# Study unravels the genetics of childhood 'overgrowth'

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Study leader, Professor Nazneen Rahman, Head of Genetics at The Institute of Cancer Research, London, and The Royal Marsden Hospital NHS Foundation Trust Credit: The Institute of Cancer Research, London

Researchers have undertaken the world's largest genetic study of childhood overgrowth syndromes - providing new insights into their causes, and new recommendations for genetic testing.

Overgrowth syndromes describe conditions that cause children to be taller and to have a bigger head size than expected for their age, and also to have an intellectual disability or other medical problems.

Scientists at The Institute of Cancer Research, London, found many of the children with overgrowth syndromes had mutations in one of 14 different genes.

They also showed that many of the overgrowth genes are also involved in driving cancer growth, though intriguingly, the types of mutations involved in promoting human growth and cancer growth are often different.

The researchers collected samples and information from 710 children with an overgrowth syndrome through an international study, funded by Wellcome.

They used a technique called exome sequencing to analyse the DNA of all the genes in each child and discovered a genetic cause for their overgrowth syndrome in 50 per cent of the children.

These children had genetic mutations in one of the 14 genes, and usually the mutation started in the child with the overgrowth syndrome and was not inherited from either parent.

Amongst the 14 genes was HIST1H1E, which has not been previously linked to a human disorder. The other genes have been linked with human disorders before, but their contribution to overgrowth syndromes was not known.

Importantly, the study showed that the major genes causing overgrowth syndromes are involved in epigenetic regulation, which means they control how and when other genes will be switched on and off.

Mutations in epigenetic regulation genes were the cause of overgrowth in 44 per cent of the children in the study, which is published today (Thursday) in the *American Journal of Human Genetics*.

Study leader, Professor Nazneen Rahman, Head of Genetics at The Institute of Cancer Research, London, and The Royal Marsden Hospital NHS Foundation Trust, said:

"The control of growth is a fundamental process important in development and many diseases, including cancer. We are pleased our work has provided both new insights into the mechanisms that control growth and new strategies by which genetic testing can be used efficiently to diagnose children with overgrowth syndromes."

Co-study lead Dr Katrina Tatton-Brown, Reader in Clinical Genetics at St George's, University of London, Consultant Geneticist at The Institute of Cancer Research, London, and the South West Thames Regional Genetics Service, St Georges University Hospitals NHS Foundation Trust, said:

"Our study suggests that offering an exome sequencing genetic test to children with overgrowth and intellectual disability would be a practical and worthwhile way to try to identify the cause of their problems. This would allow us to provide children with more personalised management and to give better information to families about risks to other members of the family."

Provided by Institute of Cancer Research