UNIVERSITÉ DE GENÈVE

Hôpitaux Universitaires Genève

PRESS RELEASE

Geneva | 3 September 2025

Blood cancers: predicting the success of cell transplants

A team from UNIGE and HUG has identified the key genetic characteristics of compatibility when transplanting blood cell-producing stem cells.

High resolution pictures

Transplanting haematopoietic stem cells from healthy individuals is one of the possible treatments for blood cancers. In Switzerland, it concerns nearly 300 patients per year. However, nearly half of transplants fail, mainly due to complications related to imperfect genetic compatibility between the donor and recipient. By comparing the genetic profiles of nearly 1,250 donor-patient pairs with the clinical results of the transplants with unprecedented accuracy, a team from the University of Geneva (UNIGE) and Geneva University Hospitals (HUG), in collaboration with all Swiss hematopoietic stem cell transplant centers, has demonstrated the crucial importance of the KIR gene system in predicting treatment outcomes. These results, published in the journal *Haematologica*, call for the systematic inclusion of gene profiling to ensure the greatest possible compatibility and increase the chances of survival.

Haematopoietic stem cells (HSCs), located in the bone marrow, can give rise to all specialised cells that make up the blood system. In blood cancers, such as leukaemia and lymphoma, one possible treatment is HSC transplantation. This involves replacing diseased HSCs with HSCs from a healthy donor to rebuild the blood cells and develop new immune cells capable of targeting and destroying tumour cells.

"The success of this treatment depends on the genetic compatibility between the donor and the recipient, and on the reaction of the patient's immune system to the transplanted cells," says Jean Villard, full professor in the Department of Medicine and the Geneva Centre for Inflammation Research at UNIGE Faculty of Medicine and head of the Cell Therapy and Transplantation Laboratory Platform at the HUG, who led the research. "At the heart of this mechanism is the HLA system, a set of genes regulating proteins that enable the immune system to distinguish between healthy cells and cells that are diseased, infected or from another individual, as in the case of a transplant. But other factors are also at play."

A delicate immune balance

The effectiveness of the transplant therefore depends on a dual effect: the reconstitution of blood cells and the production of anti-tumour immune cells. "However, this effect depends on interactions between the HLA molecules of the sick person and another group of proteins, KIR receptors, which are present on the transplanted cells," explains Antonia Schäfer, a research physician in Prof. Villard's laboratory and first author of the study. "Which KIR profiles are most effective at recognising cancer cells and thus limiting the risk of relapse? That is the question." However, the complexity of the KIR-HLA system, combined with significant genetic variability between individuals, makes studying these interactions particularly difficult.

Looking at 1,247 pairs of donors and recipients, the research team carried out high-resolution genotyping of the KIR genes of the former, then analysed the impact of KIR-HLA interactions on patient outcomes in terms of survival, cancer progression and the occurrence of serious side effects where the transplanted cells attack the host organism. "By examining KIR profiles at a level of precision never achieved before, we have identified the exact genetic parameters that need to be taken into account in order to maximise the chances of success," says Antonia Schäfer enthusiastically. "Our results show that selecting the best cells must be based not only on HLA compatibility, as is currently the case, but also on KIR parameters, whose role has been greatly underestimated until now."

Towards personalised medicine in transplantation

When patients do not have compatible siblings, physicians turn to people listed in national or international registries, which include nearly 40 million volunteers. This discovery will make it possible to identify optimal immunogenetic profiles. "We are therefore calling for the widespread use of high-resolution KIR genotyping in order to select the best person for each patient and thus improve their chances of survival after transplantation," conclude the authors.

This project was supported by the Fondation privée des HUG, the Swiss Red Cross Humanitarian Foundation and an ISREC Tandem Fund.

contact

Jean Villard
Full Professor
Department of Medicine
Geneva Centre for Inflammation Research
Faculty of Medicine
UNIGE

Head
Cell Therapy and Transplantation Laboratory Platform
HUG
+41 22 372 93 94
Jean.Villard@hug.ch

Antonia Schäfer
Staff Physician
Platform for Cell Therapy and Transplantation Laboratories
HUG

Department of Medicine
Faculty of Medicine
UNIGE

Antonia.Schafer@unige.ch

DOI: 10.3324/haematol.2024.287061

UNIVERSITÉ DE GENÈVE
Communication Department
24 rue du Général-Dufour
CH-1211 Geneva 4

Tel. +41 22 379 77 17

media@unige.ch
www.unige.ch