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Dysregulated inflammatory responses lead to enhanced infection and impaired healing in diabetic wound

Persistent unresolving inflammation and enhanced bacterial infection are major co-morbidities that contribute to impaired healing in chronic diabetic foot ulcer. Given that the role of inflammatory leukocytes is to combat infection and to jumpstart healing processes, there appears to be a disconnect in the current paradigm that blames impaired healing as a culprit responsible for enhanced infection and holds enhanced infection responsible for persistent non-resolving inflammation in diabetic wound. We have used the cutaneous full-thickness wound models in STZ-injected type-1 diabetic (T1D) rats and db/db T2D mice, to study the early dynamics of inflammatory responses and bacterial infection control in normal and diabetic wound tissues. Our data indicate that in contrast to chronic diabetic foot ulcers which are locked in persistent unresolving inflammation, the acute phase of inflammatory response which is needed to counter invading pathogens early after injury and to jumpstart healing processes is significantly delayed in diabetic wound, thus rendering diabetic wound vulnerable to enhanced infection and impaired healing. Our data further suggest that normal wound tissues express pathogen-specific antimicrobial peptides that preferentially target pathogenic bacteria amongst commensals by recognizing specific virulence structure(s) that are only found in pathogenic but not commensal bacteria. In contrast, pathogen-specific antimicrobial defenses are impaired in diabetic wounds, due to inadequate inflammatory responses early after injury, thus setting the stage for the microbiome shift toward pathogenic bacteria. We further demonstrate that the inability to control pathogenic bacteria leads to persistent inflammatory state and impaired healing in diabetic wound. Importantly, we show that restoring inflammatory responses in diabetic wound early after injury enhances antimicrobial defenses and promotes healing in diabetic wound, indicating that inadequate inflammatory response early after injury in diabetic wound is just as harmful as the persistent inflammatory state that dominates these wounds as they become chronic.

Biography

Sasha Shafikhani has completed his undergraduate and PhD studies at University of California at Berkeley and Postdoctoral studies at University of California at San Francisco. He is currently an Associate Professor in the Department of Medicine at Rush University Medical Center. He serves on Editorial Board of six reputable journals. As a Cellular Microbiologist, his group conducts projects that involve bacterial pathogenesis, cancer biology and chronic wound healing.

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