Injectable hydrogels for the delivery of miRNA-loaded lipoplexes in cardiac regeneration

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Introduction Myocardial infarction leads to the gradual formation of a non-contractile fibrotic scar. Alginate-based injectable hydrogels are promising for cardiac regeneration and currently investigated in clinical trials[1]. However, alginate presents poor degradability and no cell adhesion *in vivo*. Herein, degradable alginate dialdehyde (ADA) hydrogels were prepared, able to encapsulate and release therapeutic miRNAs-loaded lipoplexes triggering transdifferentiation of cardiac fibroblasts into cardiomyocytes.

Experimental methods ADA was synthesized by oxidation of sodium alginate using sodium metaperiodate and characterized by ATR-FTIR and ^{13}C MAS NMR analyses. Novel miRNA-loaded lipoplexes (6.7-13.4 µg/mL) were physically encapsulated in 2-4% w/v ADA hydrogels formed by calcium ions crosslinking and rheological properties were analyzed[2]. Cy5-labelled lipoplexes release was monitored under a fluorescence microscope and miRNA release was studied by Qubit fluorimetric assays.

Results and discussion Under optimal conditions, ADA was prepared with an oxidation degree of 23% at an average yield of 68%. ATR-FTIR and ^{13}C MAS NMR analyses confirmed the successful formation of aldehyde groups. Injectable hydrogels with different viscoelastic properties were obtained by using different amounts of calcium ions. Lipoplex distribution and progressive release was followed under a fluorescence microscope. Release studies showed a prolonged miRNA release over time, reaching 100% release after 9 days.

Conclusion ADA injectable hydrogels releasing miRNAs-loaded lipoplexes were designed for myocardial regeneration. In the future ADA will be functionalized with bioactive molecules able to improve transdifferentiation of cardiac fibroblasts into cardiomyocytes.

References

[1]Cattelan *et al.*, Front. Bioeng. Biotechnol., 2020. [2]Nicoletti *et al.*, submitted to ACS Nano.

AcKnowledgments This project is supported by ERC BIORECAR- EU H2020 GA N° 772168.