

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

[†] Presented at Cells, Cells and Nothing but Cells: Discoveries, Challenges and Directions, 6–8 March 2023; Available online: <https://cells2023.sciforum.net/>.

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 fasciculation, 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



Citation: Dityatev, A. Regulation of Extrasynaptic Glutamatergic Signaling by Polysialylated NCAM in Health and Disease. *Biol. Life Sci. Forum* **2023**, *21*, 30. <https://doi.org/10.3390/blsf2023021030>

Academic Editor: Alexander E. Kalyuzhny

Published: 3 April 2023



Copyright: © 2023 by the author. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

Funding: This work has been supported by the Italian Institute of Technology and DZNE, the European Union's Horizon 2020 Research and Innovation Programme under the Marie Skłodowska-Curie grant agreement no. 642881 (ECMED), and DFG SFB 1436 TP A03 (Project-ID 425899996).

Institutional Review Board Statement: All treatments and behavioral procedures were conducted in accordance with animal research ethics standards defined by German law and approved by the Ethical Committee on Animal Health and Care of the State of Saxony-Anhalt (42502-2-1159 DZNE, 42502-2-1343 DZNE, and 42502-2-1346 DZNE) or by the Italian Committee on Animal Health and Care of the governmental body in Rome.

Informed Consent Statement: Not applicable.

Data Availability Statement: Data will be made available on request.

Acknowledgments: I thank Jenny Schneeberg and Katrin Boehm for excellent technical assistance, Inseon Song for helpful discussions of patch-clamp recordings, Rahul Kaushik for helpful discussions of immunohistochemistry, Maura Ferrer for help with spine imaging, Pierre Paoletti for the GluN1 expression vector, and Hristo Varbanov, Shaobo Jia, Gaga Kochlamazashvili, Subhrajit Bhattacharya, Manal Ali Buabeid, Mohamed El Tabbal, Hussam Hayani, Stoyan Stoyanov, Weilun Sun, Oleg Senkov, Hauke Thiesler, Iris Röckle, Herbert Hildebrandt, Eckart Gundelfinger, Vishnu Suppiramaniam, and Rita Gerardy-Schahn for their contributions and support in analysis of polySia functions.

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*.

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.