Synopsis: Migraine is the most common neurological disorder and is among the most common pain conditions. However, the pathophysiological mechanisms that contribute to migraine are not well understood. Studies in the Dussor laboratory focus on events within the cranial meninges that lead to activation of meningeal nociceptive signaling as this system likely mediates the pain phase of migraine. This lecture will focus on the role of acid-sensing ion channels (ASICs) and interleukin-6 (IL-6) in meningeal afferent signaling, plasticity that develops with repetitive stimulation, and how this system may be unique in its signaling and sensitization mechanisms.