

miRNA-Set for Induction of Cardiomyocyte Regeneration as Treatment Option in Cardiac Diseases

Ref. No.: CH942

Background

In adults, cardiac injury results in loss of cardiomyocytes (CM) and subsequent scar formation with heart failure symptoms. Despite progress made over the last decades, heart failure remains the most significant health issue and the leading cause of death worldwide. In 2015, 110 million cases are estimated to suffer from ischemic heart disease (IHD), with approximately 9 million deaths due to IHD. Current therapeutic approaches focus primarily on catheter-based or surgical re-perfusion strategies to minimize loss of contractile tissue and medical therapies to prevent adverse cardiac remodeling. However, the damaged myocardium cannot be cured and a therapy that stimulates cardiomyocyte proliferation to re-muscularize the heart does not exist. There is a strong need for novel therapeutic approaches which induce cardiomyocyte proliferation and regeneration.

Technology

In a screening approach, 2019 different miRNAs were transfected in human induced pluripotent stem cell (hiPSC)-derived cardiac myocytes (CM) and tested for proliferative effects after imitation of ischemia-reoxygenation by short period of hypoxia (0,5% O₂ for 2 hours). miR-515-3p, hsa-miR-519e-3p and miRNA-517c-3p, belonging to the chromosome-19 miR-cluster, have been identified to have strong proliferative effects on the hiPSC-CMs. Moreover under hypoxic conditions, the proliferative effect of mi-R-515 and miR-519 was even higher than under normoxic conditions. miR-515-3p and hsa-miR-519e-3p are known to regulate genes involved in sarcolemn organization, cell cyclus activity and cell division. In addition, also miRNA-371a-3p has been found to have proliferative effect on hiPSC-CM. The pro-proliferative effect of miR-mimic-519e-3p could also be demonstrated in a myocardial infarct mice model induced by permanent ligation of the left anterior descending (LAD) artery in which miR-mimic-519e-3p was injected intra-myocardially.

A significant increase in EdU-positive cardiomyocytes in miR-mimic-519e-3p treated mice as compared to miR-scrambled could be found, indicative of induction of cell cycle activation. These set of miRNAs are promising new drug candidates for treating cardiac diseases associated with a loss of CMs.

Benefits

- ✓ Effective *in vitro* as well as *in vivo* (mice myocardial infarct model)

Application

Treatment for cardiomyopathies, myocardial infarction, chronic ischemic heart diseases, atherosclerosis-associated diseases

Commercial Opportunity

Searching for a licensing or developing partner

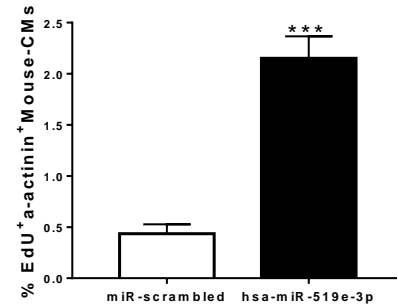


Fig. 1: Edu-positive cardiomyocytes are significantly increased in miR-519e-3p treated mice in myocardial infarct mice model compared to negative control miR-scrambled-treated group (N= 4 per group)

Key words

miRNA-515 miRNA-519, miRNA-517-13p, cardiomyocytes, regeneration, cardiac disease, cardiomyopathy, atherosclerosis

Developmental Status

in vivo

IP Status

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PCT patent application (07/2021)
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Patent Owner

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