

## **KCC2 ion transporter as a novel therapeutic target for epilepsy**

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The Cl<sup>-</sup>-extruding transporter KCC2 (SLC12A5) critically modulates GABA<sub>A</sub> receptor signalling via its effect on neuronal Cl<sup>-</sup> homeostasis. Previous studies have shown that KCC2 was downregulated in both epileptic patients and various epileptic animal models. We discovered that the in vitro dual phosphorylation of Thr906 and Thr1007 in the intracellular carboxyl (C)-terminal domain of KCC2, mediated by the Cl<sup>-</sup>-sensitive WNK-SPAK serine-threonine protein kinase complex, maintains the depolarizing action of GABA in immature neurons by antagonizing KCC2 Cl<sup>-</sup> extrusion capacity. This indicates that dephosphorylation of KCC2 at Thr906 and Thr1007 is a potent activator of KCC2 activity, and small molecular targets WNK-SAPK kinase signalling may be a novel therapeutic strategy for epilepsy.