

Biologist explains why no two people or cells age the same way, and what this means for anti-aging interventions

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You likely know someone who seems to age slowly, appearing years younger than their birth date suggests. And you likely have seen the opposite—someone whose body and mind seem much more ravaged by time than others. Why do some people seem to glide though their golden years and others physiologically struggle in midlife?

I have worked in the field of aging for all of my scientific career, and I



teach the cellular and molecular biology of aging at the University of Michigan. Aging research doesn't tend to be about finding the one cure that fixes all that may ail you in old age. Instead, the last decade or two of work points to aging as a multifactorial process—and no single intervention can stop it all.

What is aging?

There are many different definitions of aging, but scientists generally agree upon some common features: Aging is a time-dependent process that results in increased vulnerability to disease, injury and death. This process is both intrinsic, when your own body causes new problems, and extrinsic, when environmental insults damage your tissues.

Your body is comprised of <u>trillions of cells</u>, and each one is not only responsible for one or more functions specific to the tissue it resides in, but must also do all the work of keeping itself alive. This includes metabolizing nutrients, getting rid of waste, exchanging signals with other cells and adapting to stress.

The trouble is that every single process and component in each of your cells <u>can be interrupted or damaged</u>. So your cells spend a lot of energy each day preventing, recognizing and fixing those problems.

Aging can be thought of as a gradual loss of the ability to <u>maintain</u> <u>homeostasis</u>—a state of balance among body systems—either by not being able to prevent or recognize damage and poor function, or by not adequately or rapidly fixing problems as they occur. Aging results from a combination of these issues. Decades of research has shown that nearly every <u>cellular process</u> becomes more impaired with age.

Repairing DNA and recycling proteins



Most research on <u>cellular aging</u> focuses on studying how DNA and proteins change with age. Scientists are also beginning to address the potential roles many other important biomolecules in the cell play in aging as well.

One of the cell's chief jobs is to maintain its DNA—the instruction manual a cell's machinery reads to produce specific proteins. DNA maintenance involves protecting against, and accurately repairing, damage to genetic material and the molecules binding to it.

Proteins are the workers of the cell. They perform chemical reactions, provide structural support, send and receive messages, hold and release energy, and much more. If the protein is damaged, the cell uses mechanisms involving special proteins that either attempt to fix the broken protein or send it off for recycling. Similar mechanisms tuck proteins out of the way or destroy them when they are no longer needed. That way, its components can be used later to build a new protein.

Aging disrupts a delicate biological network

The cross-talk between the components inside cells, cells as a whole, organs and the environment is a complex and ever-changing network of information.

When all processes involved in creating and maintaining DNA and protein function are working normally, the different compartments within a cell serving specialized roles—<u>called organelles</u>—can maintain the cell's health and function. For an organ to work well, the majority of the cells that make it up need to function well. And for a whole organism to survive and thrive, all of the organs in its body need to work well.

Aging can lead to dysfunction at any of these levels, from the subcellular to the organismal. Maybe a gene encoding an important protein



for DNA repair has become damaged, and now all of the other genes in the cell are more likely to be repaired incorrectly. Or perhaps the cell's recycling systems are unable to degrade dysfunctional components anymore. Even the <u>communication systems</u> between cells, tissues and organs can become compromised, leaving the organism less able to respond to changes within the body.

Random chance can lead to a growing burden of molecular and cellular damage that is progressively less well-repaired over time. As this damage accumulates, the systems that are meant to fix it are accruing damage as well. This leads to a cycle of increasing wear and tear as cells age.

Anti-aging interventions

The interdependence of life's <u>cellular processes</u> is a double-edged sword: Sufficiently damage one process, and all the other processes that interact with or depend on it become impaired. However, this interconnection also means that bolstering one highly interconnected process could improve related functions as well. In fact, this is how the most successful anti-aging interventions work.

There is no silver bullet to stop aging, but certain interventions do seem to slow aging in the laboratory. While there are ongoing clinical trials investigating different approaches in people, most existing data comes from animals like nematodes, flies, mice and nonhuman primates.

One of the best studied interventions is <u>caloric restriction</u>, which involves reducing the amount of calories an animal would normally eat without depriving them of necessary nutrients. An FDA-approved drug used in organ transplantation and some cancer treatments <u>called rapamycin</u> seems to work by using at least a <u>subset of the same pathways</u> that calorie restriction activates in the cell. Both affect signaling hubs that direct the cell to preserve the biomolecules it has rather than



growing and building new biomolecules. Over time, this cellular version of "reduce, reuse, recycle" removes damaged components and leaves behind a higher proportion of functional components.

Other interventions include changing the levels of certain metabolites, selectively <u>destroying senescent cells</u> that have stopped dividing, changing the gut microbiome and <u>behavioral modifications</u>.

What all of these interventions have in common is that they affect core processes that are critical for cellular homeostasis, often become dysregulated or dysfunctional with age and are connected to other cellular maintenance systems. Often, these processes are the central drivers for mechanisms that protect DNA and proteins in the body.

There is no single cause of aging. No two people age the same way, and indeed, neither do any two <u>cells</u>. There are countless ways for your basic biology to go wrong over time, and these add up to create a unique network of aging-related factors for each person that make finding a one-size-fits-all anti-aging treatment extremely challenging.

However, researching interventions that target multiple important cellular processes simultaneously could help improve and maintain health for a greater portion of life. These advances could help people live longer lives in the process.

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