**Introduction**

The Nav1.8 TTX resistant (TTX-r) voltage-gated sodium channel is expressed exclusively in the nociceptor sub-population of primary afferent neurones and has slow inactivation kinetics and rapid recovery from inactivation (Cummins & Waxman 1997; Akopian et al., 1996). These biophysical properties mean that Nav1.8 contributes to both electrogenesis and the maintenance of repetitive firing of action potentials (Blair & Bean 2002; Renganathan et al., 2001; Waxman et al., 2001). The expression and biophysical properties of Nav1.8 can be modulated by pro inflammatory mediators and findings in the literature support a key role for Nav1.8 in pain signalling (England et al., 1996; Roza et al., 2003; Kerr et al., 2001; Coward et al., 2000; Akopian et al., 1999). Although the biophysical properties and pharmacology of native Nav1.8 currents has been investigated extensively in rodent DRGs, there is little reported data for human DRGs. Here we have characterised Nav1.8 current from TTX-r channels in human DRG and compared the biophysical properties with those of recombinantly expressed hNav1.8 channels. This work shows that the properties of the recombinantly expressed hNav1.8 channels closely match those of native TTX-r channels recorded from human DRG and that Nav1.8 has a functional role in these neurones.

**Materials and Methods**

Electrophysiological recordings were made in voltage clamp mode from HEK cells expressing human recombinant Nav1.8β1 and in also from human DRGs within 12-24 hours of isolation, containing native TTX-r channels. For the latter, recordings were also made in current clamp mode. The biophysical properties and pharmacology of the channels was determined using a variety of protocols and commercially available compounds. In order to eliminate contamination by Nav1.9 currents recordings from human DRG were made from a holding potential of -80 mV at which there is little Nav1.9 conductance available for activation.

**Results & Conclusion**

In this poster we have characterised the rapidly inactivating TTX-r current recorded from human DRG and proven pharmacologically using a selective blocker that the current recorded is Nav1.8. TTX-r currents have previously been reported in human DRGs, however, as the dataset was small, the currents were not fully characterised (Waxman et al., 1999).

The biophysical properties of recombinantly expressed hNav1.8 channels in a variety of neuronal and non-neuronal backgrounds closely matched those of the TTX-r current recorded from human DRGs. The V_{1/2} activation for human TTX-r is -9.8 mV, which is approximately 9 mV more hyperpolarised than V_{1/2} activation of recombinantly expressed hNav1.8β1 in HEK-293 cells (V_{1/2} activation -0.98 mV). V_{1/2} activation of human TTX-r more closely matches V_{1/2} activation values reported for hNav1.8 expressed in neuronal background (e.g. SH-SY5Y: -11 mV, Dekker et al., 2005; ND7-23: -2.7 & -9.4 mV, Browne et al., 2009; John et al., 2004). The V_{1/2} activation of human TTX-r is also similar to values reported for TTX-r in rat DRG (-17 mV, John et al., 2004; -16 mV, Rush et al., 1998). The V_{1/2} fast inactivation of human TTX-r was -35.4 mV compared to -42.3 mV for hNav1.8β1 in HEK-293 cells. This is within the range of published values for hNav1.8 expressed in various neuronal backgrounds (SH-SY5Y: -50 mV, Dekker et al., 2005; ND7-23: -30.8 mV, John et al., 2004). V_{1/2} fast inactivation values reported for rat TTX-r are clustered around -25 and -46 mV (Rush et al., 1998).

Recovery from inactivation was fitted with a single exponential for the recombinantly expressed hNav1.8β1, which is approximately 9 mV more hyperpolarised than V_{1/2} activation values reported for the human TTX-r channel (τ_{fast} = 4.5 ms and τ_{slow} = 2403 ms). Two exponential components have also been reported for recombinantly expressed Nav1.8 and rat TTX-r: τ_{fast} = 5.9 ms and τ_{slow} = 83.7 ms; τ_{fast} = 22.7 ms and τ_{TTX-r} = 15.7 ms and τ_{TTX-r} = 119.3 ms (Browne et al., 2009; John et al., 2004).

Application of a selective Nav1.8 blocker A803467, inhibited the TTX-r current in human DRG with an IC_{50} of 5 nM. Application of 100 nM A803467 inhibited 76 % of the current in Nav1.8β1 in HEK-293 cells, which suggests that A803467 has similar potency against both human TTX-r and heterologously expressed Nav1.8. This is further demonstrated by previous data from recombinantly expressed human Nav1.8 using an identical voltage protocol (A803467 IC_{50} = 8 nM, Jarvis et al., 2007). Using current-clamp recordings from human DRGs, 100 nM A803467 reduced firing in response to increasing current injections as seen previously in rat DRG neurones (Jarvis et al., 2007).

Therefore, under these recording conditions we have shown both biophysically and pharmacologically that Nav1.8 is present and functional in human DRG and that the properties of recombinantly expressed hNav1.8 channels expressed in a variety of neuronal and non-neuronal backgrounds, closely resemble those of the native channel.

**References**


**Cummins TR, Waxman SG (1997) Downregulation of tetrodotoxin resistant sodium currents and upregulation of a rapidly repressing tetrodotoxin resistant sodium current in small spinal sensory neurons after nerve injury. J. Neuroscience 17:3503-3511.**


Reference images have been uploaded. The poster is based on the published work of Liz Payne et al., 2004; Victor A. Panchenko et al., Andrea Ghetti et al., Ari Alexandrou et al., Paul E. Miller et al.