Seminar

Wednesday, April 4, 2018

11:00 AM – 206 Furnas Hall

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Systems bioengineering dissection of skeletal muscle stem cell fate and function

Muscle stem cells (also called satellite cells) reside in defined microenvironmental compartments in skeletal muscle tissue and are essential for its homeostasis and regeneration throughout adulthood. After muscle damage, muscle stem cells (MuSCs) divide through self-renewal, yielding progeny that both retain a Pax7-expressing stem-cell phenotype and also differentiate into myogenic progenitor cells (myoblasts), which further commit and fuse to repair myofibers. In aging and inherited muscular dystrophies, MuSC contributions to muscle repair are defective, owning to an altered regulation of self-renewal fate outcomes resulting in aberrant differentiation and premature senescence. We have recently identified that aging-related MuSC dysfunction is due in part to a heterogeneous and cell-autonomous activation of the p38 MAPK pathway and devised an *ex vivo* strategy, based on mechanosensitive signaling, to rejuvenate aged MuSCs. In this talk, I will discuss recent and on-going efforts to dissect the MuSC cell-fate regulatory networks using systems-level gene expression and phosphoprotein network models. We have employed single-cell mass cytometry and RNA-sequencing to provide a refined set of molecular definitions to the muscle stem and progenitor cell functional hierarchy and discovered dysfunctional MuSC subpopulations that are increasing observed in advanced aging. Based on these insights, we have designed combinatorial biomaterial-based microenvironments to engineer the selective expansion of transplantable MuSCs, and have resolved biomanufacturing approaches for autologous muscle cell therapies at the clinical scale.

Refreshments at 10:45

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