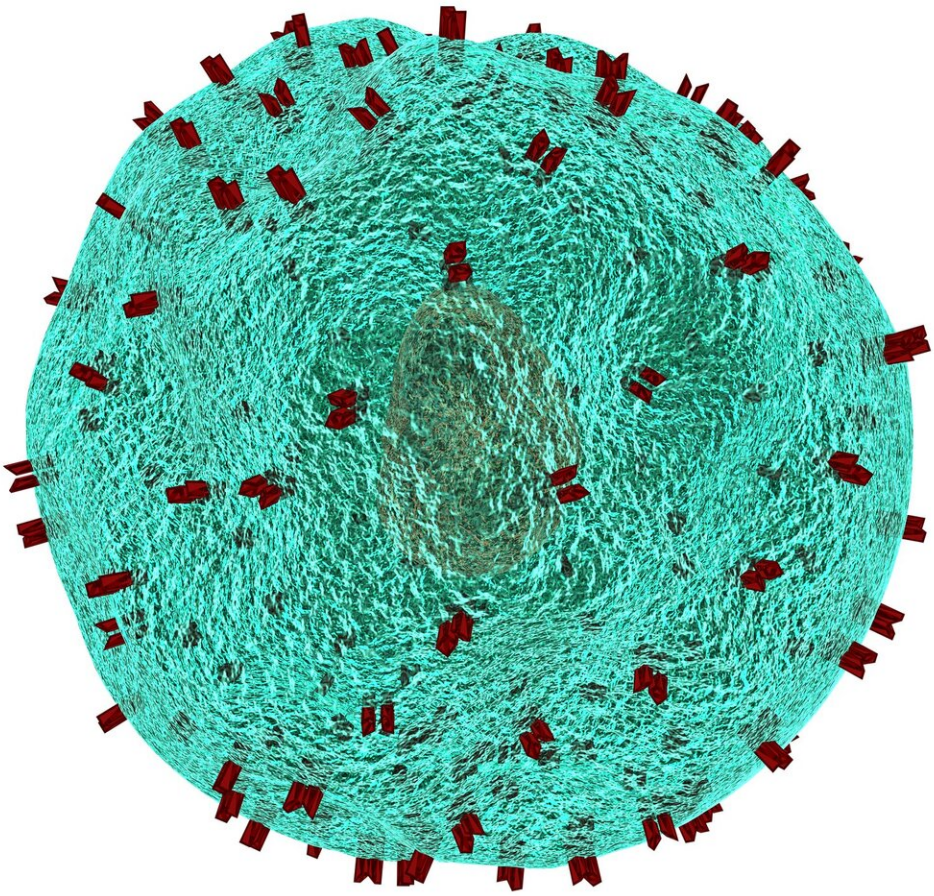
Novel method produces life-saving T cells from mesenchymal stromal cells

April 30 2020



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A new study released today in *Stem Cells* suggests for the first time that regulatory T-cells (Treg) induced by mesenchymal stromal cells can yield an abundant replacement for naturally occurring T-cells, which are vital in protecting the body from infection. Led by Rita I. Azevedo, Ph.D., at the Instituto de Medicina Molecular in Lisbon, Portugal, this study could yield new treatments for a long list of chronic inflammatory diseases that includes everything from cancer and asthma to inflammatory bowel disease, rheumatoid arthritis and more.

"Treg play a critical role in immune tolerance," Dr. Azevedo said. "In stem cell transplantation to treat leukemia and other blood diseases, for example, lower Treg counts are associated with the development of chronic graft-versus-host disease. However, Treg are very scarce. Finding alternative sources of stable Treg induction might produce a large enough number for effective treatment uses."

Mesenchymal stromal cells (MSCs) have been suggested as one way to achieve this. These multipotent progenitor cells, which can be isolated from a wide range of adult and postnatal tissues, are able to differentiate into diverse cell types. And like Treg, MSCs constitute an important immunoregulatory population by inhibiting both innate and adaptive immune responses.

"But thus far, the potential of MSC to recruit Treg has been poorly understood," Dr. Azevedo said.

Previous studies suggest that MSC-mediated immunomodulation may be partly driven by Treg induction and/or expansion. However, these reports have not assessed Treg yield in terms of absolute counts, nor

characterized the resulting Treg-like cells in detail. In the present study, Dr. Azevedo's team sought to determine whether MSC are able to induce and/or expand Treg in vitro, as well as the mechanisms of Treg enrichment by MSC.

To conduct the study, they collected human peripheral blood mononuclear cells—including T-cells—from healthy donors and co-cultured them with allogeneic bone marrow-derived MSC. Fourteen days later, the results showed an increase in the count and frequency of Treg cells—four- and six-fold, respectively.

The MSC-induced Treg-like cells resemble Treg functionally, and importantly, their DNA methylation profile closely resembles that of natural Treg, indicating that this population is stable. DNA methylation is an important component in numerous cellular processes, including embryonic development. Errors in the methylation have been linked to several human diseases.

"Our data sheds new light into the origin, functional potential and stability of MSC-induced Treg-like cells, which are key features for their potential applicability in the clinical setting." Dr. Azevedo concluded. "The co-administration of MSC and Treg might have the potential to constitute a more effective cellular therapy approach by harnessing the suppressive capacity of both these immunomodulatory populations."

"This is an exciting advance", said Dr. Jan Nolta, Editor-in-Chief of *Stem Cells*. "Dr. Azevedo and her team have defined important MSC-based mechanisms to induce and enrich Treg cells, which could have important future implications for the treatment of chronic diseases."

More information: "Mesenchymal stromal cells induce regulatory T cells via epigenetic conversion of human conventional CD4 T cells in

vitro," *Stem Cells* (2020). stemcellsjournals.onlinelibrar … bs/10.1002/stem.3185

Provided by AlphaMed Press