Clonal hematopoiesis: A new causal risk factor for cardiovascular disease

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Advances in DNA sequencing methodology reveal that somatic mutations leading to clonal events are remarkably prevalent in aging individuals. In the hematopoietic system this condition is referred to as clonal hematopoiesis or clonal hematopoiesis of indeterminant potential (CHIP). Epidemiological studies indicate that clonal hematopoiesis is associated with increased mortality due in large part to an increase in cardiovascular disease risk. Our work supports the concept that clonal hematopoiesis is a causal risk factor for cardiovascular disease, and we have defined aspects of its mechanism. This work has shown that expanding mutant clones in hematopoietic stem cells, attributed to mutations in *TET2*, *DNMT3A*, *JAK2* and other driver genes, give rise to progeny leukocytes with altered phenotypic properties. While different mutant driver genes confer distinct phenotypes to their progeny leukocytes, a growing body of experimental evidence suggests that activation of IL-1beta and/or IL-6 expression is a common mechanistic feature shared by multiple forms of clonal hematopoiesis, and that targeting inflammation can reduce the increased risk of disease that is conferred by clonal hematopoiesis. Overall, these findings reveal that clonal hematopoiesis represents a new mechanism of cardiovascular disease development that shares features with hematologic malignancy. Further research in this area could provide a mechanistic framework for personalized anti-inflammatory therapies to treat individuals who carry specific somatic mutation clones within their hematopoietic cell populations.