Immune system cell clones created before birth may last for decades

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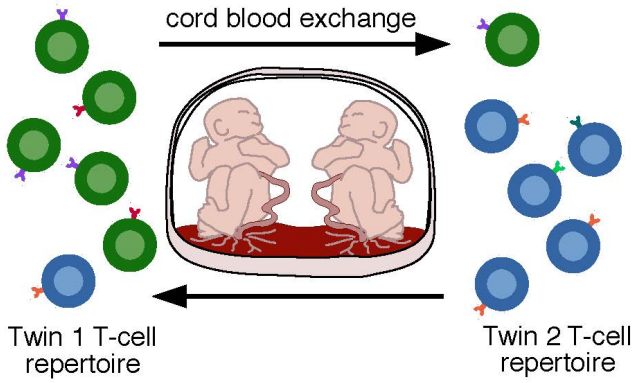

Twins exchange T-cells in utero through shared placenta. Credit: Kevin Dufendach (2008), retrieved from commons.wikimedia.org/wiki/File:Placentation.svg, CC BY, adapted and modified by M.V. Pogorelyy.

Key immune system cells produced before birth may survive well into adulthood, according to new research published in *PLOS Computational Biology*.

The findings provide new insights into the immune system's T cells, each of which possesses receptor proteins that allow it to recognize a specific pathogen. Throughout life, every person maintains a unique but highly diverse set of different T cells with receptors that recognize different pathogens. This enables protection against a wide range of diseases.

Since unique T cell receptors are created through a random process of DNA arrangement, even genetically identical twins differ in their precise set of distinct T cells. However, previous studies have shown that identical twins share more T cell receptors than would be statistically expected.

In the new study, Mikhail Pogorelyy and colleagues from the Ecole normale supérieure in Paris, and the Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, Moscow, address this excess of T-cell clone sharing between genetically identical twins.

The team used a statistical model of T cell receptor formation to analyze receptor DNA sequences in blood samples from adult pairs of identical twins. The analysis suggests that the degree of T-cell clone sharing between twins is greater than can be explained simply by shared genomes. Instead, the scientists propose, twin embryos may exchange T cells through cord blood before birth.

"As a result, the immune system of one twin has cells that were generated in the other twin and vice versa," says study co-author Thierry Mora.

These findings, combined with further statistical analysis of T cell receptor DNA sequences from unrelated adults of varying ages, suggest that some T cell clones created before birth may persist in the body for about 40 years. "This longevity of clones implies that any 40 year old person can still have clones that were produced before birth," Mora says.

These results could shed new light on the observation that the exact same T cell receptors are sometimes found in multiple unrelated adults. If T cell clones created before birth can stick around for decades, they might account for a substantial amount of shared T cells between any two unrelated people. Indeed, the diversity of T cell receptors generated before birth is known to be lower than in adults, increasing the odds of two unrelated people sharing the same receptor.

More information: Pogorelyy MV, Elhanati Y, Marcou Q, Sycheva AL, Komech EA, Nazarov VI, et al. (2017) Persisting fetal clonotypes influence the structure and overlap of adult human T cell receptor repertoires. *PLoS Comput Biol* 13(7): e1005572. doi.org/10.1371/journal.pcbi.1005572