## Early changes in neuronal cells derived from isogeneic pair of normal and genomic edited Alzheimer's disease (AD)-iPSCs

**John Yu[1, 2], Ming-Wei Kuo[1]** and **Sheng-Wen Chen[1]**
[1]Linkou Chang Gung Memorial Hospital, Taiwan
[2]Academia Sinica, Taiwan

While patient-derived AD-induced pluripotent stem cells (iPSCs) can recapitulate AD phenotypes, the lack of isogenic pair of normal and AD-iPSC with identical genetic background for comparison may impede the detailed analysis of subtle pathophysiological changes in early stage of disease. We had developed a robust MS-based proteomic platform to explore these early changes of pathogenesis by comparing the protein expression in isogeneic pair of normal and AD-iPSCs derived neuron cells. In proteome-wide label-free quantitation of the isogenic pair-derived neural progenitor and neuron cells, the changes of proteome context are proportional to the neuronal differentiation, when compared to their iPSC state, as indicated by the Pearson's correlation coefficient of triplicate datasets. We then explored the changes caused by D678H mutation in amyloid-beta precursor protein (APP) by comparing the proteome between the isogenic pair during their neuronal differentiation process. Our results suggested that the differential display of proteome between WT and AD is more significant at the state of mature neuron at day 15 (NM15). Using Perseus to identify the statistically different expressed proteins between the isogenic pair of 71-WT-NM15 and 71-AD-NM15, we found 299 proteins with significant difference based on the significance criteria of false discovery rate (FDR) 0.01 and small positive constant (So). The 299 proteins were subjected to cluster analysis and presented by the heatmap, which revealed the up- or down-regulation of protein cluster caused by D678H-APP. Launching from these MS-based technology platform, we are now focusing on finding potential pathological/diagnosis markers for AD. We selected candidate genes from these 299 proteins and confirm the changes of mRNA expression during neuron differentiation in the iPSC pair. We also found that alterations of these gene expressions in iPSC lead to changes of amyloid 40/42, characteristics of AD phenotypes.

### Speaker Biography

John Yu is Distinguished Chair Professor/Director at Institute of Stem Cell/Translational Cancer Research, CGMH. He is also Distinguished Visiting Research Fellow at Institute of Cellular and Organismic Biology, Academia Sinica, and was the Director for the same Institute (2002-2009). He is the founding President for Taiwan Society for Stem Cell Research. He was elected to serve in ISSCR Committees (USA), the Steering Committee of Asia-Pacific Stem Cell Network, and Advisor for Stem Cell Biology, Kumamoto Univ. He was the Director of Exp. Hematology (1998-2002) at Scripps Research Institute, USA. He has received an Established Investigatorship Award from American Heart Assoc. and many other awards.

**e:johnyu@cgmh.org.tw**

*Notes:*