THERAPEUTIC POTENTIAL AND ANTI-AMYLOIDOSIS MECHANISM OF TERT-BUTYLHYDROQUINONE FOR ALZHEIMER’S DISEASE

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Introduction and aim: Alzheimer's disease (AD) is a major cause of dementia in the elderly with no effective treatment. The aim of this study is to explore the therapeutic potential of a synthetic phenolic antioxidant tert-butyl hydroquinone (TBHQ), which has been used in a wide range of food and cosmetic products as a preservative, for the treatment of AD.

Methods: APP/PS1 transgenic mice, a well established mouse model of AD, were fed with a diet supplemented with 1% TBHQ for 6 weeks.

Results: Brain Abeta burden is dramatically reduced, associated with decreases in the amounts of alpha- and beta-C-terminal fragments of APP. Interestingly, only male, not female, APP/PS1 mice show TBHQ-mediated anti-amyloidosis effect. Furthermore, we show that TBHQ feeding increases the abundance of low density lipoprotein related protein 1 (LRP-1) in brain blood vessels and Abeta levels in the plasma, and inhibits the expression of plasminogen activator inhibitor-1 (PAI-1), a physiological inhibitor of tissue type and urokinase type plasminogen activators (tPA and uPA), which has been shown in our previous study to play a critical role in promoting Abeta accumulation in AD.

Conclusion: These data suggest that TBHQ can reduce brain Abeta burden by

1) inhibiting gamma-secretases expression/activity and thus Abeta synthesis;

2) increasing LRP-1 expression in brain blood vessel and thereby Abeta efflux from the brain; and

3) inhibiting PAI-1 expression, leading to increased tPA/uPA activity and Abeta degradation.

The results presented in this study suggest that TBHQ have therapeutic potential in the treatment of AD.