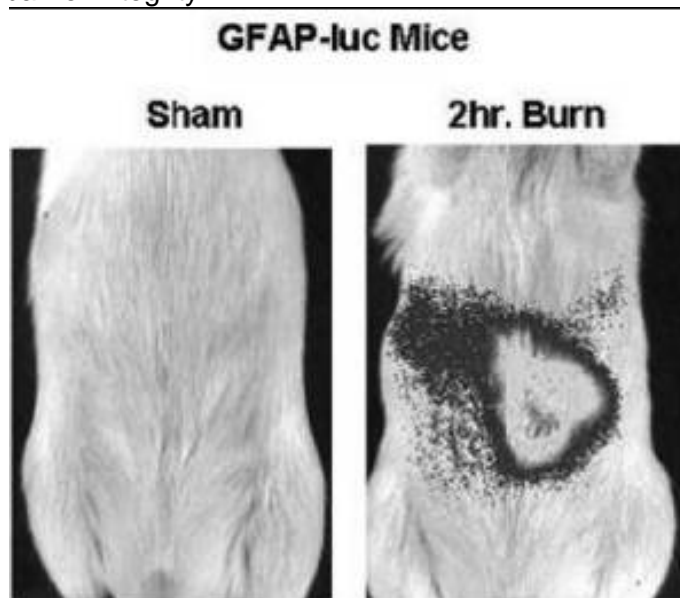


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GUT BARRIER INJURY IS ASSOCIATED WITH ACTIVATION OF ENTERIC GLIA CELLS

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Introduction: Severe injury results in intestinal barrier breakdown and may be the source of the systemic inflammatory response (SIRS), sepsis, and multiple organ failure responsible for significant morbidity and mortality. We have previously shown that gut barrier injury following burn is related to decreased expression of tight junction proteins. The enteric nervous system may play an important role in modulating gut barrier response to disease through activation of enteric glia cells. In vitro studies have shown that enteric glia activation improves intestinal epithelial barrier function through increased expression of tight junction proteins. We postulated that severe injury would increase expression of glial fibrillary acidic protein (GFAP), a marker of enteric glial cell activation, and provide insight into the enteric nervous systems role in restoring gut barrier integrity.



Methods: We utilized a 30% total body surface area (TBSA) steam burn as a murine model of severe injury. Reporter mice expressing the luciferase gene under transcriptional control of the GFAP promoter (GFAP-luc mice) were used to perform imaging of the in vivo response to injury. Non-invasive images of gut bioluminescence from GFAP-luc mice were obtained using the Xenogen IVIS Lumina imaging system. Distal small intestine was also harvested at various time points following burn to investigate changes in GFAP expression using quantitative

polymerase chain reaction (PCR) and confocal microscopy.

Results: Gut bioluminescence imaged in GFAP-luc mice at 2 hours following severe burn showed increased expression of intestinal GFAP. The degree of abdominal bioluminescence decreased at later time points following burn. Quantitative PCR showed that GFAP mRNA expression increased 9-fold over sham at 2 hours following injury, and remained elevated by 3-fold over sham at 6 hours following injury. GFAP mRNA expression returned to baseline by 24 hours following burn. Confocal microscopy images of distal ileum showed increased GFAP expression post-injury, with GFAP staining glial cells localized to the submucosal plexus extending into the intestinal villi.

Conclusion: Intestinal GFAP expression is increased at 2 hours following severe burn. These results suggest that enteric glial cell activation occurs at early time points following severe injury. The enteric nervous system may play an important role in restoring barrier integrity and attenuating the SIRS response to injury.