

MCM7 gene Expression versus risk of malignancy index (RMI) for prediction of ovarian malignancy

Thesis

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List of abbreviations

(NH₄)₂SO₄	Ammonium sulfate
AJCC	American Joint Committee Of Cancer
AR	Androgen receptors
ARID1A	AT-rich interactive domain-containing protein 1A
ATP	Adenosine triphosphate
AUC	Area Under The Curve
BIM	Bcl-2-interacting mediator of cell death
BMI	Body Mass Index
Bmi-1	B-Lymphoma Moloney Murine Leukemia Virus Insertion Region-1
BRAF	V-Raf Murine Sarcoma Viral Oncogene Homologe B1
BRCA	Breast Cancer Gene
CA 19-9	Carbohydrate antigen 19-9
CA125	Cancer Antigen 125
cdc45	Cell Division Cycle 45
CDC47	Cell cycle-regulated nuclear import and export
Cdc6	cell division cycle 6
CDK12	Cyclin-Dependent Kinase 12
CDKs	Cyclin dependent kinases
cDNA	Complementary Deoxy Ribonucleic Acid
Cdt1	chromatin licensing and DNA replication factor 1
CIN	Cervical intraepithelial neoplasia
CT	Computerized Tomography
CT	Crossing Threshold
CTNNB1	Catenin (Cadherin-Associated Protein), Beta 1
DNA	Deoxy Ribonucleic Acid
E2F	E2F Transcription Factor or Retinoblastoma-Associated Protein
EOC	Epithelial Ovarian Cancer
ERT	estrogen replacement treatment

FDA	U.S. Food and Drug Administration
FH	Family history
FIGO	International Federation of Gynecology and Obstetrics
FLH	FLYWCH zinc finger transcription factor homolog
GAPDH	glyceraldehyde-3-phosphate dehydrogenase
GC	Guanine and cytosine content
GINS	Gypsy Retrotransposon Integrase
HBOC	Hereditary Breast - Ovarian Cancer
HCT116	HCT116
HE4	Human epididymis protein 4
HER2	Human epidermal growth factor receptor 2 OR v-erb-b2 avian erythroblastic leukemia viral oncogene homolog 2
HGSC	High grade serous carcinoma
HNF1	Hepatocyte nuclear factor 1-alpha
HNPCC	Hereditary nonpolyposis colorectal cancer
HPV- E6	The Human Papillomavirus E6 protein
HP-α	Haptoglobin- α
HRT	Hormonal replacement treatment
ILK	Integrin Linked Kinase
IMR90	Human Caucasian fetal lung fibroblast
IOSE	Immortalized ovarian surface epithelial
KCl	Potassium chloride
KRAS	Kirsten rat sarcoma viral oncogene homolog
LGSC	Low-grade serous carcinoma.
LNCaP	Lymph Node Carcinoma of the Prostate
LPA	Lysophosphatidic acid
M	Menopausal state
Mat-1	Methionine Adenosyltransferase 1A
MCM	Minichromosomal maintaince complex
MCM7	Minichromosomal maintaince component 7
Mg²⁺	Magnesium ion
MgCl₂	Magnesium chloride

miR	Micro RNA
ml	Milliliter
MLH	MutL Homolog
MMR	mismatch repair
MP	Multipara
mRNA	Messenger Ribonucleic Acid
MS	Menopausal State
MSH-2	mutS homolog 2
MYC	V-Myc Avian Myelocytomatosis Viral Oncogene Homolog
MYCN	V-Myc Avian Myelocytomatosis Viral Oncogene Neuroblastoma
N	Lymph Node
nm	Nanometer
No	Number
NP	Nulliparous
NSCLC	Non-Small Cell Lung Cancer
°C	Centigrade
OCT	Oral contraceptive treatment
OD	Optical Density
ORC	Origin recognition complex
OVX1	Ovarian cancer antigen X1
p53	Tumor Suppressor P53
PCOS	polycystic ovarian syndrome
PI	predictive value
Pmol	Picomole
PMS 1 & 2	Postmeiotic Segregation Increased 1
PTEN	Phosphatase and tensin homolog (Tumor suppressor)
qPCR	Quantitative polymerized chain reaction
Rb	Retinoblastoma protein
RMI	Risk of malignancy index
RNA	Ribonucleic acid
RNase	Ribonuclease
ROC	Receiver operating characteristic

ROCA	Risk Of Ovarian Cancer Algorithm
ROMA	Risk of Ovarian Malignancy Algorithms
RQ	Relative Quantification
RT	Reverse Transcription
RT-PCR	Reverse Transcriptase Polymerase Chain Reaction
Saos2	Cell Line derived from human primary osteogenic sarcoma
SBT	Serous Borderline Tumor
SD	Standard Deviation
sFas	Serum Stimulator of Apoptosis Fragment
siRNA	Small interference ribonucleic acid
ssDNA	Single stranded deoxy Ribonucleic acid
T	Tumour Grade
Taq DNA	Thermus Aquatica Deoxy Ribonucleic Acid
TGFB1	Transforming Growth Factor Beta 1
Tm	Melting temperature
TNM	Tumor-Nodes-Metastases
TP53	Transcription Factor P53
TVUS	Transvaginal ultrasound
U	Ultrasound
U/ml	International Unit/Milliliter
U2OS	The human osteosarcoma cell line
US	Ultrasound
UUT-TCCs	Upper urinary tract transitional cell carcinomas
WHI	Women's Health Initiative
WHO	World Health Organization
ΔCT	Delta Crossing Threshold

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ABSTRACT

Minichromosomal Maintenance protein 7 (MCM7), a member of the MCM family of proteins critical to the DNA replication complex, has recently been shown to improve the sensitivity and specificity of Epithelial Ovarian Cancer (EOC) diagnosis but its function in cancer cells is not clear. We evaluated MCM7 expression, RMI and CA125 serum level as diagnostic tools of primary ovarian cancer in Egyptian women. The MCM7 gene expression was evaluated by real time PCR in ovarian cancer of 50 Egyptian women. Ovarian cancer tissues were studied for the detection of the gene expression of MCM7 by Quantitative Real Time PCR (Q RT-PCR). Serum Human cancer antigen 125 (CA 125) was measured in the serum of all participants of the study using immune sorbent assay (ELISA). The MCM7 showed significant difference among ovarian malignant tumors patients compared to the control subjects ($p < 0.01$). The best cutoff value 1.96 at which MCM7 sensitivity was 100% and specificity was 96%. There was a significance correlation between MCM7, RMI and CA125 in all patients of the study ($p \neq 0.01$ for both). The mRNA expression of MCM7 was significantly high versus the control group in early stages and low grades of the disease ($p = 0.00, 0.01$, respectively). As well as, there was Increased MCM7 expression in the late

stages of the disease suggesting that it may be associated with poor prognosis as well. The MCM7 could be considered as a good prognostic marker for ovarian cancer that increases the sensitivity of the CA 125 to absolute value without affection of CA125 accuracy and its positive predictive value.

Key words: Ovarian Cancer, RMI, MCM7, real time PCR, CA 125