Disease caused by reduction of most abundant cellular protein identified

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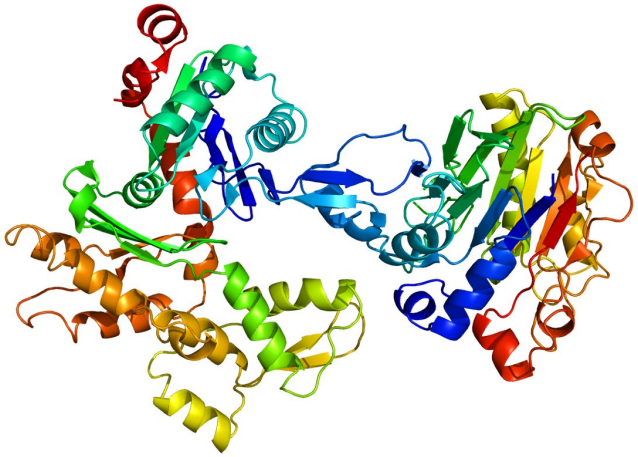

Credit: University of Manchester

An international team of scientists and doctors has identified a new disease that results in low levels of a common protein found inside our cells.

The study, led by Dr Siddharth Banka from The University of Manchester and the Manchester Centre for Genomic Medicine, St Mary's Hospital, is published in the reputed *American Journal of Human Genetics*.

?-actin is the cell's most abundant protein, providing shape and allowing them to move. It is fundamental to a number of biological functions.

The team say the new disease is caused by gene mutations which result in half of the normal ?-actin levels.

Dr Sara Cuvertino, a Research Associate at The University of Manchester and first author of the paper, said: "?-actin is so vital to our cells that it was very surprising for me that patients could still survive on just half the normal levels of this critical protein".

Dr Banka said, "Although patients born with these mutations have developmental delay, heart and kidney abnormalities, it is remarkable that several are leading a reasonably healthy life.

"Some affected individuals also have neurological problems such as epilepsy."

Dr Cuvertino studied the cells of patients affected with this new disease and found several subtle defects such as unusual shape, reduced capacity to move and divide.

"The ?-actin of a worm is very similar to the human protein. This remarkable conservation across millions of years of evolution reflects the importance of this protein for life," said Dr Cuvertino.

Dr Banka added "In our study we have described 33 patients, which is a large number for a first paper on a rare genetic disease. I am sure that this discovery will lead to identification of more patients from across the world, who have not yet been diagnosed."

Dr Cuvertino said, "Our studies of patient cells have provided some very interesting clues to the underlying mechanism of the disease that may provide a foundation for developing treatments".

Dr Banka's group is now studying how reduction in ?-actin causes the disease with a goal to develop possible treatments for these patients.

The doctors and scientists is unable to deal; with individual enquires from the public. However, patients should in the first instance contact their GP who may refer them on to a local geneticist.

More information: Sara Cuvertino et al. ACTB Loss-of-Function Mutations Result in a Pleiotropic

Developmental Disorder, *The American Journal of Human Genetics* (2017). DOI: 10.1016/j.ajhg.2017.11.006