Fabrication and Characterisation of Lactate Releasing PLGA Particles for cardiac regeneration

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Background

Lactate is known to be utilised as a fuel and regulator in a range of cellular processes including immune tolerance, memory function, ischaemic tissue injury, cancer growth, metastasis, and wound healing.[1] Systemic or local delivery of lactate in mice with ischemic wounds increased reparative angiogenesis through endothelial progenitor cell recruitment and deposition of extracellular matrix leading to accelerated wound healing and reduced skeletal muscle atrophy.[2] Recent work by our group also showed that lactate promoted neuronal stem cell/progenitor maintenance and cardiomyocyte cell cycle progression.[3,4] Here we set out to fabricate particles that release sufficient lactate to initiate such responses.

Materials and methods

Utilising a well-defined synthesis method, water-oil-water emulsion, we fabricated poly(lactic-co-glycolic) (PLGA) particles loaded with lactate and characterised their properties such as size and lactate release. Tuning the polymer length and the ratio of lactic to glycolic acids within the PLGA used to synthesise particles, as well as the method for fabrication (e.g., polymer concentration, ultrasonication intensity and time) used has allowed tuning of their size and biodegradation rate, and so their lactate release profile.[5] A cryoprotector was used to prevent particle aggregation during the freeze-drying process and the degradation products were assessed for cytotoxicity in cardiomyoblast (H9c2) and endothelial cells (HUVEC).

Results

In this study PLGA particles with sizes between 200 and 300 nm that release up to 5 mM of lactate per mg have been achieved, reaching biological active concentrations . The degradation products of the particles showed no cytotoxicity.

Acknowledgements

Financial support for the BIOCARDIO project was received in the form of a grant from the Spanish Ministry of Economy and Competitiveness (MINECO/FEDER, RTI2018-096320-B-C21), and the EuroNanoMed3 project nAngioDerm funded through the Spanish Ministry of Science and Innovation (ref. PCI2019-103648).

References

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Figures

Figure 1. Fabrication of PLGA particles, with 5 steps to control their size, and so degradation and lactate release. (1) Polymer concentration + molecular weight (high (HMw) vs low (LMw)), (2) Lactide monomer concentration, (3) PVA concentration, (4) Intensity of ultrasonication, and (5) Duration of sonication.

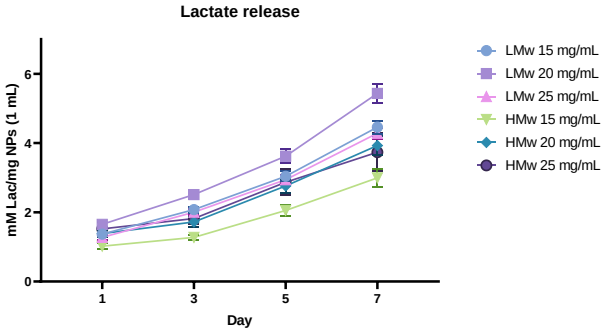

Figure 2. Lactate release of PLGA nanoparticles loaded with lactide monomer over 7 days.