New therapy substitutes missing protein in those with muscular dystrophy

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Researchers at the University of Minnesota Medical School have discovered a new therapy that shows potential to treat people with Duchenne muscular dystrophy, a fatal disease and the most common form of muscular dystrophy in children.

In the mouse model, researchers were able to substitute for the missing protein - dystrophin, which forms a key part of the framework that holds muscle tissue together - that results in the disease, effectively repairing weakened muscle tissue.

Researchers injected dystrophic mice with a protein called utrophin - a very close relative of dystrophin - that was modified with a cell-penetrating tag, called TAT.

The study is the first to establish the efficacy and feasibility of the TAT-utrophin-based protein as a viable therapy for the treatment of muscular dystrophy as well as cardiac muscle diseases caused by loss of dystrophin.

The research is published in the May 26, 2009 issue of *PLoS Medicine*.

"This unique approach can replace the missing protein without the complexities of gene replacement or stem cell approaches," said James Ervasti, Ph.D., principal investigator of the study and a professor in the Department of Biochemistry, Molecular Biology & Biophysics.

Muscular dystrophy causes the muscles in the body to progressively weaken. Duchenne is the most common and severe form of childhood muscular dystrophy. About one of 3,500 boys are born with the crippling disease. Symptoms usually begin in children who are 2 to 3 years-old, most are in a wheelchair by age 12, and many who have the disease pass away by their late teens to early 20s. Current treatment, limited to corticosteroids, are minimally effective and can cause serious side effects.

Research underway to battle muscular dystrophy with gene therapy and stem cell treatment shows promise, but major hurdles must be overcome before these approaches are viable in human patients, Ervasti said.

Delivering treatment to every muscle cell via gene therapy or stem cells is difficult because muscle tissue makes up such a large portion of the human body. Furthermore, the immune system may reject the cell or gene treatment because patients would treat the newly introduced cells or genes as a foreign substance.

Ervasti's method may conquer both of those problems. Upon injection, the TAT-utrophin combination spreads around the entire body efficiently and is able to penetrate the muscle cell wall to substitute for missing dystrophin. Because every cell in the body makes utrophin naturally, TAT-utrophin circumvents immunity issues associated with other therapeutic approaches.

"Our protein replacement approach most directly and simply addresses the cause of Duchenne muscular dystrophy," Ervasti said.

This new method is not a cure for muscular dystrophy. Rather, it would be a therapy most likely administered on a regular basis. If the treatment works in larger animal models and humans, it's most likely researchers would develop a drug for patients. Ervasti is hopeful the therapy can

move into human clinical trials within 3 years.

Source: University of Minnesota (news : web)