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參展科別 醫學與健康科學科

作品名稱 **Expression of TRPV5 in Astrocytes: Implications for Ischemic Stroke**

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國　　家 Singapore

就讀學校 NUS High School of Math and Science

作者姓名 Tan Wei Liang Byorn

ABSTRACT OF EXHIBIT
TAIWAN INTERNATIONAL SCIENCE FAIR

Elevation of intracellular calcium secondary to increased calcium influx along with increased gliosis are implicated in the pathogenesis of focal ischemic stroke. In astrocytes, which play a major role in maintaining homeostasis in brain ischemia, the identities of the ion channels responsible for increased calcium influx during ischemia is relatively unknown although several Ca2+-permeable transient receptor potential (TRP) channels have been identified to have contributing roles. The transient receptor potential vanilloid 5 (TRPV5) channel is a Ca2+-permeable cationic channel expressed primarily in kidney epithelial cells and at low levels in the brain, but the exact localization and role this channel plays in the brain has not been explored. To investigate the possible role TRPV5 plays in astrocytic calcium influx in ischemia, we examined the functional expression of TRPV5 in astrocytes subjected to hypoxia-ischemia in vitro and in rat models of ischemic stroke in vivo. We hypothesize that TRPV5 contributes to increased calcium influx in ischemia. By treating astrocytes with culture conditions without glucose and with low oxygen levels, we found that TRPV5 is upregulated with increasing durations of simulated hypoxia-ischemia in vitro. Similarly, rat models of ischemic stroke with middle cerebral artery occlusion also show TRPV5 upregulation in reactive astrocytes, suggesting a possible role of TRPV5 in reactive gliosis in vivo. Microfluorimetric intracellular calcium imaging using Fura-2 on primary cultured astrocytes show a voltage-independent increase in astrocytic calcium influx after hypoxia-ischemia in vitro that is selective for extracellular Ca2+ concentration and is reduced by inhibition of TRPV5 with ruthenium red. Electrophysiology measurements using the whole-cell patch clamp technique on primary cultured astrocytes reveal a non-selective cation current similar to that of TRPV5 that is inhibited by Mg2+, another inhibitor of TRPV5. Preliminary results on astrocyte cell viability during hypoxia-ischemia with TRPV5 inhibition by ruthenium red also suggest that inhibition of TRPV5 could enhance astrocyte survival and reactive gliosis in vitro, indicating a beneficial role in blocking non-selective Ca2+ entry via TRPV5 into astrocytes. Since TRPV5 is highly selective for Ca2+ and an important channel for Ca2+ absorption in various epithelial cells, TRPV5 upregulation may contribute significantly to elevated Ca2+ influx in astrocytes in hypoxia-ischemia. Also, Ca2+ influx has been

demonstrated to play a crucial role in reactive gliosis, further suggesting that TRPV5 upregulation is involved in reactive gliosis. We propose that TRPV5 is involved in ischemia-induced calcium influx in astrocytes, and might participate in the pathogenesis of focal ischemic stroke.

評語

The design and execution of the experiments are superior.