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ROSSINI

peRsistence Of tranSient neuronS In Neurodevelopmental dIsorders

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Neurodevelopmental disorders are disabilities involving brain dysfunction as a result of altered brain assembly during embryonic development. They include autism, attention-deficit/hyperactivity disorder, intellectual disability, cerebral palsy, and various forms of epilepsy. Understanding deficits involved in these disorders is of utmost importance in the search for therapeutic strategies to cure these patients. A variety of mechanisms may be involved in abnormal brain development, including the generation of neurons, their migration and their proper connections. In addition, a form of 'programmed cell death' is emerging as a novel, yet poorly studied, mechanism for proper brain development. Some neurons (including a group of neurons called 'Cajal-Retzius cells') appear transiently during brain development where they are involved in the construction of neural circuits and are programmed to die at the end of brain maturation. Aberrant survival of these neurons has been found in patients with neurodevelopmental disorders associated with epilepsy. Our teams have discovered that forcing just some of these neurons to survive after birth perturbs brain wiring, leading to aberrant brain activity and epileptic seizures. The ROSSINI project gathers European experts in brain development and function using complementary advanced techniques to study how the aberrant survival of Cajal-Retzius cells in mice and humans leads to altered brain activity in neurodevelopmental disorders. In this project, we aim to identify key mechanisms of 'programmed cell death' during brain development and evaluate its role in neurodevelopmental disorders associated with epilepsy, paving the way towards identification of novel targets or strategies for therapeutic intervention in these disorders.