

Expression of Human Papillomavirus Type 18 L1 Virus-Like Particles in Methylophilic Yeast, *Pichia Pastoris*

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Abstract : Human papillomavirus type 16 and 18 are closely associated with the development of human cervical carcinoma, which is one of the most common causes of cancer death in women worldwide. At present, HPV type 18 accounts for about 34 % of all HPV infections in Iran and the most promising vaccine against HPV infection is based on the L1 major capsid protein. The L1 protein of HPV18 has the capacity to self-assemble into capsomers or virus-like particles (VLPs) that are non-infectious, highly immunogenic and allowing their use in vaccine production. The methylotrophic yeast *Pichia pastoris* is an efficient and inexpensive expression system used to produce high levels of heterologous proteins. In this study we expressed HPV18 L1 VLPs in *P. pastoris*. The gene encoding the major capsid protein L1 of the high-risk HPV type 18 was isolated from Iranian patient by PCR and inserted into pTG19-T vector to obtain the recombinant expression vector pTG19-HPV18-L1. Then, the pTG19-HPV18-L1 was transformed into *E. coli* strain DH5 α and the recombinant protein HPV18 L1 was expressed under IPTG induction in soluble form. The HPV18 L1 gene was excised from recombinant plasmid with XhoI and EcoRI enzymes and ligated into the yeast expression vector pPICZ α linearized with the same enzymes, and transformed into *P. pastoris*. Induction and expression of HPV18 L1 protein was demonstrated by BMGY/BMMY and RT PCR. The parameters for induced cultivation for strain in *P. pastoris* KM71 with HPV16L1 were investigated in shaking flask cultures. After induced cultivation BMMY (pH 7.0) medium supplemented with methanol to a final concentration of 1.0% every 24 h at 37 degrees C for 96 h, the recombinant produced 78.6 mg/L of L1 protein. This work offers the possibility for the production of prophylactic vaccine for cervical carcinoma by *P. pastoris* for HPV-18 L1 gene. The VLP-based HPV vaccines can prevent persistent HPV18 infections and cervical cancer in Iran. The HPV-18 L1 gene was expressed successfully in *E.coli*, which provides necessary basis for preparing HPV-18 L1 vaccine in human. Also, HPV type 6 L1 proteins expressed in *Pichia pastoris* will facilitate the HPV vaccine development and structure-function study.

Keywords : *Pichia pastoris*, L1 virus-like particles, human papillomavirus type 18, biotechnology

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