TALK 31 MAI – 1:10 TO 2:30 PM , TAICHUNG

PROF KIM Q. DO

TITLE & ABSTRACT

Exploring Psychosis Heterogeneity: Circuit-Based Biomarkers Paving the Way for Precision Psychiatry

In this presentation, I will discuss a translational program aimed at early detection and intervention in schizophrenia. It requires mechanism-based biomarkers that capture neural circuitry dysfunction, enabling better patient stratification, personalized treatments and disease progression monitoring.

I will illustrate how the interplay between genetic and environmental risk factors during neurodevelopment converges upon a central hub characterized by neuroinflammation, NMDA receptor hypofunction, mitochondrial dysfunction, dopamine dysregulation, and disrupted redox balance. These factors give rise to oxidative stress, reinforcing one another in a detrimental feedforward mechanism. This cascade affects parvalbumin interneurons (PVI), including their associated gamma synchronization, and impacts myelination. Consequently, structural and functional alterations emerge within local microcircuits and long-range connections, both of which are pivotal for cognitive, affective, and social functioning.

I will review the challenges and prospects encountered when translating preclinical models into clinical trials, particularly those involving the supplementation of antioxidants in individuals at the early stages of psychosis. Furthermore, I will delve into a newly discovered molecular mechanism linking mitochondrial bioenergetics and oxidative stress, which leads to impairments in PVI microcircuits. These resultant biomarkers exhibit remarkable accuracy in patient selection for treatments targeting brain mitochondria dysregulation, and they also serve as a means to validate the clinical and functional efficacy of forthcoming clinical trials.