Patient Jack Crick

2004	Born in May
2004	X-SCID is diagnosed in September. The search for a suitable bone marrow donor unsuccessful. Gene therapy using the patient's own blood stem cells is successful, even without chemotherapy.
2011	Patient has had no symptoms since.

Attending Physician

Bobby Gaspar, Great Osmond Street Hospital, London

X-SCID

SCID stands for severe combined immunodeficiency;
A weakening of the immune system due to the absence or lack of lymphocyte function; mutations in genetic information (DNA) cause the disruption of T cell development. The patients' immune systems cannot cope with the pathogens in our normal environment and the affected children must therefore live in a sterile environment.

Therapy

Collection of hematopoietic stem cells (CD34-positive); inserting the corrected gene into the test tube using a retroviral vector (taken from the mouse leukemia virus); stem cells are returned to the patient.
Advantages: Use of own cells instead of foreign cells; low risk of rejection or incompatibility; no suitable donor necessary.

Discussion

The introduction of a new gene can lead to changes in cell properties or to degeneration (cancer). Cases are known where patients developed leukemia. The trigger seems to be the retroviral vector. Research is being carried out on the use of newer HIV-derived lentiviral vectors, for example, which have a much better safety profile.

Search terms
Bubble Boy, David Vetter

Patient Timothy Ray Brown

1966	Born in Seattle, USA
1995	Diagnosis: HIV positive
until 2006	Treatment using highly active antiretroviral therapy (HAART): 600 mg Efavirenz, 200 mg Emtricitabine and 300 mg Tenofovir
2006	Diagnosis of acute myeloid leukemia (AML); chemotherapy treatment
2007	Treatment by allogeneic stem cell transplantation from a donor with a mutation in the CCR5 cell surface receptor. The mutation prevents the HI virus from penetrating the cells.
since 2007	HI virus no longer detectable using common procedures
2008	Leukemia identified again; second stem cell transplantation (same donor)
since 2008	HI virus undetectable using common procedures; leukemia treatment successful; neurological disorders diagnosed
2020	Died because of another leukemia occurance

HLA type: B57

Attending Physician

Dr. Gero Hütter, Benjamin Franklin Campus Charité Berlin (until 2009)

Bone marrow donor

HLA type: B57

Mutation: delta 32 on receptor CCR5

Therapy

Transplantation of allogeneic stem cell transplantation of a donor with a mutation in the cell surface receptor CCR5. The mutation prevents the HI virus from entering the cells.

Discussion

It is not clear whether this individual case is reproducible. The procedure is very expensive. In 2012, Steven Yukl (University of California, San Francisco) investigated nine billion patient blood cells using polymerase chain reaction (PCR). After several attempts he identifies fragments of the virus genome in the blood plasma. Douglas Richman (University of California, San Diego) also conducts blood tests and finds no residues. He considers contamination in the Yukl test possible; in addition, PCR is highly sensitive and error-prone.

Search terms

The Berlin Patient, Mississippi Baby, The London Patient

Patient Hassan

Born in 2008	started treatment at the age of 7
2015:	After fleeing from Syria to Germany, he suffered infections and chronic skin lesions as a result of the inherited disorder epidermolysis bullosa.
2015-2016:	Skin graft involving 80 percent of the patient's skin. Since then, the patient has been largely free of symptoms.

Doctors involved

Tobias Rothoeft, Kinderklinik Bochum

Tobias Hirsch, Universitätsklinikum Bergmannsheil (plastic surgeon)

Michele De Luca, Center for Regenerative Medicine at the University of Modena (stem cell researcher)

Epidermolysis bullosa

Epidermolysis bullosa is an inherited disorder. Children with this condition are sometimes called butterfly children, because their skin is as fragile as a butterfly's wings. This is because the upper layer of the skin (epidermis) is not properly attached to the layer underneath (dermis). People with this disease have a defective LAMB3 gene. This gene encodes the laminin-332 protein.

Treatment

Skin cells from Hassan were sent to Italian experts in Modena for culturing. The scientists used retroviral vectors to insert a healthy LAMB3 gene into the skin cells. Retroviral vectors are viruses which have been specially modified to carry genes into cells. The genetically modified stem cells in the piece of skin were then cultured in a clean room laboratory to produce large pieces of skin suitable for grafting. Over a series of three operations in Germany, scientists then grafted the cultured tissue. In total, they replaced 80 percent of Hassan's skin.
The new skin contains roughly the same amount of the laminin-332 anchor protein as normal, healthy skin.

Discussion

There are around 35,000 children with epidermolysis bullosa in Europe. The severity of the disease varies greatly. Until now, no treatment aimed at eliminating the underlying cause of the condition has been available. All gene therapies carry a risk that the new gene could be inserted into the wrong place in the genome, however. This can disrupt cell regulatory processes and cause cancer.
The treatment Hassan underwent was risky and laborious. It was justified by the extent of his suffering and the fact that there was no prospect of his suffering being relieved by any other treatment.

Search terms

Patient Hassan, butterfly child
(https://www.spiegel.de/gesundheit/diagnose/gentherapie-junge-erhaelt-neue-haut-a-1177073.html)