David Schaffer is a Professor of Chemical Engineering, Bioengineering, and Neuroscience at University of California, Berkeley, where he also serves as the Co-Director of the Berkeley Stem Cell Center. He graduated from Stanford University with a B.S. degree in Chemical Engineering in 1993. Afterward, he attended Massachusetts Institute of Technology and earned his Ph.D. also in Chemical Engineering in 1998 with Professor Doug Lauffenburger. Finally, he did a postdoctoral fellowship in the laboratory of Fred Gage at the Salk Institute for Biological Studies in La Jolla, CA before moving to UC Berkeley in 1999. At Berkeley, Dr. Schaffer applies engineering principles to enhance stem cell and gene therapy approaches for neuroregeneration. This work includes mechanistic investigation of stem cell control, as well as molecular evolution and engineering of viral gene delivery vehicles. David Schaffer has received an NSF CAREER Award, Office of Naval Research Young Investigator Award, Whitaker Foundation Young Investigator Award, and was named a Technology Review Top 100 Innovator. He was also awarded the Biomedical Engineering Society Rita Shaffer Young Investigator Award in 2000, the American Chemical Society BIOT Division Young Investigator Award in 2006, and was inducted into the College of Fellows of the American Institute of Medical and Biological Engineering in 2010.

Molecular Engineering of Extrinsic and Intrinsic Cues to Control Stem Cell Function

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Stem cell microenvironments present complex repertoires of signals to regulate the processes self-renewal and differentiation. There has been considerable progress in studying soluble signals that regulate stem cell function, but comparatively less work has focused on investigating the “solid phase” of the microenvironment, in large part due to experimental complexities in manipulating matrix and other components. Recent work demonstrates that bioactive, synthetic materials can be harnessed to emulate and thereby study the effects of solid phase, biophysical cues on cell function. By using a modular, bioactive material, we have found that that the matrix modulus profoundly impacts neural stem cell self-renewal and differentiation, and mechanistic analysis implicates key mechanotransductive pathways in this process. Furthermore, immobilization of biochemical signals to the solid phase of a natural niche can lead to nanoscale organization of these signals, and nanostructured biological-polymeric conjugates likewise serve as potent effectors of neural stem and human embryonic stem cell function. Finally, the combinatorial presentation of different matrix motifs from a material can generate synthetic systems capable of supporting the self-renewal and differentiation of both neural stem cells and human embryonic stem cells, thereby enabling the dissection or distillation of the ECM into key individual signals necessary to support stem cell function. Biomimetic materials can thus be employed to study mechanisms by which the solid phase of a stem cell microenvironment regulates cell function, as well as offer safe, scaleable, and robust systems to control stem cells for biomedical application.

In addition to engineering the microenvironment, one can control a cell’s behavior by editing its genome. Viral vectors offer a number of advantageous properties, including the potential for safe and efficient gene delivery; however, they face a number of challenges including inefficient delivery to some therapeutically relevant cells such as stem cells. Such shortcomings arguably arise from the fact that viruses did not naturally evolve to be utilized as human therapeutics, and

we have thus been developing directed evolution – the iterative generation of large libraries genetic mutants and selection for enhanced properties – as an approach to create new viruses with useful properties. For example, we have evolved adeno-associated virus for enhanced gene delivery to and gene targeting in neural stem cells. Engineering both extrinsic and intrinsic cues thus provides strong capabilities to study natural mechanisms of stem cell fate regulation, as well as to control these choices for therapeutic applications.