Public Abstract

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Title:IDENTIFICATION OF FACTORS THAT PROMOTE SATELLITE CELL MOTILITY

An important but poorly understood aspect of stem cell-mediated skeletal muscle regeneration is stem cell recruitment and migration within the damaged tissue; a failure to spread after therapeutic engraftment is also a key stumbling block in cell-based therapies for muscle disease. Acute muscle damage results in the local release of diffusible factors, many of which have potential to promote increased movement, but to date no comprehensive survey of damage-induced proteins that increase movement has been published. We generated crushed muscle extract (CME) to obtain a physiologically-relevant sample of secreted factors from damaged muscle; we propose that components of CME will promote satellite cell movement within the injured tissue in a concentration-dependent manner. Using benchtop tests of movement and migration, we have shown that total CME as well as known components increase migration for primary mouse satellite cells. To identify other active components, we used chromatography to fractionate CME and test the fractions for migration potential. Utilizing this approach we have identified and validated a novel factor, Wnt5b, as a satellite cell motogen. Wnt-5b increases both movement and migration for primary mouse satellite cells in a dose dependent manner. Additional fractionation of CME chromatography has identified Annexin A2 and Galectin-1 as putative movement factors present in high activity fractions of CME. Ongoing work is aimed at validating Annexin A2 and Galectin-1 as increasing either movement or migration. Identification of these signals and an understanding of their activity individually and collectively will add significantly to our understanding of skeletal muscle regeneration.