To keep a 117-Year-Old Healthy Study Explains how Genetics and Lifestyle Combinedly Work

An international team of researchers conducted a comprehensive multiomics analysis of the world's oldest living person and compared her data with matched cohorts.

They identified factors underpinning her resistance to typical age-related conditions: low inflammation, protective genetic variants, a younger epigenome, and a youthful microbiome, thereby pointing toward hypotheses for potential strategies and candidate biomarkers of healthy aging.

Study

To explore the processes that enable extreme longevity, researchers conducted an extensive multiomics analysis that examined multiple molecular layers of biology. Most analyses were performed on blood collected at 116 years and 74 days, with saliva, urine, and stool providing complementary data. Maria Branyas Morera's data were systematically compared with those from non-supercentenarian populations to identify distinguishing features of extreme aging.

A range of biological samples, including blood, urine, saliva, and stool, was collected, along with detailed records of her lifestyle and medical history. Peripheral blood mononuclear cells were isolated and preserved for cellular and genetic analyses.

Chromosomal structure was evaluated using standard karyotyping, while telomere length (a well-established biomarker of aging) was measured with advanced imaging techniques.

High-molecular-weight deoxyribonucleic acid (DNA) extracted from blood cells was subjected to optical genome mapping, and DNA from multiple tissues underwent whole-genome sequencing.

Detected genetic variants were compared with those of a Spanish control cohort to identify rare or potentially protective alleles. Further analyses included tests for clonal hematopoiesis, single-cell ribonucleic acid (RNA) sequencing to characterize immune cell populations, and proteomic profiling of plasma extracellular vesicles.

Serum samples were analyzed using metabolomics, with a focus on lipid profiles, amino acids, and glycoproteins, providing insight into metabolic efficiency and cardiovascular health.

The gut microbiome was studied through the genetic sequencing of stool samples and compared with publicly available datasets, providing insight into microbial contributions to longevity.

Together, this multiomics approach produced a highly detailed picture of her genetics, immune function, metabolism, and microbiota.

Results

One of the striking observations was that, despite having extremely short telomeres (~8 kb mean, with 40% below the 20th percentile), Maria Branyas Morera remained healthy. This suggests that telomere shortening may reflect chronological age without necessarily predicting the onset of illness. The authors hypothesize that extreme telomere attrition may act as a clock rather than a disease marker and speculate that it could even constrain malignant clones.

Genetic analysis revealed rare variants in genes associated with immune system function, cardiovascular protection, neurological health, and mitochondrial function. No single variant explained longevity, and the canonical FOXO3A longevity allele was absent; instead, multiple rare alleles across pathways appeared to contribute collectively.

Blood testing uncovered mutations typical of clonal hematopoiesis (SF3B1 and TET2), a process often tied to cancer and cardiovascular disease. Yet Maria Branyas Morera displayed no such conditions. Instead, her immune profile was characterized by expanded cytotoxic T cells and age-associated B cells, along with specific "young-like" expression features in selected pathways and upregulation of IgG genes, all of which indicated immune resilience despite her advanced age.

Mitochondrial function in her blood cells was robust, as indicated by assays that suggested a preserved energy production capacity compared to controls.

Metabolomic studies have demonstrated efficient lipid metabolism, characterized by low triglyceride levels, reduced "bad" cholesterol, elevated "good" cholesterol, and decreased markers of inflammation.

These features are associated with protection against cardiovascular disease and dementia. Her extracellular vesicles carried proteins that promoted immune defense, lipid transport, and protection against oxidative stress, reinforcing the picture of robust biological defenses. Notably, the SAA1 protein was elevated compared to that of younger postmenopausal controls, yet she showed no signs of neurodegenerative disease.

Analysis of the gut microbiome revealed unusually high levels of Bifidobacterium, a beneficial bacterium typically reduced in elderly individuals, but known for its anti-inflammatory effects and links to healthy aging. She consumed approximately three yogurts daily, each containing Streptococcus thermophilus and Lactobacillus delbrueckii, which can support Bifidobacterium growth. The authors note that this dietary link is plausible but unproven without longitudinal sampling.

Epigenetic testing revealed distinctive DNA methylation patterns. Remarkably, her "biological age" was significantly younger than her chronological age, with an rDNA methylation age of ~23.17 years younger and a negative age pace of −17.34 years, indicating preserved genomic stability and a decelerated epigenetic aging process. In addition, she retained hypermethylation of repetitive elements (LINE-1, ALU, ERV) that typically lose methylation with age, potentially contributing to genomic protection.

Conclusion

Overall, Maria Branyas Morera's extraordinary longevity resulted from a convergence of protective genetic variants, resilient immune function, efficient metabolism, robust mitochondrial performance, a favorable gut microbiome, and stable epigenetic regulation, collectively preserving her health into extreme old age.

These traits interacted to preserve health into extreme old age, illustrating that aging and disease can, under certain circumstances, be decoupled.

A major strength of this study is its comprehensive multiomics approach, which provided an unprecedented depth of analysis across multiple biological layers. However, as a cross-sectional, blood-centric study of a single individual, causal inference and broad generalizations remain limited.

Future research should examine larger cohorts of long-lived individuals and test targeted interventions, such as dietary changes, exercise, metabolic therapies, and microbiome modulation. It is also important to note that some epigenetic interventions may require caution due to the protective role of repeat hypermethylation.

Source:

https://www.news-medical.net/news/20250925/Study-explains-how-genetics-and-lifestyle-combined-to-keep-a-117-year-old-healthy.aspx