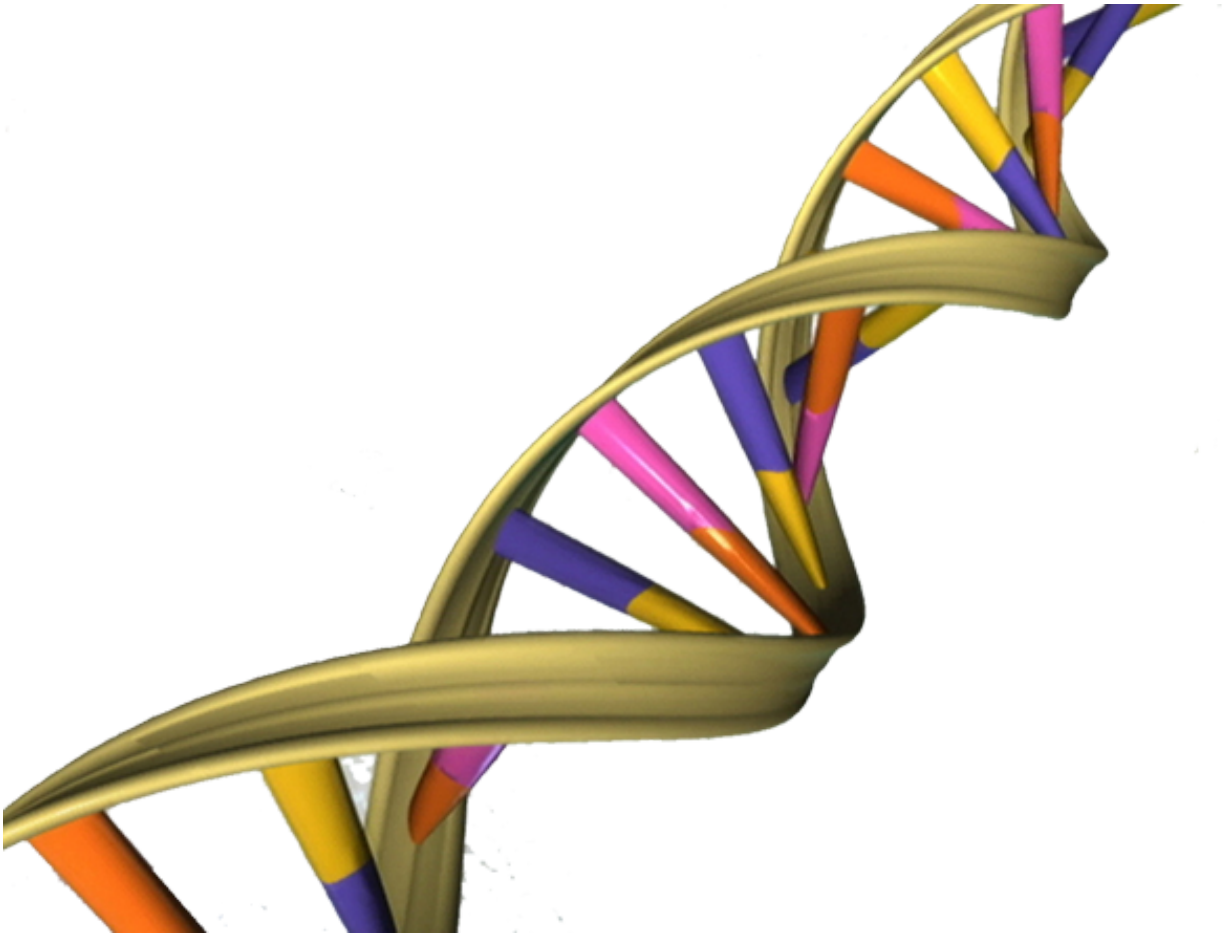
Aged DNA may activate genes differently

October 31 2017, by Kim Krieger



A depiction of the double helical structure of DNA. Its four coding units (A, T, C, G) are color-coded in pink, orange, purple and yellow. Credit: NHGRI

Grey hair, wisdom, and wrinkles on our skin mark us as we age, but it's the more subtle changes beneath the surface that make us old. Now,

researchers have discovered that our chromosomes also wrinkle with age, changing how our immune system renews itself.

Our chromosomes are our instruction manuals. They tell how to make every protein we need to live. They look like long necklaces of DNA, coiled and curled in the center of every cell in the body. Some parts of the necklace are open and loose, others are coiled tightly or obscured by other sections of the chain. If a part is tightly coiled, it's harder for the cell's machinery to access the DNA in that section and activate the genes that DNA describes.

New research by a team from UConn Health and the Jackson Laboratory for Genomic Medicine (JAX-GM) shows that our chromosomes age along with us, with some sections of the chromosome curling and closing up and making it harder to access DNA that might be critical to defend our bodies against disease. The paper appeared in the *Journal of Experimental Medicine* on Sept. 13.

"In young people, thousands of sites are open, seemingly ready to activate genes and make protein. There are genes and pathways that are very active in younger people that appear to lose their activity in older adults," says George Kuchel, UConn Health geriatrician and director of the UConn Center on Aging. "The portions that are open and the portions that are closed look very different" in younger people versus older people, he adds.

Kuchel worked with JAX-GM's immunologist Jacques Banchereau and computational biologist Duygu Ucar to determine the regions of chromosomes and genes that lose their activity with aging. The large amount of data and its diversity required Ucar and her team to invent new analysis techniques to get meaningful results from it. The close collaboration between researchers at UConn Health and JAX-GM is what makes this type of complex study possible.

The researchers recruited 75 healthy young people between the ages of 22 and 40 years, and 26 healthy seniors aged 65 and older to participate in the study. Each person gave a blood sample, and the research team then isolated immune cells from the blood. They investigated how the immune cells' gene activation changed with aging.

The differences between younger people and older made a clear signature, one that had never been seen before in genomic analysis. Regions of chromosome coding for genes that encourage the development and differentiation of T-cells, which help defend us against flu and other viral infections and some cancers, are more likely to be open in young people compared to the elderly. On the other hand, regions of chromosome coding for genes associated with cell death and inflammation appeared to be more open in the elderly than in the young.

Kuchel, Banchereau, and Ucar have new studies now underway that will apply this type of genomic analysis to pneumococcal vaccine response, as well as to overall disease resilience in the elderly.

More information: Duygu Ucar et al. The chromatin accessibility signature of human immune aging stems from CD8+T cells, *The Journal of Experimental Medicine* (2017). DOI: 10.1084/jem.20170416

Provided by University of Connecticut