### 計畫主持人 Professor Chao-Ching Huang (黃朝慶, MD).

### 得獎與榮譽

1999 國科會傑出研究獎

2002 國科會傑出研究獎

2001 台灣小兒科醫學會獎

2006 台灣醫學會學術演講獎

2019 日本小兒神經醫學會,福山幸夫紀念講座獎

2024 國家科學及技術委員會 113 年度傑出特約研究員

### 重要學術研究成果

Dr Huang is a pediatrician and a child neurologist. His leadership experience in research include the Chairperson in the Graduate Institute of Clinical Medicine, College of Medicine, National Cheng Kung University (2005/4~2011/7), the Dean, College of Medicine, Taipei Medical University (2013/9~2017/7), and the Vice President for Research, Taipei Medical University (2017/8~2018/12). He was also the Distinguished Professor (2003~2018) and Chair professor (2019/1~2024/1) in the College of Medicine, National Cheng Kung University. He is now the Chair professor in the College of Medicine, Taipei Medical University (2024/2~). His research awards include Distinguished Research Award of Taiwan National Science Counsel (2000, 2002); Award of Taiwan Pediatric Association (2001); Formosa Academic Lecture Award (2006); Yukio Fukuyama Memorial Lecture Award, Japanese Society of Child Neurology, Nagoya, Japan (2019); and Distinguished Researcher Award of Taiwan National Science Counsel (2024). He also has led clinical teams and also organized cross disciplinary teams to execute the PPGs from NSTC approved in 2017 and 2020.

He and his collaborators has three original articles published in the New England Journal of Medicine, which include: 1) the first to delineate the neurological staging of severity and outcome, and the MR neuroimaging correlates of enterovirus 71 encephalitis in young children (*NEJM*, 1999); 2) the first to depict urinary metabolites (lactate/creatinine ratio) detected within 6 hours after birth by MRS can be used to early predict the occurrence of hypoxic-ischemic encephalopathy and their long term neurodevelopmental outcome in term infant with hypoxic-ischemic brain injury (*NEJM*, 1999); and 3) the first to demonstrate the long-term neurocognitive adverse effect at school age of postnatal use of steroids for chronic lung disease in very preterm infants (*NEJM*, 2004).

His team in translational Neuroscience Research has been focusing on the brain injury especially in neonates by characterizing: (1) the early biomarkers of neonatal brain injury; (2) the shared protective/injurious mechanism in the neurovascular unit of neonatal brain injury in term and preterm infants; (3) the risk factor and outcome of epilepsy/febrile seizures; and (4) CNS infection including enterovirus 71 in young children. His works have been published in *Radiology, Annals of Neurology, Neurology, Critical Care Medicine, Stroke, J Cerebral Blood Flow & Metab, Journal of Neuroscience, Pediatrics, J Neuroinflammation, Molecular Neurobiology, Epilepsia, Pediatr Res, and Brain Communication.* 

### The followings are our recent integrated brain research summary for preterm infant.

## The Distinct Outcomes of Preterm-birth Children

### **They Are Different**

### **Hearing impairment**

-Severe haemodynamic-respiratory instability and intraventricular hemorrhage was associated with permanent hearing loss.

Yu et al., 2023 Dev Med Child Neurol

### Autism (ASD)

-Compared to term-birth children with ASD, preterm-birth ASD exhibited a specific behavioral phenotype of reciprocal social interaction.

Chen et al., 2019 Molecular Autism

### **Epilepsy**

An elevated incidence of epilepsy, and particularly in those with significant neonatal brain injury or severe NEC. They are prone to have neurodevelopmental disability and drug-resistant epilepsy.

Tu et al., 2019 Epilepsia



Preterm-birth children have a higher rate of FS, and postnatal corticosteroid treatment associated with FS susceptibility. Tu et al., 2016 Pediatrics

### Cerebral palsy and white matter injury

- -Altered inflammatory responses in TLR4-Tak1-NF-kB signaling is asscoiated with white matter injury induced CP
- -TNFR1-JNK signaling is a shared pathway of neuroinflammation and neurovascular damage after LPSsensitized hypoxic-ischemic
- -CXCL5-CXCR2 signaling is a shared pathway of neuroinflammation and blood-brain barrier injury contributing to white matter injury

Lin et al., 2010 Ann Neurol Wang et al., 2012, 2014, 2016 Ped Res, Neonatology; J Neuroinflam Chen et al, 2018 AJNR

### The Trend Change Study



### **Acute kidney injury**

2005~2018 Risk exposures associated with trends of acute kidney injury in extremely preterm-birth Infants.

Chen et al., 2021 Clinical J Am Soci Nephrol



**Necrotizing enterocolitis-Growth** 2006~2019 Trends in growth outcomes of NEC in infants born extremely preterm: A Taiwan population cohort study with propensity score matching.

Wang et al., in submission

### **Neurodevelopmental impairment**

1995~2016 Trends in gestational age-related survival, neonatal morbidity and NDI outcome of very preterm infants in southern Taiwan.

### Wang et al., 2021 J Formosan Med Assoc

2011~2020 Impact of severe brain injury on the trends of gestational age-related NDI outcomes in very preterm infants: A population cohort study.

Wang et al., 2024 Dev Med Child Neurol

### Cognitive impairment

2001~2015 Trends of gestational age intelligence outcomes of school-age children born very preterm in Taiwan.

Wang et al., 2023 J Pediatr

## The X-Brain Axis Disorders of Prematurity



## **Kidney-Brain**

- -Significant neurodevelopmental impairment after neonatal AKI in very preterm-birth children.
- -Preceding risks and mortalities of oliguric acute kidney injury in very preterm infants.

Chen et al., 2021 Clin J Am Society Nephrology; 2023 Pediatr Res; **Kidney International Reports** 



# Lung-Brain

- -Early-life respiratory trajectories associated with neurodevelopmental outcomes in preterm infants.
- -The developmental phenotype of motor delay in preterm infants following earlylife respiratory adversity is influenced by brain dysmaturation in parietal lobe. Yu et al., 2022 Dev Med Child Neurol; 2024 J **Neurodev Disorder**

### Pituitary-Brain

-Low-end of TSH within days after birth associated with severe RDS and brain injuries. -TSH persistently in the lowest quartile at early postnatal days and discharge screening had highest NDI risk.

Chen et al., 2023, Neonataology; 2024 J Epidemiol



## Postnatal Steroid-Brain

A Multi-center double-blinded RCT Early-life use of postnatal steroid protected immature lung but damaged developing brain Yeh et al., 2004 New England J Med



-Gestational age-related associations between feeding trajectories and growth outcomes in preterm infants -Enteral feeding progression associated with head growth faltering and neurodevelopmental impairment outcomes in preterm infants.

Lin et al., 2022, 2023 Nutrients



### Retina-Brain

Mild ROP and severe ROP are independent neonatal morbidities associated with NDI

Chang et al., 2022 Neonatology