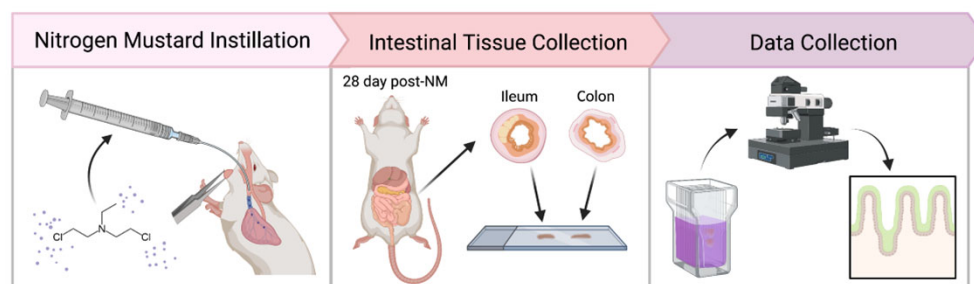


# Pulmonary Exposure to Nitrogen Mustard Induced Damage to Small Intestines in Rats

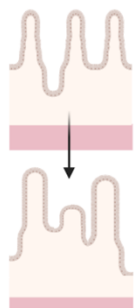
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Gastrointestinal toxicity (GI) is a characteristic response of humans to mustard vesicants, regardless of the exposure route. In present studies, we characterized GI toxicity in Wistar rats following pulmonary exposure to nitrogen mustard (NM). Rats were euthanized 28 d after exposure to aerosolized NM (0.125 mg/kg) or phosphate buffer saline (control). NM caused significant damage to the ileum including inflammation, ulceration, and blunting of villi which was adjacent to a thinned submucosa. A significant decrease in the thickness of the muscularis externa was also observed in the ileal structure ( $66.6 \pm 4.5 \mu\text{m}$  in control and  $50.4 \pm 2.5 \mu\text{m}$  in NM). Mucin-2, a gel-forming glycoprotein released from goblet cells essential for epithelial protection, was expressed in the crypts of control and released into the interstitial space. NM suppressed mucin-2 release into the interstitial space. F4/80, a murine monocyte-macrophage marker indicative of inflammation, increased following NM exposure in ileum compared to control. Serum bile acids, which are known to exert hormone-like functions via activation of nuclear and membrane-bound receptors, can modulate intestinal integrity and immunity, were found to be markedly reduced in NM animals ( $65.73 \pm 15.65 \mu\text{Mol/L}$  in control and  $19.19 \pm 3.51 \mu\text{Mol/L}$  in NM). These data demonstrate that NM causes damage to the ileal villi and crypts. Combined with alterations in bile acid homeostasis, this likely impacts normal intestinal function. Further studies will investigate mechanisms of NM damage, 3 day post-NM exposure damage, and the use of synthetic bile acid, obeticholic acid, in mitigating NM injury in rat intestines. Supported by NIH U54AR055073 and R25ES020721.

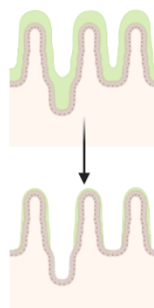


## Nitrogen Mustard Caused

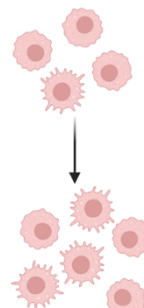
Disrupted Intestinal Structure



Decreased Mucin-2 Release



Increased Inflammation



Decreased Serum Bile Acid

