



Funded by the amfAR Research Consortium on HIV Eradication (ARCHE)

Start of an international research consortium to reproduce the only successful case of a person cured of HIV

- **European researchers co-led by the Institute for AIDS Research IrsiCaixa, in Barcelona, and the University Medical Center Utrecht (UMCU), in the Netherlands, have initiated an ambitious project with the aim to reproduce the only case of a person cured of HIV, the Berlin patient. Experts from the Catalan Institute of Oncology (ICO), the Gregorio Marañón Hospital, in Spain, the Oxford University, in the United Kingdom, the University Medical Center Hamburg and Celle xGmbH, in Germany are collaborators in this project.**
- **The Berlin patient received a stem cell transplant from a donor naturally resistant to the virus to treat him of leukemia in 2007. However, this is a high-risk procedure, only indicated for patients with life-threatening cancer disease. Doctors around the world have tried to cure other patients with similar conditions, but no other patient has been cured of HIV infection so far.**
- **The international consortium, named EPISTEM, is sponsored by the amfAR Research Consortium on HIV Eradication (ARCHE), a program from the US Foundation for AIDS Research amfAR. The project aims to improve the interventions to cure these patients and to better understand the implication of stem cell transplants in the control and eradication of HIV.**

The only person cured from HIV infection is known as the Berlin patient. This patient underwent stem cell transplantation and received bone marrow from a donor who had a rare genetic mutation, which conferred him resistant to HIV infection. This mutation is present in approximately 1% of people with European origin.

The strategy raised tremendous scientific interest as it opened new prospects of viral eradication. However, this success is not scalable to cure HIV infection, as it is a high-risk procedure only indicated for HIV+ patients with life-threatening hematological disease, as was the case in the Berlin Patient.

Several researchers around the world have tried, so far unsuccessfully, to reproduce this HIV cure strategy, and to understand the crucial factors for success of the intervention. The rare genetic mutation of the donor, which confers resistance to HIV, seems to be the main factor for success, but there are other steps in the clinical process that may also have contributed.

Improving the strategy to cure HIV infection

A European consortium of researchers co-led by the Institute for AIDS Research IrsiCaixa, and



the University Medical Center Utrecht have just initiated an ambitious project to try to improve the interventions to cure these patients with the additional aim to better understand the implication of stem cell transplantation in the control and eradication of HIV infection.

This team led by the ICREA researcher at IrsiCaixa Javier Martínez-Picado, and the clinical virologist at University Medical Center Utrecht Annemarie Wensing received the largest award in this round of grants of the amfAR Research Consortium on HIV Eradication (ARCHE). The consortium is formed by hematologists, infectious disease specialists, virologists, and immunologists with expertise in the field of HIV, including Gero Hütter, the oncologist credited with the Berlin patient's cure. Experts from the Catalan Institute of Oncology (ICO), the Gregorio Marañón Hospital, in Spain, the Oxford University, in the United Kingdom, the University Medical Center Hamburg, and Cellex GmbH, in Germany also collaborate in this project.

“We need to understand the specific reasons of the HIV cure in the Berlin patient if we want to move forward in the eradication of this infection. We also want to use umbilical cord blood as a source of stem cells to increase the chances of compatibility between donors and patients”, states Martínez-Picado.

Using stem cells from umbilical cord blood has a clear advantage, as they are far more compatible than the ones extracted from the bone marrow. With this new approach, the chances to find a donor that is compatible and additionally has the rare genetic mutation conferring HIV resistance is raised more than 100 fold.

In parallel, also with additional financial support from amfAR, an inventory of umbilical cord blood grafts will be created by Oxford University, led by Vanderson Rocha, that allows to identify which of the 10.000 cord blood units available in the North European cord blood banks contain the rare genetic mutation that confers resistance to HIV. These units will be immediately available for transplantation in HIV positive patients requiring transplantation.

Some patients are already monitored with an improved approach

The researchers have already started to implement this strategy in HIV positive people in need of stem cell transplantation with encouraging results. In addition, the project provides guidance to colleagues who take care of HIV-infected patients in need of a stem cell transplantation states Annemarie Wensing. As the team is still enrolling HIV patients who will receive a SCT, physicians, researchers and citizens can name potential candidates to join the project (contact can be made through, A.vanKessel-4@umcutrecht.nl).

The consortium is undertaking an exhaustive study and follow-up of these patients to collect complete information on the chemotherapy, transplantation procedure, donor selection, HIV variability and treatment, and is also collecting samples to be stored before and after the transplantation. These samples are used to measure the size and genetic make-up of the HIV



reservoirs in Barcelona and Utrecht, using the most cutting edge technologies available in the field.

During the first year the experts do not plan to consider antiretroviral treatment interruptions, as it was recently demonstrated that two transplanted patients who received bone marrow cells lacking the specific mutations had viral rebound after being a few months out of treatment.

Project reference: EpiStem: Allogeneic stem cell transplant in HIV-1-infected individuals

Consortium members:

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This project has been given the largest award in this year's round of grants of the amfAR Research Consortium on HIV Eradication (ARCHE). This program is an initiative launched in 2010 to explore potential strategies for eliminating HIV infection. The new grants, totaling nearly \$2.4 million, will support the work of seven teams of scientists worldwide. amfar.org

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