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What makes the biological clock tick? La Jolla scientists link tw aging

UCSD researchers work to pave the way for new therapies to slow or reverse the process

Zane Koch and Trey Ideker are authors of a study out of the UC San Diego School of Medicine on aging. (UC San Diego)

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In the continuing quest to find the cause of aging and a pathway to slow or even reverse it, a recent study out of the UC San Diego School of Medicine in La Jolla has linked two leading theories.

In doing so, researchers hope to better understand the aging process and develop new therapies.

“Everyone gets that we age, and most people would like to age in a healthy manner or to a prolonged age, whether that’s beauty-related or the health care aspect and onset of disease,” said study co-author Trey Ideker. “This has led to intensified interest in the last few decades, because if you can understand the molecular level, you could reverse it or slow it. That’s what people are after.”

According to UCSD, there are two prevailing theories about the relationship between aging and our DNA.

The somatic mutation theory suggests aging is caused by an accumulation of mutations leading to permanent changes in the DNA sequence that occur randomly.

The epigenetic clock theory suggests aging occurs due to accumulation of epigenetic modifications, or minor changes to the chemical structure of DNA that do not alter the underlying sequence but instead change which genes are on or off.

Comparing this in the body to the hardware and software in a computer, the study’s first author, Zane Koch, said DNA serves as the “hardware” such as a keyboard or a memory chip and the epigenome is the “software,” or the programs that provide functions.

“One theory is that the software gets buggy; the other is that the physical hardware stops working,” he said.

Looking to link the two rather than target one or the other, researchers analyzed data from 9,331 patients catalogued in the Cancer Genome Atlas and the Pan-Cancer Analysis of Whole Genomes. By comparing genetic mutations and epigenetic modifications, they determined that mutations were predictably correlated. They also found that a single mutation could cause a cascade of epigenetic changes across the genome, not just where the mutation occurred.

“Our paper shows that as the hardware of the computer breaks down, that causes the software to break down,” Koch said.

Modifications to the epigenome can be reversed in some cases, Koch said, so scientists are working to develop therapeutics that target them.

But, he added, “efforts to simply wind back or reset the software ignore the errors in the hardware.”

With the findings in the paper, scientists can “double down on therapies that reduce damage to the ‘hardware’ in the first place,” Ideker said. “Because of this paper, we now know the reduction in DNA damage leads to less reprogramming at the ‘software’ level.”

With the caveat that research driven by these findings is in its “early stages,” Koch said the next project is to investigate a pathway into cells that responds to DNA damage, and develop a therapy. ♦