The Role of Bone Lineage Cells During Digit Tip Regeneration in Adult Mice

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Limb loss poses an important challenge to society, as humans have limited regenerative potential. The murine digit is used to study mammalian regeneration because it can regenerate after distal amputation by activating local progenitor cells. Previous studies suggest that cells from bony tissues participate in regeneration, but it is unknown to what extent they are needed. I hypothesize that bone lineage cells are required for successful regeneration. By implementation of a custom computer code for image analysis, I evaluated the role of bone lineage cells during regeneration. I obtained microscope images of digits of two different mouse strains from my lab. The first strain, Osx-CreERT2;Ai9 mice, were used to trace osterix-positive (Osx+) bone lineage cells after different levels of digit amputation to quantify the proportion of Osx+ cells in various tissues throughout regeneration. Dividing cells were also labeled with EdU to determine the proportion of proliferating Osx+ cells. The second strain, 3.6Col1a1-tk mice, were used to ablate proliferating bone lineage cells, and test whether bone lineage cells were required for regeneration. Results show that proliferating Osx+ cells derived primarily from the periosteum and endosteum regenerated the digit bone after distal amputation. In contrast, proximal amputation led to scarring, which was driven by Osx-negative cells. When proliferating bone lineage cells were removed, the remaining cells failed to regenerate the bone after amputation. Taken together, these findings show that bone lineage cells are critical for digit tip regeneration.

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