Insight into cause of rare disorder may aid quest for treatments

12 December 2018

Fresh discoveries about a rare genetic disorder that affects mainly boys may inform the development of therapies to treat the condition.

The disease, known as MeCP2 duplication syndrome, leads to severe intellectual disability, seizures and impaired motor function.

Scientists have examined molecular details of the biological causes behind the disorder, which is caused by duplication of a section of DNA, including a gene known as MeCP2. The same gene is linked with Rett syndrome, a neurological disorder that affects mostly girls.

Researchers carried out studies in mice to better understand how an abundance of protein produced by the extra gene gives rise to the condition.

Scientists at the University of Edinburgh found that disease symptoms depend on a key part of the MeCP2 protein binding to another set of proteins known as NCoR. When this happens in excess, disease symptoms arise.

Researchers examined a key component of NCoR that is known to interfere with DNA, but they were surprised to find that removing this part had no effect on symptoms.

This suggests that drugs targeting this component's function would not relieve the condition.

Research is now focused on drugs that could block the interaction between MeCP2 and NCoR, as a way to prevent the symptoms associated with an excess of protein.

Dr. Martha Koerner, of the University of Edinburgh's School of Biological Sciences, who led the study, said: "We have effectively ruled out a key possible biological mechanism behind duplication syndrome. Our research points towards other avenues that might prove fruitful in the quest for treatments."

The research is published in *Genes & Development*.

More information: Martha V. Koerner et al, Toxicity of overexpressed MeCP2 is independent of HDAC3 activity, *Genes & Development* (2018). DOI: 10.1101/gad.320325.118

Provided by University of Edinburgh