

July 05-07, 2018
Vienna, AustriaLiangping Li et al., Insights Allergy Asthma Bronchitis 2018, Volume: 4
DOI: 10.21767/2471-304X-C1-003

ANTITUMOUR T CELLS GENERATED FROM EMBRYONIC STEM CELLS MODIFIED BY TUMOUR ANTIGEN SPECIFIC TCR

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TCR-T cell therapy is a promising immunotherapy for cancer patients. A large number of tumour-reactive TCR genes are cloned and need the preclinical experiments. Therefore, it is very important to establish an experimental animal model to quickly and effectively evaluate the function of TCR. The development of stem cell technology provides a new way to solve these technological bottlenecks. Embryonic stem cells (ES) / inducible pluripotent stem cells (iPS) can grow infinitely *in vitro*, are easy to culture, and maintain normal cell karyotype and have the potential to differentiate into various normal cells, including T cells. Therefore, we propose to combine TCR and ES technology to produce single specific T cells using TCR modified ES cells. In order to mimic human HLA-TCR recognition system in mouse T cells, we use human and mouse hybrid molecular system of MHC and TCR. The MAGEA1-specific TCR1367 contained human V (D) J and mouse C gene fragment was sub cloned into lentiviral vector for the transduction of mouse ES cells, and then OP9-DL1-HHD cell line was generated with HHD retroviral vector which express the chimeric MHC molecule HHD to create human HLA-TCR antigen recognition system in mouse T cells, TCR1367-ES, OP9 and OP9-DL1-HHD cells were subcutaneously co-injected into NOD/SCID or NSG mice to generate ES cell-derived teratoma. 8 weeks later, mature T cells which have single antigen specificity for anti-tumour antigen could be detected in peripheral blood and spleen. After isolating these T cells, we found that they could specifically recognize MAGEA1 epitopes, and kill MAGEA1+ cells. Using this simple and low cost TCR-ES cell differentiation technique, NOD/SCID or NSG mice can be used as a biological generator to produce antitumor T cells, which can be used to test the functions of various human TCR genes in preclinical animal experiments.

Biography

Liangping Li has completed his PhD from Humboldt-Universität zu Berlin and Postdoctoral studies from Max-Delbrück-Centrum für Molekulare Medizin, Berlin, Germany. He is the director of Institute of Clinical Oncology, Jinan University, First Affiliated Hospital, Guangzhou, China. He has published several important papers in reputed journals such as Nature Medicine, Nature Protocol, Blood, Cancer Res. et al. and has been serving as an Editorial Board Member of several journals.

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