The scientific and clinical concept of microribonucleic acid (miRNA) in human diseases

(Essay)

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بسم الله الرحمن الرحيم

قال تعالى : "{قَالُواْ سُبْعَانَكَ لاَ عِلْمَ لَنَا إِنَّكَ أَنِهَ الْعَلِيمُ الْحَكِيمُ} إِلاَّ مَا عَلَّمْتَذَا إِنَّكَ أَنِهَ الْعَلِيمُ الْحَكِيمُ}

[سورة البهرة أية (٣٢)]

Abstract:

Keyword: microRNA

MicroRNAs are single-stranded RNAs of 19–25 nucleotides in length. MicroRNAs have emerged as central post- transcriptional repressors of gene expression. MicroRNAs have been implicated in regulation of cellular processes such as differentiation, proliferation, apoptosis, metabolism, haematopoiesis, cardiogenesis. MicroRNAs represent a class of genes with a great potential for use in diagnosis, prognosis, therapy and are a new frontier for molecular medicine.

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List of abbreviation

A Adenine

Ago argonaute proteins
ALD alcoholic liver disease

AMO anti-miRNA oligonucleotide

aP2 Adipocyte protein 2

ARE AU-rich 3`UTR regulatory sequence

ASO antisense oligonucleotides AT1R angiotensin II type 1 receptor

Bcl-2 B-cell lymphoma 2

C Cytosine

C/EBPα CCAAT-enhancer-binding proteins alpha

CAT-1 cationic amino acid transporter-1

Cav2 caveolin 2

CD4 cluster of differentiation 4 CDK2 cyclin-dependent kinase 2 CLL chronic lymphocytic leukemia

CNS central nerve system

CNV choroidal neovascurization

CP capping protein

CREB-1 cAMP-response-element binding protein

CTGF connective tissue growth factor

CYP1B1 cytochrome P450, family 1, subfamily B, polypeptide 1

DCP2 decapping enzyme

DGCR8 DiGeorge Syndrome Critical Region 8

DNA deoxyribonucleic acid DNMTs DNA methyl transferases

dsRBP double-stranded RNA-binding protein

dsRNA double-stranded RNA
ED endothelial dysfunction
eIF eukaryotic initiation factors

eNOS endothelial nitric oxide synthase

ER Endoplasmic reticulum

ERKS extracellular-signal-regulated kinases

ES Embryonic stem

Exp 5 Exportin 5

Fab fragment antigen-binding

FMR1 fragile X mental retardation 1

FMRP fragile X mental retardation protein

FOS FBJ murine osteosarcoma FoxA2 fork head box protein A2

G Guanine

Gag group-specific antigen GAX growth arrest homeobox

GK Goto-Kakizaki

GLUT4 insulin-sensitive glucose transporter,

GM-CSF granulocyte-macrophage colony stimulating factor

GSIS glucose-stimulated insulin secretion

Hand2 Heart- and neural crest derivatives-expressed protein 2

HBV hepatitis B virus
HCV hepatitis C virus
HDAC4 histone deacetylase 4
HDL High density lipoprotein
HIF hypoxia inducible factor

HIV Human immunodeficiency virus hnRNA heterogenous nuclear RNA

HOXB8 homeobox B8

HSC hepatic stellate cells HSL hormone sensitive lipase

IFN-beta interferon beta IL Interleukin

Insig1 insulin-induced gene 1

IRAK1 interleukin-1 receptor-associated kinase 1

IRES internal ribosome entry sites IRS Insulin receptor substrate

KATP ATP-sensitive potassium channel Kir6.2 inwardly-rectifying potassium channel LATS2 large tumour suppressor homologue 2

LDL Low-density lipoprotein
Limk1 LIM domain kinase-1
LNA Locked nucleic acid
m7G 7-methylguanosine

MAFB v-maf musculoaponeurotic fibrosarcoma oncogene homolog B

MAPK7 mitogen-activated protein kinase 7

Mef2 myocyte enhancer factor-2

miRISC miRNA induce silencing complex

miR- miRNA Mimic technology

Mimic

miRNA MicroRNA

miRNPs miRNA containing ribonucleoprotein particles

mRNA messenger RNAs

Mtpn Myotrophin MyoD myogenic D

NAFLD non-alcoholic fatty liver disease

ncRNA non-coding RNA NFI-A nuclear factor I/A NF- κ B nuclear factor κ B cell NMD nonsense mediated decay

NO Nitric oxide

Noc2 nucleolar complex protein 2

nPTN Neuroplastin Nt Nucleotid

Onecut2 one cut homeobox2

p53 protein 53

PABP1 poly(A)-binding protein 1

PACT protein activator of the interferon-induced protein kinase

PAZ Piwi, Argounate, Zwille PBC Primary biliary cirrhosis

Pdx1 pancreatic and duodenal homeobox 1

PEG polyethylene glycol (

PFV-1 primate foamy virus type 1 PN peripheral neuropathy PNA peptide nucleic acids

Pol II polymerase II

PPAR-2 peroxisome proliferator-activated receptor

pre-miRNA prieursor miRNAs pri-miRNA primary miRNA

PTEN phosphatase and tensin

PTGS post-transcriptional gene silencing

PVD peripheral vascular disease

Ran-GTP RAs-related Nuclear protein-guanine triphosphatase

RISC RNA-induced silencing complex

RNA ribonucleic acid

RNAi ribonucleic acid interference

RNases Ribonuclease RNAs Ribosomal RNAs SGs stress granules siRNA Small Interfering RNA SLITRK1 Slit and Trk-like 1

SMA Spinal muscular atrophy SMN survival of motor neuron snoRNA Small nucleolar RNA snRNA Small nuclear RNA SRF serum response factor

sRNA small RNA

ssRNAs single-stranded RNAs SuFu suppressor of fused Sur1 sulfonylurea receptor

T Thymine

T1D Type 1 diabetes T2D Type 2 diabetes

TBP TATA binding protein
TFIID Transcription Factor II D
TGF Transforming growth factor

TLRs toll like receptors
TNF tumor necrosis factor

TNFα tumor necrosis factor alpha

TRAF6 TNF receptor-associated factor 6

TRBP transactivation-response element RNA-binding protein

TRNA Transfer RNA

TS Tourette's syndrome TSP-1 thrombospondin-1

TUSC2 tumour suppressor candidate 2

U Uracil

UTR untranslated region

VCAM 1 vascular cell adhesion molecule 1 VEGF vascular endothelial growth factor

VIG Vasa intronic gene

VSMCs vascular smooth muscle cells

XRN1 exoribonuclease 1

ZOP Zonula occludens protein

3-day transfer, inoculum 3 x 105 cells

5-Aza-CdR 5-Azacytidine

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INTRODUCTION AND AIM OF WORK

Introduction

Human gene expression is the process by which DNA is transcribed into RNA to be translated into proteins which produce essential cellular function. This process is usually under strict regulation (Wang, 2009).

MicroRNAs (miRNA) are single-stranded RNA molecules of 21-23 nucleotides in length, which regulate gene expression. MiRNAs are encoded by genes from whose DNA they are transcribed but are not translated into protein (Lee et al, 1993).

A miRNA is complementary to a part of one or more messenger RNAs (mRNA). Animal miRNAs are usually complementary to a site in the three prime untranslated regions (3'UTR) whereas plant miRNAs are usually complementary to coding regions of mRNAs (Wang, 2009).

The function of miRNAs appears to be in gene regulation. Perfect or near perfect base pairing with the target RNA promotes cleavage of the RNA. In animals, microRNAs more often only partially base pair and inhibit protein translation of the target mRNA. They can also speed up de-adenylation causing mRNAs to be degraded sooner. MicroRNAs occasionally also cause DNA methylation of promoter sites and therefore affecting the expression of targeted genes (Williams, 2009).

The elevated tissue-specific expression of some miRNA genes suggests that they might be involved in tissue differentiation and maintenance of cell-type identity; miRNAs would share such a role with tissue-specific transcriptional factors (**Kawasski et al, 2004**).