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## **Antinociceptive targets for spider toxins in adult dorsal root ganglia neurons**

Tânia C. GONCALVES<sup>1,2</sup>, Evelyne BENOIT<sup>2,3,\*</sup>, Michel PARTISETI<sup>1</sup>, Denis SERVENT<sup>2</sup>

<sup>1</sup>Sanofi R & D, Integrated Drug Discovery – High Content Biology, F-94440 Vitry-sur-Seine, France. <sup>2</sup>DRF, Institut des Sciences de la Vie Frédéric Joliot, SIMOPRO, CEA de Saclay, Université Paris-Saclay, F-91191 Gif-sur-Yvette, France. <sup>3</sup>Institut des Neurosciences Paris-Saclay, UMR CNRS/Université Paris-Sud 9197, F-91198 Gif-sur-Yvette, France.

\* Corresponding author; E-mail: evelyne.benoit@cea.fr

Although necessary for human survival, pain may sometimes become pathologic if long-lasting and associated with alterations in its signaling pathway. Opioid painkillers are officially used to treat moderate to severe, and even mild, pain. However, the consequent strong and not so rare complications that occur, including addiction and overdose, combined with pain management costs, remain an important societal and economic concern. In this context, animal venom toxins represent an original source of peptides for therapeutic treatment to fight against pain and avoid central side effects, and the most appropriate targets seem to be those of neurons located in the dorsal root ganglia (DRG) which convey pain from the skin and tendons to the central nervous system (CNS). Hence, the DRG neurons are well-known to express various families of transmembrane proteins, including ion channels, G-protein-coupled receptors and gap junctions/pannexins. Among the ion channel family, the most studied target for pain treatment is the voltage-gated sodium (Nav) channel subtype Nav1.7. The attraction of scientists for this channel subtype is due to its validation by human genetic diseases as a pain target. Many studies have been reported in the literature to describe gating modulators or pore blockers that affect the functional properties of Nav1.7 channel subtype. The present overview will focus on the fascinating spider venom toxins which represent an original source of proteins possessing complex structures associated with specific electrophysiological effects and prone to be more selective for the Nav1.7 channel subtype mainly expressed in DRG neurons. It will detail (i) the characteristics of these primary sensory neurons, (ii) the electrophysiological properties of the different Nav channel subtypes expressed in these neurons, with a particular attention on the Nav1.7 subtype, and (iii) the features of spider venom toxins, shaped of inhibitory cysteine knot motif, that present high affinity for the Nav1.7 subtype associated with evidenced analgesic efficacy in animal models.

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**Keywords:** spider toxins, dorsal root ganglia neurons, pain, voltage-gated sodium channels, electrophysiology

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