult. Therefore, the discovery of active agents capable of stimulating the proliferation of cardiomyocytes, which are able to stimulate the regeneration of damaged portions of cardiac tissue, is of paramount importance.

Description of the invention: the present invention refers to the discovery that 37 human microRNAs are able to markedly increase the proliferation of isolated mouse and rat neonatal cardiomyocytes and of human cardiomyocytes derived from stem cells. The inventors also discovered that some of these microRNAs also increase the proliferation of cardiomyocytes in various animal models, in particular after their intracardiac injection in the form of short, synthetic RNAs, or upon delivery in the context of viral vectors. Strikingly, administration of these microRNAs after myocardial infarction induced by coronary artery ligation was found to markedly improve cardiac function, strongly supporting their therapeutic use.

Applications/Suggested use: the present invention identifies a subset of microRNAs able to increase proliferation of cardiac myocytes from different species, including human cells. The results, which were obtained in well assessed and accepted animal models, allow for the development of medicaments for the treatment of cardiac diseases in human patients. As such the microRNAs disclosed in the present invention are at the basis of the development of novel therapeutic approaches against cardiac diseases in humans. Such approaches include the delivery of these microRNAs, upon appropriate formulation, to patients with myocardial infarction, heart failure or various kinds of cardiomyopathy involving loss of cardiac contractile function.

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