TARGETING MECHANOBIOLOGICAL CUES WITHIN THE STEM CELL NICHE TO DRIVE OSTEOGENESIS AND BONE REGENERATION

Abstract: Osteoporosis affects millions globally and current anti-catabolic treatments are limited by significant side-effects. Osteoporosis arises when skeletal stem cells (SSC) no longer sufficiently replenish osteoblasts, leading to net bone loss. A key regulator of SSC recruitment, proliferation and osteogenic differentiation is physical loading, yet the mechanisms by which SSCs sense and respond to changes in their mechanical environment are virtually unknown. This talk will explore two mechanisms by which SSCs are mechanically regulated in bone. Initially, it will be shown that fluid shear can directly drive SSC osteogenic lineage commitment and the mechanistic role of the primary cilium in this process will be explored. Primary cilia are nearly ubiquitous ‘antennae-like’ cellular organelles that have very recently emerged as extracellular chemo/mechano-sensors and thus, are strong candidates to play an important role in regulating SSC responses in bone. This study will also demonstrate a second indirect mechanism whereby mechanically stimulated bone cells coordinate SSC recruitment and osteogenic differentiation in a paracrine manner. The role of bone derived extracellular vesicles in this mechanically activated paracrine signalling will be also be explored. Finally, it will be shown that targeting these direct and indirect mechanisms of biophysical regulation of SSC behaviour represent novel mechanotherapeutic avenues to enhance SSC contributions to bone and new anabolic treatments for osteoporosis. These mechanotherapeutics can also be combined with bone mimetic fibrous scaffolds produced through Melt Electrospinning Writing, resulting in novel mechano-biomimetic materials which have great potential as an effective strategy to guide bone regeneration.
Bio: Dr. David Hoey is an Associate Professor in Biomedical Engineering within the Department of Mechanical and Manufacturing Engineering and PI within the Trinity Centre for Bioengineering in Trinity College Dublin (TCD). After being awarded his PhD in Mechanical Engineering from TCD in 2009, he undertook a postdoc in Columbia University in the area of Skeletal Mechanobiology before returning to Ireland to establish his own research team in the University of Limerick in 2012. Since relocated to TCD in 2015 Dr. Hoey now leads a multidisciplinary experimental mechanobiology and biomaterials research group where his goal is to integrate mechanics into the understanding of the molecular basis of skeletal physiology and disease. Dr. Hoey's research has discovered novel mechanisms by which bone can sense and respond to a biophysical stimulus. In particular, he is focused on determining indirect and direct biophysical regulation of skeletal stem cell contributions to bone formation and repair and how this is altered in disease. These platforms have potential to result in new therapeutics and biomaterials that mimic the beneficial effect of biophysical stimuli and treat orthopaedic diseases such as osteoporosis. He was awarded the European Research Council Starting Grant (2013) and Proof of Concept (2018) and his group is also funded by the Irish Research Council, MSCA and Science Foundation Ireland Research Centres ‘AMBER’ and ‘CURAM’.

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