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# Entire T-cell receptor repertoire sequenced revealing extensive and unshared diversity

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T-cell receptor diversity in blood samples from healthy individuals has been extensively cataloged for the first time in a study published online today in *Genome Research*, setting the stage for a better understanding of infectious disease, cancer, and immune system disorders.

Adaptive immunity is mediated by T-cells, a white blood cell that identifies and attacks cells that may be infected with viruses or contain cancer-causing mutations. To recognize a wide array of potentially infectious agents or cancer-causing mutations, gene shuffling creates a highly variable and diverse collection of T-cell receptor sequences.

While the diversity of sequences in immune cell repertoires has been investigated previously, no study had yet been able to capture the entire range present in an individual sample. Now, using next-generation sequencing technology, researchers in Canada have identified essentially all T-cell receptor variants in blood samples, identifying more than one million unique sequences.

Dr. Robert Holt of the BC Cancer Agency and Simon Fraser University, senior author of the report, explained that this study is the first to establish that while there is high T-cell diversity in a standard blood sample, it does not give the entire picture. "This is only part of the diversity that would be present within a person's entire body," Holt said, "but now we know that although the diversity is very large, it is ultimately limited, and it is measureable."

The group found that some T-cell receptor sequences are common, some are rare, and the repertoire can change over time. The individual repertoire was then compared to that of two other individuals, showing that only a minority of sequences is shared between them.

Interestingly, they noted that for sequences that were shared, different gene shuffling events had often generated the same sequence. "This shows that certain sequences are more favored than others, most likely because they are more effective in recognizing specific types of infections or mutations," said Holt.

By cataloging the baseline diversity of the immune repertoire in a healthy individual, Holt explained that future studies would be able to then recognize how the repertoire is disturbed in cases of immune challenge, such as infectious disease or organ transplantation, and furthermore, may assist in the development of new vaccines.

**More information:** Warren RL, Freeman JD, Zeng T, Choe G, Munro S, Moore R, Webb JR, Holt RA. Exhaustive T-cell repertoire sequencing of human peripheral blood samples reveals signatures of antigen selection and a directly measured repertoire size of at least 1 million clonotypes. *Genome Res* doi:10.1101/gr.115428.110

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