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Development of a DNA vaccine against human breast cancer

Yap Fei Ling[1], Rozita Rosli[1], Cheong Soon Keng[2]

[1]Department of Human Growth and Development, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor, Malaysia.
[2]Department of Pathology, Faculty of Medicine, Universiti Kebangsaan Malaysia, 56000 Kuala Lumpur, Malaysia.
E-mail: feilingyap@yahoo.com

Breast cancer is the most common malignancy among women in Malaysia. While the specific etiology of breast cancer remains unknown, DNA vaccines directed at eliciting an immune response toward tumors appear to offer promise for both the prophylactic and therapeutic treatment of cancer. In this study, DNA encoding human breast tumor antigen, MUC-1 and cytokine, interleukin-18 (IL-18) are being investigated as potential candidates for the DNA vaccine against human breast cancer. The cDNAs of human MUC-1 with 22 tandem repeats and IL-18 were cloned into mammalian expression plasmid, pVax1. Subsequently, IL-18 cDNA was subcloned into pTrcHis2-TOPO plasmid and expressed in *Escherichia coli*. To express the MUC-1 protein, the pVax1/MUC-1 clones were transfected into COS-7 cells by liposomal mediated transfection. Translated proteins were detected by SDS-PAGE followed by Western blotting. Indirect immunofluorescence staining of fixed COS-7 cells was also performed using the monoclonal antibody anti-human MUC-1 and the binding visualized using a fluorescein isothiocynate (FITC)-conjugated goat anti-mouse. The results revealed the presence of MUC-1 in about 40 % of the transfected cells, demonstrating that MUC-1 was indeed expressed in the membrane. These successfully expressed clones were then be tested in dendritic cell (DC) and mouse studies. In dendritic cell study, autologous T cells were stimulated *in vitro* with untransfected DC or with DC transfected with plasmid expressing various genes to investigate the capacity of gene-modified DC to prime naive T cells, as measured by T cell proliferation response in mixed leukocyte reaction. The most significant T cell proliferation was observed after stimulation with IL-18/ MUC-1-DC. In addition, enhanced cytotoxic activity of these stimulated T cells as the effector cells was also augmented against the target cells T47D and MDA-231. Immunization with pVax1/MUC-1 in BALB/C mice showed MUC-1 specific antibody response. Most importantly, administration with pVax1/MUC-1 and pVax1/IL-18 led to the potent generation of Th1 cytokine (IL-18). These results indicate that DNA vaccine coexpressing tumor antigen MUC-1 and cytokine IL-18 can be used as an immunogen and its immunization may be an effective strategy for a successful therapeutic vaccination.