


**MIGRATION**

## Exchange to migrate

Activation of GABA<sub>A</sub>Rs (γ-aminobutyric acid type A receptors) leads to the elevation of intracellular Ca<sup>2+</sup> concentration ([Ca<sup>2+</sup>]<sub>i</sub>) in immature neurons, through a well-established signalling pathway that is important for neuronal migration. NG2 cells — a group of glial precursors — also express GABA<sub>A</sub>Rs; however, the function of these receptors in NG2 cells was unknown. Tong *et al.* have now shown that the

activation of GABA<sub>A</sub>Rs in NG2 cells triggers a different Ca<sup>2+</sup> signalling pathway that involves reversal of the activity of the Na<sup>+</sup>-Ca<sup>2+</sup> exchanger 1 (NCX1) and is required for the migration of NG2 cells during development.

The authors showed that activation of GABA<sub>A</sub>Rs led to increased [Ca<sup>2+</sup>]<sub>i</sub> in cultured NG2 cells as well as in hippocampal slice preparations from juvenile rats, but not if the expression of non-inactivating Na<sup>+</sup> channels or NCX1 was downregulated by small interfering RNAs or if these proteins were inhibited pharmacologically. They concluded that stimulation of GABA<sub>A</sub>Rs in NG2 cells activates non-inactivating Na<sup>+</sup> channels, resulting in increased [Na<sup>+</sup>]<sub>i</sub> that triggers reversal of the activity of NCXs and ultimately leads to increased [Ca<sup>2+</sup>]<sub>i</sub> by exchanging intracellular Na<sup>+</sup> for extracellular Ca<sup>2+</sup>.

The authors next tested whether this signalling mechanism is important for the migration of NG2 cells. NG2 cells in culture and from brain explants migrated towards a source of

GABA. Pharmacological inhibition of GABA<sub>A</sub>Rs, Na<sup>+</sup> channels or NCX1, or downregulation of Na<sup>+</sup> channels or NCX1 expression using small interfering RNAs, impaired migration, providing evidence that the Ca<sup>2+</sup> signalling mechanism investigated is important for the migration of NG2 cells.

This study shows that the signalling mechanisms that underlie GABA-induced Ca<sup>2+</sup> elevation in NG2 cells and immature neurons, which is required for their migration, are very different. In neurons Ca<sup>2+</sup> elevation is driven by voltage-gated Ca<sup>2+</sup> channels and activation of N-methyl-D-aspartate receptors, whereas NG2 cells use the Ca<sup>2+</sup> signalling pathway described above. It will be interesting to determine whether this signalling mechanism is also used by other migrating cells.

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**ORIGINAL RESEARCH PAPER** Tong, X.-p. *et al.* Ca<sup>2+</sup> signaling evoked by activation of Na<sup>+</sup> channels and Na<sup>+</sup>/Ca<sup>2+</sup> exchangers is required for GABA-induced NG2 cell migration. *J. Cell Biol.* **186**, 113–128 (2009)

