UNIVERSITY of HOUSTON | ENGINEERING

Department of Biomedical Engineering

Biomedical Engineering Department Distinguished Lecture Series

Friday, September 6, 2024, 10AM

Location: TSO Auditorium, Health & Biomedical Sciences 1 (HBS 1) Building

4401 Martin Luther King Blvd, Houston TX 77204

Understanding and Exploiting Cancer Mechanobiology

Adam J. Engler, Ph.D.
Professor and Chair
Shu Chien-Gene Lay Department of Bioengineering
UC San Diego

Abstract

Epithelial cells 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 tumors that one can detect with manual palpation, 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. Contrary to previous observations, we find that collective decisions by mammary epithelial cells in 3D aggregates–called acini–indicate partial protection from the stiffened niche via molecular mechanisms that interpret stiffness. After cells leave this niche, however, mechanical changes can be remembered. In a parallel story, I will share our results on oral cancer, where cells that disseminate from the niche exhibit "mechanical memory" of their surroundings, and that memory can be used to "educate" their neighboring epithelial cells. I will conclude my presentation with the discovery of a physical marker–adhesion strength–that predicts both metastatic potential and survival rates. Cells disseminating from mammary tumors are weakly adherent, and when presorted by adhesion,

primary tumors created from strongly adherent cells exhibit fewer lung metastases than weakly adherent cells or unsorted populations. Admixed cancer lines can be separated by label-free adhesive signatures using a next-generation flow chamber. When applied to metastatic tumors, the chamber retrospectively predicted metastatic disease from stromal samples with 100% specificity, 85% sensitivity, and AUC of 0.94. The chamber can also differentiate more weakly adherent human metastatic mammary tumors, e.g., invasive ductal carcinoma (IDC) or invasive lobular carcinoma (ILC), from non-invasive tumors, e.g., ductal carcinoma in situ (DCIS). These results together suggest how, unlike other senescent cells, metastatic cancer cells use weak adhesion to navigate against stiffness gradients and how we can use this to our advantage to assess metastatic potential of patient tumors.

Biosketch

Dr. 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. Dr. Engler is also holds the Kenneth Bowles Endowed Chair and 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 120 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 and 2023), 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), the Biomedical Engineering Society (2021) and the International Academy of Medical and Biological Engineering (2024).