USC University of Southern California

Department of Biomedical Engineering
Systems Cellular-Molecular Bioengineering Distinguished Speaker Series

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Friday, September 22, 2017 11:00am – 12:00pm
UPC – Denney Research Center (DRB), Room 145

"Information from cell shape controls cellular responses"

Abstract: The shape of the cell is connected to its function however we do not fully understand the underlying mechanism by which global shape regulates cell function. We used a combination of theory, experiments and simulation, to investigate how global cell curvature can control signaling. We find that in vascular smooth muscle cells global cell curvature regulates organelle location, inter-organelle distances and differential distribution of receptors in the plasma membrane. A combination of these factors leads to the modulation of signals transduced by the M3 muscarinic receptor/Gq/PLCβ pathway at the plasma membrane, amplifying Ca^{2+} dynamics in the cytoplasm and the nucleus as determined by increased activity of myosin light chain kinase in the cytoplasm and enhanced nuclear localization of the transcription factor NFAT. Taken together, these observations show a systems level phenomenon whereby global cell curvature affects subcellular organization to regulate dynamics of biochemical signaling.

Since the shape of a cell can represent the history of chemical and physical signals that it encounters we determined if information from cell shape by itself can regulate cellular phenotype as assessed by expression and appropriate subcellular localization of physiologically relevant proteins. Using optimal control theory to constrain reaction-diffusion schemes that are dependent on different surface-to-volume relationships, we find that information from cell shape can be resolved from mechanical signals. We used microfabricated 3-D biomimetic chips to validate predictions that shape sensing occurs in a tension-independent manner through β3 integrin signaling pathway in human kidney podocytes and smooth muscle cells. Differential proteomics and functional ablation assays indicate that β3 integrin transduces shape signals through the ezrin-radixin-moesin (ERM) family. We used experimentally determined diffusion coefficients and experimentally validated simulations to show that shape sensing is an emergent cellular property enabled by multiple molecular characteristics of β3 integrin. We conclude that 3-D cell shape information transduced through tension-independent mechanisms can regulate phenotype.

Biography: Dr. Iyengar is a Dorothy H. and Lewis Rosenstiel Professor in the Department of Pharmacology and Systems Therapeutics. He is the Director and Principal Investigator of the NIGMS funded Systems Biology Center New York. Dr. Iyengar completed his undergraduate and masters degrees at Bombay University in India. He then moved to the University of Houston and completed his Ph.D. training in Biophysical Sciences. He was a postdoctoral fellow at the Baylor College of Medicine before starting an academic career at Mt. Sinai in 1980. The major interests of Dr. Iyengar's lab are to understand cellular regulatory networks at a systems level and use this understanding to develop therapeutic strategies and phenotypic signatures for complex diseases. Dr. Iyengar is especially interested in the role of cell shape and its relationship to extracellular spaces within tissue in information processing, and he uses a combination of experimental, theoretical and computational approaches to study these questions. Dr. Iyengar has authored more than 120 research papers, written 112 invited review articles, and edited six books. He received the NIH New Investigator Award in 1980, received the Established Investigator Award from the American Heart Association, and is a Fellow of the American Association for the Advancement of Science (AAAS).

Hosted by: Professor Stacey Finley