



Stem cell transplantation: undesirable rejection mechanism identified

(Vienna, 19 November 2020) In the treatment of leukaemia, stem cell transplantation subsequent to chemotherapy and radiation can often engender severe adverse inflammatory reactions – especially in the skin or in the gut, since these so-called barrier organs are more frequently affected. Up until now, the reason for this was unclear. A MedUni Vienna team led by Georg Stary and Johanna Strobl from MedUni Vienna's Department of Dermatology, the CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences and the Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases has now identified an immune mechanism that is partially responsible for this. The results have now been published in the leading journal "Science Translational Medicine".

The term leukaemia is used to describe a group of malignant diseases of the haematopoietic system, in which precursors of the white blood cells (leucocytes) proliferate uncontrollably. Chemotherapy and radiotherapy are used to destroy the abnormal blood cells, which are then replaced by means of a stem cell transplant. In leukaemia, the transplantation of healthy bone marrow stem cells or haematopoietic stem cells is often the only hope of recovery for patients. The process involves "replacing" all the recipient's blood cells that were previously destroyed by the treatment with donor cells.

However, the MedUni Vienna dermatologists have now found that there are so-called skin-resident and inactive T cells in the endogenous immune system that survive chemotherapy and radiotherapy intact and go on to survive for a further ten years between and beneath the epithelial cells of the skin, while the circulating T cells are destroyed.

"We were able to demonstrate that T cells surviving in the skin tissue are responsible for the inflammatory reaction following a stem cell transplant. These phenomena often occur within the first 100 days and can cause anything from mild eczema through to extensive fibrosis, hardening of the tissue, or blistering on the surface of the skin. In other words, the endogenous T cells attack the recipient (host) following stem cell transplantation." In specialist jargon, the condition is also referred to as Graft versus Host Disease (GvHD), and, for the first time, this study identified an inverse "Host-versus-graft reaction".

There were also cases in which the donor T cells further "supported", and thus intensified, this reaction. Affected patients are treated with cortisone, which causes an additional burden for patients who are already immunosuppressed following the transplantation. The study found that in patients who do not develop graft-versus-host disease, tissue-resident T cells



remaining after treatment even proved to be beneficial to the recipient, in that they assumed their role in immune defence and protecting against infection.

In the future, the exemplary study results could lead to new treatment strategies that help to avoid, or at least to minimise, undesirable and violent inflammatory reactions following stem cell transplants by manipulating the recipient's inactive T cells in advance. In addition, the manipulation of tissue-resident T cells might lead to new therapeutic approaches for other chronic inflammatory skin diseases, such as psoriasis or neurodermatitis.

Service: Science Translational Medicine

"Long-term skin-resident memory T cells proliferate in situ and are involved in human graft-versus-host disease" Johanna Strobl, Ram Vinay Pandey, Thomas Krausgruber, Nadine Bayer, Lisa Kleissl, Bärbel Reininger, Pablo Vieyra-Garcia, Peter Wolf, Maaia-Margo Jentus, Margit Mitterbauer, Philipp Wohlfarth, Werner Rabitsch, Georg Stingl, Christoph Bock, Georg Stary.
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Medical University of Vienna - short profile

Medical University of Vienna (MedUni Vienna) is one of the most traditional 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 5,500 employees, 26 departments and two clinical institutes, 12 medical theory centres and numerous highly specialised laboratories, it is also one of Europe's leading research establishments in the biomedical sector.

CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences

The mission of CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences is to achieve maximum scientific innovation in molecular medicine to improve healthcare. At CeMM, an international and creative team of scientists and medical doctors pursues free-minded basic life science research in a large and vibrant hospital environment of outstanding medical tradition and practice. CeMM's research is based on post-genomic technologies and focuses on societally important diseases, such as immune disorders and infections, cancer and metabolic disorders. CeMM operates in a unique mode of super-cooperation, connecting biology with medicine, experiments with computation, discovery with translation, and science with society and the arts. The goal of CeMM is to pioneer the



science that nurtures the precise, personalized, predictive and preventive medicine of the future. CeMM trains a modern blend of biomedical scientists and is located at the campus of the General Hospital and the Medical University of Vienna.

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Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases

The Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases (LBI-RUD) was founded by the Ludwig Boltzmann Gesellschaft in April 2016 together with the CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences, the Medical University of Vienna and the St. Anna Children's Cancer Research Institute. The three partner institutions, together with the CeRUD - Vienna Center for Rare and Undiagnosed Diseases, are the most important cooperation partners of the LBI-RUD. The aim of LBI-RUD is to bundle the expertise of its partner organizations to establish a coordinated research program that, in addition to the scientific approach, also includes social, ethical, and economic aspects of rare diseases.