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Extensive renewal of the T cell repertoire following autologous stem cell transplant in MS

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A new study describes the complexity of the new T cell repertoire following immune-depleting therapy to treat multiple sclerosis, improving our understanding of immune tolerance and clinical outcomes.

In the Immune Tolerance Network's (ITN) HALT-MS study, 24 patients with relapsing, remitting multiple sclerosis received high-dose immunosuppression followed by a transplant of their own stem cells, called an autologous stem cell transplant, to potentially reprogram the immune system so that it stops attacking the brain and spinal cord. Data published today in the *Journal of Clinical Investigation* quantified and characterized T cell populations following this aggressive regimen to understand how the reconstituting immune system is related to patient outcomes.

ITN investigators used a high-throughput, deep-sequencing technology (Adaptive Biotechnologies, ImmunoSEQTM Platform) to analyze the T cell receptor (TCR) sequences in CD4+ and CD8+ cells to compare the repertoire at baseline pre-transplant, two months post-transplant and 12 months post-transplant.

Using this approach, alongside conventional flow cytometry, the investigators found that CD4+ and CD8+ lymphocytes exhibit different reconstitution patterns following transplantation. The scientists observed

that the dominant CD8+ T cell clones present at baseline were expanded at 12 months post-transplant, suggesting these clones were not effectively eradicated during treatment. In contrast, the dominant CD4+ T cell clones present at baseline were undetectable at 12 months, and the reconstituted CD4+ T cell repertoire was predominantly comprised of new clones.

The results also suggest the possibility that differences in repertoire diversity early in the reconstitution process might be associated with clinical outcomes. Nineteen patients who responded to treatment had a more diverse repertoire two months following transplant compared to four patients who did not respond. Despite the low number of non-responders, these comparisons approached statistical significance and point to the possibility that complexity in the T cell compartment may be important for establishing immune tolerance.

This is one of the first studies to quantitatively compare the baseline T cell repertoire with the reconstituted repertoire following autologous stem cell transplant, and provides a previously unseen in-depth analysis of how the immune system reconstitutes itself following immune-depleting therapy.

Provided by Immune Tolerance Network