ABOUT DR. SMITH

Lucas R. Smith obtained his B.S. in Bioengineering from the University of Washington, followed by serving in the US Air Force as a logistics officer. Lucas Smith earned his Ph.D. in Bioengineering from the University of California, San Diego in 2011 where he studied the biomechanical basis for muscle contractures in children with spastic cerebral palsy. His subsequent postdoctoral research at the University of Pennsylvania investigated the mechanisms in which ECM functioned in regeneration and fibrosis of dystrophic mouse models. Further inquiring into ECM architecture led to postdoctoral studies in the mechanisms of bridging fibrosis and cirrhosis of the liver. In 2016, Dr. Smith was awarded an NIH/NIAMS K99/R00 award to advance a mechanistic understanding of ECM architecture in fibrotic muscle function and regeneration and to develop novel anti-fibrotic therapies. Dr. Smith started his lab in Fall 2018 at UC Davis in the Department of Neurobiology, Physiology, and Behavior with a joint appointment in Physical Medicine and Rehabilitation.

PRESENTATION

Skeletal Muscle Fibrosis: Barrier to Function and Regeneration

WHEN
Thursday, October 25, 2018
4:10 p.m. Refreshments Provided

WHERE
Genome & Biomedical Sciences
Auditorium #1005

Fibrosis, or scarring, is the pathological accumulation of extracellular matrix (ECM) material that compromises tissue function and occurs in response to injury in many tissues. Fibrosis of mechanically active tissues, such as skeletal muscle, can be especially harmful as the ECM is a major determinant of tissue mechanics. My efforts using patient biopsies have demonstrated that muscle contractures, a disabling feature in children with cerebral palsy, result from the confluence of increased ECM stiffness as well as high muscle strains. Yet, in fibrotic muscles from dystrophic mice, the amount of ECM does not scale with mechanical stiffness. This highlights the role of the ECM architectural features that we initially describe in muscle as being critical factors in muscle stiffness. The fibrotic ECM also presents a barrier to tissue regeneration by resident stem cells, further propagating the fibrotic cycle. My work has shown that muscle regeneration is dependent upon muscle stem cell ability to remodel the ECM using matrix metalloproteinases (MMPs), primarily through MMPs’ roles in cell migration. However, further studies have revealed that migration through the small pores present in fibrotic muscle damages nuclei and compromises their differentiation into muscle. My efforts will continue to shape the understanding of how fibrosis limits mechanical function through advanced imaging of ECM architecture and tissue biomechanics. Mimicking the fibrotic ECM architecture using novel biomaterials will uncover the mechanosensitive mechanisms of muscle stem cells. Together these efforts will provide new targets for anti-fibrotic therapy targeting ECM architecture to overcome the hurdles fibrosis presents in pursuit of regenerative medicine.