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Primary Research Interest:	Physiology
Description of Research:	The mucosal epithelial layer is densely innervated by nerve fibers originating from the enteric nervous system (ENS), which is essential for GI motility, ion secretion, fluid absorption, and epithelial barrier permeability. Unraveling the mechanisms of epithelial and ENS interactions remains technically challenging, and much work remains to be done regarding our understanding of how ENS influences intestinal epithelium. Lysophosphatidic acid (LPA) is a simple bioactive phospholipid that exhibits numerous biological functions acting through six widely distributed G protein-coupled receptors, LPA1-6. Our studies using mice with global loss of the LPA1 receptor have indicated a role for LPA1 signaling in intestinal epithelial barrier function and wound healing. Other have shown that the LPA1 receptor is a critical mediator of neurological function so that the lack of LPA1 receptor leads to stress hypersensitivity, anxious-depression phenotype, and dysregulation of pain perception. The proposed study is based on our preliminary findings that mice lacking the LPA1 receptor in the ENS (Lpar1?ENS) display dysregulated GI motility and reduced numbers of enteric neurons and glial cells. We will test the hypothesis that LPA1 receptor signaling in the ENS plays a role in the regulation of GI motility and intestinal barrier function and that the loss of LPA1 function in the ENS leads to intestinal inflammation associated with increased levels of stress.
Relevance to VA:	Gastrointestinal (GI) problems are common during military conflict, and these exert significant adverse effects on the health of service members involved in warfare. The onset of a GI disorder can be triggered by severe stress and infections of the digestive tract. It is becoming more evident that high levels of anxiety that military personnel face during war may contribute to the increased risk of developing GI disorders such as irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD). The GI tract is lined with a protective monolayer of epithelial cells that separates the host from the hostile environment of the GI tract and increased intestinal permeability has been linked to chronic GI symptoms in Gulf War veterans.