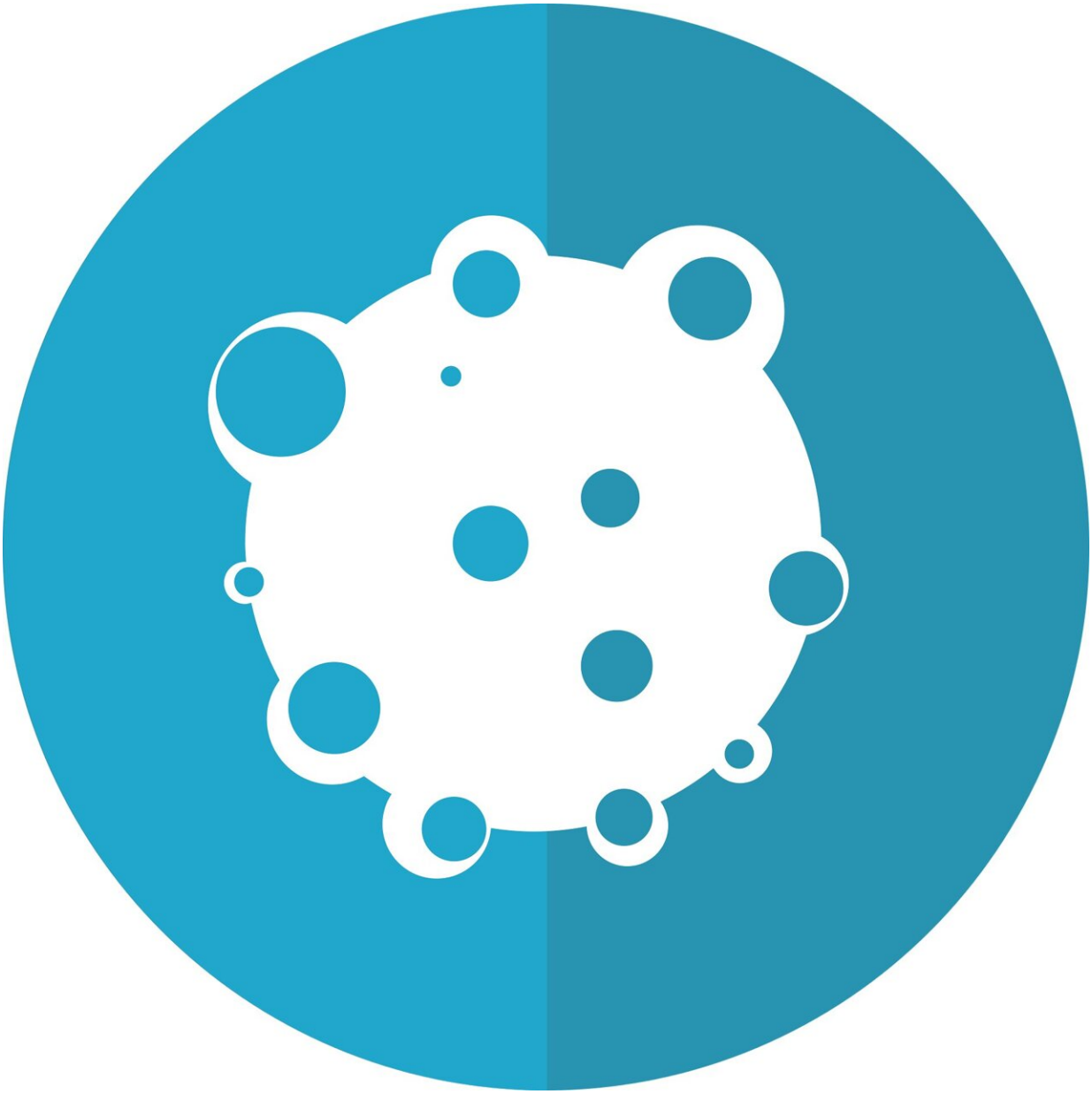
Chronologically young, biologically old: DNA linked to cancer survivors premature aging

March 22 2022



Credit: Pixabay/CC0 Public Domain

Scientists from St. Jude Children's Research Hospital have identified variants in two genes that are associated with accelerated aging in childhood cancer survivors. Their research looked at the difference between their biological age and chronological age. The study, published today in *Genome Medicine*, is the first to identify genetic risk factors for accelerated aging in pediatric cancer survivors.

Today a majority of children with cancer in the U.S. survive. However, some survivors develop diseases that typically occur in older adults. It is not totally clear why some patients are more susceptible to developing age-related conditions than others.

"This is one of a series of studies my lab has undertaken to investigate aging biomarkers in childhood cancer survivors," said corresponding author Zhaoming Wang, Ph.D., of the Departments of Epidemiology and Cancer Control and Computational Biology. "We previously evaluated non-genetic risk factors including cancer treatments, health behaviors, and chronic health conditions that contribute to age acceleration. This study focuses on the underlying genetic factors among these patients."

St. Jude follows over 6,000 childhood cancer survivors enrolled in the St. Jude Lifetime Cohort Study (SJLIFE). As part of SJLIFE, scientists have characterized genetic variations by conducting whole-genome sequencing (WGS) of survivors' DNA. Wang's group analyzed the link between common genetic variants derived from the WGS data with epigenetic age acceleration (EAA) in SJLIFE participants. EAA is a measure of the difference between "biological" and chronological age for each survivor, and it strongly correlates with the development of age-related diseases.

Finding the premature aging needle in a genetic haystack

Wang's group found variants in two genomic regions associated with the development of accelerated aging. One variant was in the SELP gene and the other in the HLA region. These genes are both involved in age-related diseases. For example, SELP is upregulated in Alzheimer's disease.

The scientists found the variants by employing an agnostic Genome-Wide Association Study (GWAS) approach. In this technique, the researchers compare the DNA variants present in survivors and community controls with different levels of biological aging (i.e., EAA). In the 3 billion base pair DNA genome, over 8 million variants were tested, and there were two single nucleotide polymorphisms (SNPs) that appeared significantly different between individuals with different levels of biological aging. These SNPs in combination with other non-genetic risk factors may allow physicians in the future to identify the survivors at higher risk of accelerated aging before they develop premature aging symptoms.

"Our work can help determine subgroups at the highest risk for accelerated aging among childhood cancer survivors," Wang said. "The findings can also identify potential drug targets for future invention studies. For example, the protein produced by the SELP gene, p-selectin, already has an inhibitor used in other diseases."

More information: Qian Dong et al, Genome-wide association studies identify novel genetic loci for epigenetic age acceleration among survivors of childhood cancer, *Genome Medicine* (2022). DOI: 10.1186/s13073-022-01038-6

Provided by St. Jude Children's Research Hospital