Martina Coletto
PhD candidate in Bioengineering and Medical-Surgical Sciences

Functionalized hybrid nanoparticles loaded with microRNA for targeting fibroblasts and cardiomyocytes in cardiac regeneration

Abstract

Background

Myocardial infarction (MI) causes irreversible cardiomyocyte loss and fibrotic remodelling leading to cardiac dysfunction [1]. Given the limited regenerative capacity of the adult heart, microRNAs therapies represent a promising strategy for cardiac repair. MiRcombo (miR-1, -133, -208, -499) induces direct reprogramming of fibroblasts into induced cardiomyocytes [2], while miR-199a-3p promotes cardiomyocyte cell-cycle re-entry [3]. However, safe and cell-selective delivery systems are required to enhance precision and translatability.

Aims

To develop targeted nanocarriers enabling selective microRNAs delivery to distinct cardiac cell populations involved in post-infarction remodelling.

Results

Hybrid polymer-lipid nanoparticles were designed for efficient microRNAs encapsulation and controlled release [4]. Fibroblast-targeting nanoparticles loaded with miRcombo were functionalized with an antibody to promote receptor-mediated endocytosis, inducing direct reprogramming and antifibrotic effects. Cardiomyocyte-targeting nanoparticles loaded with miR-199a-3p were decorated with cardiac homing peptides, enhancing uptake and stimulating proliferation.

Politecnico di Torino – Corso Duca degli Abruzzi 24, 10129 - Torino, Italia
martina.coletto@polito.it - www.polito.it

Validation in 2D and 3D human cardiac models, together with preliminary *in vivo* assessment in a murine MI model, demonstrated improved cardiac function.

Main objective

To establish a regenerative strategy addressing both fibrosis and cardiomyocyte loss after MI.

Conclusion

Targeted hybrid nanoparticles represent a promising microRNA-delivery platform for cardiac regeneration. Improved understanding of cardiac pathophysiology will guide nanocarrier optimization and enhance translational potential.

References

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