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Gene editing has saved the lives of two children with leukaemia

Immune cells can be edited to target cancer
Val Altounian / Science Translational Medicine (2017)

By **Michael Le Page**

Two children treated with gene-edited cells to kill their cancers are both doing well more than a year later. The baby girls were both given the experimental treatment only as a last resort, but clinical trials of the therapy are now getting underway in children and adults in the UK.

An 11-month-old girl called Layla was the first to get the treatment, in June 2015. When the team who treated her at Great Ormond Street Hospital in London revealed details in November 2015, they stressed that it was too soon to say if she was cured.

But 18 months on, Layla is doing well with no sign of the leukaemia returning. A second child, who was treated in December 2015 when she was 16 months old, is also healthy.

Off-the-shelf

The treatment is a form of so-called CAR-T cell therapy. This involves using a virus to add a gene to immune cells that make them target specific cancers. Dozens of CAR-T trials are already underway around the world, and some have produced dramatic results.

One of the drawbacks of the approach, however, is that people have to be treated with their own modified immune cells. If non-individual, "off-the-shelf" cells were used, they would see the patient's body as foreign and attack it. This makes CAR-T therapies very expensive, and it is not always possible to extract enough immune cells from very young or ill patients for the technique to work.

This prompted the Paris-based pharma company Cellectis to develop a gene editing tool that disables the gene that causes donor immune cells to attack their host. This can be used to create batches of cells, called UCART19, for treating anyone with the particular form of leukaemia that Layla had (B-cell acute lymphoblastic leukaemia).

Turning to CRISPR

Waseem Qasim at University College London, who led the team that treated the girls, asked Cellectis if they could try the therapy after conventional treatments failed.

The process is not perfect. The gene, called TCRαβ, was not disabled in 0.7 per cent of the cells injected into the children, and both girls developed signs of graft-versus-host disease. But the team was on the lookout for this, and treated it as soon as signs

emerged.

Once the girls' immune systems were restored, the gene-edited cells were themselves seen as foreign and killed off.

Many groups around the world hope to use gene-editing to improve immune therapies for cancer. Cellectis used an older method called TALEN to target TCRαβ, but the revolutionary new CRISPR method has made it much easier and cheaper to create gene-editing tools. Two cancer trials involving CRISPR-edited cells are getting underway in China and the US.

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