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Hydrogel microengineering: a route to better in vitro tumour models

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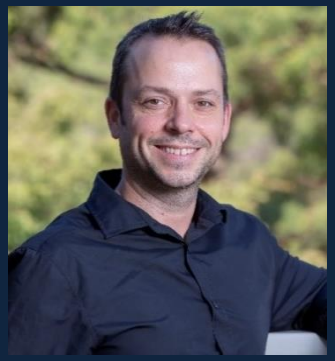
When: 12noon, Thursday 14th of June 2018

Where: Room B2.72, Trinity Biomedical Sciences Institute

The physical and chemical properties of the tissue microenvironment provides a context in which cells receive and integrate signals to drive specific outcomes. Recent studies of the tumour microenvironment points to a tight coordination between soluble signals and cell-matrix engagement during progression. We have developed micro-tumour engineering methods to explore matrix parameters that guide cancer cell state, and identified a role for matrix topology in orchestrating intracellular stem cell programs and intercellular paracrine signals to facilitate dissemination. Topology at the tumour periphery will augment fibronectin adhesion through integrin a5b1, epithelial to mesenchymal transition, and adoption of a stem cell-like phenotype. Expression of the molecular stem cell markers Oct4, Sox2, and CD271, corresponds to spatial enrichment of the histone mark H3K9Ac at perimeter features. This interfacial stem-fraction is highly tumorigenic, and will secrete pro-angiogenic molecules through signal transducer and activation of transcription (STAT) and hypoxia inducible factor (HIF1α) pathways—using mechanotransduction in lieu of low oxygen—to promote neovascularization. Taken together, these results support an "invasive niche" concept, where a growing tumour exploits the biophysical characteristics of the microenvironment to simultaneously attract new vasculature and adopt stem cell-like tumorigenic qualities. We will demonstrate the broad potential of this platform for individualized medicine, where hundreds of microtumours can be lithographically arrayed across a single chip with precise control over spatial stem fraction, towards novel high-throughput/high-content synthetic avatars for cancer research and drug development on patient derived cells.



Kris Kilian received B.S. and M.S. degrees in Chemistry from the University of Washington in 1999 and 2003 respectively. He worked for Merck Research Labs in the Methods Development group from 2000-2004 before travelling to Sydney, Australia to do his PhD with Justin Gooding at the University of New South Wales. In 2007, Kris joined the laboratory of Milan Mrksich at the University of Chicago as a NIH postdoctoral fellow to investigate new methods for directing the differentiation of stem cells. He was Assistant Professor of Materials Science and Engineering (2011-2017) and Associate Professor of Bioengineering (2017-2018) at the University of Illinois at Urbana-Champaign before returning to UNSW in 2018 as a Scientia Fellow between the School of Chemistry and the School of Materials Science and Engineering. Kris is a recipient of the Cornforth Medal from the Royal Australian Chemical Institute (2008), the NIH Ruth L. Kirchstein National Research Service Award (2008), a Kavli Fellow of the 19th German-American Frontiers of Science (2014), the National Science Foundation's CAREER award (2015), and he is a Young Innovator of Cellular and Molecular Biongineering (2017). His research interests include the design and development of model extracellular matrices for stem cell engineering and fundamental studies in cell biology.