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Delivering microRNA-31 via electrospun nanofibres for the treatment of non-healing wounds

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MicroRNA (miR) are post-transcriptional regulators of multiple genes and associated pathways, thus have excellent potential for chronic wound treatment. miR-31 was found to be downregulated in impaired wound healing in patients with diabetes and those over that age of 65. These two cohorts are highly prone to chronic wound development, therefore upregulation of miR-31 presents as a promissing wound healing therapy. To carry the therapeutic cargo into the cells, a novel peptide delivery system CHAT was utilised to created nanoparticles (NPs) with plasmid encoding for miR-31 (pmiR-31). The delivery system resulted in successful transfection of keratinocyte, endothelial, and fibroblast cells and knockdown of miR-31 target genes: Epithelial membrane protein-1 (EMP-1) and factor inhibiting hypoxia-inducible factor-1 (FIH-1), resulting in significant improvements in cellular functionality with regards to migration, proliferation, and angiogenesis. Electrospinning of hydrogels in a form of nanofibres has been identified as an advantageus platform for the development of wound dressing. Here, a crosslinked PVA nanofibre patch facilitated temporal delivery of the NPs. The efficacy of the CHAT/pmiR-31 loaded nanofibres was validated *in vitro* and *in vivo* to assess its functionality, in addition to subject to biocompatability assesment. The device resulted in transfection in fibroblast, endothelial, and keratinocyte cell lines, and successful gene knockdown of the targets of miR-31 (EMP-1 and FIH-1). In vitro, functionality improvements were evident, which translated into significant improvements *in vivo*. Treatment with the loaded nanofibres in the full thickness wound model in C57BL/6N mice resulted in thicker epidermal and stratum corneum layers, heightened blood vessel density and size, and exhibited biocompatability comparable to commerical dressing controls.

Recent Publications

1. EM McErlean, M Ziminska, C M McCrudden, et al. Rational design and characterisation of a linear cell penetrating peptide for non-viral gene delivery. Journal of Controlled Release 2021, 330.
2. M Ziminska, EM McErlean, N Dunne, H O McCarthy. Synthesis and evaluation of a thermoresponsive degradable chitosan-grafted-PNIPAAm hydrogel as a "smart" gene delivery system. Materials 2020, 13.
3. Z Guo, N Jiang, J Moore, C McCoy, M Ziminska, et al. Nanoscale Hybrid Coating Enables Multifunctional Tissue Scaffold for Potential Multimodal Therapeutic Applications. ACS Appl. Mater. Interfaces 2019, 11

Speaker Biography

Monika has completed her PhD from School of Mechanical & Aerospace Engineering, Queen's University Belfast University, UK. She is a research fellow in the School of Pharmacy, QUB, UK developing nanoparticle delivery systems and nanocomposite for wound healing and bone regeneration.

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