Mutations in ASXL3 cause problems similar to Bohring-Opitz syndrome

4 February 2013

Mutations which affect the gene ASXL3 cause a novel syndrome similar to Bohring-Opitz syndrome, finds a study published in BioMed Central's open access journal *Genome Medicine*. This molecular definition distinguishes these children from those with Bohring-Opitz, and other similar syndromes, and highlights a technique able to help define rare diseases.

When Dr Ropers from the Max-Planck Institute for Molecular Genetics in Berlin found a child with non-specific symptoms, including small size at birth, difficulties with movement and feeding, severe intellectual disability, and with distinctive facial features, he looked to see if there was a gene involved. Using genome-wide sequencing, researchers found that the child had a 'truncating' mutation in the gene ASXL3 not present in either parent.

ASXL3 is in the same family of proteins as ASXL1 and about half of all children with Bohring-Opitz syndrome have a truncating mutation in their gene for ASXL1. This results in production of a short protein unable to behave properly in the cell and, because ASXL1 is a repressor protein, disrupts the proper function of many genes which would normally be switched off.

From looking at one child it was impossible to be sure that the problem with ASXL3 was responsible for the child's condition in the same way as ASXL1 and Bohring-Opitz. However three other unrelated children, from the USA, who also had the same kind of non-specific syndrome, also had truncating mutations in ASXL3.

Dr Matthew Bainbridge from Baylor College of Medicine, who led this study explained, "Our study provides a molecular definition of this new syndrome, which is difficult to distinguish from Bohring-Opitz from the physical effects on the children alone. Although it is not curable, improving diagnosis can help parents and improve the quality of life of the child. In all of these cases the mutation was not inherited so the chances of having a second child with this syndrome was exceedingly rare."

This study also demonstrates a need for sharing genomic data from patients. Dr Bainbridge continued, "It was only by talking to doctors and researchers at the Max-Planck-Institute for Molecular Genetics, and Alfred I. duPont Hospital for Children that we discovered that there were several children with this condition. The more open data we have for these rare conditions the easier it will be to continue research."

More information: De novo truncating mutations in ASXL3 are associated with a novel clinical phenotype with similarities to Bohring-Opitz syndrome Matthew N Bainbridge, Hao Hu, Donna M Muzny, Luciana Musante, James R Lupski, Brett H Graham, Wei Chen, Karen W Gripp, Kim Jenny, Thomas F Wienker, Yaping Yang, V Reid Sutton, Richard A Gibbs and H Hilger Ropers Genome Medicine (in press)

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