شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم

HANAA ALY

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جامعة عين شمس

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تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

HANAA ALY

Evaluation of miRNA-106a and ADARB1 in Autistic Children

Thesis

Submitted for Partial Fulfillment of Master Degree in Medical Biochemistery & Molecular Biology

By

Brihan Magdy Abdu-Allah Zamil

Demonstrator of Medical Biochemistry and Molecular Biology

M.B.B.Ch.,

Faculty of Medicine - Ain Shams University

Under supervision of

Prof. Dr. Randa Ali-Labib

Professor of Medical Biochemistry and Molecular Biology

Faculty of Medicine, Ain Shams University

Dr. Eman Khairy Farahat

Assistant Professor of Medical Biochemistry and Molecular Biology

Faculty of Medicine, Ain Shams University

Dr. Walaa Youssef Youssef

Lecturer of Pediatrics

Faculty of Medicine, Ain Shams University

Faculty of Medicine

Ain Shams University

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بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

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Brihan Magdy

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Abb.	Full term
A	Adenosine
ABC	Adaptive Behavior Composite score
ADARB1	Adenosine Deaminase Acting on RNA B1
ADHD	Attention deficit/hyperactivity disorder
Ads	Autoimmune diseases
AGO	Argonaute family proteins
APP	Amyloid precursor protein
ASD	Autism spectrum disorder
AUC	Area under the curve
BBB	Blood - brain barrier
Ca	Calcium
CARS	Childhood Autism Rating Scale
cDNA	Complementary DNA
CELF	CUG-BP, Elav-like family
CMPs	Chromatin modifiers proteins
CNS	Central nervous system
CRH	Corticotropin-releasing hormone
CSF	Cerebrospinal fluid
Ct	Threshold Cycle
DGCR8	DiGeorge syndrome critical region gene 8
DM	Deaminase domain
dsRBDs	Double stranded RNA binding domains
dsRBPs	Double stranded RNA-binding proteins
DUI	daytime urinary incontinence
FN	False negatives
FP	False positives
FR	Folate receptor
G	Guanosine
GIT	Gastrointestinal tract

List of Abbreviations Cont…

Abb.	Full term
GluRs	Glutamate receptors
GSH	Glutathione
GSH-PX	Glutathione peroxidase
GW182	Glycine-tryptophan protein of 182 kDa
HDL	High density lipoprotein
HMDD V2	Human microRNA Disease Database, version 2
HT2C	Serotonin
I	Inosine
I/V	Isoleucine to valine
ICU	Intensive care unit
ID	Intellectual disability
IL	Interleukin
Imp8	Importin 8
IP6	Inositol hexakisphosphate
IQ	Intelligent quotient assessment
LBW	Low birth weight
lincRNAs	Large intergenic non-coding RNAs
lncRNAs	Long non-coding RNAs
MDD	Major depressive disorder
MECP2	Methyl CpG binding protein 2
MHC	Major histocompatibility complex
miRNAs	Micro RNAs
MREs	miRNA response elements
mRNA	Messenger RNA
MTHF	5-methylene tetra hydrofolate
MTHFR	Methylene tetra hydrofolate reductase
n	Number
NE	nocturnal enuresis
NICU	Neonatal intensive care unit

List of Abbreviations Cont...

Abb.	Full term
NLGN	Neuroligins
NMDAR	N-methyl-D-aspartate receptor
NPV	Negative predictive value
NRXN	Neurexin
nt	Nucleotides
OMSCs	Olfactory mucosal stem cells
PACT	Protein activator of the interferon-induced protein kinase
PAHs	Polycyclic aromatic hydrocarbons
PCR	Polymerase chain reaction`
piRNAs	PIWI-interacting RNAs
Pol II	Polymerase II
PPV	Positive predictive value
pre-miRNA	Precursor miRNA
pri-miRNA	Primary transcript
PTBP1/2	polypyrimidine tract binding protein 1 and 2
Q/R	Glutamine to arginine
qRT-PCR	Quantitative reverse transcription polymerase chain reaction
r	Correlation coefficient
R/G	Arginine to glycine
RA	Rheumatoid arthritis
RISC	RNA-induced silencing complex
ROC	Receiver operating characteristic
RQ	Relative quantity
rRNAs	Ribosomal RNAs
SD	Standard deviation
SHANK	SH3 and multiple ankyrin repeat domains
shRNAs	Short hairpin RNAs

List of Abbreviations Cont...

Abb.	Full term
siRNAs	Small interfering RNAs
SLE	Systemic lupus erythematosus
snoRNAs	Nucleolar RNAs
SNPs	Single nucleotide polymorphisms
snRNAs	Small nuclear RNAs
SOD	Super oxide dismutase
SPSS	Statistical Package for Social Sciences
stRNAs	Small temporal RNAs
TAR	Transactivation-responsive
TE	Tris-EDTA
TGA	Transcriptional gene activation
TGS	Transcriptional gene silencing
TN	True negatives
TNF	Tumor necrosis factor
TP	True positives
TRBP	Transactivation-responsive RNA-binding proteins
tRNAs	Transfer RNAs
T-UCRs	Transcribed ultra-conserved regions
UTR	Untranslated region
VABS	Vineland Adaptive Behavior Scales
X	Mean
Y/C	Tyrosine to cysteine
ΔCt	Delta Threshold Cycle
^{o}C	Centigrade

INTRODUCTION

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by disturbances in social interactions, language, and communication, as well as by the presence of stereotyped behaviors and restricted interests ***(Salem et al., 2013).***

In most cases, ASD symptoms are first recognized in early childhood. The average age of ASD diagnosis is 4 years. The world Health Organization estimated the prevalence of ASD in children to be 1 in 160 worldwide ***(World Health Organization, 2018).*** This increased prevalence will have enormous future public health implications, and has necessitated the need to discover predictive noninvasive biomarkers that could be index for autism before the onset of symptoms ***(Anitha and Thanseem, 2015).***

In recent years, epigenetic mechanisms, which act at the interface of genes and the environment, have been identified as a potential contributor to the pathogenesis of several neurodevelopmental abnormalities such as ASD. Epigenetic factors control heritable changes in gene expression without changing the DNA sequence. MicroRNAs (miRNAs) have recently emerged as prominent epigenetic regulators of a variety of cellular processes, including differentiation, apoptosis and metabolism ***(Vasu et al., 2014)***.

MicroRNAs (miRNAs) are small RNA molecules of approximately 22 nucleotides that regulate the expression of genes by binding to the 3’untranslated regions (3’UTR) of specific mRNAs directing translational repression or transcript degradation ***(Talebizadeh et al., 2008)***. MiRNAs are abundantly present in brain ***(Vasu et al., 2014)***, and have been found to play important roles in neurogenesis, synaptogenesis, and neuronal migration ***(Hicks et al., 2016)***.

Abnormal expression of circulating miRNAs have been reported in several neurological and neurodevelopmental disorders. Thus, miRNAs within the central nervous system (CNS) may be exported across the blood–brain barrier (BBB) by the microvesicles (exosomes) released by neurons and glial cells ***(Anitha and Thanseem, 2015)***. Serum miRNAs, which may be derived from circulating blood cells, are known to be stable and resistant to the action of RNase, suggesting the potential efficacy of serum miRNAs as noninvasive biomarkers for ASD ***(Vasu et al., 2014)***.

Based on using HMDD V2 (the Human microRNA Disease Database, version 2) and PhenomiR database, and according to ***Abu-Elneel et al. (2008)***, miRNA-106a has been reported to be differentially expressed in postmortem cerebellar cortex tissue of individuals with ASD compared to non ASD individuals. This miRNA was also deregulated in serum of astrocytoma patients, a primary brain tumor, and in whole blood samples of Alzheimer's disease as reported by ***Zhi et al,***