

“Understanding and Exploiting Cancer Mechanobiology”

Friday, March 17th, 2023
12:00 – 1:00 p.m.

McDonnell Douglas Auditorium



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Abstract: Mammary epithelial cells (MECs) are classically known to respond to differences in extracellular matrix (ECM) stiffness by transitioning to a malignant, non-polarized state on stiffer ECM, i.e. Epithelial-Mesenchymal Transition (EMT). While this is akin to stiff mammary tumors that one can detect with manual palpation, breast cancer fibrosis is dynamic and stiffening occurs over months to years. I will describe our efforts to mimic the onset of tumor-associated fibrosis using dynamic methacrylated-hyaluronic acid (MeHA) hydrogels, whose stiffness that can be modulated from normal 100 Pa to malignant 5000 Pa. Contrary to previous observations, we find that collective decisions by MECs in 3D aggregates—called acini—indicate partial protection from the stiffened niche (*PNAS* 2019). To interpret MEC mechano-signaling that result in this protection, I will also present our new understanding of the molecular mechanisms used by MECs to interpret stiffness, i.e., Hippo/YAP/TAZ/LETS (*Nature* 2018) and Twist-Lyn/EPH2A signaling (*Dev Cell* 2020). After cells leave this niche, however, mechanical changes can be exploited to improve metastatic detection. I will conclude my presentation with new data showing that we can use differences in cell-ECM adhesion strength to mark metastatic cells even in mixed or lineage committed populations (*Cancer Res* 2020; *Nature BME* 2023), and that these cells undergo adrotactic migration down stiffness gradients as shown in computational and experimental models (*Cell Reports* 2021). These data suggest potential improvements to our prognostic capacity when diagnosing and treating epithelial tumors.

Biography: Adam J. Engler is a Professor and Chair of the Shu Chien-Gene Lay Department of Bioengineering at UC San Diego, where he has been on the faculty since 2008. He also is a resident scientist at the Sanford Consortium for Regenerative Medicine. Prior to starting his independent career, Dr. Engler was awarded his PhD from the University of Pennsylvania and performed postdoctoral training at Princeton University. Dr. Engler has published more than 100 peer-reviewed manuscripts and his seminal work has shown how physical and chemical properties of the extracellular matrix influence or misregulate cell function and modify genetic mechanisms of disease. His lab currently studies this phenomenon in the context of cardiovascular diseases and cancer. Dr. Engler has received numerous awards in recognition of this research, including young investigator or mid-career awards from International Society for Matrix Biology (2008), Biomedical Engineering Society (2008), American Society of Matrix Biology (2014), American Society of Mechanical Engineering (2015), and American Society for Engineering Education (2018). Dr. Engler is a NIH New Innovator Award grantee (2009) and fellow of the American Institute for Biomedical Engineering (2018) and the Biomedical Engineering Society (2021).