

Scientists discover a new gene that causes microcephaly

Researchers from the Indian Institute of Science (IISc), Bangalore and the National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore have discovered a new gene that causes microcephaly, a congenital disorder characterized by smaller than normal sized brain and retardation affecting the cerebral cortex, mostly with a generalized reduction in the size of the entire brain.

The discovery may help develop a regular clinical screening tool to detect this disorder at the foetal stage and aid expectant mothers in detecting this deformity.

So far, four genes were known to cause microcephaly. The IISc team located the fifth gene known to cause this disorder in India. This is the first time that the gene called *STIL* has been shown to cause microcephaly. Previously mutations in four genes, *MCPH1*, *CDK5RAP2*, *ASPM* and *CENPJ* that code for centrosomal proteins have been shown to cause this disorder. Three homozygous mutations in *STIL* which codes for pericentriolar

and centrosomal proteins were identified in patients linked to the *MCPH7* locus¹.

Microcephaly is known to be caused by environmental and genetic factors. Among the environmental factors are intrauterine infections, alcohol, drugs taken during pregnancy, prenatal radiation exposure, maternal phenylketonuria and birth asphyxia². The majority of microcephalic cases are caused by a variety of genetic mechanisms, including cytogenetic abnormalities and single-gene disorders³.

The discovery is a result of a research collaboration between the teams of Satish Girimaji, Department of Psychiatry, NIMHANS and Arun Kumar, Department of Molecular Reproduction, Development and Genetics, IISc. The identification and characterization of the genes responsible for microcephaly are important for both genetic counselling and prenatal diagnosis⁴.

Doctors at NIMHANS recorded clinical data from the afflicted people, which were later taken by the IISc team for genetic analysis. The data were obtained

from a number of families in Bangalore, Mangalore, Mysore and parts of Tamil Nadu. The higher incidence of microcephaly in Karnataka, Tamil Nadu and Andhra Pradesh was attributed to the prevalence of consanguineous marriages. Kumar has identified that the most common cause of primary microcephaly is mutation in the *ASPM* gene⁴.

Owing to the smaller size of the brain, microcephaly patients have mild to severely low IQ. Although the disease is not fatal, the patients remain mentally challenged for life. This discovery is also significant from the point of view of the study of evolution of the human brain from the days of early hominids like *Australopithecus*, who had a small brain similar to the brain of microcephaly patients.



A primary microcephaly patient (Source: Kumar *et al.*¹).

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ACKNOWLEDGEMENTS. I thank Dr Arun Kumar, Department of Molecular Reproduction, Development and Genetics, IISc, Bangalore, for providing information on microcephaly.

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