

Curcumin Derivatives may Prevent Alzheimer's Disease by Promoting Amyloid- β Clearance

Dr. Rita P.-Y. Chen, an Associate Research Fellow at the Institute of Biological Chemistry and her research team has recently discovered that polyhydroxycurcuminoids, but not curcumin itself, may be useful in the prevention of Alzheimer's disease. The compounds were found to upregulate neprilysin (NEP), the most important amyloid- β peptide (A β)-degrading enzyme. Recently, many reports have shown that A β clearance is a promising strategy in the prevention and treatment of Alzheimer's disease and NEP is the most important A β -degrading enzyme. Upregulating NEP is expected to decrease A β levels in affected brains thus decreasing the risk of Alzheimer's disease progression. The research was published in *Scientific Reports*, a scientific journal published by the Nature Publishing Group, on July 13th, 2016.

The number of patients diagnosed with Alzheimer's disease has significantly increased in recent years due in part to aging populations. Since the average life expectancy after diagnosis with Alzheimer's varies from 4 to 20 years, medical and non-medical care for Alzheimer's patients can lead to significant economic and social burdens.

Alzheimer's disease is characterized by neurofibrillary tangles and senile plaques in the brain. Senile plaques are mainly composed of the A β peptides which are produced in the brain during protein catabolism. Under normal conditions, NEP and the other A β -degrading enzymes can degrade A β . However, if the rate of A β production exceeds the rate of A β degradation, A β can accumulate in the brain and form amyloid plaques resulting in the death of neurons. High plaque density regions (e.g., the hippocampus and cerebral cortex) of human Alzheimer's brains show significantly less NEP expression. Furthermore, the expression of NEP decreases with age and this suggests that there is a strong link between NEP activity and amyloid accumulation in the brains of Alzheimer's disease patients. It has also been reported that cognitive impairments and abnormal A β accumulation in the brains of transgenic Alzheimer's disease mice can be restored by the injection of stem cells or viruses that express foreign NEP.

Indian people have low incidence of Alzheimer's disease. Turmeric is a commonly used food additive in India. Curcumin is the major component of turmeric but has very poor solubility and bioavailability. The research team led by Dr. Rita P.-Y. Chen designed a highly-sensitive fluorescence-based NEP detection system to screen 25 curcumin analogs for their ability to upregulate NEP activity. Results from both in mice and in cell models indicated that polyhydroxycurcuminoids, but not curcumin itself, upregulated NEP activity.

They also found that feeding mice polyhydroxycurcuminoids upregulated NEP, decreased A β accumulation, and reduced the number of senile plaques in the hippocampus and cortex regions in

the brain. Hence, these polyhydroxycurcuminoids may represent a promising strategy in the prevention of Alzheimer's disease.

The full research article entitled "Polyhydroxycurcuminoids but not curcumin upregulate neprilysin and can be applied to the prevention of Alzheimer's disease" is available at the Scientific Reports website at: <http://www.ncbi.nlm.nih.gov/pubmed/27407064>.

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