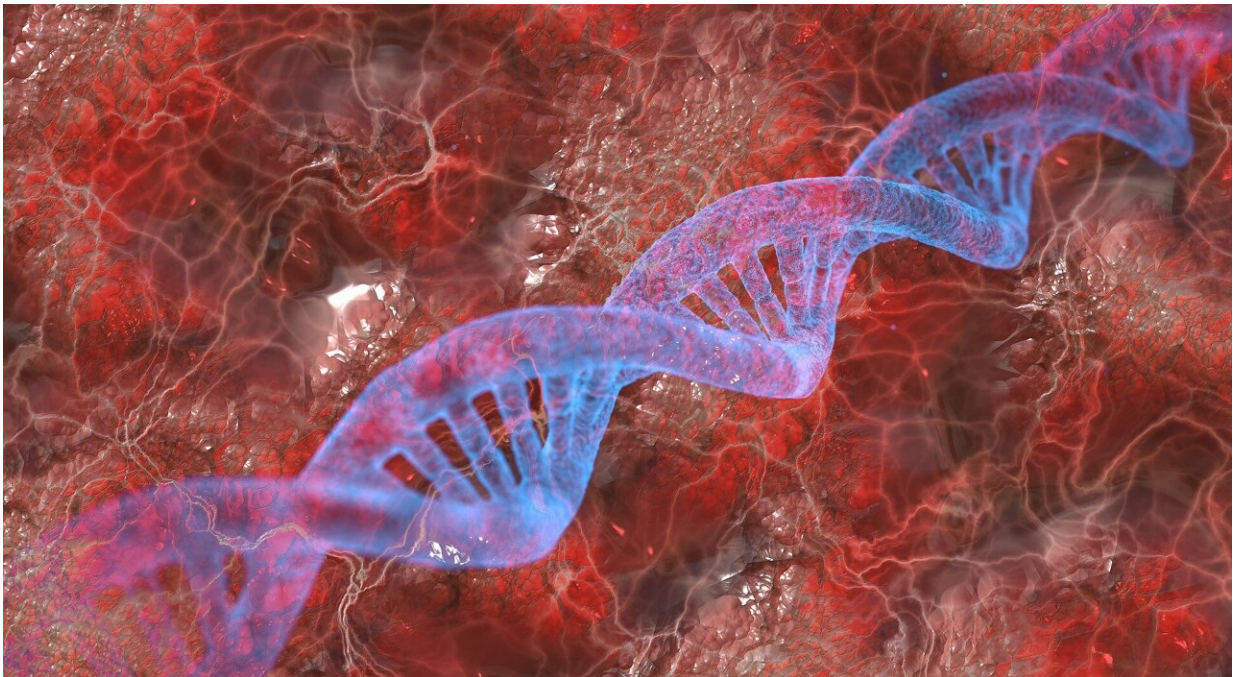


Blood levels of 'free range' DNA may signal early detection of dementia and frailty

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In a long-term prospective study of more than 600 older participants, Johns Hopkins Medicine researchers say they have evidence that higher levels of cell-free DNA circulating in the blood may signal increased risk of chronic inflammation associated with early signs of frailty and dementia.

The findings, published Oct. 11 in the *Journal of Alzheimer's Disease*, could advance the search for relatively simple blood tests that detect risk of Alzheimer's disease and other forms of cognitive decline.

Circulating cell-free genomic DNA, (ccf-gDNA) is a long identified product of natural cell death in the body. As cells die via apoptosis (programed cell death), the cells shrink, degrade their [plasma membrane](#), and ultimately rupture and release their contents into the body, including DNA fragments. These fragments end up as free-range DNA in the bloodstream.

"These ccf-gDNA fragments may trigger long-term chronic inflammatory reactions that have previously been linked to the premature destruction and aging of tissues and organs, including the brain," says Peter Abadir, M.D., associate professor of geriatric medicine and gerontology at the Johns Hopkins University School of Medicine. "The body sees these ccf-gDNA fragments as something that needs to be removed, therefore the body's immune system is running at a higher rate than it should. Such immune system overdrive may be a factor in identifying the onset of dementia."

For the new study, the researchers tested the blood of 631 people with the average age of 79 who showed no [cognitive impairment](#) when the study began. Participants received yearly physical and cognitive testing, at the time of each blood draw. Researchers found that during the eight-year study period, higher levels of ccf-gDNA in the blood were associated with increased cognitive decline and worsening frailty.

Alzheimer's disease affects an estimated 6.5 million people in the United States, according to the Alzheimer's Association, and there are no known cures or effective therapies. However, the potential of a blood test to identify those most at risk or in early stages could lead to supportive services and other interventions to plan for, compensate for or slow

down worsening symptoms.

"Our [world population](#) is aging quickly. We have so many advances that have helped extend our [life span](#), so the goal now is to live healthier as we age," says Lolita Nidadavolu, M.D., Ph.D., assistant professor of geriatric medicine and gerontology at the Johns Hopkins University School of Medicine. "Dementia and frailty are increasing in frequency. Many people know someone affected by these conditions. With a single [blood](#) draw, we may have the potential to identify people who can benefit from early interventions."

Moving forward, researchers say they hope to learn more about the cellular origins of ccf-gDNA fragments. If researchers can identify that a large amount of these fragments are coming from a specific type of cell, it is hoped that they can advance the search for drugs that target the aging and dementia process.

More information: Lolita S. Nidadavolu et al, Circulating Cell-Free Genomic DNA Is Associated with an Increased Risk of Dementia and with Change in Cognitive and Physical Function, *Journal of Alzheimer's Disease* (2022). [DOI: 10.3233/JAD-220301](https://doi.org/10.3233/JAD-220301)

Provided by Johns Hopkins University

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