# Epigenetic biomarkers predict CVD risk

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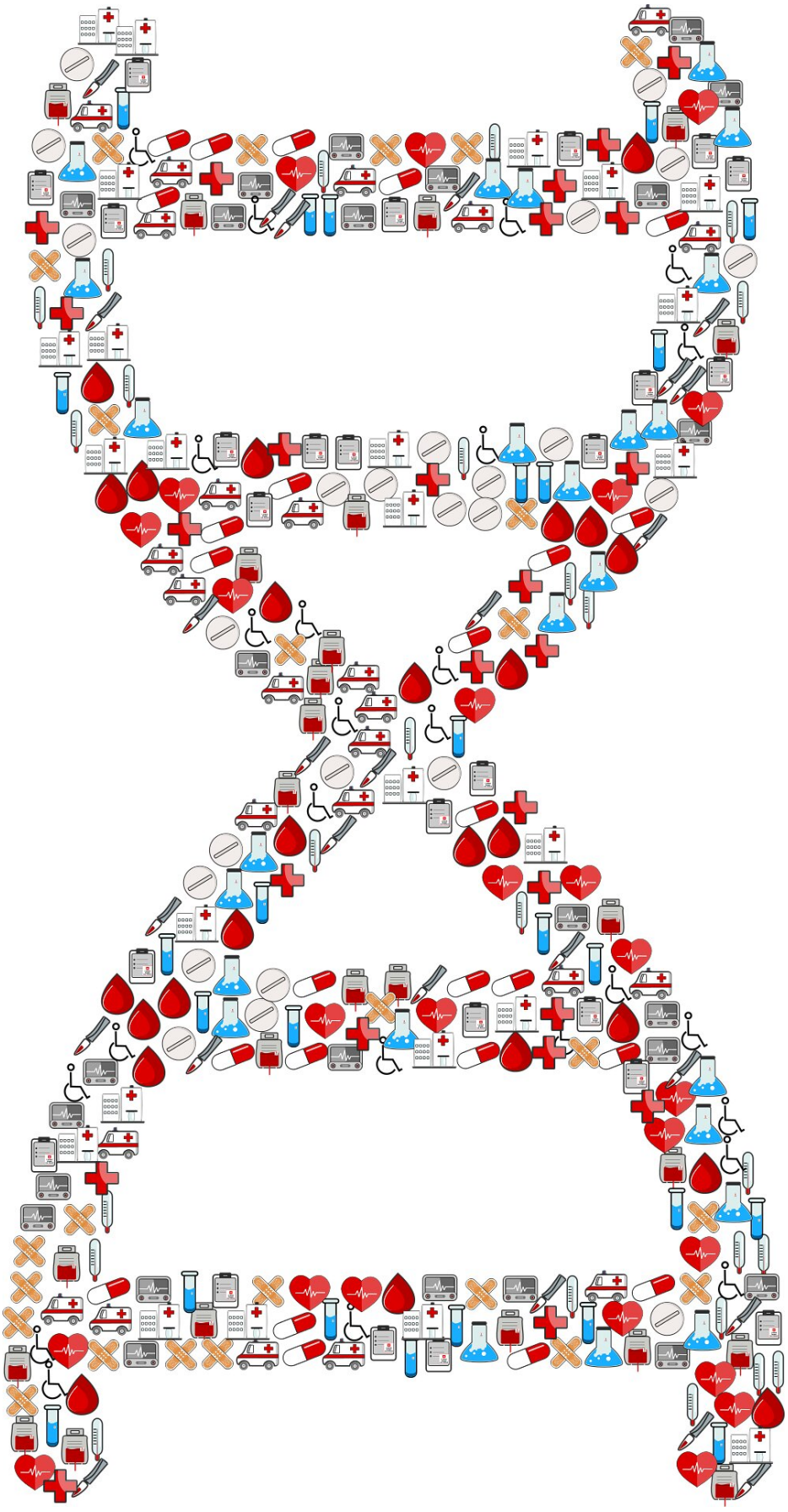

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Epigenetic biomarkers may reflect past cardiovascular health exposures and predict cardiovascular disease in the future, according to a Northwestern Medicine study published in the journal *Circulation*.

These biomarkers measured around midlife reveal valuable health information from a patient's past, according to Yinan Zheng, Ph.D., assistant professor of Preventive Medicine in the Division of Cancer Epidemiology and Prevention and lead author of the study.

"Our past exposures to obesity, elevated blood pressure, blood sugar and cholesterol leave 'epigenetic footprints' for us to better inform the development of cardiovascular diseases," Zheng said.

Cardiovascular health from young adulthood is strongly associated with future risk of cardiovascular disease (CVD) and total mortality. In the current study, investigators defined a cumulative cardiovascular health score including body mass index, blood pressure, cholesterol and fasting glucose. They applied this score to more than 1,000 patients in the Coronary Artery Risk Development in Young Adults (CARDIA) study, a long-term study of cardiovascular risk factors which began in 1983.

In addition, the scientists measured DNA methylation —epigenetic changes that regulate gene expression—in patient blood samples at two different time points collected around 40 years of age. DNA methylation can be modified gradually through long-term exposures to cardiovascular risk factors and the investigators hypothesized that it might better capture risk of CVD in conjunction with conventional CVD risk factors.

"These epigenetic markers integrate our exposures over decades to environmental factors like air pollution and to behavioral factors like our diet and physical activity," said Donald Lloyd-Jones, MD, ScM, chair and the Eileen M. Foell Professor of Preventive Medicine and co-senior author of the study. "In some ways, your epigenome is even more important than your inherited DNA code in determining your health."

The scientists found changes in 45 DNA methylation markers that were prospectively associated with 15 to 20 years of cardiovascular health prior to the measurement of the markers. For example, poorer cardiovascular health was associated with less methylation in the gene CPT1A, "switching on" expression of the gene.

The gene CPT1A codes for a lipid metabolism protein that's important for burning fat, but a long-term poor diet can "exhaust" those proteins and contribute to fat buildup and eventual CVD, Zheng said.

Investigators also created a methylation risk score and used it to predict risk of coronary artery calcification (CAC), a condition that often presages later CVD. This methylation score was able to predict future clinical CVD events in the Framingham Heart Study, another large longitudinal cohort.

"Clinicians can use the score just like the CVH metrics by applying thresholds to determine the CVD risk level, such as low, moderate or high," said Lifang Hou, MD, Ph.D., chief of Cancer Epidemiology and Prevention in the Department of Preventive Medicine and co-senior author of the study. "However, future larger population studies are needed to determine such a threshold."

**More information:** Yinan Zheng et al, Association of Cardiovascular Health Through Young Adulthood With Genome-Wide DNA Methylation Patterns in Midlife: The CARDIA Study, *Circulation*. DOI:

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