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Gene mutation can cause brain malformation in children

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Credit: Cardiff University

Researchers from Cardiff University and Université Libre de Bruxelles have identified how the function of a key gene significantly impacts nerve stem cell growth, and how it can lead to abnormal brain development in unborn babies if the system goes awry.

The new research reveals a pivotal role for the Dmrta2 gene in regulating the division of cells and the production of specialised cells.

This discovery shows that the Dmrta2 gene mutation, if inherited from

both the mother and father, leads to a form of brain malformations called lissencephaly, a rare nervous system disorder in which a baby's brain is not fully developed.

Language skills and learning

This condition occurs in the second/third trimester of pregnancy, and leaves the child with a small and smooth brain as it prevents the development of brain folds (gyri) and grooves (sulci), which are needed for language skills and learning.

"Dmrta2 is part of the machinery responsible for gauging if enough cells are being produced for an optimally balanced and developed brain," Professor Meng Li of Cardiff University explains.

"It ensures the brain's stem cells proliferate at appropriate time windows during foetal development and generate sufficient numbers of brain stem cells..."

Researchers genetically mutated the Dmrta2 gene in embryonic stem cells to examine the impact of too much or too little protein levels on brain development. The team then examined the effect of these changes on laboratory-created nerve cells, showing a direct link between Dmrta2 mutation and the causes of microcephaly (a type of lissencephaly).

Autism and learning difficulties

Lead researcher, Dr Fraser Young, comments: "Without the Dmrta2 gene maintaining the delicate balance between neurogenesis and cell cycle progression, brain development is altered.

"Errors in nerve stem cell fate decisions may contribute to other

neurodevelopmental conditions such as autism and learning difficulties.

"If we can identify why some children are potentially predisposed to nurturing neurodevelopmental disorders, we will be much better placed to look at ways of effectively treating or preventing such conditions from occurring."

The paper 'The Doublesex-related Dmrta2 safeguards neural progenitor maintenance involving transcriptional regulation of Hes1', is co-authored by Eric J Bellefroid from Université Libre de Bruxelles and published in *PNAS* journal.

More information: Fraser I. Young et al. The doublesex-related Dmrta2 safeguards neural progenitor maintenance involving transcriptional regulation of Hes1, *Proceedings of the National Academy of Sciences* (2017). DOI: 10.1073/pnas.1705186114

Provided by Cardiff University