Decreased Gut Microbiome Production of Butyrate Increases Immune Suppression Following Burn Injury

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Introduction: Secondary infections remain a leading cause of mortality following thermal injury. A major underlying factor to this increased infection risk is thermal injury-induced immune suppression. A key aspect of this is the decrease in numbers and functionality of T cells following thermal injury. Our recent data demonstrate that the gut microbiome is altered after thermal injury resulting in decreased gut butyrate levels. In this study, we hypothesized that decreased butyrate-producing bacteria within the microbiome after injury down regulates acid sphingomyelinase (Asm) that is needed to protect against T cell apoptosis.

Methods: Mice were subjected to a dorsal 28% full thickness scald injury. T cell numbers were determined by flow cytometry. Butyrate levels were assessed by HPLC. Ex vivo survival experiments were conducted using dexamethasone to induce cell death and quantified by flow cytometry.

Results: We observed that after burn injury: 1) butyrate levels are decreased and 2) T cell numbers are decreased. We next observed that T cell Asm activity is decreased after burn injury and that butyrate can increase Asm activity. Butyrate offered partial protection against dexamethasone induced T cell death in wild type, but not in mice with reduced Asm levels.

Conclusion: These data suggest that decreased butyrate levels can drive lower Asm levels that can result in increased T cell susceptibility to apoptosis. Thus, microbiome recolonization therapies may reverse burn induced T cell suppression and decrease susceptibility to nosocomial infections.

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