



Stem cell transplantation: Processes for the restoration of the immune system discovered

(Vienna, 09-02-2023) In stem cell transplants, which are used for the treatment of leukaemia, the patient's haematopoietic system is eliminated and replaced by haematopoietic cells from donors. Even though the amount of complications occurring in this process is steadily decreasing due to medical progress, the exact mechanisms for the restoration of the immune system in these patients have not yet been conclusively clarified. Researchers at MedUni Vienna, the CeMM Research Centre for Molecular Medicine of the Austrian Academy of Sciences and the Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases have now discovered processes that can contribute to the success of stem cell transplantation and to improving this therapy. The results of the study have just been published in the journal *Clinical Immunology*.

For their study, the research group led by Georg Stary from MedUni Vienna's Department of Dermatology and the CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences analysed immune cells in the blood and skin of stem cell transplantation recipients. In sequential samples, the scientists discovered regulatory processes that are involved in restoring the balance of T cells in the immune system, which is relevant for the success of stem cell transplantation.

In particular, enzymes called histone deacetylases (HDACs) proved to be essential players in this process. The medicinal inhibition of HDACs is already successfully used in cancer therapy. In order to investigate a possible application of this approach after stem cell transplantation, the team administered HDAC inhibitors to isolated cells. "By inhibiting different classes of HDACs in isolated T cells from patients after stem cell transplantation, we could modulate the imbalance of T cell subsets," report first authors Ram Vinay Pandey and Johanna Strobl from the Department of Dermatology at MedUni Vienna.

Further findings regarding complications

Within the framework of the study, it was possible to gain further insights into graft-versus-host disease (GVHD), which can occur after stem cell transplantation. The analyses in blood and skin revealed a rapid recovery of immune cells that are of importance for GVHD (such as effector T cells), while the appearance of "protective" regulatory T cells was delayed. On the other hand, the simultaneous examination of the transcriptome, i.e. all those genes that are actively read from the DNA, and the epigenome, the "readiness" of individual genes, showed strong differences between skin and blood cells. This imbalance between body tissues as well as regulatory and non-regulatory cell types could promote complications after stem cell transplantation, such as GVHD.



New approach for therapeutic options

Allogeneic haematopoietic stem cell transplantation is used as a therapy for patients with serious diseases of the haematopoietic system (e.g. acute leukaemia). Following the replacement of the patient's diseased haematopoietic system with healthy haematopoietic cells from donors, about 40 per cent of patients develop GVHD, which most commonly affects the skin. "With the potential of HDAC inhibitors to modulate T cells after stem cell transplantation, we have discovered an innovative approach to influence the epigenetics of T cells at specific time points after stem cell transplantation and to increase the safety of the therapy," says Georg Stary about the research results, which will be tested in clinical trials in the next step. "Our study underlines the importance of epigenetic regulators in restoring the immune system and shows new therapeutic possibilities for achieving T-cell balance after stem cell transplantation."

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Epigenetic regulation of T cell lineages in skin and blood following hematopoietic stem cell transplantation

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Medical University of Vienna - short profile

Medical University of Vienna (MedUni Vienna) is one of the longest-established medical education and research facilities in Europe. With almost 8,000 students, it is currently the largest medical training centre in the German-speaking countries. With more than 6,000 employees, 30 departments and two clinical institutes, 13 medical theory centres and numerous highly specialised laboratories, it is one of Europe's leading research establishments in the biomedical sector. MedUni Vienna also has a medical history museum, the Josephinum.