OMICS International conferenceseries.com
Global Summit on Stroke
Stroke 2015
August 03-05, 2015 Birmingham, UK

Amelioration of brain function through modulation of GSK3β/β-catenin and Ang1/Tie2 signaling to preserve BBB integrity and promote neurogenesis by Bu-yang Huan-wu Decoction in mice with acute ischemic stroke

Chung Kuang Lu[1], Yu-Chang Hou[2], Yea-Hwey Wang[4], Kuo-Tong Liou[5], Chang-Ming Chern[3] and Yuh-Chiang Shen[1]

[1]National Research Institute of Chinese Medicine, Taiwan

[2]Taoyuan General Hospital, Taiwan

[3]National Yang-Ming University, Taiwan

[4]National Taipei University of Nursing and Health Science, Taiwan

[5]Chinese Culture University, Taiwan

The Bu-yang Huan-wu Decoction (BHD), one of the classic traditional Chinese medicine (TCM) formula has been used for improving neurological functional recovery in stroke-induced disability in China for more than 300 years and is the most famous and popular TCM formula clinically used in Taiwan. However, whether and how BHD and its active components can protect mice against ischemic stroke-mediated excite toxicity still lacks the evidence-based study. We have previously reported the BHD can protect acute ischemic stroke (AIS) murine through impeding inflammatory responses via impairing NF-κB and GSK3β signaling, most possibly through activating ERK and PI3K/Akt pathways. This compromises the activation/infiltration of microglial and/or inflammatory cells, and activation of endogenous neurogenesis, respectively. Treatment of mice that have undergone ischemic stroke with BHD (1.0 g/kg, p.o.) at 2 hour after stroke enhanced survival rate and ameliorated neurological deficits, brain infarction, neural dysfunction and massive oxidative stress due to enormous free radial production and severe breakdown of blood-brain barrier (BBB). The goal of this study is to further study whether BHD can promote BBB remodeling through which to mediate neuronal cell survival and neuronal progenitor cell migration for neurogenesis and tissue repair. Our data revealed that BHD decreases BBB leakage through dramatically increasing vascular integrity (BBB remodeling) via up-regulating tight junction protein (occludin) expression and Ang1/Tie2 signaling most possibly through inactivating GSK3 to activate Wnt/-catenin signaling in the ischemic brain after stroke. This results explains why BHD can increase neuroblast(DCX+, a neuroblast marker) survival and migration which is closely associated with vascular remodeling and angiogenesis through enhancing neovascularization (CD34+/BrdU+staining) with upexpression of occludin, Ang1 and Tie2, as well as activation of Wnt/-catenin signaling. Our data provide evidence to show that BHD is superior than t-PA in ameliorating AIS via enhancing angiogenesis through which to massively support neuron survival (Tubβ3/Ang1 and Tie2/Ang1 staining) and promote neuroblast proliferation and migration from sub ventricular zone (SVZ) to ischemic damaged core region and peri-infarct area for neurogenesis and tissue repairmen. Besides, the analysis of UPLC fingerprints among different BHD production batches and the 6 plantamedica suggested two active components, X1 and Y1. The survival rates of ischemic stroke mice which were treated by compound X1 and Y1 together were around 65% in day 3.

Biography

Chung Kuang Lu worked as an Assistant Research Fellow, National Museum of Marine Biology & Aquarium, Assistant Professor, Institute of Marine Biotechnology, National Dong Hwa University and Assistant Professor, School Pharmacy, Taipei Medical University. His research project focuses on developing and applying biotechnology to detect, isolate, identify and evaluate novel biologically active metabolites from the highly diverse microbes. To discover new anti-cancer, cardiovascular, and reduction in blood sugar agents from microbes is the priority goal.

cklu@nricm.edu.tw