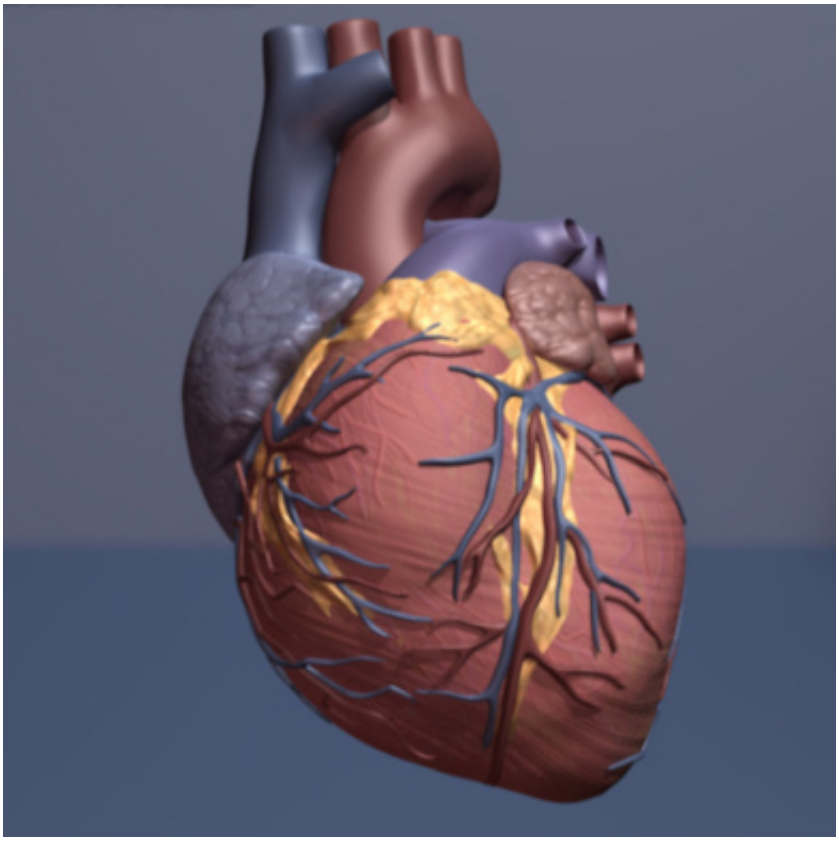
A role for mutated blood cells in heart disease?

January 19 2017



Human heart. Credit: copyright American Heart Association

A new study provides some of the first links between relatively common mutations in the blood cells of elderly humans and atherosclerosis.

Though cardiovascular disease, which is characterized in part by

atherosclerosis, or plaque build-up, is a leading cause of death in the elderly, almost 60 percent of elderly patients with atherosclerotic cardiovascular disease (CVD) exhibit no conventional risk factors, or just one. This and other data suggest that age-dependent risk factors that haven't yet been identified may contribute to CVD.

Scientists know that accumulation of somatic DNA mutations is a feature of aging, though little data exists on the role of such mutations in age-associated disorders beyond cancer. Meanwhile, recent human studies indicate that aging is associated with an increase in somatic mutations in the hematopoietic system, which gives rise to blood cells; these mutations provide a competitive growth advantage to the mutant hematopoietic cells, allowing for their clonal expansion - a process that has been shown to be associated with a greater incidence of atherosclerosis, though specifically how remains unclear.

In this study, researchers at Boston University School of Medicine (BUSM) investigated whether there is a direct relationship between such mutations and atherosclerosis. They generated an experimental model to investigate how one of the genes commonly mutated in blood cells of elderly humans, TET2, affects plaque development. Plaque formation accelerated in the models transplanted with Tet2-deficient bone marrow cells, likely through increasing macrophage-driven inflammation in the artery wall. The results strengthen support for the hypothesis that hematopoietic mutations play a causal role in atherosclerosis.

"Our studies show that mutations in our white blood cell cells, that we acquire as we age, may cause cardiovascular disease. Understanding this new mechanism of cardiovascular disease could lead to the development of new therapies to treat individuals who suffer from heart and blood vessel ailments due to these mutations," explained corresponding author Kenneth Walsh, PhD, professor of medicine at BUSM. "Furthermore, because these mutations become prevalent starting at middle age, these

studies suggest that genetic analyses of blood samples could add to the predictive value of traditional risk factors - high cholesterol, hypertension, diabetes and smoking - that are currently monitored."

The study is published in the journal *Science*.

More information: "Clonal hematopoiesis associated with Tet2 deficiency accelerates atherosclerosis development in mice," *Science*, science.sciencemag.org/lookup/ … 1126/science.aag1381

Provided by Boston University Medical Center