# New vitamin-based treatment that could reduce muscle degeneration in muscular dystrophy

23 October 2012

Boosting the activity of a vitamin-sensitive cell adhesion pathway has the potential to counteract the muscle degeneration and reduced mobility caused by muscular dystrophies, according to a research team led by scientists at the University of Maine.

The discovery, published 23 October in the open access journal PLOS Biology, is particularly important for congenital muscular dystrophies, which are progressive, debilitating and often lethal diseases that currently remain without cure. The researchers found that they could improve muscle structure and function in a zebrafish version of muscular dystrophy by supplying a common cellular chemical (or its precursor, vitamin B3) to activate a cell adhesion pathway.

Muscle cells are in themselves relatively delicate, but derive important additional mechanical strength from adhesion protein complexes; these anchor the muscle cells to an external framework known as the basement membrane, thereby helping to buffer the cells against the extreme forces that they experience during muscle contractions. Mutations in the genes that encode these adhesion proteins can weaken these attachments, making muscle cells more susceptible to damage and death.

The resulting muscle degeneration can eventually lead to progressive muscle-wasting diseases, such as muscular dystrophies. A major component of the basement membrane, a protein called laminin, binds to multiple different receptors on the muscle cell surface and forms a dense, organized network.

The study was led by UMaine Associate Professor of Biological Sciences, Clarissa Henry, whose laboratory focuses on understanding how cell adhesion complexes contribute to muscle development. The researchers discovered that a pathway involving a common cellular chemical called nicotinamide adenine dinucleotide (NAD+) plays a role in the formation of organized basement membranes in muscle tissue, during development of the fish embryo. As disordered basement membranes are seen in many different types of muscular dystrophies, the researchers wondered whether activating this pathway might reduce the severity of some muscular dystrophies.

In the current study, the researchers show that NAD+ improves the organization of laminin in a zebrafish version of muscular dystrophy. Zebrafish lacking either of the two main receptors for laminin have a disorganized basement membrane, causing muscle degeneration and difficulties with movement. However adding extra NAD+, or even a vitamin packet containing vitamin B3 (niacin, a precursor to NAD+), significantly reduced these symptoms.

The research team found that the main protective effects of NAD+ come from enhancing the organization of the laminin structure in the basement membrane, which helps to increase the resilience of diseased muscle fibers.

Because the same cell adhesion complexes are found in humans, the research team is optimistic that these findings may one day positively impact patients with muscular dystrophies. "Although there is a long way to go, I'm hopeful that our data could eventually lead to new adjuvant therapies," says University of Maine Ph.D. student Michelle Goody, who led the research team with Prof. Henry.

Prof. Henry summarizes; "One of my favorite aspects of this study is that it is a poster child for how asking basic biological questions can lead to exciting discoveries that may have future

therapeutic potential."

**More information:** *PLoS Biol* 10(10): e1001409. doi:10.1371/journal.pbio.1001409