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Peak satellite cell proliferation for regenerative myogenesis takes place 24-72h post injury in mouse muscles

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Skeletal muscle regeneration is accomplished by muscle resident satellite cells (SC). While the majority of studies evaluating the myogenic potential of SC has been performed *in vitro*, not many studies have assessed the function of these cells *in vivo* - proper muscle regeneration depends on the interaction between different cell types and their secreted factors. Also, our previous work showed that genetic modifiers can influence muscle regeneration in mouse models of Duchenne muscular dystrophy with genetic backgrounds. **PURPOSE:** our purpose was 2-fold: 1) determine the rate of SC proliferation and fusion during the subsequent days post-injury *in vivo*; 2) evaluate whether regenerative myogenesis differs in mice with different genetic backgrounds - C57BL/10ScSnJ (B10-WT) and DBA/2J (D2-WT) mice. **METHODS:** 24d old B10-WT and D2-WT mice were anesthetized with isoflurane prior to receiving intramuscular injections of the myotoxin notexin. Following injury, we administered 5'-bromo-2'-deoxyuridine (BrdU), a thymidine analog, in the drinking water at different time-intervals to label proliferating cells: either 24–48h (day 1 BrdU), 48–72h (day 2 BrdU), 72–96h (day 3 BrdU), and 96–120h (day 4 BrdU). Mice were euthanized and tissues harvested at 3 days post cessation of BrdU administration, and muscles were subsequently sectioned on slides for immunostaining with specific antibodies. To evaluate fusion of myogenic cells, we counted the number of BrdU+ centrally nucleated fibers (CNFs) and expressed it as a percentage of total myofibers throughout muscle sections. **RESULTS:** In B10-WT muscles, our findings demonstrate that both day 1 and 2 have a similar pattern of SC proliferation, which is shown by the %BrdU+ CNFs (day 1: 49.3% BrdU+ CNFs; day 2: 45.1% CNFs). By day 3 and 4, the rate of proliferation already decreased by 10-fold, as shown by only 4.2% and 3.0% myofibers with BrdU+ CNFs, respectively. Lastly, we found that regenerative myogenesis was severely comprised in muscles from D2-WT mice compared to B10-WT mice (%BrdU+ CNFs - day 1: 4.9%, day 2: 6.9%, day 3: 1.8% day 4: 0.9% BrdU+ CNFs). **CONCLUSION:** our data demonstrates that peak SC proliferation happens within 72h after muscle injury, and that genetic modifiers, which potentially alter the muscle niche, influence the function of SC in the D2-WT genetic background.

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