A team from ULB, HUDERF and (IB) ² improves the genetic decoding of neurodevelopmental disorders

A result that will help in the future diagnosis of children with neurodevelopmental disorders, such as intellectual disability, autism or schizophrenia. A video illustrates this scientific analysis with medical applications.

A key question in biology is understanding how brain works. Its basic working units, the neurons, transmit information in the form of electrical impulses and chemical signals. Alterations in the function of the neurons can lead to neurological and psychiatric disorders. Neurodevelopmental disorders (NDDs) are a group of frequent and often severe pediatric conditions, that can manifest, for example, as intellectual disability, autism or early-onset psychiatric symptoms. The recent development of higher resolution genetic diagnostic tools (like having better telescopes in astronomy) has underlined the prevalence of genetic anomalies, such as copy number variations (for example, loss of a gene), in children with NDDs.

Two HUDERF patients with neurodevelopmental disorders (here cognitive and behavioral symptoms) showed partial loss (deletion) of the *DLG2* gene, which plays an important role in the development, plasticity, and stability of synapses (the zone where two neurons touch each other allowing them to exchange information).

A research team led by Dr. Guillaume Smits, Nicolas Deconinck and Catheline Vilain of HUDERF and Professor Gianluca Bontempi of ULB (Machine Learning Group) collaborated through the Interuniversity Institute of Bioinformatics in Brussels, (IB) ², a joint research institute at the Université libre de Bruxelles (ULB) and the Vrije Universiteit Brussel (VUB). Together, they worked at integrating large genomic, epigenomic, transcriptomic and clinical datasets. The computational experiments, performed by Claudio Reggiani, a PhD student funded by the Belgian Kids' Fund for Pediatric Research and Innoviris, pinpointed two novel *DLG2* promoters and coding exons conserved in human and mouse and present in the fetal brain. The deletion of these new regions were found statistically associated with developmental delay and intellectual disability in two independent patient cohorts, supporting the pathogenic role of these new elements into the neurodevelopmental symptoms of both HUDERF patients. The results of this work have been published in the international journal *Genome Medicine* and are presented in this video.

From a medical perspective, the findings will help medical doctors in improving future diagnosing of children with NDDs, intellectual disability, autism and schizophrenia. From a scientific point of view, this work shows how the *in silico* integration of multiple large

datasets can bring knowledge about the genome. It also provides elegant progress into the molecular cause of neurodevelopmental disorders and improves fundamental knowledge about the *DLG2* gene.

Genome Medicine

Novel promoters and coding first exons in DLG2 linked to developmental disorders and intellectual disability.

Reggiani C, Coppens S, Sekhara T, Dimov I, Pichon B, Lufin N, Addor MC, Belligni EF, Digilio MC, Faletra F, Ferrero GB, Gerard M, Isidor B, Joss S, Niel-Bütschi F, Perrone MD, Petit F, Renieri A, Romana S, Topa A, Vermeesch JR, Lenaerts T, Casimir G, Abramowicz M, Bontempi G, Vilain C, Deconinck N, Smits G.

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About HUDERF

The Queen Fabiola Children's University Hospital (QFCUH) is the only hospital exclusively dedicated to children and adolescents in Belgium. Our missions are:

- To take care of children, adolescents and his/her relatives and accompany them through a global, multidisciplinary, humanist approach of excellence
- To ensure high-level teaching and research through a continuous process of innovation and knowledge development
- To actively contribute to health education

By making every effort to ensure the well-being of the child, our hospital helps children become actors of their own development and self-fulfillment. The QFCUH is member of Brussels public hospitals network IRIS, CHU Bruxelles and Pôle Hospitalier Universitaire de Bruxelles.

www.huderf.be

About d'(IB)²

The ULB/VUB Interuniversity Institute of Bioinformatics in Brussels (ibsquare.be) brings together the research groups of the VUB and ULB specialized in bioinformatics analysis of large scale omics data, into an interuniversity, cross-faculty (Medicine, Sciences, and Applied Sciences, of ULB and VUB) laboratory. The main missions of the (IB)2 are:

- Design and use of large-scale omics driven bioinformatics, biostatistics and computational biology to achieve a better understanding of the physio- and pathological mechanisms of living organisms.
- Enable interdisciplinary and interuniversity research collaborations in bioinformatics by providing a physical location for research, meetings, collaborations, seminars.

- Create in the Brussels Region a critical mass of researchers in bioinformatics and computational biology.
- Increase National and International visibility by participation into projects, seminar organizations, national and international conference hosting.

Ibsquare.be

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