



Trinity College Dublin

Coláiste na Tríonóide, Baile Átha Cliath

The University of Dublin

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## Biomaterial delivery of synergistic therapeutics to manipulate bone metabolism and promote repair

**Speaker:** Ciara Murphy, Tissue Engineering Research Group (TERG) & Science Foundation Ireland (SFI) Advanced Materials and Bio-engineering Research (AMBER), Royal College of Surgeons in Ireland (RCSI), Dublin, Ireland

**When:** 4pm on Friday 12<sup>th</sup> of October 2018

**Where:** Stanley Quek Lecture Theatre, Trinity Biomedical Sciences Institute

Healthy bone metabolism is a tightly coupled dynamic process that relies on a balance between bone resorption (catabolism) by osteoclasts and bone formation (anabolism) by osteoblasts. Traditionally, tissue-engineering approaches for non-union fracture repair employ local anabolic therapeutic delivery strategies that target mesenchymal stem cells (MSCs) and osteoblasts to induce bone formation, however, the challenge of healing non-union defects depends on the cause of defect e.g. trauma or disease, and targeting bone formation alone is often not sufficient. Our research focuses on utilising both anabolic therapeutics, including recombinant human bone morphogenetic protein (rhBMP) -2 and parathyroid hormone (PTH)<sub>(1-34)</sub>, and anti-catabolic bisphosphonates (BPs) to target bone metabolism. A major challenge with harnessing a combined dosing regimen is controlling the release of the individual therapeutics to target cells. We have developed a number of polymer-ceramic based biomaterial delivery systems, including injectable and implantable scaffolds, for the controlled release of rhBMP-2 and the BP zoledronic acid (ZA) and demonstrated their efficacy *in vivo*. A dual therapeutic load provided a synergistic enhancement of bone regeneration, demonstrating significantly increased bone formation and remodelling compared to anabolic therapies alone. Utilising hydroxyapatite as the ceramic phase in our scaffolds further increased bone formation, demonstrating the polymer-ceramic scaffolds to be osteoconductive in the absence of therapeutics. In addition, we have demonstrated the manipulation of bone metabolism through a specific dosing regimen of PTH<sub>(1-34)</sub>, a therapeutic traditionally used as an anabolic, to induce bone remodelling and drive healing in BP loaded fractures. Our research to date has shown that optimising the delivery and regimen of anabolic and anti-catabolic therapeutics to control bone metabolism, augments the bone regenerative potential of these therapeutics in orthopaedic applications.



**Dr Ciara Murphy** received a BSc in Biological Sciences from the National University of Ireland (NUI), Maynooth, and then went on to complete her PhD in Biomedical Engineering with Prof Fergal O'Brien at the Royal College of Surgeons in Ireland (RCSI) (2010), studying the effect of collagen-based scaffold architecture on bone and stem cell behaviour. In 2011, she began a post-doctoral fellowship in Prof David Little's orthopaedic research group in University of Sydney, Australia. It was during this time that her research focus moved towards orthopaedic medicine, whereby she applied her experience in tissue engineering with Prof Little's expertise in orthopaedic drug therapies, developing novel therapeutic approaches to augment bone healing in challenging orthopaedic defects. In 2015, Ciara returned to Ireland, taking up a position as Assistant Professor in the School of Medicine in University College Dublin (UCD) before returning to the Tissue Engineering Research Group (TERG) and RCSI as a StAR Research Lecturer in 2017. Ciara is the recipient of the prestigious New Investigator Recognition Award (NIRA) from the Orthopaedic Research Society (ORS) (2014) and Marie Skłodowska-Curie Fellowship (2016). She has produced 19 publications in top tier journals that have achieved over 2000 citations. Her research interest is in developing advanced biomaterials as innovative platforms for disease model systems and targeted therapeutic delivery systems for tissue repair. The focus of her research is the study of cell-matrix interactions in metabolic bone disease, such as osteoporosis, to design bone metabolism targeted therapies and technologies to treat metabolically impaired bone defects.