Researchers discover potential new treatment for rare muscle-wasting disease

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Dr Fabrizio Pertusati and Dr Michaela Serpi. Credit: Cardiff University

A team of Cardiff University researchers has uncovered a potential new way to treat a very rare genetic disorder that causes muscles in the arms and legs to become increasingly weak.

GNE myopathy is a debilitating condition that affects young adults in their 20s or 30s, typically leaving them in a wheelchair within years.

It is caused by a mutation in a gene called GNE.

The faulty gene causes a deficiency in an enzyme which is essential to the production of sialic acid, a sugar derivative that is vital for healthy muscle development and function.

There are no approved treatments, but patients can be supplied with key sugars.

However, the high daily dose causes side effects such as an increase in weight and cholesterol, liver problems and diarrhoea.

Researchers at the School of Pharmacy and Pharmaceutical Sciences have now found a way to deliver a chemical product that bypasses the faulty enzyme and re-establishes the body's production of sialic acid. This in turn powers up the proteins needed for muscles to function and develop effectively.

The team, led by Dr. Fabrizio Pertusati and Dr. Michaela Serpi, have been working on this project since March 2018.

Dr. Pertusati said: "It's like a van trying to deliver food to a location but is stuck in a traffic jam.

"If you open a new route to bypass the bottleneck, the food will be delivered as normal.

"By administering our compound, sialic acid synthesis can be performed again by the cell machinery and its normal function is then restored."

The team hope the results of the study, published in the *Journal of Medicinal Chemistry*, will lead to the development and trial of effective drugs to tackle the condition.

The researchers first need to further improve the chemical properties of the compound to make it more water soluble so it can be administered orally.

They would then need to carry out trials in an animal model, followed by clinical trials in humans.

"We are in the early stages of this research, but it's exciting to think about the potential to develop and trial a new drug to decrease the symptoms, severity and progression of muscle weakness and wasting to enable patients to enjoy greater mobility and quality of life," said Dr. Pertusati.

The charity Muscular Dystrophy UK regards GNEM as "very rare", estimating the worldwide prevalence to be just one person in a million.

Dr. Kate Adcock, director of research and innovation at the charity Muscular Dystrophy UK,

said: "This is a promising first step in the journey.

"They are using a cell-based assay, so are a long way from patient studies, but it's promising to see these early stage studies for a rare condition."

Provided by Cardiff University