Researchers reveal pathogenesis and therapeutic strategy of pre-engraftment syndrome

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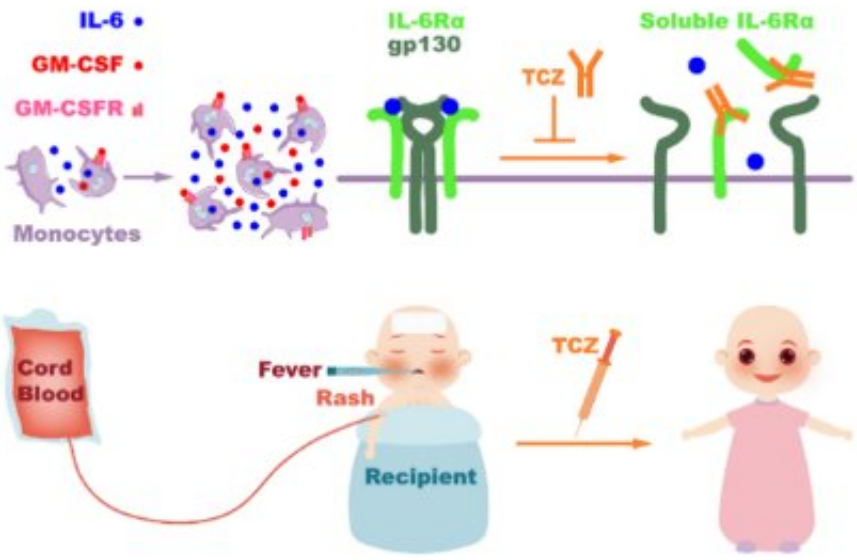

Diagram of cytokine dysregulation in PES. Credit: JIN Linlin et al.

The research team led by Prof. Wei Haiming and Prof. Tian Zhigang from Division of Life Sciences and Medicine, University of Science and Technology of China (USTC) of the Chinese Academy of Sciences (CAS), collaborating with the research group led by Prof. SUN Zimin from the First Affiliated Hospital of USTC revealed the pathological

mechanism of severe pre-engraftment syndrome (PES) after umbilical cord blood transplantation, not only providing a treatment strategy for patients with PES, but significantly guiding for further improvement in the curative effect of unrelated cord blood transplantation (UCBT). This study was published in *Nature Communications*.

UCBT is an important means to cure hematological malignancies, hematopoietic failure, congenital immunodeficiency and some genetic metabolic diseases. The incidence of chronic graft-versus-host disease (GVHD) after transplantation is low and mild, so that the quality of life of patients is high. The First Affiliated Hospital of USTC has so far completed 1519 cases of UCBT since the first successful case using this method in the treatment of children's malignant hematological diseases in 2000, which makes it an internationally recognized umbilical cord blood transplantation treatment center, encouraging the emergence of more and more relevant clinical and scientific research achievements

Unfortunately, however, in the early stage after UCBT, 70-80% of recipients will suffer PES, which is characterized by high fever, rash, diarrhea, and other clinical findings. Severe PES increases the transplant-related mortality, but its mechanism is still unclear. Further study and revelation of the pathogenesis of PES after UCBT is of great clinical significance for the treatment of PES patients and the reduction of transplantation related mortality.

Faced with this problem, the research group analyzed the peripheral blood of recipients after UCBT and found significantly increasing number of monocytes in patients with PES. These monocytes derived from cord blood had inflammatory characteristics and produced proinflammatory cytokines such as GM-CSF and IL-6. After UCBT, monocytes expanded rapidly in the recipient body, increasing the levels of GM-CSF and IL-6 in serum, which led to the occurrence of PES.

Based on the pathogenesis study of PES, the team applied for a clinical trial using tocilizumab to block the IL-6 receptor at http://www.chictr.org.cn (Reference: ChiCTR1800015472) among patients with severe PES. The results showed that the use of tobuzumab for intervention treatment significantly controlled the clinical symptoms of PES and reduce the mortality of patients.

This study, lasting nearly 8 years, provides practical guidance for USTC to propose and implement treatment plan (tobuzumab) for patients with severe COVID-19 pneumonia. This treatment plan (tobuzumab) has been currently approved by U.S. Food & Drug Administration (FDA) and National Health Service (NHS) in clinical application.

More information: Linlin Jin et al, Inflammatory monocytes promote pre-engraftment syndrome and tocilizumab can therapeutically limit pathology in patients, *Nature Communications* (2021). DOI: 10.1038/s41467-021-24412-1

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