Sulfur Mustard-Induced Changes in Swine Skin Integrity

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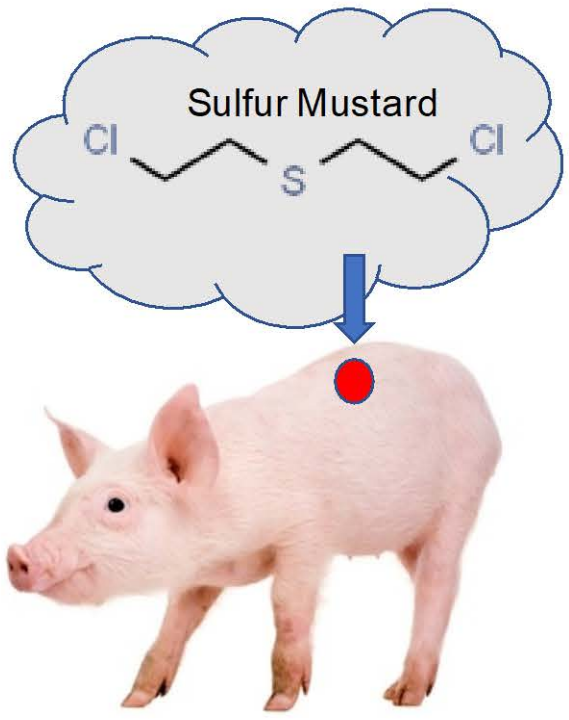
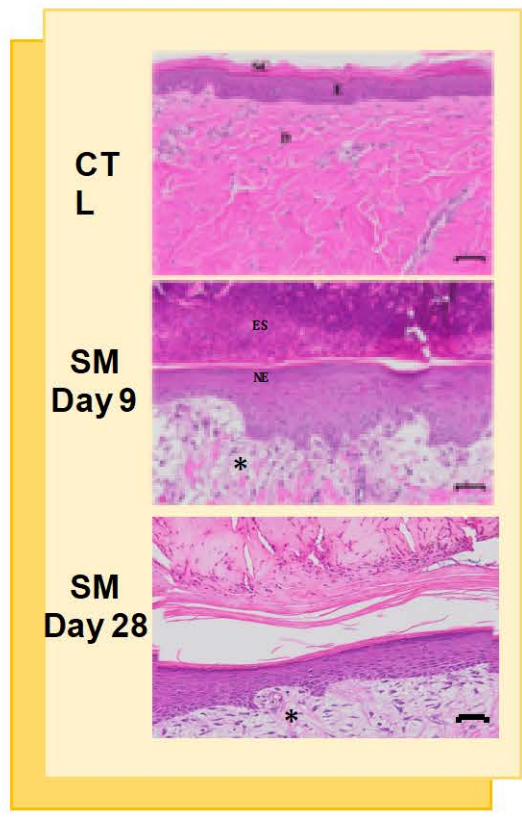
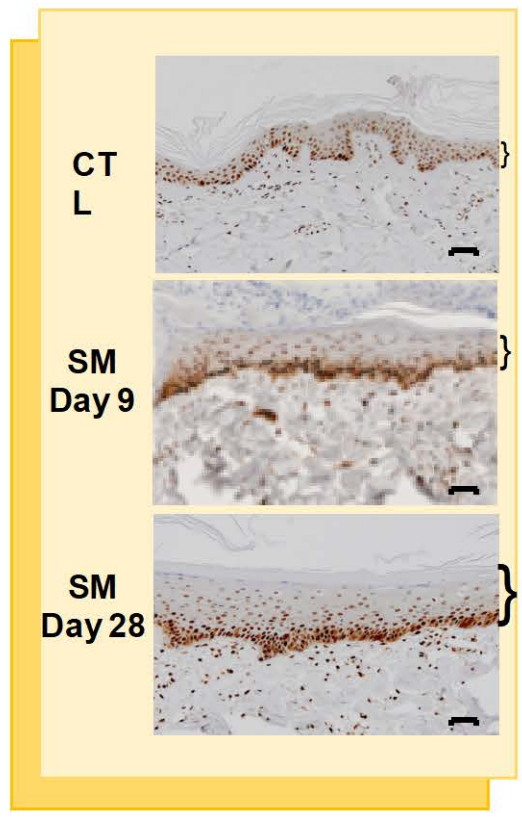
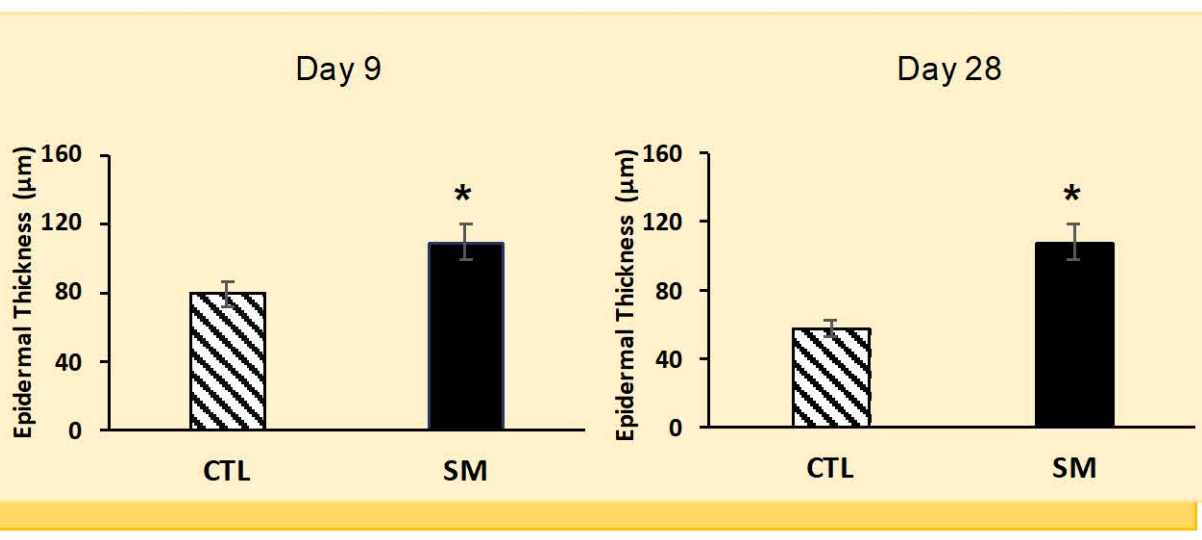
Sulfur mustard (SM) is a bifunctional alkylating chemical warfare agent. SM is known to cause epidermal erosions, dermal inflammation, edema and blistering. Saturated SM vapor caps were placed on the dorsal flanks of 3-month-old male Gottingen minipigs for 90 minutes to create wounds in the skin (MRI-Global, Kansas City MO). Forty-eight hours post SM, skin was debrided daily for 7 days with wet to wet saline gauze soaks. Eschar formation was observed 3 days post-SM and were still present by day 28. Animals were sacrificed on days 9 and 28 days post-SM; full thickness skin biopsies were prepared for histology and immunohistochemistry. We hypothesize that SM-induced damage will compromise normal skin function due to changes in epithelial cell differentiation and epidermal thickness. Hematoxylin and eosin and Gomori's trichrome stains were used to visualize structural changes, including dermal inflammation and epidermal hyperplasia. SM induced a 37.5% increase to epidermal thickness compared to control by 9 days, interestingly by 28 days post-exposure there was an 86% increase in the epidermal thickness compared to matched control. Stratum corneum shedding, basal cell karyolysis and elongated rete ridges composed of multilayered columnar cells were evident in the neo-epidermis by 9 and still evident 28 days after SM exposure. Proliferating cell nuclear antigen (PCNA) expression, a marker of cellular division, was found to be a contiguous monolayer along the basal layer of the control tissue. By 9 days, there was an upregulation of PCNA expression at the dermal-epidermal junction and in the dermis, with some flattened nuclei and parakeratosis observed in the stratum corneum. By 28 days, PCNA expression was observed in the basal-suprabasal layers and in the dermis, while parakeratosis was no longer evident. In summary, a single SM exposure induced wounding, followed by cellular proliferation and epidermal thickening. Taken together, these data suggest that SM caused damage to the skin's structural integrity which was still observed 28 days after exposure though a contiguous neo-epidermis was evident. Further studies will include studying biomarkers to examine wound repair in swine skin. Supported by NIH AR055073, ES020721 and the School of Graduate Studies.









SM increased dermal inflammation and epidermal hyperplasia