DBT-CDFD study finds the cause for a new type of intellectual disability

New Delhi, July 03: Identification of disease causing genetic mutations has important value in prenatal diagnosis and genetic counseling. Once the culprit mutation is identified, families can look for the presence of it in their offspring through genetic testing even before the birth of the child and plan accordingly. This also has immense importance in basic research towards understanding gene functions and mechanisms of disease that may help in development of new therapeutic options.

Advances in human genetic research and simultaneous development of new high throughput diagnostic tools like next generation sequencing now make it possible to quickly and cost effectively identify genetic mutations responsible for a particular disease using just a few affected individuals.

In a recent discovery, researchers at the Department of Biotechnology's Centre for DNA Fingerprinting and Diagnostics (DBT-CDFD) have identified the genetic mutation associated with a novel syndrome. Two siblings - a brother and a sister, born of consanguineous parents from southern India, were evaluated for intellectual disability with other developmental abnormalities. A mutation in a gene called *HERC1* was identified as the likely cause of the disease, using one of the cutting edge next generation technology (exome sequencing) followed by DNA microarray analysis. Conventional sequencing confirmed the presence of this mutation in both siblings.

Interestingly, the parents were also found to be carriers for the same mutation. However, they both were unaffected. Further functional analysis with the RNA from the affected individuals indicated a possible deleterious effect of the mutation on the protein by changing the structure

and function of *HERC1* mRNA that may lead to decreased production as well as loss of important functional domains of the protein.

More research is needed to ascertain the pathophysiological (disordered physiological processes) role of *HERC1* in brain development and disease. This discovery of a new intellectual disability syndrome will be helpful in future genetic testing of patients with similar abnormality. It has also led to the advancement of scientific knowledge regarding brain development.

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