MedicalXpress

Gene discovery sheds light on growth defects linked to dwarfism

February 13 2017

Credit: CC0 Public Domain

A new study shows how errors in a specific gene can cause growth defects associated with a rare type of dwarfism.

During the study, published today in *Nature Genetics*, an international team of scientists led by the University of Birmingham looked at genetic information from more than 250 people around the world with

microcephalic dwarfism, a group of disorders characterised by short stature and reduced head size.

They found that 29 of the individuals had faulty versions of a gene called DONSON.

Tests on cells growing in the laboratory revealed that this gene plays a crucial role in ensuring DNA is copied correctly when cells divide and grow.

Cells from patients with mutations in the DONSON gene had difficulty in efficiently replicating their DNA and protecting it from uncontrolled damage, ultimately leading to the growth defects typical of microcephalic dwarfism.

This research raises the potential of more accurate diagnoses for patients with genetic microcephaly, in addition to providing an insight into how similar rare hereditary diseases are caused.

Professor Grant Stewart, from the Institute of Cancer and Genomic Sciences at the University of Birmingham, says: 'Despite DNA replication being a process that is fundamental to life, there is still a lot we don't know. This research sheds new light on the mechanisms underlying DNA replication, and the effect on human health when this process goes wrong.'

Professor Andrew Jackson, of the University of Edinburgh's Institute for Genetics and Molecular Medicine, says: 'Identification of DONSON as a microcephaly gene has given us new insights into how the genome is protected during DNA replication, and has only been possible through the close collaboration and contributions of families, clinicians and scientists from many countries around the world.'

Professor Christopher Mathew, from the National Institute for Health Research (NIHR) Biomedical Research Centre at Guy's and St Thomas' and King's College London, adds: 'This is a good example of how unravelling the genetics of rare human disorders can provide profound insight into basic biological processes.'

Professor Fowzan Alkuraya, from the King Faisal Specialist Hospital and Research Center, also adds: 'The DONSON story is a remarkable example of how loss of a very basic cellular function can result in a phenotype that ranges from embryonic lethal to one characterized by growth deficiency of brain and body depending on the severity of the mutation. It is also a reminder of the contribution of tricky deep splicing mutations to human disease.'

More information: Reynolds et al. (2017) 'Mutations in DONSON disrupt replication fork stability and cause microcephalic dwarfism' *Nature Genetics* DOI: 10.1038/ng.3790

Provided by University of Birmingham