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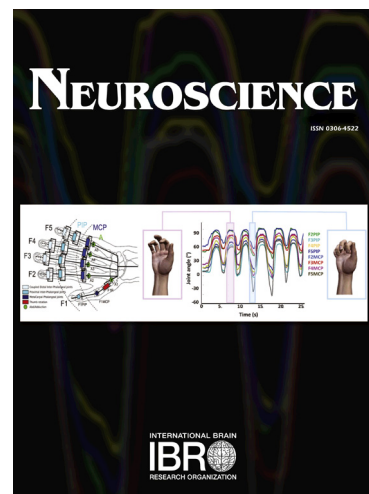
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## **Sonic hedgehog induces GLT-1 degradation via PKC delta to suppress its transporter activities**

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**Keywords:** sonic hedgehog, GLT-1, PKC, astrocytes.

**Abbreviations:** SHH, sonic hedgehog; PKC $\delta$ , PKC delta; Smo, Smoothed; STP, staurosporine; Bis II, Bisindolylmaleimide II; MTT, thiazolyl blue tetrazolium bromide; TfR: transferrin receptor; CYC, cyclopamine; Asp, Aspartate; PMA, phorbol 12-myristate 13-acetate; UCPH, UCPH101; WAY, WAY213613.

**Abstract**—GLT-1 is mainly expressed in astrocytes and has a crucial role in glutamate uptake. Sonic hedgehog (SHH) can inhibit glutamate uptake and its pathway is activated in many brain diseases related with glutamate excitotoxicity. However, whether SHH regulates GLT-1 to affect glutamate uptake is not clear. Here, we use pharmacological and genetic methods to show that SHH induces GLT-1 degradation in astrocytes in a manner that is dependent on PKC delta (PKC $\delta$ ) to regulate GLT-1 activities. GLT-1 protein levels are reduced as early as 2 hs in astrocytes after incubation with SHH, whereas its mRNA levels are not

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