Gene Therapy (2017) **24,** 122

www.nature.com/gt

EDITORIAL

Double TALEN-edited T-cells kick B-ALL into touch

Gene Therapy (2017) **24,** 122; doi:10.1038/gt.2017.17

CAR19 T cells can be highly effective against refractory-B-cell acute lymphoblastic leukaemia (B-ALL), but a significant limitation is the need to engineer cells for every individual patient. If engineered allogenic cells are used, there is a significant risk of host-mediated rejection of such cells and/or graft versus host disease (GvHD). In a recent study, Qasim *et al.*[1] reported a significant step towards so-called universal CAR19 T cells (UCART19) in two paediatric patients with refractory-relapsed B-ALL using TALEN-edited allogeneic CAR19 T cells. The TALENs were used to disrupt the *TRAC* gene encoding the TCR alpha subunit to prevent rejection of the cells and GvHD. The gene for CD52 was also disrupted with TALENs so that the incoming CAR19 T cells would not be depleted by any residual alemtuzumab, an anti-CD52 antibody used to lymphodeplete B-ALL patients prior to T-cell infusion. A third modification was expression of a 'sort/suicide' gene, *RQR8*, to allow enrichment via a CD34 epitope during cell preparation, and a CD20 epitope to give the option for immunodepletion with rituximab in case of an adverse reaction. The overall clinical outcome was successful with both patients showing molecular remission within 1 month, which enabled bridging of both individuals to successful allogeneic stem cell transplants. While this approach is a positive step in the direction of universal CAR cells, it highlights the challenges and complexities of gene engineering, bordering on the field of synthetic biology.

AUTHOR BIOGRAPHY

PTH has directed a gene editing research group at University College Cork in Ireland since 2005 using ZFNs, TALENs and CRISPR to study a range of genetic diseases including cystic fibrosis and cystinosis, and skin disorders such as atopic dermatitis. He is also a Principal Investigator in the Cork SynBioCentre. His scientific journey began at his home university in Liverpool, before a long and winding journey to Cork which encompassed Glasgow (three times), Cambridge, Vienna and Edinburgh. With a background in virology, virus vectors, immunoreceptors and gene editing, he is delighted to have the opportunity to serve as Associate Editor (Europe) of *Gene Therapy* and looks forward to working with Rafael and the rest of the team during a very exciting era of advanced gene and cell therapies.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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