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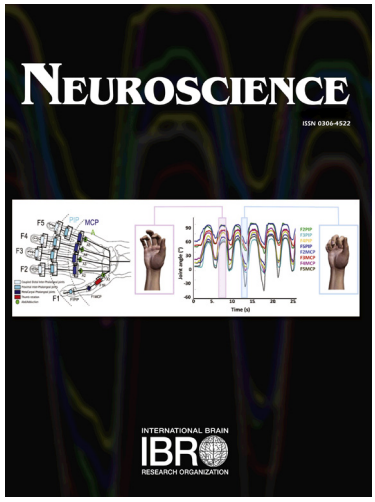

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Sonic hedgehog induces GLT-1 degradation via PKC delta to suppress its transporter activities

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

Abbreviations: SHH, sonic hedgehog; PKCδ, PKC delta; Smo, Smoothened; STP, straurosporine; 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 (PKCδ) 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