Introduction
Alcohol intoxication, which is present in 25-40% of trauma patients with orthopaedic injuries, is a known modulator of the immuno-inflammatory pathway. However, the influence of ethanol intoxication on the inflammatory response following orthopaedic trauma is currently not well understood.

Both acute and chronic alcohol intake have been shown to independently influence the inflammatory response. Chronically, ethanol intake results in immunosuppression, although patients with chronic ethanol-induced liver injury increase their production of both hepatic and systemic inflammatory markers. In contrast, acute alcohol intake has been shown to result in a diminished injury-induced induction of inflammatory markers and the expression of early lung proinflammatory cytokines in rats. However, acute alcohol ingestion has been associated with increased levels of lung inflammation and neutrophil infiltration following burn injury, and is known to impair hemodynamic and neuroendocrine counterregulation following hemorrhagic shock. Ultimately, the influence of alcohol on the post-injury response is unknown despite the prevalence of ethanol intoxication within the trauma population.

Surgical intervention has been shown to propagate the magnitude of the inflammatory response beyond that of the initial traumatic injury. An ill-timed surgical procedure prior to restoration of physiologic balance following injury may result in a hyper-inflammatory state with potential to cause systemic disease including ARDS or MOFS. To avoid these complications, an increased emphasis has been placed on the evaluation of the underlying post-injury inflammatory status to help guide clinical decisions and base surgical timing. Thus, the aim of this investigation is to examine the influence of orthopaedic trauma and alcohol binge on measurable markers of inflammation. We hypothesized that markers of inflammation would be elevated following orthopaedic trauma, and that acute alcohol intake prior to injury would modify these markers.

Methods
Eighty-Five (85) Sprague Dawley rats were administered either saline or alcohol in binge fashion for three days, followed by a either a sham operation or bilateral femoral intramedullary pinning and mid-diaphyseal closed fracture via blunt guillotine. Alcohol was administration by a single daily IP injection to achieve peak blood alcohol concentrations (BAC) of approximately 200 mg/dL. Animals were euthanized at various time points after injury. Serum and lung tissue were collected and 24 inflammatory markers were analyzed by commercially available immunoassay.

Results
Bilateral femur fracture significantly increased serum markers of inflammation including IL-2, IL-6, IL-10, GM-CSF, GRO/KC, MCP-1, and WBC. Alcohol binge resulted in significant depression of post-injury serum levels of IL-6, of IL-2, IL-10, CRP, and WBC. However, alcohol binge significantly increased lung levels of the proinflammatory markers IL-6 at 6 hours, and IL-1b, IL-2 and MIP-1a at 48 hours following injury compared to controls.

Discussion
Results from the current study indicate that acute alcohol intake is associated with depressed levels of multiple serum inflammatory markers following orthopaedic trauma. Despite this, lung levels of specific proinflammatory markers were found to be significantly elevated after injury when compared to controls. Alcohol binge may have a proinflammatory influence on pulmonary tissue which is not observed on serum evaluation.

Excessive alcohol consumption is a well-known risk factor for metabolic bone disease and delayed fracture healing. However, despite the prevalence of alcohol intoxication within the trauma population, the significance of ethanol intoxication on the inflammatory response following trauma is currently not well understood. Acute alcohol intake has been shown to suppress the injury-induced mRNA induction of inflammatory markers including IL-6, IL-12 and interferon-α, and attenuates the in-vitro production of toxic superoxide by neutrophils. In addition, acute alcohol administration before septic shock is associated with suppressed lung proinflammatory cytokine expression. However, in burn injury, acute alcohol ingestion causes increased levels of lung inflammation and neutrophil infiltration, and is associated with impairment of neuroendocrine counter-regulation and hemodynamic stability following hemorrhage. Ultimately, clinical evaluation of the inflammatory response in intoxicated patients has been difficult to interpret.

In the present study, we found that alcohol binge resulted in significant depression of post-injury serum levels of IL-6, of IL-2, IL-10, CRP, and WBC. However, acute alcohol administration was associated with significantly increased post-injury lung levels of the proinflammatory markers IL-6, IL-1b, IL-2, and MIP-1a. These findings indicate that acute alcohol intake may have a proinflammatory influence on pulmonary tissue which is not observed on serum evaluation, and should be taken into account when evaluating the inflammatory response in intoxicated trauma patients with orthopaedic injuries.