THE ROLE OF AURKA GENE EXPRESSION AS A MARKER IN COLORECTAL CANCER

Thesis

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ABSTRACT

Background and Objectives:

The centrosome-associated kinase aurora A (AURKA) is involved in genetic instability and is over-expressed in several human carcinomas including colorectal cancer (CRC). It plays a critical role in cancer cell development, proliferation, motility and survival. It is suggested that the Aurora kinase A expression in colorectal cancer significantly increase, which may play an important role in development of colorectal cancer.

Design and Methods:

In this study, the expression of AURKA gene was analyzed in 15 malignant patients, 13 premalignant patients and 23 control patients. AURKA gene expression was analyzed using a Real-Time Quantitative Reverse-Transcriptase Polymerase Chain Reaction (RTQ-PCR) to examine the copy number gains and mRNA level of AURKA in CRC.

Results:

AURKA gene expression was highly expressed in (33.3%, 5 of 15 CRC studied patients) with (mean 213.4, P value=0.005) indicated highly significant difference between control, premalignant and malignant groups.

Conclusions:

These findings indicated that colorectal cancers exhibit different mechanisms of aurora A regulation and this may impact the efficacy of aurora-A targeted therapies.

Key words:

Colorectal cancer; AURKA, RTQ-PCR .

LIST OF CONTENTS

LIST OF FIGURES.....i
LIST OF TABLES.....iii
LIST OF ABBREVIATION……vi

INTRODUCTION……1

REVIEW OF LITERATURE
CHAPTER 1……4
CHAPTER II……24

MATERIALS AND METHODS…….41
RESULTS……..60
DISSCUSION……82
SUMMARY……...90
REFERENCES…….93
ARABIC SUMMARY…….118

LIST OF FIGURES

Figure	*Description*	*Page*
1	*Anatomical and staging illustrations for colorectal cancer*	*4*
2	*Stagging of colorectal cancer*	*15*
3	*Domain organisation of Aurora kinases A–C*	*24*
4	*Schematic cell cycle diagram showing phases of cell cycle and checkpoints*	*27*
5	*Localization of Aurora-A and -B kinases during the cell cycle*	*28*
6	*Comparative localization of Aurora A and B*	*29*
7	*Regulation of Aurora-A activity by Ran–GTP and TPX2*	*34*
8	*Mechanisms of Aurora-A promoted tumorigenesis*	*35*
9	*The two step RT-PCR*	*42*
10	*Basics of the 5´ Nuclease Assay*	*43*
11	*Coloured illustration of the RT & PCR assay*	*44*
12	*Amplification Plot shows higher level of expression in patients*	*55*
13	*Demographic features in patients groups according to sex*	*61*
14	*Family history of colorectal lesions in all patients groups*	*61*
15	*Percentage distribution of all patients as regards colonoscopy indication*	*62*

16	*Percentage distribution of all patients as regards type of sedation*	*63*
17	*Percentage distribution of all patients as regards colonoscopy findings*	*66*
18	*Percentage distribution of pathology*	*69*
19	*Comparison between control, premalignant and malignant groups as regards age*	*70*
20	*Comparison between non malignant and malignant groups as regards RQ of AURKA gene expression*	*72*
21	*Comparison between control, premalignant and malignant groups as regards RQ of AURKA gene expression*	*73*
22	*Comparison between control, premalignant and malignant groups as regards sex*	*74*
23	*Correlation between age and AURKA gene expression*	*75*
24	*Relation between sex and RQ of AURKA gene expression*	*76*
25	*Correlation between RQ of AURKA gene expression and tumor grade*	*77*
26	*Receiver Operating Characteristic (ROC)-curves (RQ)*	*79*

LIST OF TABLES

Table	***Description***	***Page***
1	*Symptoms associated with CRC*	*11*
2	*TNM Classification of Colorectal Cancer*	*16*
3	*Staging Systems for Colorectal Cancer*	*17*
4	*Adverse Prognostic Indicators in Colorectal Cancer*	*19*
5	*Aurora substrates/interacting proteins and mitotic processes*	*30,31*
6	*Aurora kinase inhibitors*	*37*
7	*The RT mix*	*49*
8	*Thermal profile of RT*	*50*
9	*PCR assay mix*	*53*
10	*Thermal profile of PCR*	*53*
11	*Demographic features in patients groups according to age, sex and family history*	*60*
12	*Percentage distribution of all patients as regards colonoscopy indication*	*62*
13	*Percentage distribution of all patients as regards type of sedation*	*63*

Table	***Description***	***Page***
14	*Percentage distribution of all patients as regards colonoscopy extent*	*64*
15	*Percentage distribution of all patients as regards colonoscopy findings*	*65*
16	*Anatomical site of colorectal lesions as determined by colonoscopy*	*67*
17	*Percentage distribution of pathology*	*68*
18	*Comparison between control, premalignant and malignant groups as regards age*	*70*
19	*RQ of AURKA gene expression in all studied patients*	*71*
20	*Comparison between non malignant and malignant groups as regards RQ of AURKA gene expression*	*71*
21	*Comparison between control, premalignant and malignant groups as regards RQ of AURKA gene expression*	*73*
22	*Comparison between control, premalignant and malignant groups as regards sex*	*74*

Table	***Description***	***Page***
23	*Correlation between age and RQ of AURKA gene expression in all studied patients*	*75*
24	*Relation between sex and RQ of AURKA gene expression in all patients*	*76*
25	*Correlation between RQ of AURKA gene expression and tumor grade.*	*77*
26	*Odds ratio of AURKA gene expression among studied group*	*78*
27	*Sample size*	*79*
28	*ROC-curve of AURKA gene expression among malignant and non malignant groups*	*80*

LIST OF ABBREVIATION

ADRM1	Adhesion regulating molecule 1
AJCC	American Joint Committee on Cancer
AMPK	AMP-activated kinase
APC	Adenomatous polyposis coli
AURKA	Aurora kinase A
AURKA-CN	Aurora kinase A gene copy number
AXIN1	Axis inhibition protein 1
BAX	Bcl2-associated X protein
BRCA-1	Breast cancer 1
BUB1	Budding uninhibited by benzimidazoles 1 homolog
BUBR1	Bub1-related kinase
cDNA	Complementary DNA
cdc20	Cell division cycle 20 homolog
CDC25B	Cell division cycle 25 homolog B
C20orf24	Chromosome 20 open reading frame 24
Cdh1	Cadherin 1
CEA	Carcinoembryonic antigen
CENP-A	Centromere Protein -A
CGH	comparative genomic hybridization
CIN	Chromosomal Instability
CIMP	CpG island methylator phenotype
CPEB	Cytoplasmic polyadenylation element-binding protein isoform 1
CRC	Colorectal Cancer

CTNNB1	catenin (cadherin-associated protein), beta 1
DCC	Deleted in Colorectal Cancer
DCBE	Double contrast barium enema
DNA	Deoxyribose Nucleic Acid
dNTP	Deoxynucleotid triphosphate
Eg5	Kinesin-related motor protein
FGFR1	Fibroblast growth factor receptor 1
FLT3	Fms-related tyrosine kinase 3
FOBT	Fecal occult blood test
Gadd45a	Growth arrest and DNA-damage-inducible, alpha
GSEA	Gene set enrichment analysis
GWAS	Genome-wide association studies
H3	Histone
HEF1	Enhancer of filamentation 1
histone H2A	Histone cluster 2
HURP	Hepatoma up-regulated protein homolog
IkBaLpha	Nuclear factor of kappa light polypeptide gene enhancer in B-cells 1
INCENP	Inner centromere protein antigens
KEN	Kendrin
KRAS	Kirsten rat sarcoma viral oncogene homolog
LATS2	Large tumor suppressor, homolog 2
LCK	Lymphocyte cell-specific protein-tyrosine kinase
LIM protein	Lipophilic protein

MAPKAP-K1	Mitogen activated protein kinase-activated protein kinase 1
MCAK	Kinesin family member 2C
mCRC	metastatic colorectal cancer
MEK	MAP kinase-ERK kinase
MSI	Microsatellite Instability
MKK1	MAP kinase/ ERK kinase 1
MMR	mismatch repair
NKD1	Naked cuticle 1 homolog
NSCLC	Non-small cell lung carcinoma
PAK1	P21 protein (Cdc42/Rac)-activated kinase 1
P53-RB	P53- Retinoblastoma pathway
PCR	Polymerase chain reaction
PDGFRB	Platelet-derived growth factor receptor, beta polypeptide
PHK	Phosphorylase kinase
PI3K	Phosphoinositide 3-kinase
PLK1	Polo-like kinase 1
PP1-2A	Protein phosphatase 1-2A
PTEN	Phosphatase and tensin homolog
P- value	Probability value.
QMPSF	quantitative multiplex polymerase chain reaction of short fluorescent fragments
RASSF1A	Ras association domain family member 1
RNPC1	RNA binding motif protein 38
RNA	Ribose Nucleic Acid
ROC	Receiver Operating Characteristic

RT-PCR	Reverse transcriptase-PCR
RTQ-PCR	Real-Time Quantitative Reverse-Transcriptase Polymerase Chain Reaction
SMAD2,4	Mad (D. melanogaster) homologs 2 and 4
SNPs	Single nucleotide polymorphisms
SPARC	Secreted protein, acidic, cysteine-rich (osteonectin)
SRC	Sarcoma viral oncogene
SSSCA1	Sjogren syndrome/scleroderma autoantigen 1
STK15	S/T kinase 15
TACC/ Maskin	Transforming, acidic coiled-coil containing protein 3
TCF7L2	Transcription factor 7-like 2
TGF-β	Transforming growth factor
TH1L	TH1-like (Drosophila)
TNM	Tumor,Node,Metastasis
TP53	Tumour protein p53
TPX2	Targeting protein for Xklp2
Wnt pathway	Wingless pathway