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Research group identifies GLUT2 protein's role in zebrafish brain development

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Researchers from the University of Barcelona (UB) have described the key role that GLUT2 protein plays in embryonic brain development in zebrafish. A new article —highlighted on the cover of the January issue of the *Journal of Cerebral Blood Flow & Metabolism*— proves that this molecule depletion alters the development of brain basic structures involved in glucose sensing.

The study points the use of zebrafish (Danio rerio) as a model to study diseases produced by GLUT2 alterations, such as the Fanconi-Bickel syndrome (FBS), a rare glycogen storage disease characterized by the absence of GLUT2 which causes severe liver and kidney dysfunction. The study is led by Josep Planas, university lecturer in the Department of Physiology and Immunology and researcher at the Institute of Biomedicine of the UB. Researchers from Leiden University collaborate in the study too.

Glucose: a key factor to cellular metabolism

GLUT2 is a glucose transporter that facilitates the entry of glucose—a monosaccharide crucial for proper brain function— inside cells. In order to investigate GLUT2 function in embryonic brain development, the UB group knocked down GLUT2 in zebrafish embryos and examine the anomalies that took place. "Glucose deprivation induces apoptosis (programmed cell death)", says Josep Planas. "Moreover —he adds—, the brain region proved to be involved in the detection of glucose level

changes in mammals is altered. This region also regulates feeding behaviour, energy metabolism, and glucose homeostasis".

The system detects, for instance, the lack of glucose after a fast or its excess caused by food intake, and organise endocrine response to maintain the glucose levels needed to survive.

"The study first proves the crucial role that GLUT2 plays in early development. Moreover, it relates GLUT2 depletion to the alteration of the brain structures that take part in the regulation of brain glucose", summarises Josep Planas.

A model for studying metabolic diseases

The study may have implications for the treatment of diseases characterised by glucose deprivation like the Fanconi-Bickel syndrome. "People who suffer the syndrome present psychomotor developmental problems as a consequence of the alteration of cerebellum development and glucose regulation mechanism", affirms Planas. Zebrafish embryos without GLUT2 present features which are similar to the ones that characterise this syndrome. Researchers consider that zebrafish can be used as a model to study in deep the strategies to treat this type of diseases.

The zebrafish is a species that develops quickly out of the mother's body. Besides, genetic manipulation is easier than in other animal models (for example, mice). So zebrafish embryos provide a unique opportunity to unravel the mechanisms following this rare disease.

The UB research group will develop new studies to analyse the consequences that knocking out GLUT2 has on adult zebrafish. "It will be a key evidence to better understand the functional role that GLUT2 has in glucose regulation, and to identify what neurons that undergo

apoptosis die and change their expression pattern without this transporter", concludes the researcher.

More information: Rubén Marín Juez, Mireia Rovira, Diego Crespo, Michiel van der Vaart, Herman P. Spaink y Josep V. Planas. "GLUT2-mediated glucose uptake and availability are required for embryonic brain development in zebrafish". *Journal of Cerebral Blood Flow & Metabolism*, October 2014. DOI: 10.1038/jcbfm.2014.171

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