Molecular Intervention of Parkinson's disease

Essay

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التدخل الجزيئى فى علاج مرض الباركنسون

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توطئة للحصول على درجة الماجستير

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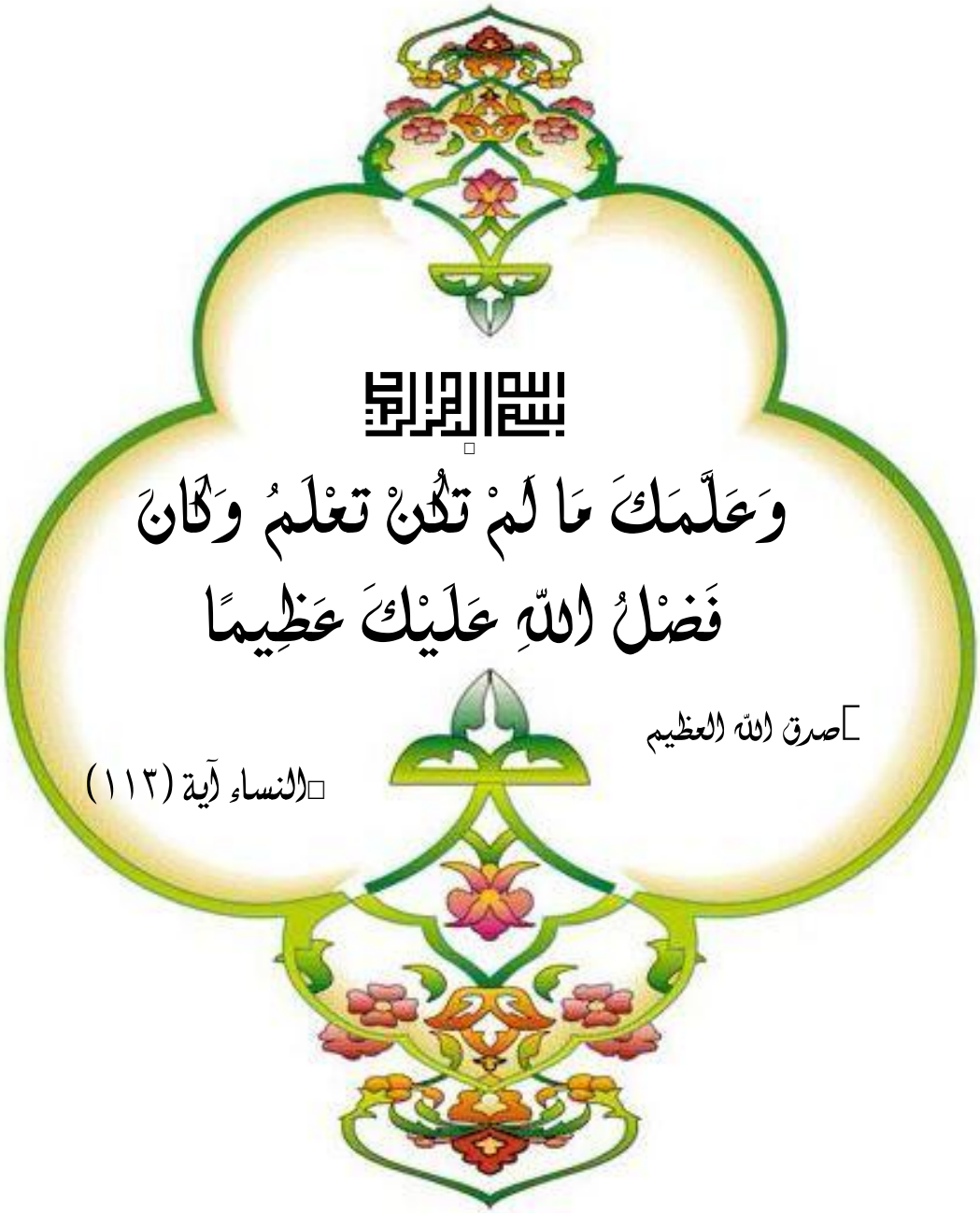

بسم الله الرحمن الرحيم

وَعَلَّمَكَ مَا لَمْ تَكُنْ تَعْلَمُ وَكَانَ فَضْلُ اللّهِ عَلَيْكَ عَظِيمًا

صدق الله العظيم

النساء آية (١١٣)

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List of Abbreviations

ANT2/ANT3	Neutarin 2 & Neutarin 3
A2A	Adenosine-2A
AADC	Aromatic amino acid decarboxylase
AAV2	Adeno associated virus 2
ACC	Anterior cingulate cortex
Ach	Anticholinergic
AD	Autosomal dominant
AMPA	α-amino-3-hydroxyl-5-methyl-4-isoxazole-propionate
AR	Autosomal recessive
ARJP	Autosomal recessive juvenile Parkinsonism
ASC	Adult stem cells
ATP	Adenosine triphosphate
BAG1	Bcl-2–associated athanogene 1
BDNF	Brain derived neurotrophic factor
bFGF	Basic fibroblast growth factor
BFGF	Basic fibroblasts growth factors
BMSC	Bone marrow stromal cell
BMSCs	Bone marrow stem cells
CAP	Capsid
CDNF	Cerebral dopamine neurotrophic factor
CeM	Central medial thalamic nuclei
CL	Central lateral thalamic nuclei
cm	Centimeter

CNS	Central nervous system
CNTF	Ciliary neurotrophic factor
COMT	Catechol-0-methyl transferase
CREB	cAMP response element binding
CSF	Cerebrospinal fluids
CSP	Co-operative Study program
D1R	Dopamine receptor 1
D2R	Dopamine receptor 2
DA	Dopamine
DARPP-32	Dopamine and cAMP-regulated phospho-protein
DBS	Deep brain stimulation
DG	Dente gyrus
dPL	Dorsal prelimbic cortices
DR3	Dopamine receptor 3
Erk1/	Erk2 extracellular signal-related kinase 1 / 2
ESC	Embryonic stem cells
FD	Fluro dopa.
GABA	Gamma-aminobutyric acid
GAD	Glutamic acid decarboxylase
GDNF	Glial cell derived neurotophic factor
GID(s)	Graft-induced dyskinesias
Glut	Glutamate
GP	Globus pallidus
GPe	Globus pallidus, externa
GPi	Globus pallidus, interna

GSH	Gluthione .
HD	Huntington's disease
hESC	(human) embyonic stem cell
HSV	Herpes simplex virus
Hz	Hertz
IL	Infralimbic cortex
IMD	intermediodorsal thalamic nuclei
IPSC	Induced pluripotent stem cells
KB	Kilo byte
LD	Levodopa
LDB	Dementia with lewy bodies
LID(s)	Levodopa-induced dyskinesias
LRRK2	leucine rich repeat kinase 2 gene
MANF	Mesencephalic astrocyte derived neurotrophic factor
MAO-B	Monoamine oxidase-B
MAP	Mitogen-activated protein kinase
MD	Movement disorders
MEK	Mitogen-activated protein kinase kinase
Mi RN	Micro Ribonucleic acid
MIBG	Metaiodobenzlguaindine
Mm	Millimeter
mos	Months
MPTP	1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine
mRNA	Messenger ribonucleic acid
MSC	Mesenchymal stem cells

MSN	Medium spiny neuron
NICD	Notch 1 intracellular domain
NMDA	N-methyl-D-aspartic acid
NR1	NMDA receptor subunit 1
NR2A	NMDA receptor subunit 2A
NR2B	NMDA receptor subunit 2B
NR4A2	Nuclear receptor subfamily4.
NTFS	Neurotrophic factors
PARK 8	Parkinson's disease 8
PARS	Parkinson's associated risk syndrome
PCN	Paracentral thalamic nuclei
PD	Parkinson's disease
PET	positron emission tomography;
PFC	Prefrontal cortex
PINK1	PTEN induced putative kinase 1.
PKA	Protein kinase A
PKC	Protein kinase C
PNS	Peripheral nervous system
PPN	Pedunculopontine tegmental nucleus
PSP	Progressive supranuclear palsy
PSTP	Physician Scientist Training Program
PVN	Paraventricular thalamic nuclei
R	Rostral
RBD	Rapid eye movement sleep behavior disorder
REP	replication

RM-ANOVA	Repeated measures - analysis of variance
ROS	Reactive oxygen species
RPEC	Retinal pigmented epithelial cell
Sh RNA	Short hair pin Ribonucleic acid
SNCA	Synuclein, alpha
SNpc	Substantia nigra, pars compacta
SNpr	Substantia nigra, pars reticulate
SOD	Superoxid dismutase.
SPECT	Single Photon Emission Computerized Tomograghy
sq	Subcutaneous
SSRI	Selective Sertonine reuptake inhibitors
STN	Subthalamic nucleus
SVZ	Subventricular zone
TH	Tyrosine hydroxylase
TH-ir	Tyrosine hydroxylase immunoreactive
UC-COM	University of Cincinnati College of Medicine
UCH- LI	Ubiquitin carboxy-terminal esterase L1.
um	Micrometer
UPDRS	Unified parkinson's disease rating scale
UPS	Ubiquitin proteasome system.
VA	Veterans affairs
Veh	Vehicle
VIM	Ventralis intermedius
VM	Ventral mesencephalon
vPL	Ventral prelimbic cortices

VTA	Ventral tegmental area
Wks	Weeks.
β-CIT	Beta-(4-iodophenyl) tropane.
3OMD	Three O methyl dopa
6-OHDA	6-hydroxydopamine

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Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder associated with a loss of dopaminergic nigrostriatal neurons. It is named after James Parkinson, the English physician who described the shaking palsy in 1817. It is recognized as the second most common neurodegenerative disorder after Alzheimer's disease. The likelihood of developing Parkinson's disease increases with age. Parkinson's disease is more common with advancing age. It affects as many as 1.5% of individuals older than 65 years and as many as 3.5% of individuals older than 85 years ***(Olanow et al., 2009).***

Symptoms of Parkinson's disease are slowly progressive. Well-recognized clinical features of Parkinson's disease are slowed movements, tremors, rigidity, and difficulties with gait and balance. However, other features commonly occur, including changes in olfaction, autonomic function, cognitive function, affect, sleep, and energy level ***(Burn et al., 2006)***.

Parkinson's disease is characterized pathologically by the selective loss of dopaminergic neurons from the substantia nigra, and by the presence of Lewy bodies in surviving cells and Lewy neurites in brain parenchyma. The main protein component of Lewy bodies and Lewy neurites is α-synuclein,