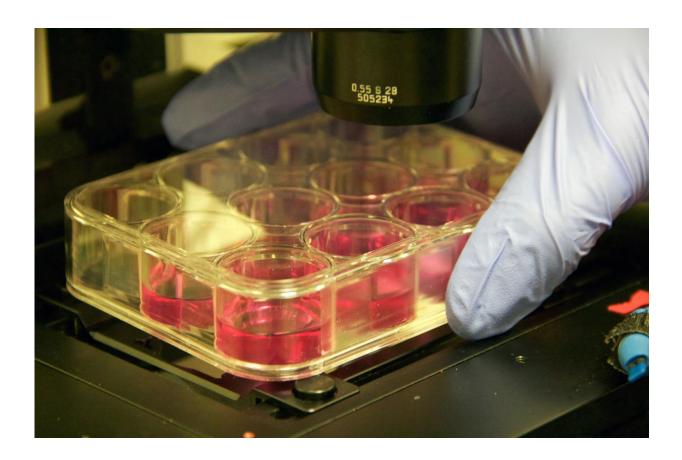


Spectrin proteins spring into action to restore nucleus

June 20 2017, by Samantha Jamison



Credit: Carnegie Mellon University College of Engineering

When you lift weights, carry heavy boxes, or engage in physical activity, the cells in your body stretch and deform to accommodate your movements. But how do your cells recover, or return to their original



state, once you set down the weights, unpack those heavy boxes, or complete your workout?

Carnegie Mellon University's Associate Professor of Chemical Engineering Kris Dahl and Chemical Engineering Ph.D. student Travis Armiger discovered that the cell's nucleus recovers from major deformations (e.g. muscle cells or bone cells that stretch during exercise) in part because of a spring-like, mechanical element that exists in the nucleus. This mechanical element, called a spectrin protein, helps transform the nucleus back into its original shape after the cell endures a period of high stress.

Before Dahl and Armiger completed their study, most scientists understood that spectrin proteins increased the elasticity of erythrocytes (<u>red blood cells</u>), regulated membrane stability in the cytoskeleton of nucleated cells, and helped repair damage to the cell's DNA.

In general, most scientists hypothesize that spectrin proteins help maintain the *structure* of the cell's nucleus, but they have not hypothesized how spectrin proteins might affect the *mechanics* of the cell's nucleus. Through their study, Dahl and Armiger confirm that spectrin proteins do in fact contribute to the resiliency of the cell's nucleus.

"What's understood about nuclear mechanics is that there's a stiff nucleoskeleton primarily composed of lamina proteins ... which as a whole, are able to deform and squeeze through spaces [in the body]," says Armiger.

"What we've shown is that there are other proteins present in the nucleoskeleton called spectrin proteins that act like springs ... and help pull the nucleus back to its original shape [after deformation]."



The nucleus contains most of the cell's genetic material in thread-like strands called chromosomes. These chromosomes also encompass portions of the human genome, or the complete set of genetic information that ultimately builds an organism, allowing it to grow and develop over time.

The genome is surrounded by a flexible shell called the nucleoskeleton, which sits along the inside of the nuclear-membrane, protecting the nucleus from permanent damage or deformation. As cells squeeze through small pathways in the body, the nucleus tends to deform. But the existence of lamina (stiff proteins that compose the nucleoskeleton), allow the nucleus to deform without rupturing. If the lamina prevent the nucleus from rupturing, then what exactly helps the nucleus return to its original shape?

"Lamin filaments are able to bend and come back [to their original shape]," says Dahl. "However, they form a network structure, and when they're in a network structure, they don't deform that easily, even though the nucleus does deform. So it [the nucleus] will crinkle, but it does need a spring to be able to pop back into its nuclear shape."

The discovery of the spring-like spectrin protein is important because scientists can now understand *how* the cell's <u>nucleus</u> recovers after major bouts of deformation. The existence of spectrin explains how an individual's muscle cells contract after lifting weights or how their cardiovascular cells respond to increased blood pressure. Scientists may also link spectrin to different muscular dystrophy diseases such as Emery-Dreifuss muscular dystrophy.

"We find this [discovery] interesting because these discoveries come from the most interesting directions," said Dahl. "We were investigating a <u>protein</u> usually found in blood <u>cells</u>. Our studies were performed in a cancer cell line. And the implications are for <u>muscular dystrophy</u>. This



happens in science all of the time: by allowing yourself to think outside the box and follow through with rigorous study, you can make the greatest discoveries."

Dahl and Armiger's research was published in volume 49 of Elsevier's *Journal of Biomechanics*.

More information: Travis J. Armiger et al, Nuclear mechanical resilience but not stiffness is modulated by ?II-spectrin, *Journal of Biomechanics* (2016). DOI: 10.1016/j.jbiomech.2016.10.034

Provided by Carnegie Mellon University, Department of Chemical Engineering

Citation: Spectrin proteins spring into action to restore nucleus (2017, June 20) retrieved 27 April 2024 from <u>https://phys.org/news/2017-06-spectrin-proteins-action-nucleus.html</u>

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