【校級神經醫學研究中心 110 年 6 月份月會】

會議紀錄

時　　間：110年6月23日(星期三) 12:10-13:30

地　　點：視訊會議-Google Meet

主　　席：蔣永孝 主任(藍亭 副主任代理)

TMU Neuroscience Research Center Monthly Meeting Record for June, 2021

Chair: Vice Director Timothy Lane

Recorded by: Professor J. Y. Wang, Secretary C. N. Huang

Host: The Vascular Dementia Team

Time: 2021/6/23 (Wednesday) 12:10-13:30

Place: Net meeting via Google Meet

Meeting Agenda (議程) :

1. Opening by Vice Director Timothy Lane
2. "Diabetes and Stroke-the Link, Risk Factors, and Prognosis" presented by Dr. Yi-Chen Hsieh (謝宜蓁老師)
3. "RBM3 in Hypothermia Mediated Neuroprotection Following Ischemic Stroke" by Dr. Chih-Hao Yang (楊志豪老師)

1. Opening

In the opening, Vice Director Timothy Lane was very delighted to have two members from the Vascular Dementia Team share their research results. The Vascular Dementia Team is led by Vice Superintendent Chaur-Jong Hu.

藍亭副主任於開場時介紹，本次月會我們邀請到由胡朝榮副院長所領導的血管性失智團隊來分享研究成果。

2. Forum hosted by the Vascular Dementia Team

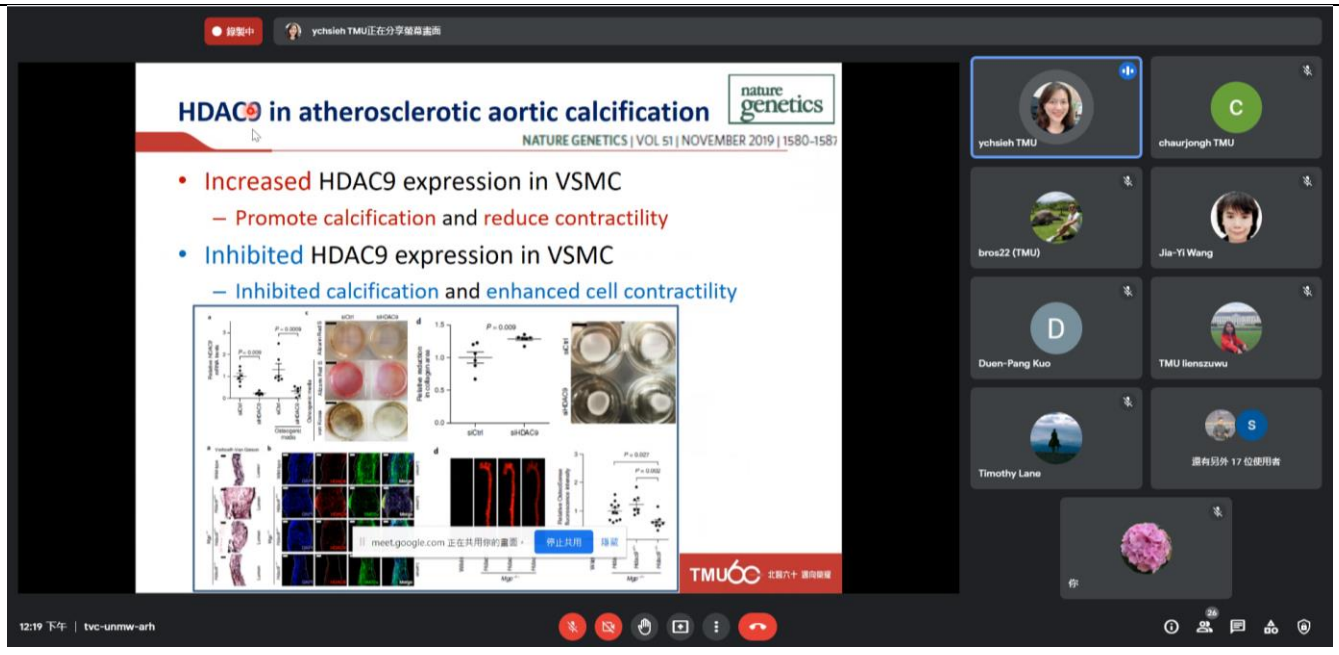
Vice Superintendent Hu introduced the first speaker, Dr. Yi-Chen Hsieh. Dr. Hsieh graduated from the School of Public Health of TMU. Her research focus on molecular epidemiology, genetic epidemiology, and especially stroke. As we know diabetes is an important risk factor and outcome determine factor of stroke. Dr. Hsieh has a lot of research in this field. Today she would talk about the research about diabetes and stroke.

胡朝榮副院長首先介紹第一位講者-謝宜蓁老師。謝老師畢業於臺北醫學大學公共衛生學系並取得博士學位，她的研究重點是分子流行病學、遺傳基因流行病學，尤其是中風研究。而糖尿病是中風的重要危險因素和結果決定因素。謝老師今天要介紹此糖尿病及中風的相關研究，

1) Diabetes and Stroke-the Link, Risk Factors, and Prognosis presented by Dr. Yi-Chen Hsieh (謝宜蓁老師)

Brief summary of Dr. Hsieh's speech:

Stroke ranks the 4th leading cause of death in Taiwan, and the annual death rate is from 60 deaths per 100,000 in 2000, gradually decreased to 51.6 deaths per 100,0000 in 2019. Several previous epidemiologic studies showed diabetes mellitus (DM) is an independent but modifiable risk factor for stroke, including both ischemic and hemorrhagic stroke. In addition, genetic heritability is also an important risk factor of stroke. Previous large scale genome-wide association studies (GWASs) found HDAC9 gene was associated with large vessel stroke, and further validated through in vitro and in vivo studies. Furthermore, HDAC family is related to insulin sensitivity through many pathways. Therefore, we conducted a study to investigate the interaction effect between HDAC and diabetes mellitus on the risk of ischemic stroke. The results showed a significant interactive effect of the polygenic risk score (PRS) and DM on the risk of ischemic stroke. A significant positive correlation between the polygenic score and a change in the plaque score in healthy controls with diabetes mellitus was also found. Next, we also wanted to identify novel genes and their regulated miRNAs that are associated with hyperglycemia-induced unfavorable stroke outcomes. We found the expression of Fas and miRNA hsa-let-7b-5p in addition to traditional risk factors could increase the discrimination and predictive ability for poor prognosis. Finally, we wanted to explore the hyperglycemia and diabetes related genes and then examine the association between these candidate genes and unfavorable stroke outcomes. A hyperglycemia/DM-derived PRS was constructed and the results showed the risk of poor outcomes after stroke at 3 months was substantially increased for those in the second, third, and fourth quartiles of the PRS compared to those in the first quartile of PRS as the reference group. Again, we performed a ROC analysis to evaluate the discriminative ability of the PRS in addition to traditional risk factors. The



Diabetes and Stroke-the Link, Risk Factors, and Prognosis presented by Dr. Yi-Chen Hsieh. (6/23, 2021)

findings showed that after integration with the PRS to the traditional risk factors, the C statistic increased to 0.907, which reached to an excellent discrimination ability. Our results further provided the evidence that even though the hyperglycemia AIS patients recovered during hospitalization, patients with higher PRS still acquired to have antidiabetic treatment when discharged. Therefore, PRS could help the clinicians to make appropriate treatment decision.

Vice Superintendent Hu then introduced the second speaker, Dr. Chih-Hao Yang (楊志豪老師). Dr. Yang graduated from the Institute of Basic Medical Science of National Cheng Kung University. He also did his research at the Johns Hopkins University School of Medicine. His research expertise includes neuropharmacology, neural stem cell development, cognitive and behavioral sciences. Today he would introduce his research about the RNA-binding motif protein 3 (RBM3).
胡副院長介紹第二位講者–楊志豪老師，楊老師畢業於成功大學基礎醫學研究所並取得博士學位，並曾於美國約翰霍普金斯醫學院進行研究。他的研究專長包括神經藥理學、神經幹細胞發育、認知和行為科學。今天楊老師將介紹關於 RBM3 的研究。

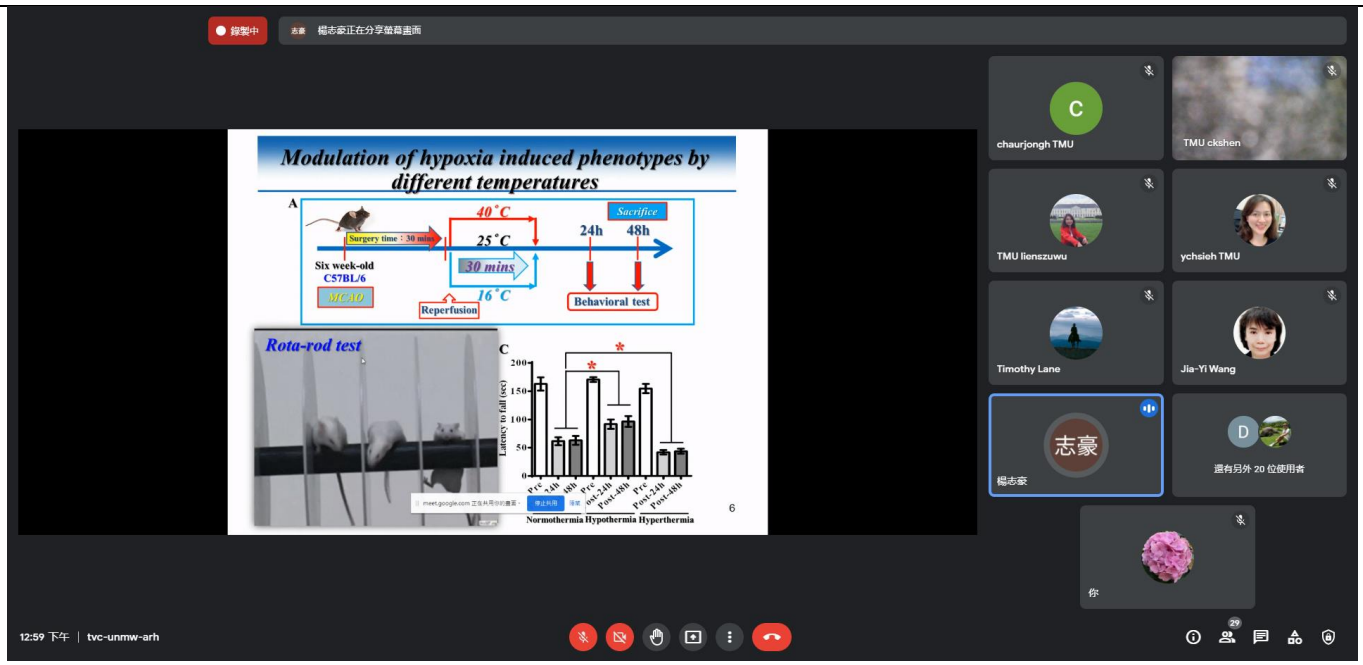
2) RBM3 in Hypothermia Mediated Neuroprotection Following Ischemic Stroke by Dr. Chih-Hao Yang (楊志豪老師)

Brief summary of Dr. Yang's speech:

Stroke represents the second leading cause of death worldwide that costs approximately 3-7% of the total health-care expenditure in high-income countries. Several key players in ischemia induced neuronal damage have been identified, including excitotoxicity, oxidative stress, and inflammatory responses. However, so far only one thrombolytic agent: rt-PA has been approved in the treatment of ischemic stroke. Unfortunately, the risk of regional bleeding and limited therapeutic time window restricts its clinical application. Therefore, there is an urgent need for developing of new therapeutic strategy for stroke. Recent evidence indicated that therapeutic hypothermia could be a potential strategy to reduce stroke induced neuronal damage and improve functional recovery afterward. However, the therapeutic time window for hypothermic treatment and also its underlying mechanisms involved in its neuroprotective effect has not been answered carefully.

Here in our current study, we found RBM3 (RNA-binding motif protein 3) could be a critical molecule that contributes to the beneficial effect by hypothermic treatment. By using the standard hypoxic rodent model (MCAO, middle cerebral artery occlusion), we have obtained evidence showing the significance of RBM3 in mediating the neuroprotective effect of hypothermic therapy in ischemic stroke. Through the analyzing of multiple indexes that reflect the hypoxia induced neuronal phenotypes, we found that changes in individual body temperature indeed affect the hypoxia induced phenotypes in the brain. Basically, the drop of ambient environmental temperature to 16℃ considerably reduces the hypoxia induced cerebral edema, infarct damage, and neurological deficits. On the other hand, rise the ambient environmental temperature to 40℃ profoundly increase in infarct size and edema ratio after hypoxic

challenge. Mechanistically, by in vitro primary culture neurons and in vivo MCAO models, we further identified that the inducibility of RBM3 instead of CIRBP negatively correlated with the excitotoxic and inflammatory events which implied that the induction of RBM3 might functional involved in hypothermia mediated neuroprotective effects toward hypoxia challenge. More importantly, by using the RIP-Seq, we have identified numerous RBM3 binding targets that might be involved in the neuroprotective of RBM3. The findings of our current study have the potential to provide a novel and promising therapeutic strategy for ischemic stroke by targeting RBM3.

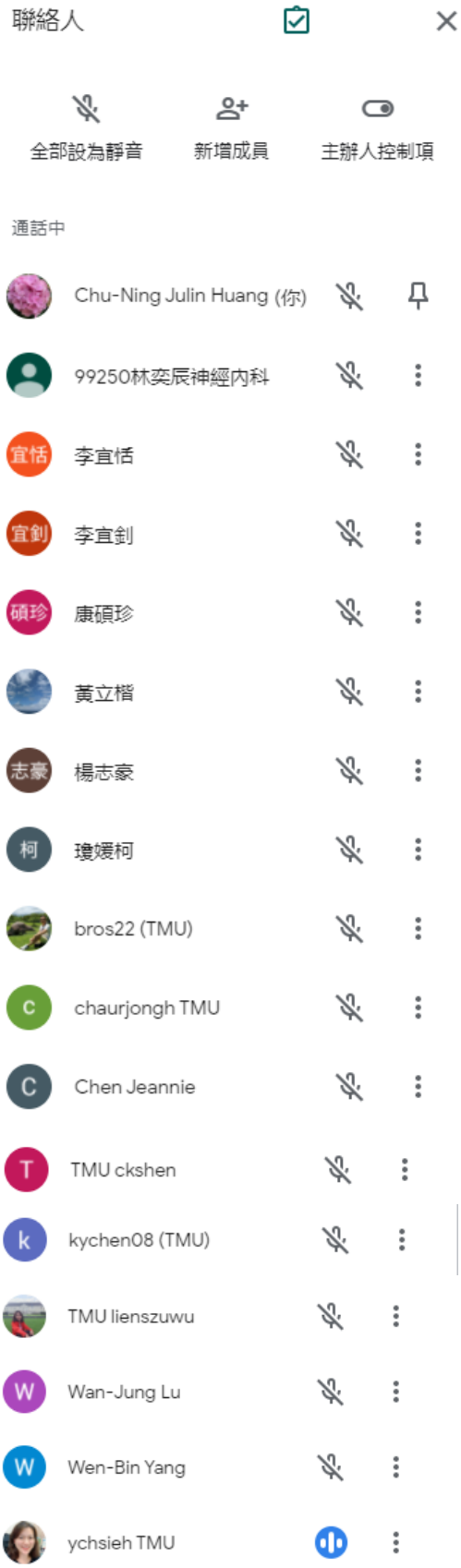


RBM3 in Hypothermia Mediated Neuroprotection Following Ischemic Stroke by Dr. Chih-Hao Yang (6/23, 2021)

3) Discussion

Prof. Lane was curious about the data source and did Dr. Hsieh have access to raw data from the cooperative institutes. Dr. Hsieh replied that the cooperative hospitals have the raw data, but they need to request access. Prof. Hu and Dr. Hsieh also discussed the polygenic risk score has the potential to be the mainstream for genetic study in the future.

會議結束時間為 13:40。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李宜釗
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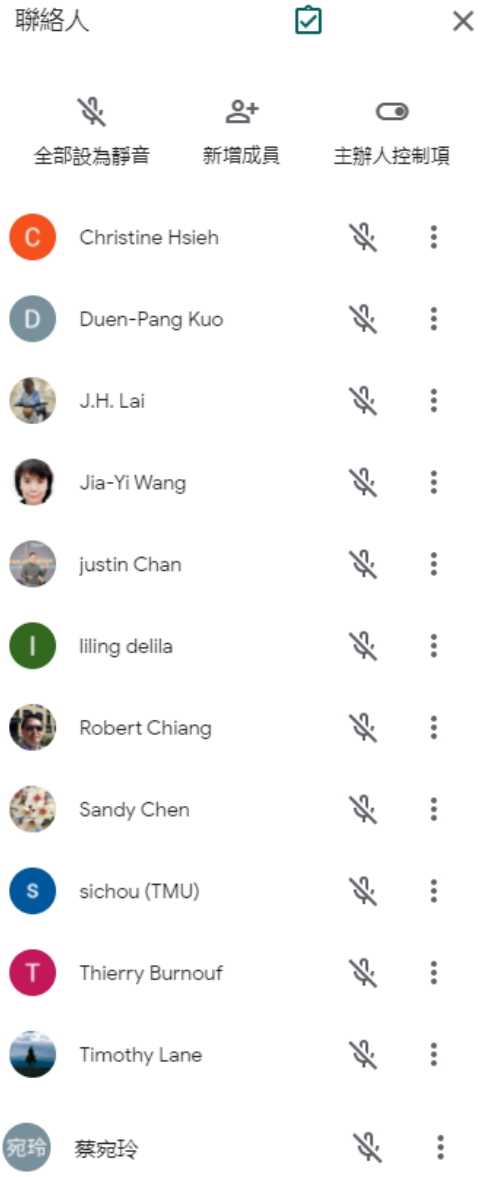
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