

“TRPC6 and Aβ production”

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Venue: Meeting Room 2-130, 1/F, Block 2, To Yuen Building

Abstract

Alzheimer's disease is the most common neurodegenerative disease leading to dementia in the aged. Over-production and accumulation of Aβ peptide is critical for the pathogenesis of AD. Generation of Aβ involves cleavage of amyloid precursor protein (APP) by γ-secretase, a protease known to cleave several substrates, including Notch. Attempts to treat AD patients by inhibiting γ-secretase activity have been disappointing.

We report that transient receptor potential canonical 6 (TRPC6) specifically interacts with APP (C99), but not with Notch, and prevents C99 interaction with presenilin 1 (PS1), leading to inhibition of γ-secretase cleavage of APP and Aβ production. A fusion peptide derived from TRPC6 also reduced Aβ levels without effect on Notch cleavage. Thus, preventing APP interaction with PS1 via TRPC6 could be a novel strategy to reduce Aβ formation. Additionally, TRPC6 expression is changed in AD patients. In the case-control study, we measured TRPC6 expression levels in the peripheral blood cells of AD patients and found a specific reduction of TRPC6 mRNA levels in four AD sets and one MCI set. In a subgroup of AD patients with brain Aβ examination, TRPC6 was associated with standardized uptake value ratio of Pittsburgh Compound B and cerebrospinal fluid Aβ42. The TRPC6 reduction in AD patients was further confirmed in blood RNA samples from The Australian Imaging, Biomarkers and Lifestyle Flagship Study of Aging, in post-mortem brain tissues from The Netherlands Brain Bank and in induced pluripotent stem cells-derived neurons from Chinese donors. We conclude that TRPC6 mRNA levels in the blood cells are specifically reduced in AD and MCI patients, and TRPC6 might be a biomarker for the early diagnosis of AD.

Biography

Prof Wang earned his Ph.D. degree from University of Laval, Canada 1991 and was a postdoctoral fellow of University of Nice, France and Case Western Reserve University, USA between 1991 and 1994. He served as a group leader in the Institute of Neuroscience or the director of State Key Lab for Neurosciences from 2001 or 2010 to 2015. He has obtained the national talented young award. He is now the director for brain science center in the Chinese Academy of Medical Sciences. His main interest is to study the neuronal survival mechanism during development and under pathological conditions.

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All are welcome !