Development of a Hydrogel-based Platform to Treat Diabetic Foot Ulcers Correcting Their Defective Micro-RNA Expression

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- 1 in 4 diabetic patients will develop DFUs, being the leading cause of non-traumatic amputation worldwide, presenting lower 5-year survival rates than breast or prostate cancer and costing £1 in every £150 the NHS spends each year according to the National Diabetes Foot Care Audit 2015-2018.

- It has been recently discovered that some of the natural regulators of a correct gene expression, named micro-RNAs (miRs), are dysregulated in DFUs. We found that miR-X, strongly involved in diabetes and the wound healing process, is upregulated in DFUs delaying the healthy healing. Hence, the inhibition of the miR-X raises as an interesting approach to tackle this medical condition.

**PROBLEM**

Diabetic wounds

miR-X overexpression leads to an impaired wound healing

miR-X

miR-X overexpression

miR-X overexpression

Impaired wound healing

Normal wound healing

miR-X

miR-X

Diabetic wounds

General wounds

**APPROACH**

Nanoparticle-loaded hydrogel

miR-X inhibitor (miR-X inh) is delivered using nanoparticles (NPs) that are released in a sustained manner over time, directly into the wound site

miR-X inhibitor

miR-X

miR-X

Cells in the wound site

**HYDROGEL**

PEG/PBAE-based injectable hydrogel (HG) was prepared to serve as the matrix of the delivery platform

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The nanoparticles were loaded into the hydrogel and tracked by tagging the core (PBAE) and the shell (PBAE). The overlap of positions shows that the particles are stable inside the HG.

**WOUND HEALING RESTORATION**

Wound healing

Restoration of the defective gene expression and proliferation similar to a non-diabetic behaviour

**CONCLUSIONS**

- PBAE nanoparticles are promising vehicles to transfec primary cells. The high transfection efficiencies obtained with the C6RH formulation open the possibility to treat other similar diseases with the same strategy.

- The injectable hydrogel presented is able to encapsulate and release the therapeutic nanoparticles as it degrades while still fulfilling the characteristic wound necessities.

- The platform herein designed could eventually be used to deliver any RNA combination to cells from different tissues, increasing its impact across medical problems with one generalizable approach.

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