Digit Amputation Level Influences Macrophage Polarization

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INTRODUCTION

Macrophages are crucial in post-injury healing, initially transforming into an inflammatory form (M1) to eliminate pathogens and then shifting to a non-inflammatory form (M2) that aids tissue repair. Previous research on mouse distal digit tip amputations has indicated the predominance of M1 in regenerative wounds. Our paper suggests that proximal scar-forming wounds are primarily associated with M2. Additionally, we propose that the wound tissue's microenvironment influences macrophage polarization.

METHODS

Amputations at the second (P2) and third (P3) phalanx were conducted on 2 hindlimb digits from 8 mice per group, resulting in 16 digits per injury type. Wound tissue was collected after a 10-day healing period. Additionally, bone marrow from 3 separate mice was cultured on L929 media infused with macrophage colony-stimulating factor, fostering the growth of naive macrophages (M0). Filtered tissue homogenate was introduced to the M0 plate for 24 hours, and the Seahorse XF96 measured the plates' metabolic capacity, illustrating the dominant macrophage type, with M1 relying on glycolysis and M2 on fatty acid oxidation, both quantifiable.

RESULTS

Macrophages exposed to P3 homogenate demonstrated metabolic qualities of M2 whereas those exposed to P2 homogenate demonstrated qualities of M1.

DISCUSSION and CONCLUSION

Since the macrophages polarized only when exposed to tissue homogenate, we validated the influence of an element within the microenvironment on their differentiation. We additionally reaffirmed the prevalence of M1 in P2 wounds and supported earlier evidence of M2 predominance in P3.

SIGNIFICANCE/CLINICAL RELEVANCE: This study's findings highlight the pivotal role of the local wound microenvironment in driving macrophage activation states during the healing process. These insights into the metabolic and cytokine expression differences between regenerative and nonregenerative injury sites hold promise for developing targeted interventions

to enhance wound healing outcomes in conditions such as non-union fractures, volumetric muscle loss, and chronic wounds.