Molecular Studies on Genotypes of Human Papillomavirus among Bladder Carcinoma Infected Patients

Thesis

Submitted for the Master Degree in Science

(Microbiology)

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Approval sheet

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TO MY GREAT PARENTS

TO WHOM I OWED MY DEEPEST GRATITUDE

MY BROTHERS

MY SISTERS

MY FRIENDS

My dear husband

&

MY SWEET DAUGHTER

“NOUR”

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LIST OF ABBREVIATIONS

AP	Alkaline phosphatase.
BCIP	5-bromo-4-chloro-3-indolylphosphate.
Bp	Base pair.
Brd4	Bromodomain-4.
BSA	Bovine serum albumin.
BTB	Bladder tissue biopsy.
DH	Dot Hybridization.
DNA	Deoxyribonucleic acid.
ds-DNA	Double-stranded deoxyribonucleic acid.
dNTP	Deoxy nucleotide tri-phosphate.
EBV	Epstein Barr virus.
E.coli	*Escherichia coli*.
EDTA	Ethylene diamine tetra-acetate.
ELISA	Enzyme Linked Immunosorbent Assay.
FDA	Food and Drug administration.
FISH	Fluorescently labeled *in situ* hybridization.
FVU	First voided urine.
HIV	Human immunodeficiency virus.
HPV	Human papillomavirus.
HR-HPV	High risk human papillomavirus.
HC2	Hybrid capture 2 assay.

ISH	*In situ* hybridization.
IR-HPV	Intermediate risk human papillomavirus.
LCR	Long control region.
LR-HPV	Low risk human papillomavirus.
LiPA	Line immune Probe Assay.
Mcm	Micrometer.
NBT	Nitroblue tetrazolium.
O.D	Optical density.
PBMCs	peripheral blood mononuclear cells.
PBS	Phosphate buffer saline.
PCR	Polymerase chain reaction.
PVDF	polyvinylidene fluoride.
RB	Retinoblastoma.
RDH	Reverse dot hybridization.
STH	Southern transfer hybridization.
SIL	squamous intraepithelial lesions.
SqCC	Squamous cell carcinoma.
STD	Sexually transmitted disease.
TAE	Tris acetate EDTA.
TBS	Tris buffered saline.
TCC	Transitional cell carcinoma.
TESPA	3-aminopropyl-triethoxysilane.
$\boldsymbol{T_m}$	Melting temperature.
TSPCR	Type specific PCR.

TUR	Transuretheral resection.
UUR	Upstream regulator region.
VLP	Virus-like particle.
WHO	World Health organization.

INTRODUCTION

Cancer of the urinary bladder is one of the most common types of urogenital cancer in the world, particularly in some parts of the world like Africa. Bladder cancer is the fourth most common type of cancer in men and the eighth most common type in women and it is two to three times more frequent in men. **(Helal *et al.,* 2006)**.

In Egypt, bladder cancer is one of the most common malignancies **(Khaled *et al.,* 2002)**. There are different kinds of carcinogenic and cocarcinogenic factors associated with bladder cancer; age, sex, smoking, alcohol abuse, long time taking of analgesic and anti-neoplastic drugs, contact with carcinogenic chemicals, Schistosomiasis and human papillomavirus (HPV) genital infections (**Sur *et al.,* 2001; Karagas and Kelsey *et al.,* 2005 and Helal *et al.,* 2006) .** The etiology of transitional cell carcinoma (TCC), which represents 90 percent of bladder malignancies, is not quite clear, while squamous cell carcinoma (SqCC) (5%) of the bladder malignancies is well associated with some factors like urinary stones and prolonged infections or parasitic infestation particularly (Schistosomiasis). HPV has been documented in the etiology of several urogenital carcinomas **(Yu *et al.,* 1993)**. Numerous studies have been performed, in recent years, on a possible association between HPV and human bladder cancer, but contradictory results have been reported. It is believed that different technical factors and geographical conditions may affect the studies results **(Barghi *et al.,* 2005).** Other reports have confirmed its role in bladder cancer **(Anwar *et al.,* 1992 and La Rue *et al.,* 1995).** However, the possible role of HPV in bladder cancer is still controversial.

HPV is a genus of *Alphapapillomaviruses* belongs to *Papillomaviridae* family and it is associated with genital or oral warts, or associated with benign genital tumors. HPV exists as more than two-hundred different types that