Rapid down-regulation of the rat glutamine transporter SNAT3 by a caveolin-dependent trafficking mechanism in *Xenopus leavis* oocytes

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The glutamine transporter SNAT3 is involved in the uptake and release of glutamine in the brain, liver, and kidney. Substrate transport is accompanied by Na^+ cotransport and H^+ antiport. In this study, treatment of *Xenopus laevis* oocytes expressing rat SNAT3 with the phorbol ester PMA resulted in a rapid downregulation of glutamine uptake in less than 20 minutes. PMA treatment of oocytes co-expressing SNAT3 and the monocarboxylate transporter MCT1 reduced SNAT3 activity only, demonstrating the specificity of the regulatory mechanism. Single or combined mutations of seven putative phosphorylation sites in the SNAT3 sequence did not affect the regulation of SNAT3 by PMA. Expression of an EGFP-SNAT3 fusion protein in oocytes established that the downregulation was caused by the retrieval of the transporter from the plasma membrane. Co-expression of SNAT3 with dominant negative mutants of dynamin or caveolin revealed that SNAT3 trafficking occurs in a dynamin-independent manner and is influenced by caveolin. While System N activity was not affected by PMA in cultured astrocytes, a downregulation was observed in HepG2 cells.