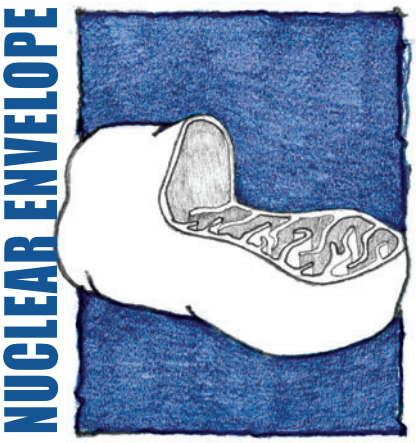

STRETCHY TO THE CORE

One of the main differences between eukaryotes and bacteria is that eukaryotes sequester their genetic material into organelles, with most of the DNA enclosed by a structure known as the nuclear envelope. The nuclear envelope is a double membrane studded with pore complexes that regulate the movement of molecules into and out of the nucleus. In higher eukaryotes, its inner membrane is lined with a two-dimensional fibrous network called the nuclear lamina. Little is known about the structure or function of the lamina, but it is known that the proteins that make it up belong to the diverse family of cytoskeletal proteins known as intermediate filaments. Intermediate filament proteins assemble into 10 nm-diameter filaments that are believed to impart cells with mechanical integrity. It is likely that the nuclear lamins do the same for the nucleus. Recently, Rowat and colleagues tested the hypothesis that the nuclear lamina behaves as an elastic solid capable of mechanically reinforcing the nucleus.

Rowat's team tested specifically whether the nuclear envelope deforms like an elastic solid or flows like a fluid when the nucleus is sucked into a micropipette. Labelling the lamin network with green fluorescent lamin proteins allowed them to analyse whether the distance between lamin molecules changes as the nucleus is drawn into the pipette. The researchers reasoned that, if the lamina is an elastic solid, the fluorescence intensity should spread out where the lamina is stretched and increase where it is compressed. Alternatively, if molecules in the lamina can diffuse freely, as in a fluid, deformation should have no effect on the average fluorescence intensity.

The team found that when the nuclear envelope in both living mammalian cells and isolated nuclei is pulled into a micropipette, the fluorescence intensity is greater than average at the mouth of the pipette and decreases exponentially as you move from the mouth inward. This suggests that the lamina is compressed at the mouth and stretched inside the pipette, which supports the idea that the nuclear envelope behaves like an elastic solid when it is supported by a lamina. Furthermore, they found evidence of buckling folds that radiated out from the mouth of the pipette in the direction of tension, which would not occur if the lamina is a two-dimensional fluid. But what happens when the deforming force is removed – does the nucleus spring back to its original shape? For quick deformations, Rowat's team found that the answer is yes, but for longer deformations (more than ten seconds), relaxation is slower. In other words, like most biological materials, the nuclear lamina is best described as a viscoelastic solid.

This work could have profound implications for understanding a mysterious group of genetic diseases known as laminopathies, which are caused by mutations in the lamin-encoding gene. These diseases are typically characterized by defects in muscle, adipose and nervous tissues, but one unique variant causes a rare syndrome in which patients appear to age prematurely and die before their teens. The cell nuclei of patients with laminopathies often exhibit irregular shapes and there is evidence that they are mechanically fragile. Rowat's team is next going to measure how nuclei isolated from these patients stand up to mechanical stress, which is an important first step to understanding the mechanisms underlying laminopathies. Furthermore, by exploring what goes wrong when nuclear lamina function is disrupted, these studies will illuminate the selective pressures that were responsible for the appearance of the nuclear lamina in higher eukaryotes.

10.1242/jeb.01650

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THAT ALL-IMPORTANT TAN…

The arthropod exoskeleton is both a blessing and a curse. It provides mechanical protection, a permeability barrier and a lightweight skeleton; but it must be moulted regularly as it becomes constricting when the animal grows. The multi-stage moulting process involves the growth of a new flexible cuticle underneath the old one, the detachment from and shedding of the old one (ecdysis), then the expansion of the new one before it is finally tanned – that is, made rigid by chemical crosslinking. Classic neck-ligation experiments (tying the neck with ligature silk to prevent soluble brain factors from reaching the rest of the body) showed that brain-derived factors are responsible for moulting. Since then, it has become clear that moulting is under multiple, sequential neurohormonal control. In March this year, two research groups simultaneously revealed an important missing link in this pathway – the last step in the process, the tanning hormone bursicon.

Bursicon is released from the insect's head after ecdysis; if an insect's neck is ligated soon enough after moulting, its cuticle does not tan. Painstaking work has shown that bursicon acts through the second messenger cyclic AMP. Second messengers signal the arrival of hormones (like bursicon) at the cell surface to target molecules in the cell. Bursicon's effects can be mimicked in neck-ligated insects by injecting their abdomen with either cyclic AMP analogues or a central nervous system-derived peptide fraction of around 30 kDa in size, too large to be a neuropeptide. That is, bursicon is a protein hormone, explaining why it has proved hard to identify.

To determine bursicon's peptide sequence, one of the groups laboriously purified