

Surface delivery of siRNA for implants

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INTRODUCTION: Using short interfering RNAs (siRNAs) we can shut down the production of any cellular protein specifically. This has many potential applications in implant and tissue engineering technology. One could for example use it to direct the differentiation of stem cells (i.e. by targetting a transcription factor or a repressor thereof) or to reduce the local immune response (i.e. by targetting an inflammatory cytokine). But for a siRNA formulation to be used together with an implant they need to be interfaced. Here we present a surface delivery system for siRNAs which can be coated onto 2 and 3 dimensional structures. The system is based on a lyophilized formulation of biocompatible siRNA nanoparticles

METHODS: siRNA particles were formed with chitosan or TransIT-TKO. Particles were added sucrose or gelatine and used to coat various surfaces including cell culture wells and PCL scaffolds which were then lyophilized. The particles released from the dried coat were studied by native PAGE, dynamic light scattering and laser doppler velocimetry. Macrophages, epithelial cells and mesenchymal stem cells were grown upon the surface and uptake and activity studied using microscopy, ELISA, flow cytometry and RT-PCR

RESULTS: We show that sucrose protects the particles during the coating process and that we can tune the release rate and localisation of the particles using gelatine. We also show that the delivery system can deliver the siRNAs into cells growing on and nearby the coated surface and silence a cellular target in these cells. Specifically we have targeted TNF- α in macrophages grown on a siRNA coated 2d surface and eGFP in epithelial cells and mesenchymal stem cells on 2D and 3D surfaces.

DISCUSSION & CONCLUSIONS: We have developed a system that could be used to silence a wide range of proteins in cells growing on surfaces. This system will advance the field of

implant technology by making them more immunocompatible and capable of directing differentiation of stem cells.

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