Optimizing Nitrogen Mustard Administration to Obtain Reproducible Model Vesicant Skin Burns

Author Block: T. Roldan[1,2], F. Al-Zubaydi[1,2], G. Wahler[2,1], D. Kakkar[1,2], L. Shike[1,2], D. Gao[1,2], N. D. Heindel[2,3], J. D. Laskin[2,1], and P. J. Sinko[1,2]. *[1]Rutgers, The State University of New Jersey, Piscataway, NJ; [2]Rutgers CounterACT Center of Excellence, Piscataway, NJ; and [3]Lehigh University, Bethlehem, PA.*

Sulfur mustard (SM) is a chemical warfare vesicant that damages exposed skin, eye, and lung tissues requiring the advancement of countermeasures to develop effective therapies. Nitrogen mustard (NM) is a primary vesicating and bifunctional agent widely used as a model vesicant surrogate for SM owing to its comparable skin injuries and similar mechanisms of cytotoxicity. A consistent NM skin injury/burn animal model is required for wound healing efficacy studies. Researchers have established consistent NM burn efficacy models with mixed levels of success. Our currently used model entails shaving the dorsal skin of female CD-1 mice at the lumbar region and delivering a 20 µmol bolus of NM in acetone to the skin using 6mm glass fiber filter discs as a wound template. The NM induced skin inflammation was evaluated by punch biopsies (on day 3) of the treated area and compared to the control groups. Although this model resulted in comparable wound severity, we could not obtain highly reproducible NM skin burns. Therefore, we hypothesized the variation was related to hair shaft height, follicle density, sequence of acetone/NM administration and dose/volume delivered. The first hypothesis tested was that shaving hair resulted in variable contact between the skin surface and filter discs. To improve contact between the skin and filter discs, a chemical depilatory, Nair™, was employed to remove the hair from the epidermal surface. Results indicate that hair removal using the depilatory appreciably reduced burn incidence inconsistencies as compared to the shaving method. After shaving, the hair shaft was present above the entire epidermis and stratum corneum, while the application of the depilatory shortened the hair shaft to beneath the epidermal surface and preserved the follicle. Histological analysis revealed improved contact surface using Nair™ with no significant alterations of skin structure. In addition, it was found that by changing the sequence, volume and concentration of acetone/NM administration, model burns could be reliably and consistently produced yielding a model that allowed for countermeasure efficacy studies in rodents. *Supported by NIH grant #U54AR055073.*