Researchers identify new model of cerebral cortex development linked to reelin protein expression

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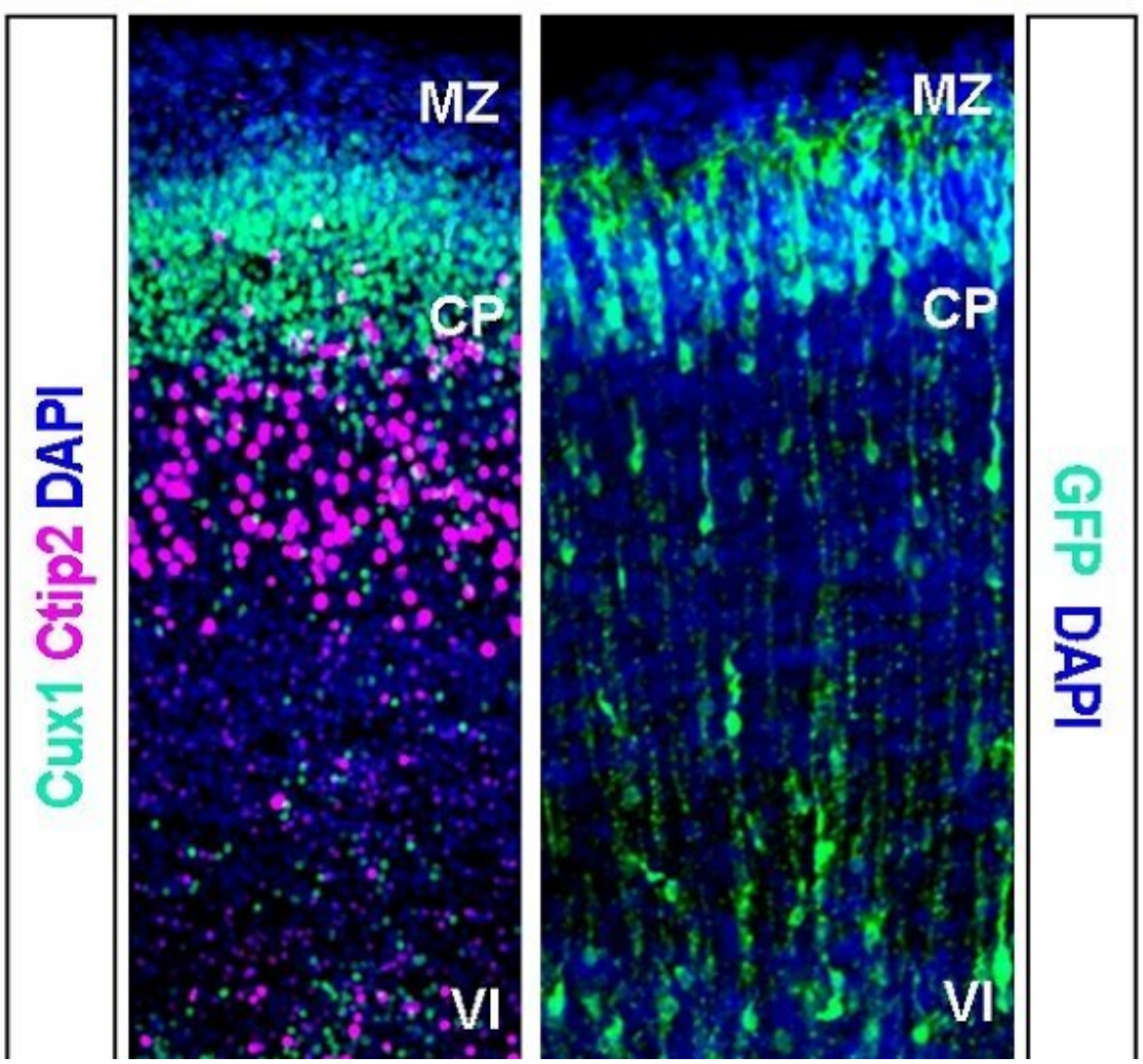

Reelin deficit in Cajal-Retzius cells during development alters the migration of

neurons destined for the upper layers (green) that become ectopically located in the lower layers of cerebral cortex (confocal microscopy images). Credit: University of Barcelona

The correct development of the brain cortex is an essential process for the acquisition of correct cognitive skills. Reelin, a key extracellular protein in neuronal migration and synaptic plasticity, is determinant in this process. For this reason, the dysfunction—genetic or at an expression level—of this protein is involved in neurodevelopmental pathologies—such as lissencephalies, epilepsy or some psychiatric disorders, particularly autism, schizophrenia and bipolar disorder—or neurodegenerative diseases.

Now, an article published in the journal *Proceedings of the National Academy of Sciences* (*PNAS*) reveals the decisive role of reelin expressed by the Cajal-Retzius pioneer neurons (CR) or cortical GABAergic neurons in the process of corticogenesis and neuronal migration. The study was led by Professor Eduardo Soriano, from the Department of Cell Biology, Physiology and Immunology of the Faculty of Biology and the Institute of Neurosciences (UBNeuro) of the UB, and the Biomedical Research Networking Center on Neurodegenerative Diseases (CIBERNED), and its first authors are the researchers Alba Vílchez and Yasmina Manso (UB-UBNeuro-CIBERNED).

The study is based on the analysis of genetically modified mice to inactivate the reelin gene in pioneer CR neurons and cortical GABAergic interneurons. While CR cells play an essential role at early stages, "the study stresses the fundamental role of the GABAergic interneuron-derived reelin in late neuronal migration," says Professor Eduardo Soriano.

A new model for reelin protein action

The team also described the existence of transient migratory deficits in some neuronal populations, a process that indicates that reelin expressed by any other of the neuronal populations is sufficient to reverse and compensate for some effects in cortical lamination in the brain. Based on this study, the authors present a new model of action for reelin in the development of the cerebral cortex based on the cooperation and the spatial, cellular and sequential specific expression of this key protein.

Several neuropsychiatric disorders are linked to alterations in neuronal migration and reelin deficits in interneurons. "Thus, this study can provide a better understanding of the mechanisms associated with human brain disorders related to reelin deficits associated with migration alteration," concludes the research team.

More information: Alba Vílchez-Acosta et al, Specific contribution of Reelin expressed by Cajal–Retzius cells or GABAergic interneurons to cortical lamination, *Proceedings of the National Academy of Sciences* (2022). DOI: 10.1073/pnas.2120079119

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