Voltage-Gated Sodium Channel Knockout Mice: Tools for Developing Therapeutics for the Treatment of Pain

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Summary

Scientists at University College London have developed Voltage-Gated Sodium Channel subtype specific conditional knockout mice which provide invaluable tools for the development of therapeutics for the treatment of pain.

The Technology and its Advantages

University College London have developed the following subtype specific knockout mice:

-"NaV1.3 flox"-Transgenic mouse expressing floxed NaV1.3 sodium channel gene

-"NaV1.7 flox"-Transgenic mouse expressing floxed NaV1.7 sodium channel gene (as described in Nassar et al. 2004)

-"NaV1.8 Cre"-Transgenic mouse expressing Cre-recombinase gene under the control of the NaV1.8 sodium channel gene promoter (as described in Stirling et al. 2005)

- A tamoxifen inducible pan-DRG Cre mouse.

Market Opportunity

Voltage-gated sodium channels underlie electrical signalling in biological tissues and low doses of channel blockers have been used for many years as analgesics. Nine voltage-gated sodium (NaVs) channels are expressed in complex patterns in mammalian nerve and muscle. It is now clear that some sodium channel subtypes are selectively expressed in specialised damage-sensing peripheral neurons (nociceptors). These channels may be the principal site of action of non-specific analgesic sodium channel blockers like lidocaine, and providing appealing targets for the development of selective blockers with fewer side effects. The four sodium channel subtypes that are of particular interest because of their restricted distribution in nociceptors are the tetrodotoxin-sensitive (TTX-S) channels NaV1.3 and NaV1.7 and the tetrodotoxin-resistant (TTX-R) channels NaV1.8 and NaV1.9. Intriguingly, a role for voltage-gated sodium channels in immune cell function has also been reported at the same

time as a crucial role for these cells in chronic pain has been established. These channels are currently regarded as being amongst the best validated targets for pain therapy and in particular have caught widespread attention following the discovery of the remarkable analgesic phenotype associated with the loss-of-function NaV1.7 mutations in humans. As a result the development of subtype selective channel blockers, whilst technically challenging, is the focus of many current pain drug discovery efforts. The channel subtype specific knockout mice developed at University College London provide an invaluable tool to support such efforts.

Further Information

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