Title: **Bioengineered skeletal muscle tissues to study regeneration and drug response**

Presenter: **Nenad Bursac,** Professor of Biomedical Engineering and Cell Biology
Duke University, USA

When: **Thursday 26 July, 2018 @ 1pm**

Venue: Room 1.81, School of Human Sciences, Anatomy Building
The University of Western Australia (off Hackett Entrance No. 2)

Abstract:

Engineering three-dimensional skeletal muscle tissues is motivated by the need for improved physiological systems that would serve for modelling and studying of muscle diseases, pre-clinical drug development, and potential muscle regenerative therapies. In this talk, I will describe first-time engineering of contractile human engineered muscle tissues made of primary myogenic cells derived from muscle biopsies and myogenic progenitors derived from induced pluripotent stem cells by transient overexpression of satellite cell marker Pax7. Resulting engineered microtissues ("myobundles") exhibit aligned architecture, multinucleated and striated myofibers, and a $Pax7^+$ cell pool. They contract spontaneously and respond to electrical stimuli with robust calcium transients, twitch and tetanic contractions. During culture, myobundles maintain functional acetylcholine receptors and structurally and functionally mature, as evidenced by increased myofiber diameter, improved calcium handling and contractile strength, and enhanced expression of maturation genes. In response to diversely acting drugs, myobundles undergo dose-dependent hypertrophy or toxic myopathy similar to clinical outcomes. When derived using cells from patients with congenital skeletal muscle disease, myobundles exhibit expected pathological phenotype. Upon implantation into immunocompromised mice for 3 weeks, the myobundles progressively vascularize and maintain functionality. I will further show that incorporation of immune system cells into the engineered myobundles enhances their regenerative potential and enables near-complete structural and functional repair after cardiotoxin injury *in vitro* and hypoxic injury *in vivo*. Overall, tissue-engineered myobundles provide an enabling platform for predictive drug and toxicology screening and development of novel therapeutics for degenerative muscle disorders.

Speaker:

Dr. Nenad Bursac is a Professor of Biomedical Engineering, Medicine, and Cell Biology at Duke University. As a PhD student in Robert Langer's group at MIT, he demonstrated the first engineering of functional heart tissues using mammalian cells. As a postdoctoral fellow in Leslie Tung's group at Johns Hopkins University, he developed novel methods to control architecture and function of cardiomyocyte cultures for studies of cardiac arrhythmias. Currently, Dr. Bursac's research involves development of novel cell, tissue, and genetic engineering therapies for heart and skeletal muscle disease. Examples of this work include engineering of first human contractile skeletal muscle tissues from primary and induced pluripotent stem cells, first fabrication of human cardiac tissue patches with clinically relevant dimensions, and use of engineered prokaryotic sodium channels as a platform for control of tissue excitability. Dr. Bursac has authored more than 90 scientific articles and has mentored more than 30 PhD students and postdoctoral and medical fellows. He co-directs Regeneration Next Initiative at Duke University. He is a recipient of the Stansell Family Distinguished Research Award and Stem Cell Innovation Award. In 2014, Dr. Bursac was the president of the North Carolina Tissue Engineering and Regenerative Medicine Society. Since 2015, Dr. Bursac has been a Fellow of American Institute for Medical and Biological Engineering.

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