Regeneration of Soft Tissues is Promoted by MMP1 Administration after Digit Amputation in Mice

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INTRODUCTION:
The ratio of matrix metalloproteinases (MMPs) to the tissue inhibitors of metalloproteinases (TIMPs) in wounded tissues strictly control the protease activity of MMPs, and therefore regulate the progress of wound closure and scar formation (1-2). In some amphibians (i.e., axolotl/newt), a critical role of MMPs was demonstrated for complete regeneration of missing or wounded digits and even limbs. Similarly, mammalian wound healing re-establishes the tissue integrity, but at the expense of scar tissue formation. The differences in the healing process can be attributed to the greater ratio of MMPs to TIMPs in amphibian tissue, which is similar to the scarless healing seen after mammalian fetal wounds (3). Among the various MMPs, our previous studies have demonstrated the ability of MMP1 to effectively promote skeletal muscle regeneration by favoring extracellular matrix (ECM) remodeling to enhance cell proliferation and migration (4). In this study, MMP1 was administered to the amputated digits of adult mice and observe its effect on digit regeneration.

METHODS:
Digit Amputation: The wild type mice (C57BL/6J, male, 5 weeks of age, Jackson lab, Bar Harbor, Maine) were used in this study. After being cleaned with 70% alcohol, the middle digits of both hind feet of mice were amputated by blades, through the middle phalanges, bones, as demonstrated in Figure 1. The wounded digits in both legs were cleaned with water and treated with antibiotics to avoid bacterial infection.

MMP1 Administration: Within the first 10 days after amputation, MMP1 was applied directly to the exposed area of the amputated digit of the left legs (300ng of MMP1 in 3μl of PBS) and injected with a microsyringe 3 mm away from the edge of the severed tip. From day 10 to day 25 after amputation (after wound closure), MMP1 was injected. MMP1 injection was repeated every 4 days after digit amputation. The amputated digits on the right leg were administered PBS to serve as a control.

RESULTS:
1. MMP1 treatment accelerated wound closure and healing of soft tissue in the amputated digits, but not the elongation of the skeletal tissue (Fig. 1 and Fig. 2)

CONCLUSION:
These results indicate that the regeneration of soft tissue and wound closure was significantly improved by MMP1 administration, but the elongation of the skeletal tissue remained unaffected up to 25 days after injury. During digit regeneration, more capillary vasculature and neuromuscular-related tissues were observed in MMP1 treated digits, in addition, there was less fibrotic tissue discovered in the MMP1 treated digits. In general, MMP1 was found to be effective in promoting wound healing in amputated digits of adult mice.

REFERENCE:

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