

Study gives clues to causes of Motor Neurone Disease and Parkinson's Disease

March 10 2017, by Chris Melvin





The team produced 11 3D images of mutant versions of angiogenin. Credit: University of Bath



Scientists at the University of Bath have made further progress to understanding the role of one of the proteins that causes the neurodegenerative disorder Amyotrophic Lateral Sclerosis (ALS) and Parkinson's Disease (PD).

The scientists studied a protein called angiogenin, which is present in the spinal cord and brain, which protects neurons from cell death. Mutations in this protein have been found in sufferers of ALS and PD and are thought to play a key role in the progression of the condition.

ALS/PD triggers progressive weakness, muscle atrophy and muscle twitches and spasms. The diseases affect around 130,000 people in the UK.

The team of cell biologists and structural biologists have produced 3-D images of 11 mutant versions of angiogenin to see how these mutations changed the structure of the molecule and damaged its function.

The study, published in the journal *Scientific Reports*, provides insights into the causes of ALS and related conditions such as PD. The detailed experimental structural study on these mutations will have implications in understanding the molecular basis underlying their role in ALS and PD.

Previously the team had looked at the effects of the malfunctioning proteins on neurons grown from <u>embryonic stem cells</u> in the laboratory. They found that some of the mutations stopped the protein being transported to the cell nucleus, a process that is critical for it to function correctly. The <u>mutations</u> also prevented cells from producing stress granules, the neuron's natural defence from stress caused by low oxygen levels.



The research was led by structural biologist Professor K. Ravi Acharya and cell biologist Dr Vasanta Subramanian, both from the Department of Biology & Biochemistry.

Professor Acharya said: "We hope that the scientific community can use this new knowledge to help design new drugs that will bind selectively to the defective protein to protect the body from its damaging effects."

The research was funded by the Wellcome Trust and extensively made use of Diamond Light Source, the high brightness, state of the art international X-ray facility located at Didcot to discern the 3-D mutant structures at the highest precision.

More information: William J. Bradshaw et al. Structural insights into human angiogenin variants implicated in Parkinson's disease and Amyotrophic Lateral Sclerosis, *Scientific Reports* (2017). DOI: 10.1038/srep41996

Provided by University of Bath

Citation: Study gives clues to causes of Motor Neurone Disease and Parkinson's Disease (2017, March 10) retrieved 2 May 2024 from <u>https://medicalxpress.com/news/2017-03-clues-motor-neurone-disease-parkinson.html</u>

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