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Cues at the interface: A role for physical and chemical signals during cancer metastasis

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Abstract: During development cells experience force, and integrate physical and chemical signals into specific activities. Cancer will coopt numerous of these programs for survival and growth, but also for coordinating metastatic spread—the primary cause of suffering and death. In this seminar I will present our work in developing synthetic tumor models for deconstructing the cues that orchestrate cancer progression and metastasis. Using a robotic spotter to array hundreds of combinations of short peptides, we have identified several combinations of peptides derived from matrix proteins and growth factors that promote a cancer stem cell (CSC)-like state in adherent melanoma cells. Since these CSCs are a rare and difficult to study cell type (often < 0.1% of cells in a tumor)—that is believed to be at the heart of both recurrence and metastasis—we are exploring these peptide reagents as tools to amplify the CSC state for therapeutic development. Next I will show how microengineered hydrogels reveal a surprising role for interfacial geometry in guiding the CSC state. Hydrogel stiffness and convex features at the perimeter of model tumors will guide mesenchymal-to-epithelial transitions and initiation of pluripotency signaling networks. These perimeter cells show significantly enhanced metastatic potential and tumorigenicity in mouse models. Using several 3-D hydrogel patterning approaches with multiple cell types, to better recapitulate tumor architecture, we demonstrate interfacial cues that coordinate the appearance of this elusive and deadly cell type. Screening a panel of cancer cells from different human solid tumors suggests that interfacial geometry may prove a conserved mechanism underlying metastasis. Advanced materials systems that can accurately model signaling in developing tumors, are proving to be transformational in understanding the processes underlying cancer metastasis. These tools may ultimately provide a solution for modelling oncogenesis in the clinic, using patient derived cells, for personalized medicine.

Bio: Professor Kristopher 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. His doctoral research involved the development of nanostructured porous-silicon based photonic crystals and their chemical modification for optical biosensors and biomaterials. In 2007, he 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. Kris joined the faculty of the University of Illinois at Urbana-Champaign as Assistant Professor of Materials Science and Engineering in 2011. Kris is a 2008 recipient of the NIH Ruth L. Kirchstein National Research Service Award, and a 2015 recipient of the National Science Foundation's CAREER award. His research interests include the design and development of model extracellular

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