

PRESS RELEASE

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Researchers discover gene essential to cerebellum formation

Scientists have identified a molecular switch that causes the differentiation of neurons in the cerebellum, a part of the brain that helps to regulate motor functions. Their work appears online this week in *Proceedings of the National Academy of Sciences USA*.

A study published this week in the scientific journal PNAS provides new information on the origin of different cells in the cerebellum, an important component of the central nervous system found in all vertebrates, including humans, and the part of the brain that controls movement. The study was completed by researchers from the Institute for Research in Biomedicine (IRB Barcelona), the Department of Cell Biology of the University of Barcelona (UB), the IMIM-Hospital del Mar, Pompeu Fabra University (UPF) and Vanderbilt University (Nashville, Tennessee, USA). The main authors of the study are Dr. Marta Pascual (IRB Barcelona and UB) and Ibane Abasolo (IMIM-Hospital del Mar-UPF).

Co-author of the study, Francisco X. Real, coordinator of the Research Unit on Cell and Molecular Biology at IMIM-Hospital del Mar and Professor at the UPF, explains that “this discovery sheds new light on the mechanisms of brain formation and has potential future applications for regenerative medicine. It provides crucial insight into the manipulation of truncal nerve cells (or stem cells) and their selective differentiation into ‘gabergic’ neurons, or cells that contain the neurotransmitter gamma-aminobutyric acid (GABA) and that act as inhibitors.

Eduardo Soriano, Principal Investigator of the Developmental Neurobiology and Regeneration laboratory at IRB Barcelona, and professor at the UB, maintains that the study explains two important principles: first, “that the protein Ptf1a/p48 is needed for the production and differentiation of Purkinje neurons, the most important cells in the cerebellum”; and second, “that in the absence of this protein, the progenitor cells that should produce Purkinje neurons do not differentiate correctly and instead produce a different type of neuron, granular cells, indicating that Ptf1a/p48 acts as a molecular switch.”

The researchers hypothesized that a transcription factor, whose function is well known in the pancreas and which appears to play a role in the nervous system, is also involved in the development of the cerebellum. In order to test their idea, and characterize the new mechanism of cell differentiation, the authors used laboratory rats with a deactivated gene that codes for the Ptf1a/48 protein, and compared them with rats that express the gene normally. Their conclusions provide new insight into origin of nerve cells that form the cerebellum in higher organisms.

In a second research project, led by Francisco Real and Eduardo Soriano and funded by the Fundación La Caixa, the scientists aim to explore the potential of this gene to produce Purkinje neurons in a laboratory setting. The researchers will investigate whether the expression of Ptf1a/p48 can induce the production of Purkinje cells from stem cells and neurospheres, progenitor cells of adult neurons. This study is an important step toward understanding rare diseases, such as cerebellar ataxias, which is characterized by the degeneration of Purkinje cells. Producing this type of cell in the lab may lead to future neuronal replacement therapy. ■

Source article: Pascual M, Abasolo I, Mingorance-Le Meur A, Martínez A, Del Rio JA, Wright CVE, Real FX and Soriano E (2007) Cerebellar GABAergic progenitors adopt an external granule cell-like phenotype in the absence of Ptf1a transcription factor expression. Proceedings of the National Academy of Sciences USA

About IRB Barcelona

The Institute for Research in Biomedicine (IRB Barcelona) is an international centre of excellence in basic and applied biomedical research, funded by the Government of Catalonia and located at the Parc Científic de Barcelona on the University of Barcelona campus. At present, it comprises 25 research groups organised into five Programmes: Cell and Developmental Biology, Chemistry and Molecular Pharmacology, Molecular Medicine, Oncology and Structural and Computational Biology. Director: Joan Guinovart; Adjunct Director: Joan Massagué. www.irbbarcelona.org

About IMIM Hospital del Mar

The IMIM-Hospital del Mar is a public research institute, created by the City Council of Barcelona in 1947, focused on scientific research in biomedicine and health, as well as on the training of highly qualified researchers in these fields. It comprises 18 multidisciplinary research units whose activities include: basic, clinical, and epidemiological cancer, clinical and epidemiological studies on drugs and substance abuse, studies on the effectiveness of health care services, cardiovascular diseases, respiratory medicine and environmental health, and biomedical informatics. Direction: Miguel López-Botet. www.imim.es