Zsuzsanna Izsvak et al., J Immunome Res 2017, 13:1 (Suppl)
http://dx.doi.org/10.4172/1745-7580.C1.010

8th Molecular Immunology & Immunogenetics Congress

Zsuzsanna Izsvak[1], Mario Bunse[1], Julian Clauss[1], Wolfgang Uckert[1], Julian Claus[1], Mario Bunse[1] and Zoltan Ivics[2]

[1]Max Delbruck Center for Molecular Medicine, The Helmholtz Society, Germany
[2]Paul Ehrlich Institute Langen, Germany

Non-viral *Sleeping Beauty* transposon-based vector for immunotherapy

The specificity of T cells can be redirected by stable expression of a tumor-reactive T cell receptor (TCR) or chimeric antigen receptor (CAR). This strategy has been successfully used in immunotherapy to treat various cancer patients. Widespread application of this new therapy depends on the availability of a robust and cost-efficient gene transfer system. The *Sleeping Beauty* (SB) transposon has been demonstrated to mediate the stable gene transfer into the genome of various mammalian cell types, including human T cells. Non-viral, transposon-based gene delivery vectors are an emerging alternative to viral vectors for the generation of engineered T cells. In fact, regarding safety, flexibility, cost and time of T cell engineering, the use of transposon-based vectors confers an advantage over retro/lentiviral vectors. To cope with the poor gene transfer efficiencies, cell lines presenting the antigen of the transferred receptor and co-stimulatory signals can be used to expand engineered T cells. This strategy has reached the clinic. While this approach results in the rapid outgrowth of gene-modified T cells, it might compromise functionality. Alternatively, we aimed at developing an improved protocol for generating transposon vector-modified T cells. Using a combination of minicircle transposon and a hyperactive transposase mRNA (SB100X), we achieved stable expression of transgenic TCR in ~50% of primary human T cells in a donor-independent and reproducible manner. In addition, we optimized our transposon-based TCR expressing vector with enhanced functionality and a reduction of mixed TCR dimers on the surface of TCR-modified T cells. Using transposon minicircle vectors encoding a genetically optimized TCR and miRNAs for the silencing of the endogenous TCR, we generated TCR-modified T cells with superior TCR surface expression and antigen-specific functionality. The transposon vector could match the need in personalized form of TCR gene therapy, in which tumor-specific mutations are targeted that are unique for each patient.

Biography

Zsuzsanna Izsvak has joined Max-Delbrück-Center, Berlin in 1999, where she works on mobile DNA. She has also worked at the Hungarian Academy of Sciences, University of Minnesota and Netherlands Cancer Institute. Her academic background includes molecular genetics, genome manipulation, gene therapy and stem cell research. She is one of the inventors of the *Sleeping Beauty* transposon-based, non-viral gene transfer system. She is a recipient of European Young Investigator Award, European Science Foundation supported by ERC-Advanced (European Research Council), TRANSPOSOstress (PI) and EvoGenMed (co-PI).

zizsvak@mdc-berlin.de

Notes: