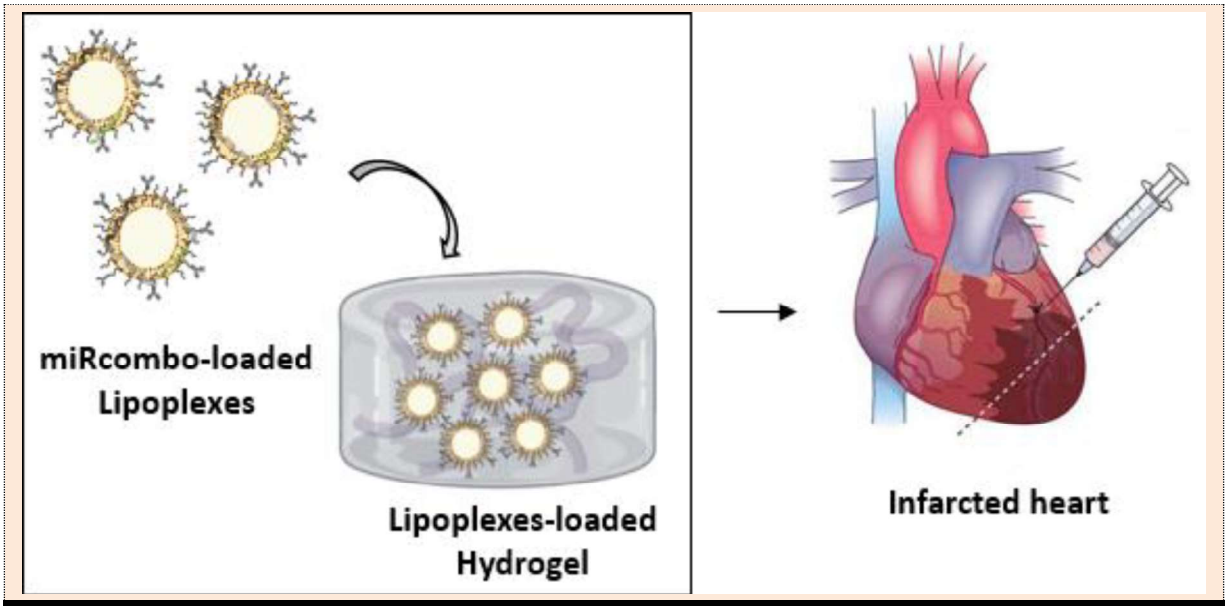
Novel lipoplexes for efficient microRNA delivery to human cardiac fibroblasts



Novel lipoplexes for efficient microRNA delivery to human cardiac fibroblasts

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Myocardial infarction causes the irreversible loss of cardiomyocytes and the formation of a dysfunctional fibrotic scar. Among advanced therapies for myocardial regeneration, *in situ* release of specific microRNAs (miRNAs) is under evaluation to promote cardiomyocyte proliferation or transdifferentiation of cardiac fibroblasts (CFs) into cardiomyocytes [1, 2].

In this work, new miRNAs-loaded lipoplexes were designed for efficient encapsulation and delivery of miRNAs to human CFs, aimed at triggering their direct reprogramming into cardiomyocytes. Lipoplexes containing negmiR or miR-1 were prepared at different N:P ratios, showing 99% encapsulation efficiency, hydrodynamic diameter ranging from 372 nm to 876 nm and average zeta potential ranging from +40 mV to -26 mV with decreasing N:P ratio from 3.0 to 0.35. Based on stability experiments in different media at different temperatures (4°C and 37°C), lipoplexes with N:P 3 were selected for *in vitro* tests with human CFs, showing more efficient miR-1 release to CFs, as compared to a commercial agent. Direct reprogramming experiments are in progress using miRcombo (miR-1, 133, 208, 499) to validate the newly developed lipoplexes as efficient vectors for direct cardiac reprogramming compared to a commercial agent [2].

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2. Paoletti C, Divieto C, Tarricone G., Di Meglio F, Nurzynska D, Chiono V (2020). **MicroRNA-Mediated Direct Reprogramming of Human Adult Fibroblasts Toward Cardiac Phenotype.** Front Bioeng Biotechnol. 8, 529.