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Folate-modified chitosan nanoparticles containing the IP-10 gene promote melanoma-specific cytotoxic $CD8^+CD28^+$T lymphocyte responses

Background: Adoptive cytotoxic T-cell (CTL) therapy has great potential for the treatment of several malignant cancers; however, promotion of the CTL anti-tumor immune responses is a key limiting factor. This study aimed to investigate the anti-tumor response of a combination therapy employing folate-modified chitosan nanoparticles containing IP-10 plus melanoma TRP2-specific $CD8^+CD28^+$T cells.

Methods: We prepared folate-modified chitosan nanoparticles containing the mouse IP-10 gene (FA-CS-mIP-10) and induced melanoma TRP2-specific $CD8^+CD28^+$T by culturing artificial antigen-presenting cells with TRP2180-188 peptide and anti-CD28 antibody in the presence of IL-21 and IL-15. B16-bearing mice were treated with FA-CS-mIP-10, melanoma TRP2-specific $CD8^+CD28^+$T cells, a combination of both, or saline control. Tumor volumes and mice survival were recorded. The proportion of myeloid-derived suppressor cells (MDSCs) and $CXCR3^+CD8^+$T cells infiltrating the tumor microenvironment and regulatory T cells (Tregs) in spleen was analyzed by flow cytometry. We also detected tumor proliferation and angiogenesis by immunohistochemistry and apoptosis in vivo by TUNEL.

Results: The combination therapy prevented the progression of melanoma in vivo. Compared with other treatments, it more efficiently inhibited tumor growth and increased mice survival. After treatment with combination therapy, the proportion of MDSCs and Tregs decreased, while the percentage of $CXCR3^+CD8^+$T cells increased. Moreover, combination therapy prevented proliferation and promoted apoptosis of tumor cells and significantly inhibited tumor angiogenesis in vivo.

Conclusion: We provide a novel strategy for improving the anti-tumor response of $CD8^+CD28^+$CTLs by combining them with FA-CS-mIP-10 nanoparticles.

Biography

Xiaoling Lu has completed her PhD from Huazhong University of Science and Technology, China. She is the Vice-director of National Center for International Research of Biological Targeting Diagnosis and Therapy of China, the leader of Changjiang Scholars and Innovative Research Team in University of China and candidate for New Century Excellent Talents in University of China. She has published more than 30 papers in SCI journal as first or corresponding author, and 15 patents.

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