

Brain Disorders and Therapeutics

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Pharmacotherapy with Sertraline improves Brain development and Behavior in a mouse model of CDKL5 Deficiency Disorder

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CDKL5 deficiency disorder (CDD) is a rare neurodevelopmental disease caused by de novo mutations in the X-linked CDKL5 gene. The consequent misexpression of the CDKL5 protein in the nervous system leads to a severe phenotype characterized by intellectual disability, motor impairment, visual deficits and early-onset epilepsy. No therapy is available for this devastating disorder. Recent studies have implicated alterations in serotonin (5-HT) signaling in neurodevelopmental disorders (NDDs), such as autism spectrum disorders, RTT and Down syndrome, suggesting that drugs targeting the 5-HT system might be a valid treatment option for NDDs. Interestingly, we found a deregulation of the 5-HT_{2A} receptor expression, an important player in cognitive processes, in the hippocampus and cortex of an animal model of CDD, the Cdkl5 knockout (KO) mouse, suggesting a Cdkl5-dependent dysregulation of the 5-HT system. Importantly we found that treatment with Sertraline, a

selective serotonin reuptake inhibitor, improved brain development and behavior in Cdkl5 KO mice. Our result might represent a fundamental pre-clinical step with a high translational impact for the amelioration of CDKL5-related symptoms.

Speaker Biography

Elisabetta Ciani, PhD, Neurophysiologist. Professor of Physiology at the Medical School of the University of Bologna. Trained in genetic, molecular and cellular biology during her postdoc at the Max Planck Institute, Munich (1995-1999). Dr. Ciani is an expert in dendrite and synapse development in the Central Nervous System. In particular, she studies development of dendritic spines and neuronal maturation in various models of neurodevelopmental disorders including Down syndrome and CDKL5 disorder. Her group has collaborated to develop a first mice model of the CDKL5 disorder. She has developed a protein therapy for CDKL5 disorder (inventor, Patent WO2015128746A3). She has 76 publications, and her publication H-index is 35.

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