STARSTEM hedding new light on regenerative medicine

NanoSTARS Imaging for Stem Cell Therapy for Arthritic Joints Niamh Duffy¹, Declan Byrnes¹, Georgina Shaw¹, Mary Murphy¹, Frank Barry¹, VJ Raghavan², Martin Leahy² Work Plan Background Mesenchymal stem/stromal cells Highly sensitive / Deep tissue pathophysiological information (MSCs) present Nanostars potential for cell-Nanostai tagged MSC Structural mediated therapy in Functiona many diseases such Magnetic nanoparticle **Multi-spectral** Biocompatible layer as osteoarthritis (OA). However, a major Molecular Optoacoustic (OA) CO-NH **Receptor antibo** NIR challenge to clinical translation is a lack of Imaging avelength understanding about engraftment of laser delivered cells and their biological activity in situ. STARSTEM, an EU horizon 2020 project Wide-band aims to develop a novel nanotechnology-Ultrasound enhanced optoacoustic imaging (OAI) platform for MSCs. **Optoacoustic Imaging (OAI)** MRI-MSOT Multi-spectral **Co-registration** The underlying principle of optoacoustic Co-registered OA/MRI Image **Optoacoustic (OA) Images** imaging is the photoacoustic effect: the conversion of light energy into acoustic Production (2,4) waves. The tissue of interest is illuminated Partners with nanosecond laser light pulses. Chromophores in the tissue absorb the light Phase 1 clinical tria 1. Regenerative Medicine Institute (REMEDI), National University of Ireland energy, converting it to heat and causing a Galway, Galway, Ireland thermoelastic expansion of the tissue. This 2. Tissue Optics & Microcirculation Imaging (TOMI), National University of generates acoustic waves, which are then Ireland Galway, Galway, Ireland detectable by ultrasound sensors. 3. Università degli Studi di Genova, Genoa, Italy 4. The Institute of Photonic Sciences, Barcelona, Spain ulsed I 5. University of Cambridge, Cambridge, UK 6. Technical University of Munich, Munich, Germany 7. iThera Medical GmbH, Munich, Germany Ultrasonic **NS-loaded MSC Characterization** Laser/ RF pulse Absorption Ultrasonic Image MSCs have been successfully loaded with nanostars as can Dark Field Phalloidin be seen with dark field microscopy. Uptake of nanostars has not altered the cell phenotype in terms of viability, surface Gold Nanostars (AuNS) marker expression and tri-lineage differentiation capacity. The contrast medium of choice, a gold Viability of NS-loaded cells Surface Marker Expression nanoparticle, shaped like a star (the Chondrogenesis 12 4.5 nanostar), amplifies the signal response in Control NS 10 OAI. Nanostars absorb light at around 3.5 au/au) 1100nm, which is 2.5 6 GAG/DNA within the near-2 infrared II biological 1.5 window (NIR-II), also 1 0.5 known as the optical No NS 0.2pM NS 2pM NS 1pM 0.2pM 0.1pM 0.02pM Control 21 pM 10.5 pM 2pM on the star on the the set we we

Undifferentiated

Control: 2pM NS

window, as there is minimal absorption by tissue chromophores such as haemoglobin, melanin and fat (Smith et al., 2009).

Undifferentiated

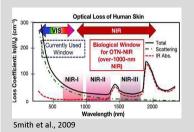
Control: No NS

Adipogenic

Osteogenic

REMEDI

Test: No NS



The STARSTEM platform will be capable of tracking MSCs and MSC-derived exosomes, labelled with nanostars, at unprecedented depth and sensitivity.

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Test: 2pM NS

Future Work

superparamagnetic iron oxide particles (SPIONs) to

the nanostar surface to allow for multi-modal imaging

with MRI. MSCs will be characterized once more with

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these new nanoparticles. Small animal experiments

will then begin to track MSC/exosomes in the joint.

Current work focuses on conjugation of