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The Thing Inside Your Cells That Might Determine How Long You Live

You may have forgotten about the nucleolus since you took biology class, but scientists think this structure inside every cell in your body may play an important role in aging.

By JoAnna Klein

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Once there was a mutant worm in an experiment. It lived for 46 days. This was much longer than the oldest normal worm, which lived just 22.

Researchers identified the mutated gene that had lengthened the worm’s life, which led to a breakthrough in the study of aging — it seemed to be controlled by metabolic processes. Later, as researchers studied these processes, all signs seemed to point to the nucleolus.

Under a microscope, it’s hard to miss. Take just about any cell, find the nucleus, then look inside it for a dark, little blob. That’s the nucleolus. If the cell were an eyeball, you’d be looking at its pupil.

You’ve got one in every nucleus of every cell in your body, too. All animals do. So do plants, and yeast — and anything with a cell with a nucleus. And they’ve become much more important in our understanding of how cells work.

“We think the nucleolus plays an important role in regulating the life span of animals,” said Adam Antebi, a cellular biologist at the Max Planck Institute for Biology of Ageing in Germany. He’s an author of a new review published last week in Trends in Cell Biology that examines all the new ways that researchers have fallen in love with the nucleolus — especially its role in aging.

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You may have forgotten this from biology class, but the nucleolus is the cell’s ribosome factory. Ribosomes are like micro-machines that make proteins that cells then use for purposes like building walls, forming hairs, making memories, communicating and starting, stopping and slowing down reactions that help a cell stay functioning. It uses about 80 percent of a cell’s energy for this work.

But there’s more to the nucleolus than just making ribosomes.
If building a cell were like building a building, and the DNA contained the blueprint, the nucleolus would be the construction manager or engineer. “It knows the supply chain, coordinates all the jobs of building, does quality control checks and makes sure things continue to work well,” said Dr. Antebi.

How well it balances these tasks influences a cell’s health and life span. And in certain cells, its size has something to do with it.

The nucleolus can wax and wane in response to a body’s available nutrients and growth signals.

The more growth signals it intercepts, the more machines, or ribosomes, it makes. It gets bigger to contain them, but mysteriously this also shortens a cell’s or organism’s life. When food is restricted, or a metabolic pathway is silenced or slowed down, nucleoli shrink, making fewer ribosomes, and cells live longer.

Dr. Antebi thinks that as the nucleolus gets smaller, it also starts remodeling the things it would create to make the best of available supplies.

This is a highly coordinated process, he said. And life span can be thought of as how well the nucleolus balances the need to grow with the need to repair, correct mistakes and make sure everything works.

A drug called rapamycin, that blocks the signals of one metabolic pathway, extends life in different species from yeast, worms and fruit flies to mice. Centenarians tend to have cells in which there is reduced signaling in another pathway that involves insulin.

Researchers have found that modest dietary restriction and exercise shrunk nucleoli in muscle cells of some people over age 60. People with diseases like cancer or progeria, a kind of accelerated aging, tend have enlarged nucleoli.

You can see these kinds of effects in many different species. “It’s amazing — even if genetically identical, some live a short life and some live a long life,” said Dr. Antebi.

“We think that the smaller nucleoli may be a cellular hallmark of longevity” in certain cells under certain conditions, he added.

More research is needed to see if the size of these structures are just markers for longevity or aging or if they actually cause it.

“We’ve spent lots of money on trying to find biomarkers of longevity or aging, and maybe it’s just sitting under the microscope for us to see,” said Dr. Antebi.