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Expression of microRNA-96 and it relationship to matrix metalloproteinase regulator- RECK in Retinoblastoma

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التعبير عن الحامض النووي الريبي الميكروى ٩٦ فى الأورام الخبيثة بشبكية العين (ريتنوبلاستوما) و علاقته بالانزيم الفلزى المحلل لبروتينات النسيج الخلوى RECK

رسالة

توطئة للحصول على درجة الماجستير

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Abstract

Background: Retinoblastoma is the most common malignancy that develops in children's eyes. MiR- 96 was identified as an oncogenic micro-RNA. The RECK protein downregulates matrix metalloproteinases (MMP-2, MMP-9 and MT1-MMP) and suppresses tumor invasion, angiogenesis and metastasis. RECK mRNA was reported as a target of miR-96 in many cancers. This study aimed at evaluating the expression of miRNA-96 and the level of the matrix metalloproteinase regulator- RECK in 14 patients newly diagnosed with retinoblastoma before and after treatment, and in 14 controls, in order to give insights on their possible role as potential diagnostic and prognostic biomarkers in retinoblastoma.

Methods: MiR-96 and RECK protein were evaluated using sera of three groups of samples, retinoblastoma group before treatment, controls, and retinoblastoma group after treatment by quantitative reverse transcription real time polymerase chain reaction (qRT-PCR) and Enzyme Linked Immunosorbent Assay (ELISA), respectively.

Results: The expression of miR- 96 was significantly higher in the sera of patients than the control group ($P<0.05$). The concentration of RECK protein was significantly decreased in the patients compared to control group ($P<0.05$). Furthermore, the level of miR- 96 was significantly decreased ($P<0.05$), and concentration of RECK protein was significantly increased ($P<0.05$) in the sera after treatment in patients who responded to globe salvage treatment. Moreover the expression of RECK protein, and miR- 96 was negatively correlated with each other in the patients before treatment as well as after treatment and in the control group with r (-0.809), r (-0.926), r (-0.615), respectively.

Conclusion: Serum level of miR-96 and RECK protein concentration may serve as potential biomarkers in retinoblastoma.

KEYWORDS:

Retinoblastoma; MicroRNA; MiR-96; RECK.

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List of abbreviations

Ago ……...Argonaute protein

AML…….Acute myeloid leukemia

ANT2……Adenine nucleotide translocase 2

ARE……...AU-rich element

AUC …….Area under the curve

c-Myc……Cellular Myelocytomatosis

C_T……..Cycle threshold

CDK……..Cyclin dependent kinase

CDKN1A……..Cyclin dependent kinase inhibitor 1A

CNS……...Central nervous system

CT…….....Computed tomography

DD…….Disc diameters

DDR……..DNA damage response

DEPC……Diethylpyrocarbonate

DNA……..Deoxyribonucleic acid

ECM……..Extra-cellular matrix

EGF ……..Epidermal growth factor

EGFR……Epidermal growth factor receptor

EGCG ……..Epigallocatechin 3 gallate

EMQN……..European molecular quality network

FAK……..Focal adhesion kinase

FOXO1……Forkhead box protein O1

FOXO3a……..…Forkhead box protein O3a

FXR1……...Fragile-X-mental-retardation-related protein 1

HAT……Histone acetyltransferases

HbF……. Fetal hemoglobin

HDAC1……...Histone deacetylase 1

HCC……Hepatocellular carcinoma

HIF-1alpha……..Hypoxia-inducible factor 1-alpha

HIF-2α ……Hypoxia-Inducible Factor-2-alpha

HPV ……....Human papilloma virus

ICRB ……..International classification of retinoblastoma

ISH …….In situ hybridization

JNK ……....c-Jun N-terminal kinase

Kda……..Kilo Dalton

m7G……7-methylguanosine-cap

miR……..Micro ribonucleic acid

miRNA……Micro ribonucleic acid

µg ……....Micro gram

mL……...Mille liter

MMP……...Matrix metalloproteinases

MRI ……Magnetic resonance imaging

mRNA…….Massager RNA

MTSS1…….Metastasis suppressor-1

ng……..Nano gram

nm…… Nano meter

NSCLC ……Non-small cell lung cancer

OD……Optical density

ORF …….Open reading frame

OS…….Overall survival

PACT ……...Protein ACTivator of the interferon- induced protein kinase

PFS……Progression-free survival

pRb……RB1 protein

pri-miRNA……....primary micro RNA

qRT-PCR …….Quantitative reverse transcription Polymerase Chain Reaction

RB1.....Retinoblastoma gene

RE ……Reese-Ellsworth classification

RFS……...Relapse-free survival

RECK……Reversion inducing cysteine rich protein with kazal motifs

RIM……..RECK Intron-1 Methylation

RISC…….RNA induced silencing complex

RNase……...Ribonuclease

ROC…….Receiver-Operating Characteristic

RPM……..RECK Promoter/exon-1 Methylation

SACC ……...Salivary adenoid cystic carcinoma

SAMD9…….Sterile alpha motif domain-