Clonal expansion of hematopoietic cells carrying acquired mutations in epigenetic modifiers, such as DNMT3A and TET2, is common in older adults. This phenomenon, referred to as age-related clonal hematopoiesis (ARCH), is associated with increased risks of blood cancers and cardiovascular disease. Epigenetic mechanisms underlying these disease associations are poorly understood. Using human pluripotent stem cell-derived macrophages, we investigate the impact of ARCH-associated mutations on DNA methylation and immune gene expression. Our results reveal a broad impact of epigenetic modifier dysfunction on immune gene expression and shed light on the mechanism of immune dysfunction associated with aging.