Abstract

Regulation of Extrasynaptic Glutamatergic Signaling by Polysialylated NCAM in Health and Disease †

Alexander Dityatev 1,2,3

1 Molecular Neuroplasticity Group, German Center for Neurodegenerative Diseases (DZNE), 39120 Magdeburg, Germany; alexander.dityatev@dzne.de
2 Medical Faculty, Otto-von-Guericke-University of Magdeburg, 39120 Magdeburg, Germany
3 Center for Behavioral Brain Sciences (CBBS), 39106 Magdeburg, Germany
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Abstract: The neural cell adhesion molecule NCAM is known to mediate cell–to–cell and cell–to–extracellular matrix (ECM) adhesion via homophilic and heterophilic interactions. During brain development, NCAM and the associated glycan, polysialic acid (polySia), play important roles in cell migration, proliferation, neurite outgrowth, and synaptogenesis. In the adult rodent brain, NCAM regulates synaptic plasticity, learning, and memory. Dysregulated cortical expression of NCAM and polySia has been reported in Alzheimer’s disease and schizophrenia. Our data demonstrate i) the importance of polySia–NCAM in the balancing of signaling through synaptic/extrasynaptic NMDA receptors and ii) the therapeutic value of short defined-length polySia fragments to restrain GluN2B-mediated signaling in several animal models of neurological and psychiatric diseases.

Keywords: LTP; synaptic plasticity; polysialic acid; schizophrenia; Alzheimer’s disease; NMDA receptor

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Conflicts of Interest: A.D. filed an international patent application on “Polysialic acid and derivatives thereof, pharmaceutical composition and method of producing polysialic acid”, WO2020025653A2. A.D. is the editor-in-chief in Cell microenvironment section of Cells.
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