Voltage Sensor Probes as an efficient tool to screen for new modulators of voltage-gated sodium channels

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Auteur	Coquerel, Quentin [1], Le Ray, Anne-Marie [2], Said-Hassane, Charifat [3], Mattei, César [4], Guérineau, Nathalie C [5], Bréard, Dimitri [6], Siegler, Benjamin [7], Richomme, Pascal [8], Legros, Christian [9]
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Mots-clés	Alkaloids [10], voltage sensor probes [11], Voltage-gated sodium channel [12]
Résumé en anglais	Voltage-gated sodium channels (Nav) constitute the molecular targets of clinically used drugs for treatments of various diseases (epilepsies, chronic pain, cardiac arrythmies…) and also of numerous toxins from animals and plants. The development of useful screening assay for the discovery of new ligands in/ from chemicals libraries or animal venoms and either plant extract still represents a challenge of great interest. Here, we used a mammalian GH3 cells that constitutively express at least three different brain Nav channels isoforms (Nav1.1, Nav1.2, Nav1.3 and Nav1.6) in order to identify in a library of in-house natural alkaloids, novel compounds of therapeutical interest. For this screening, we developed a method based on the use of Voltage Sensor Probes (VSPs) that we adapted to detect both activators and blockers of Nav channels. Among 62 compounds tested, 5 isoquinolines appeared as potent Nav channels inhibitors. Other compounds were characterized as specific gating modifier of Nav channels. While most of these alkaloids have been already described in the literature, their abilities to act on Nav channels were unknown. In conclusion, we demonstrated the potency of this novel screening method using VSPs to identify novel ligands of Nav channels of therapeutical interests. References: 1. Salat, K. et al. (2014) EOID 23:1093-1104 2. Yu, F.H. et al (2003) Genome Biol. 4:
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