Expression of the neuronal voltage-gated sodium channel *Scn8a* in mouse and guinea pig small intestine

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Scn8a ($Na_v1.6$) is a voltage-gated Na^+ channel alpha subunit expressed in many CNS neurons, *e.g.*, hippocampal pyramidal neurons, cerebellar Purkinje neurons, and spinal motor neurons, as well as in dorsal root ganglion neurons. Functionally, *Scn8* contributes to the large transient inward Na^+ current of the neuronal action potential with *Scn1* (aka $Na_v1.1$, RB-I) and/or *Scn2* ($Na_v1.2$, RB-II). In some neurons, it also mediates persistent sodium current and resurgent sodium current. These subthreshold Na^+ currents are two orders of magnitude smaller than the total transient current, but have a substantial effect on neuronal excitability because of the high input resistance of the membrane in the voltage range at which they are active. Two spontaneous mutations in *Scn8a* in mice have been shown to diminish resurgent and persistent current in cerebellar Purkinje neurons. The reduction in these subthreshold currents reduces the tendency of Purkinje neurons to generate repetitive spikes, reduces the average number of spikes when multiple action potentials are observed, and increases the inter-spike interval.

While the spatial expression pattern of *Scn8a* in brain and spinal cord has been the subject of several studies and we are beginning to understand its function in a few neuronal subtypes in the CNS, nothing is known about its role in the enteric nervous system. If *Scn8a* is expressed in this system, its ability to carry subthreshold currents and thereby affect excitability could be functionally important. We are conducting pilot studies to assess the potential role of *Scn8* in the enteric nervous system. As a first step, we used RT-PCR to detect *Scn8a* message in small intestinal wall from mouse and guinea pig. Using *Scn8a*-specific primers, we were able to amplify fragments of *Scn8a* message from preparations of longitudinal and/or circular smooth muscle plus the associated neuronal plexus from mouse and guinea pig jejunum. This is consistent with expression of *Scn8a* in enteric neurons—which has not previously been reported—but does not provide quantitative information or identify the specific cell type(s) involved. Given this lack of cellular specificity and the very high sensitivity of PCR-based detection methods, further studies will be conducted to assess the functional significance of this finding by immunohistochemistry and electrophysiological analysis of the effect of a null mutation in the mouse on the functional properties of enteric neurons.