



Northeastern University

College of Engineering

Please join us for a
Special Chemical Engineering & Bioengineering Seminar

Friday, January 25, 2013
108 West Village H
11:45 a.m. – 1:00 p.m.

“A More Youthful Self-renewal: Bioengineering Solutions to Rejuvenate Dysfunctional Muscle Stem Cells in Aging”

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ABSTRACT

In aging, the ability of tissue-specific stem cells to contribute to tissue homeostasis and regeneration progressively declines leading multiple pathophysiologies afflicting the elderly including sarcopenia (skeletal muscle wasting). Rare tissue-specific stem cells maintain and regenerate tissues through stem-cell self-renewal, in which dormant stem cells are activated to divide and produce differentiated progeny and additional stem cells. This process is integratively governed by biomolecular, biochemical, and biophysical cues from supportive microenvironmental niches. In my postdoctoral research, I leveraged advances in murine skeletal muscle stem cell (MuSC) isolation and sensitive monitoring of their regenerative contributions in living mice through molecular imaging to provide novel evidence that aged MuSCs accumulate inherent molecular defects which limit their ability to regenerate damaged muscle tissue. I developed an *ex vivo* therapeutic approach to overcome the dysfunction of aged MuSCs through culture in pliant hydrogel microwells engineered to have biophysical properties mimicking native MuSC niches in synergistic combination with a small molecule pharmacological treatment that targets a signaling pathway that is inherently dysregulated in aged MuSCs. This *ex vivo* therapeutic strategy is capable of rejuvenating self-renewal in aged MuSCs and expanding their numbers such that they robustly improve stem-cell repopulation and muscle strength following transplantation into injured muscles of aged recipients. These findings could yield a potent autologous cell-therapy strategy for muscle wasting in the elderly. In this talk, I will also describe on-going and future efforts to elucidate the mechanisms underlying defective self-renewal in aged muscle stem cells through the fusion of systems-level cell signaling analyses with niche microenvironment engineering and molecular imaging approaches.

BIOGRAPHY Dr. Benjamin D. Cosgrove completed his Ph.D. in Bioengineering at the Massachusetts Institute of Technology under the joint supervision of Dr. Douglas Lauffenburger and Dr. Linda Griffith. Supported by a Whitaker Foundation Graduate Research Fellowship, Dr. Cosgrove's Ph.D. research developed on experimental and computational systems biology tools to elucidate autocrine and phosphoprotein signaling network mechanisms regulating liver hepatocyte cell-fate decisions. This research was earned Dr. Cosgrove a Biomedical Engineering Society (BMES) Graduate Research Award. Dr. Cosgrove's postdoctoral research with Dr. Helen Blau at Stanford University has focused on engineering *ex vivo* strategies employing biomimetic hydrogel niche cultures to rejuvenate and expand aged muscle stem cells to treat aging-associated muscle wasting. Dr. Cosgrove's postdoctoral work has been supported by a Stanford Molecular Imaging Scholars Fellowship and a NIH Pathway-to-Independence Award.

Refreshments will be served.