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Bonn Lecture Series in Neuroscience

Negr1 and FGFR2 cooperatively regulate cortical development and core behaviors related to autism disorders in mice (the other side of the PCHD19 story).

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Life & Brain, Seminar Room, Ground Floor

Autism spectrum disorders (ASD) are neurodevelopmental conditions with diverse etiologies, all characterized by common core symptoms, such as impaired social skills and communication, as well as repetitive behavior. Cell-adhesion molecules (CAMs), receptor tyrosine kinases (RTKs) and associated downstream signaling have been strongly implicated in both neurodevelopment and ASD. We found that downregulation of CAM Negr1 or RTK FGFR2 similarly affects neuronal migration and spine density during mouse cortical development in vivo and results in impaired core behaviors related to ASD. Mechanistically, Negr1 physically interacts with FGFR2 and modulates FGFR2-dependent ERK and AKT signaling by decreasing FGFR2 degradation from the plasma membrane. Accordingly, FGFR2 overexpression rescues all defects due to Negr1 knockdown in vivo. Negr1 KO mice present phenotypes similar to Negr1-downregulated animals. These data indicate that Negr1 and FGFR2 cooperatively regulate cortical development and suggest a role for defective Negr1-FGFR2 complex and convergent downstream ERK and AKT signaling in ASD.

Selected Publications

Szczurkowska J, Cwetsch AW, Dal Maschio M, Ghezzi D, Ratto GM, **Cancedda L** (2016) Targeted in vivo genetic manipulation of the mouse or rat brain by in utero electroporation with a triple-electrode probe. Nature Protocols, Mar;11(3):399-412.

Deidda G, Parrini M, Naskar S, Fernandez I, Contestabile A°, **Cancedda L°** (2015) Reversing excitatory GABAAR signaling restores synaptic plasticity and memory in a mouse model of Down Syndrome. Nature Medicine, 21(4):318-26.

Deidda G, Allegra M, Cerri C, Naskar S, Bony G, Zunino G, Bozzi Y, Caleo M*, **Cancedda L*** (2015) Early depolarizing GABA controls critical-period plasticity in the rat visual cortex. Nature Neuroscience, 18(1):87-96.

Perlini LE, Szczurkowska J, Ballif BA, Sacchetti S, Piccini A, Giovedì S, Benfenati F*, **Cancedda L*** (2015) Synapsin III Acts Downstream of Semaphorin 3A/CDK5 Signaling to Regulate Radial Migration and Orientation of Pyramidal Neurons in Vivo. Cell Reports, 11(2):234-48.

Dal Maschio M, Ghezzi D, Bony G, Alabastri A, Deidda G, Brondi M, Sulis Sato S, Proietti Zaccaria R, Di Fabrizio E, Ratto GM, **Cancedda L** (2012) High-performance and Site-directed in Utero Electroporation by a Triple-electrode Probe. Nature Communications, 3:960.

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