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Large-scale harvesting of rare immune system cells could lead to effective treatments for immunity-related disorders

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Therapies based on natural immune system cells hold great potential for treating autoimmune diseases and reducing the number of graft rejections. However, harvesting enough cells from healthy donors in their pure, uncontaminated form is a significant challenge. Now, A*STAR researchers have up-scaled a technique to collect large numbers of one particular rare cell type for the first time.

A subpopulation of white blood cells known as Foxp3+ regulatory T cells (Tregs) work to control inflammation and excessive immune reactions in the body. Providing patients undergoing graft procedures with a dose of pure Tregs may dramatically reduce the risk of rejection. For example, Tregs therapy could be used for the treatment of 'Graft vs. Host Disease' (GvHD), a common and potentially fatal complication of stem cell therapies given to leukemia patients.

"GvHD occurs when donor T cells grafted alongside the stem cells attack the 'foreign' cells in host tissues," explains Sebastien Bertin-Maghit, senior project manager at the A*STAR Singapore Immunology Network, who manages clinical trials using the new technique developed by A*STAR's Olaf Rotzschke. "A Tregs-based therapy could help reduce the risk of GvHD, but Tregs are a very rare population amongst blood cells. For our therapy to work, we needed a large supply of pure, 'untouched' Tregs, that are uncontaminated with other cell types."

When it came to isolating pure Tregs on a large scale, existing isolation methods proved inefficient. Rather than isolating the cells by 'plucking' them out of a donor sample—a method which comes with the risk of unwanted modification or activation of some cells—Rotzschke's group devised a depletion method for selecting Tregs in their pure, untouched state.

"We depleted all unwanted cells in donor samples using isolation reagents," says Bertin-Maghit. "This allowed us to harvest Tregs in their natural state. We took great care to wash out the isolation reagents in the final product."

The team has since proven that this single-step depletion process can be scaled up to harvest highly pure Tregs at levels suitable for clinical trials, and their procedure complies with rigorous current standards. While previous attempts to collect Tregs produced a final product with 60 per cent pure Tregs, while this new method generates over 90 per cent pure Tregs.

"The first clinical trial using our Treg product is currently ongoing at the Singapore General Hospital," says Bertin-Maghit. "We are assessing the safety of Tregs in the treatment of GvHD in 12 leukemia patients. We believe our procedure will open doors to a new era in cell therapy."

More information: Doreen Haase et al. Large-scale Isolation of Highly Pure "Untouched" Regulatory T Cells in a GMP Environment for Adoptive Cell Therapy, *Journal of Immunotherapy* (2015). DOI: 10.1097/CJI.0000000000000083

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