Researchers show that positive selection is major force shaping clonal hematopoiesis

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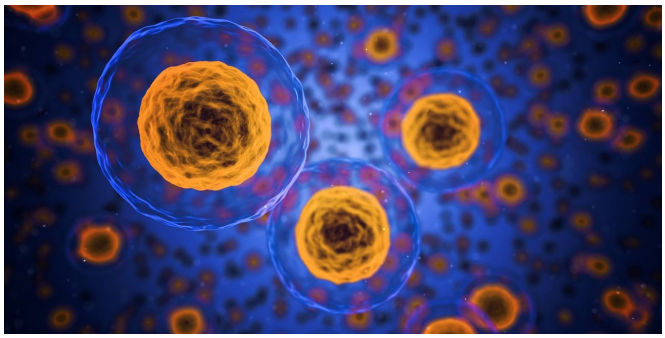

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A team of researchers from the University of Cambridge, Stanford University and Washington University School of Medicine has found evidence indicating that positive selection (as opposed to drift) is the major force shaping clonal hematopoiesis. In their paper published in the journal *Science*, the group describes their study of clonal hematopoiesis and what they learned about it. Christina Curtis with Stanford University School of Medicine has published a Perspective piece on the work by the team in the same journal issue.

Living creatures, including human beings, persist via cell division—it is how body parts are constantly rejuvenated. But sometimes, mutations are introduced, which may or may not be a good thing. Such mutations are the drivers of evolution, but some others are behind the development of cancerous tumors. Prior research has found that over time, as people age, mutations can accrue, which also may or may not be beneficial. And unfortunately, despite the important role that mutations play in living creatures, scientists still do not fully understand the process.

Prior research has shown that clonal hematopoiesis is a common age-related phenomenon in which hematopoietic stem cells or other progenitor cells in the blood take part in the formation of a population of blood cells that are genetically distinct from regular blood cells. Furthermore, some mutations can be benign, but others have been found to initiate premalignancies. The researchers with this new effort sought to learn more about this process.

The work involved analyzing information from nine public databases of blood tumor data on over 50,000 cancer patients. They catalogued the variant allele frequencies (VAFs) for each of the samples. They then used the data to build a stochastic branching model representing hematopoietic stem cell dynamics. Among other things, their model showed neutral mutations either went extinct very rapidly or grew slowly and remained at low VAFs. And it also showed that beneficial mutations grew exponentially. Taken together, the model suggested that positive selection for beneficial mutations dictate the genetic diversity of blood, rather than genetic drift.

More information: Caroline J. Watson et al. The evolutionary dynamics and fitness landscape of clonal hematopoiesis, *Science* (2020). DOI: 10.1126/science.aay9333