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Delivery of a microRNA ‘cocktail’ by electrospun PVA/alginate/ciprofloxacin nanofibres: A novel genetic nanomedicine for impaired wound healing

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Delays in wound healing are a significant financial burden to the NHS with annual costs estimated to be £3.2 billion. Wound healing is regulated by microRNAs (miRs), which impact multiple aberrant genetic pathways. miR-31 and miR-132 can promote re-epithelialisation, neoangiogenesis, and anti-inflammatory responses by targeting different molecular pathways. In this study, we have encapsulated single-stranded RNA with the sequence of these miR into nanoparticles (NP) by electrostatic interaction with RALA, a novel 30-mer amphipathic pH-responsive peptide that is designed to overcome biological barriers. A wound dressing with potential for NP loading and delivery has been fabricated using electrospinning. Polyvinyl alcohol was chosen as the carrier polymer owing to its ability to be electrospun, sodium alginate was incorporated for its wound healing ability and ciprofloxacin was added as a wide-spectrum antibiotic. The NP cocktail has been proven to efficiently enter cells with no cytotoxicity and to upregulate miR levels. Our NP-loaded electrospun nanofiber technology has demonstrated *in vitro* antimicrobial activity against *Pseudomonas aeruginosa* and *Staphylococcus aureus*, as well as biocompatibility and the promotion of keratinocyte

migration in wound scratch assays. Treatment with the loaded nanofibres in a full thickness wound model in C57BL/6N mice resulted in thicker epidermal and stratum corneum layers, as well as a heightened blood vessel density and size.

Recent Publications

1. Mulholland E J. et al. Delivery of RALA/siFKBP1 nanoparticles via electrospun bilayer nanofibres: An innovative angiogenic therapy for wound repair. *J Control Release*, (2019) 316:53-65
2. Juncos Bombin, A D. et al. Electrospinning of natural polymers for the production of nanofibres for wound healing applications. *Materials Science and Engineering: C* (2022)114, 110994
3. Mulholland E J. et al. Design of a novel electrospun PVA platform for gene therapy applications using the CHAT peptide. *Int J Pharm*, (2021) 598:120366.

Speaker Biography

Adrian Dario Juncos Bombin, at the age of 26 years, is a final year PhD student and early stage researcher at Queen’s University Belfast, UK under the Marie Skłodowska-Curie Actions H2020 programme. He is also a research assistant within professor McCarthy’s nanomedicine group based in the School of Pharmacy at QUB. Each of his publications have been cited over 40 times.

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