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Transgene IL-6 engineered dendritic cell-stimulated CD8+ T-cells – Role in potent immunotherapy

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Adoptive transfer of CD8+ T-cells specific for tumor-antigens is an attractive strategy for anti-tumor therapy. In this study, the subsets TA and TB were used to represent the population of CD8+ T cells generated by culturing the respective cells with irradiated dendritic cells (DCs) pulsed with ovalbumin (OVA) protein and transfected with adenoviral vector constructs. Naive OVA specific CD8+ T cells were isolated from the spleen of OVA-specific T-cell receptor transgenic OTI mice. The subsets TA and TB were then generated by activating the population of CD8+ T cells with OVA-pulsed DCs transfected with IL-6-expressing adenoviral vector (AdvIL-6) or the control vector (AdvNull). To assess their *in vivo* immunotherapeutic effects, TA- or TB-cells were *i.v.* transferred into C57BL/6 mice bearing EG7 thymoma. TA-cells displayed higher level expression of CD62L, IL-7R, FasL, perforin and CCR6; exhibited more potent *in vitro* cytotoxicity to OVA-expressing EG7 thymoma cells via perforin- and Fas/FasL-mediated apoptosis than TB-cells. CD8+ T-cell survival was kinetically analyzed in C57BL/6 mice adoptively transferred with TA- or TB-cells by flow cytometry. We found that the adoptively transferred TA-cells had prolonged survival and enhanced T-cell memory development, compared to TB-cells. In addition, TA-, but not TB-cells were able to eradicate well-established EG7 thymomas in all 8/8 tumor-bearing mice. Our data suggested that AdvIL-6-transfected DC-stimulated CD8+ T cells with potent cytotoxicity and survival advantage may serve as an effective adoptive CD8+ T-cell immunotherapy strategy for anti-tumor treatment.

Biography

Kalpana Kalyanasundaram Bhanumathy has completed her Master's and PhD degree in Biotechnology from Annamalai University, India. During her Master's, she has received several awards for her academic excellence and has bagged the "Best women student award" among the Departments in the Faculty of Science. Her PhD research was related to field of "Radiation Oncology" and she was the recipient of the "Senior Research Fellow (SRF) Award" instituted by the "Indian Council of Medical Research (ICMR)", Government of India during her PhD programme. After completing her PhD, she moved to Saskatoon, Canada to pursue her Post-doctoral work in the field of Immunology under Dr. Jim Xiang, Senior Scientist and Professor at the University of Saskatchewan. She was then awarded the prestigious "Terry fox Post-doctoral fellow" - by the Saskatchewan Health research foundation (SHRF), Saskatchewan, Canada. She also received various travel awards to present her work in International conferences. She has published eight papers as first author and two papers as co-author in peer reviewed international journals.

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