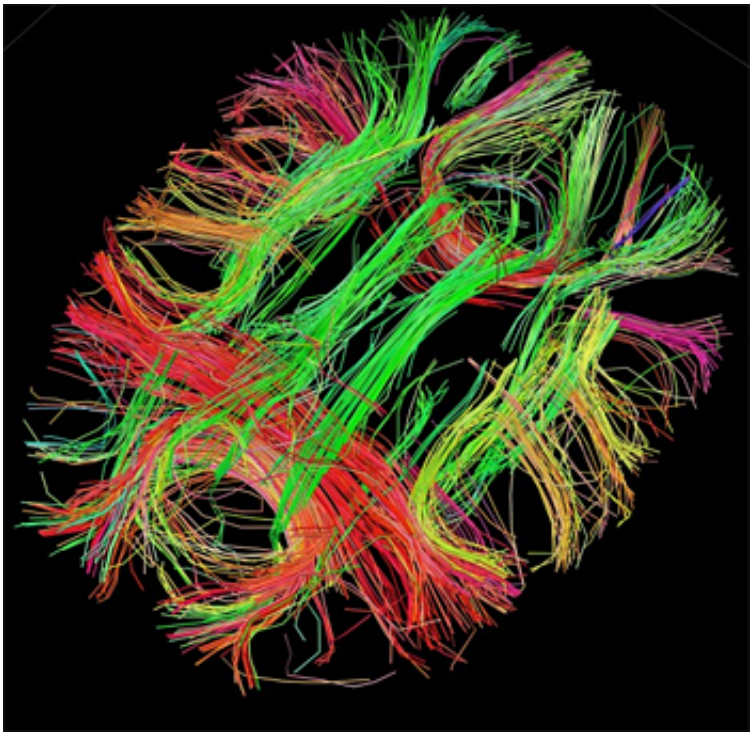
Scientists discover gene critical for proper brain development

December 19 2014



White matter fiber architecture of the brain. Credit: Human Connectome Project.

Scientists at A*STAR's Institute of Medical Biology (IMB) and Institute of Molecular and Cellular Biology (IMCB) have identified a genetic pathway that accounts for the extraordinary size of the human brain. The team led by Dr Bruno Reversade[1]KATNB1, as an essential component in a genetic pathway responsible for central nervous system development

in humans and other animals. from A*STAR in Singapore, together with collaborators from Harvard Medical School, have identified a gene,

By sequencing the genome of individuals of normal height but with a very small head size, the international team revealed that these individuals had mutations in the KATNB1 gene, indicating that this gene is important for proper human brain development. Microcephaly (literally meaning "small head" in Latin) is a condition often associated with neurodevelopmental disorders. Measured at birth by calculating the baby's head circumference, a diagnosis of microcephaly is given if it is smaller than average.

Microcephaly may stem from a variety of conditions that cause abnormal growth of the brain during gestation or degenerative processes after birth, all resulting in a small head circumference. In general, individuals with microcephaly have a reduced life expectancy due to reduced brain function which is often associated with mental retardation.

The team also carried out further experiments to determine the function of KATNB1, whose exact mode of action was previously unknown in humans. Using organisms specifically designed to lack this gene, they realised that KATNB1 is crucial for the brain to reach its correct size. Zebrafish and mice embryos without this gene could not live past a certain stage and showed dramatic reduction in brain and head size, similar to the human patients. Their results were published in the 17 December 2014 online issue of *Neuron*, the most influential journal in the field of neuroscience.

Sequencing and screening for this particular gene before birth or at birth might also help to detect future neurocognitive problems in the general population. Dr Reversade said, "We will continue to search for other genes important for brain development as they may unlock some of the

secrets explaining how we, humans, have evolved such cognitive abilities."

Prof Birgit Lane, Executive Director of IMB, said, "This is one of a small number of genes that scientists have found to be vital for brain development. The work is therefore an important advance in understanding the human brain. The team's findings provide a new platform from which to look further into whether - and how - this gene can be used for targeted therapeutic applications."

Prof Hong Wanjin, Executive Director of IMCB, said, "This coordinated effort shows the increasingly collaborative nature of science. As the complexity and interdisciplinary nature of research evolves, so do the networks of collaborations between research institutes at A*STAR and across continents."

More information: "Katanin p80 Regulates Human Cortical Development by Limiting Centriole and Cilia Number" *Neuron* DOI: dx.doi.org/10.1016/j.neuron.2014.12.017

Provided by Agency for Science, Technology and Research (A*STAR), Singapore