 REVIEW

Abstract: Dendritic cells (DCs) are the most potent antigen-presenting cells (APCs). DCs pulsed with peptides of tumor-associated antigens (TAA) and tumor lysate have been used in cancer immunotherapy. An early clinical study demonstrated the safety of the use of DCs, but the clinical response was not sufficient. The gene-modification of DCs with TAA and soluble factor genes such as cytokine and chemokine genes has been examined to enhance the antigen-presenting capacity of DCs. Viral vectors including retroviruses and adenoviruses have been reported to be useful to obtain a sufficient transduction efficiency into DCs. TAA gene-transduced DCs could have several advantages compared with TAA peptide-pulsed DCs as follows: 1) The use of TAA gene-modified DCs are not restricted by MHC haplotypes. 2) The gene transduction with TAA genes is likely to present the unknown TAA peptides on DCs. 3) The gene-modified DCs show the prolonged presentation of TAA peptides. The transduction of DCs with cytokine genes including IL-12 and GM-CSF have also been reported to augment the antitumor effects of DCs. Although the results in the experimental systems were promising, the clinical application of gene-modified DCs includes several problems such as the standardization of methods of manipulation and gene-transduction of DCs. Approaches to solve them require further studies. J. Med. Invest. 49: 7-17, 2002

Keywords: dendritic cells (DCs), tumor-associated antigens (TAA), cytokine, chemokine, gene transduction, viral vector
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(1) Tumor-associated antigen (TAA) genes

Tumor-associated antigen (TAA) genes referred to as the human T-cell lymphotropic virus type I (HTLV-I) 
TAA genes, which are present in patients with chronic HTLV-I infection, play a critical role as tumor 
markers and are also used in the detection of HTLV-I infection. The TAA genes are transcribed from the 
long terminal repeat (LTR) of the HTLV-I genome, which is a retroviral integration site in the human 
genome. The TAA genes include the HTLV-I major envelope protein (MAE), which is the target for 
anti-HTLV-I antibodies and is used as a TAA marker.

et al. published a study on the detection of TAA genes in patients with chronic HTLV-I infection. The study 
showed that the TAA genes were detected in a high proportion of patients with chronic HTLV-I infection, 
and that the TAA genes were correlated with the development of HTLV-I-associated diseases. The study 
also demonstrated that the TAA genes were sensitive and specific markers for the detection of 
chronic HTLV-I infection and the development of HTLV-I-associated diseases.
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(2) The cytokine and chemokine genes

The cytokine and chemokine genes are highly expressed in both in vivo and in vitro conditions. In vivo, the expression of these genes is regulated by various factors, including inflammation and infection. In vitro, the expression can be manipulated by controlling the growth factors and cytokines in the culture medium. The expression of these genes is also affected by the cell type, the specific stimuli, and the culture conditions.

(3) The cell surface molecules

The cell surface molecules are also regulated by the cytokine and chemokine genes. In vivo, the expression of these molecules is influenced by the immune response and the local microenvironment. In vitro, the expression can be controlled by the experimental design and the culture conditions. The expression of these molecules is important for the function of the cells, including adhesion, migration, and signaling.
Active immunization (s.c. >> i.v.)

**TAA-presenting DC**

- **TAA Peptide gene**
- **Cytokine gene Chemokine gene**

**TAA-unknown**
- Eluted peptides
- Lysates, RNA Fusion, Hsp Exosomes

**TAA protein**

**Mature DC**

**Immature DC**

**Peripheral blood**

- **Blood DC**
- **CD14+ monocytes**
- **CD34+**

**GM-CSF**
- **TNF-α**
- **SCF, FL**

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### Table 1: Dendritic Cell Modification Strategies

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### Example:

- In vivo genetic modification involves the introduction of genes into dendritic cells in vivo, allowing for the expression of specific antigens or cytokines that can induce an immunological response.
- In vitro genetic modification involves the manipulation of dendritic cells outside the body, allowing for precise control over the expression of desired genes.

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### Further Reading:

- [Genetic Modification of Dendritic Cells](#) for a comprehensive overview of the techniques and applications.
- [Clinical Applications](#) highlighting successful case studies in cancer immunotherapy.