Autophagic dysfunction in Alzheimer?s disease: Cellular and molecular mechanistic approaches to halt Alzheimer?s pathogenesis

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Autophagy is a preserved cytoplasmic self-degradation process and endorses recycling of intracellular constituents into bioenergetics for the controlling of cellular homeostasis. Functional autophagy process is essential in eliminating cytoplasmic waste components and helps in the recycling of some of its constituents. Studies have revealed that neurodegenerative disorders may be caused by mutations in autophagy-related genes and alterations of autophagic flux. Alzheimer?s disease (AD) is an irrevocable deleterious neurodegenerative disorder characterized by the formation of senile plaques and neurofibrillary tangles (NFTs) in the hippocampus and cortex. In the central nervous system of healthy people, there is no accretion of amyloid ? (A?) peptides due to the balance between generation and degradation of A?. However, for AD patients, the generation of A? peptides is higher than lysis that causes accretion of A?. Likewise, the maturation of autophagolysosomes and inhibition of their retrograde transport creates favorable conditions for A? accumulation. Furthermore, increasing mammalian target of rapamycin (mTOR) signaling raises tau levels as well as phosphorylation. Alteration of mTOR activity occurs in the early stage of AD. In addition, copious evidence links autophagic/lysosomal dysfunction in AD. Compromised mitophagy is also accountable for dysfunctional mitochondria that raises Alzheimer?s pathology. Therefore, autophagic dysfunction might lead to the deposit of atypical proteins in the AD brain and manipulation of autophagy could be considered as an emerging therapeutic target. This review highlights the critical linkage of autophagy in the pathogenesis of AD, and avows a new insight to

search for therapeutic target for blocking Alzheimer?s pathogenesis.

Alzheimer?s disease

amyloid ?

autophagy

lysosomal dysfunction

mitophagy

neurofibrillary tangles

senile plaques

amyloid beta protein

carbamazepine

dimebon

lithium

mammalian target of rapamycin

metformin

minoxidil

nicotinamide

nootropic agent

peptidomimetic agent

rapamycin

resveratrol

smer 28

tau protein

trehalose

unclassified drug

MTOR protein, human

target of rapamycin kinase

aging

Alzheimer disease

autolysosome

autophagosome

autophagy

bioenergy

brain cortex

brain mitochondrion

cell death

central nervous system

drug effect

drug mechanism

drug targeting

gene mutation

hippocampus

homeostasis

housekeeping gene

human

lysosome

mitophagy

mTOR signaling

nerve degeneration

neurofibrillary tangle

neuropathology

nonhuman

pathogenesis

pathophysiology

priority journal

protein degradation

protein phosphorylation

Review

senile plaque

xenophagy

Alzheimer disease

autophagy

cytoplasm

genetics

metabolism

mitochondrion

pathology

signal transduction

Alzheimer Disease

Amyloid beta-Peptides

Autophagosomes

Autophagy

Cytoplasm

Humans

Mitochondria

Mitophagy

Proteolysis

Signal Transduction

TOR Serine-Threonine Kinases