Estrogen Induces Pro-Inflammatory Effects during Wound Healing


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ABSTRACT

The American Burn Association estimates over one million people with burn injuries in the US need medical care each year, with ~5,000 dying. Mortality is due to bacterial infection as a consequence of severe cytokine dysregulation and impaired wound healing. Previous research has shown females have worse outcomes that males following burn injury. We hypothesize that concentrations of Estrogen can impact wound healing. We developed an in vitro cell model using human Oral Epithelial Cells (OECs) and human Airway Epithelial Cells (AECs). We simulated a wound by removing the cell insert and treating cells with concentrations of estradiol (0.1-10 μM). Images were taken at 0, 6, 24, and 72 hour and wound closure quantified. We also adapted this model to include a means for remote students to examine the cell cultures. Supernatants were harvested and analyzed for IL-6, TNFα, and VEGF (important regulators of wound healing) via ELISA. We observed an increase in percent wound closure in the AECs, and no difference in OECs. We observed an increase in IL-6 ELISA following stimulation with estradiol at different rates for each cell type and corresponding reduction in TNFα and VEGF expression. Taken together, these data suggest that estrogen affects the rate of wound healing, possibly by inducing a negative feedback loop in epithelial cells and therefore may play a role in profound immune dysregulation following burn.

METHODS

1. Scratch Assay (see schematic)

In mice and small animals, human epithelial cells (OECs) and human oral epithelial cells (AECs) were used to assess wound closure using a scratch assay. The cells were cultured at a density of 500,000 cells per well in complete media (D-MEM). The cells were treated with different concentrations of estradiol (0.1-10 μM), and images were obtained at 0, 24, and 72 hours. Images were analyzed using ImageJ software for wound closure.

3. Image Analysis

Images were taken at 0, 6, 12, and 24 hour time points. Cell type?

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