Metabolic and Microenvironmental Regulation of Cancer and Stem Cells

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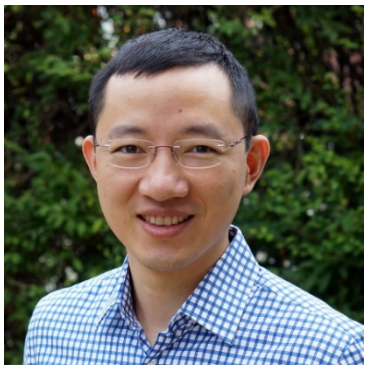
Abstract: In vivo, tissue structure and local cell-cell/cell-matrix interactions define the microenvironment and regulate a complex landscape of cellular phenotypes and metabolism in tumors and stem cell niches. Such dynamics and heterogeneity often contribute to treatment failures in cancer and regenerative medicine. Identifying the precise microenvironmental cues that trigger the phenotypic or metabolic changes will thus enable discovery of new targets for cancer or stem cell therapies. However, it is challenging to pinpoint such cues and track cellular dynamics/heterogeneity in a complex microenvironment in vivo. Our laboratory is focused on creating biologically inspired in vitro platforms to recapitulate the scale of cell signaling in tissue microenvironments from subcellular to tissue levels, and developing single-cell tools to enable dynamic, long-term tracking of metabolic heterogeneity and changes in rare cells. We have built in vitro hypoxic tumor models to recapitulate the metabolic landscapes in solid tumors, to determine/overcome the key factors that impedes the therapeutic efficacy of chimeric antigen receptor (CAR) T cells. We have also developed micropatterned tumor models to understand the mechano-regulatory mechanisms and mito-nuclear communications in cancer metastasis. Using fluorescence lifetime imaging microscopy, we created a set of non-invasive metabolic optical biomarkers to identify hematopoietic stem cells (HSCs) from their progenitor counterparts and track their metabolic dynamics during cell division at the single-cell level. With a lipid bilayer model, we have further discovered a unique role of membrane-bound factors on niche stromal cells in determining the morphology and adhesive function of HSCs in the bone marrow. Our long-term goal is to develop novel strategies for cancer immunotherapy and bone marrow transplantation.



Short biography: Dr. Keyue Shen received his Bachelor of Engineering in Mechanical Engineering and Master of Science in Biophysics from Tsinghua University of China. He earned his Ph.D. degree in Biomedical Engineering at Columbia University in 2010. He then pursued postdoctoral training in the Center for Engineering in Medicine at Harvard Medical School and Massachusetts General Hospital, where he won an MGH Fund for Medical Discovery Award. Keyue joined the Department of Biomedical Engineering at the University of Southern California in 2015. He received a Broad Innovation Award from the Eli and Edythe Broad Foundation (2016), a Marni Levine Memorial Research Career Development Award from STOP CANCER (2017), a Trailblazer Award from the NIH NIBIB (2017), and a Rising Star Award from the Biomedical Engineering Society – Cellular and Molecular Bioengineering SIG (2020). His research has been supported by NIH NIBIB and NCI. His group is focused on creating in vitro tissue models of solid tumors and bone marrow niches. His goals are to understand how tumor microenvironments regulate mitochondrial/metabolic functions of cancer and immune cells in cancer progression and therapy, and how to improve hematopoietic stem cell transplantation and biomanufacturing.