

指導單位



衛生福利部
Ministry of Health and Welfare

主辦單位



中華民國人類遺傳學會
TAIWAN HUMAN GENETICS SOCIETY



國家衛生研究院
National Health Research Institutes



台大醫院 基因醫學部
Department of Medical Genetics

合辦單位



國立臺灣大學醫學院附設醫院兒童醫院
National Taiwan University Children's Hospital

THGS SPRING SYMPOSIUM

Deciphering Challenging Conditions : New Insights into Diagnosis

04/12 | NTUH INTERNATIONAL CONVENTION CENTER ROOM 301

滿意度調查

(點擊前往)





**中華民國人類遺傳學會
Taiwan Human Genetic Society**

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秘書長

簡穎秀

Deciphering Challenging Conditions : New Insights into Diagnosis

Table of Content

Symposium Agenda	01
The Taiwan Precision Medicine Initiative: Building the Largest non-European Cohort for Precision Health	03
MODERATOR: Prof. Fuu-Jen Tsai SPEAKER: Prof. Jer-Yuarn Wu	
Spatial Biomarkers in Ovarian Cancer	06
MODERATOR: Prof. Shih-Feng (Peter) Tsai SPEAKER: Prof. Yun-Ju Huang	
Navigating Clinical Genomics Test: When Panel Is Not Enough	09
MODERATOR: Prof. Shuan-Pei Lin SPEAKER: Dr. Seung Woo Ryu	
DNA Methylation Episignatures: Clinical Biomarkers for Rare Diseases and Beyond	12
MODERATOR: Prof. Hung-Yi Chiou SPEAKER: Prof. Bekim Sadikovic	
Experience sharing–Part I	15
MODERATOR: Dr. Shao-Yin Chu SPEAKER: Dr. Chen-Hao Lee	
Experience sharing–Part II	18
MODERATOR: Dr. Ju-Li Lin SPEAKER: Dr. Po-Jung Lai	
Experience sharing–Part III	21
MODERATOR: Dr. Yen-Yin Chou SPEAKER: Dr. Yu-Ming Chang	
Experience sharing–Part IV	24
MODERATOR: Dr. Chung-Hsing Wang SPEAKER: Dr. Hsin-Ru Wu	
Experience sharing–Part V	27
MODERATOR: Dr. Tung-Ming Chang SPEAKER: Dr. Hsu-Heng Lin	
Experience sharing–Part VI	30
MODERATOR: Dr. Hsiang-Yu Lin SPEAKER: Dr. Chung-Lin Lee	
Oral presentation I	33
MODERATOR: Prof. Wuh-Liang Hwu SPEAKER: Kai-Hung Chen	
Oral presentation II	36
MODERATOR: Prof. Wuh-Liang Hwu SPEAKER: Ya-Ping Yen	
Oral presentation III	38
MODERATOR: Prof. Wuh-Liang Hwu SPEAKER: Chia-Yi Li	
Oral presentation IV	40
MODERATOR: Prof. Wuh-Liang Hwu SPEAKER: Agnes Dwi Ariyanti	
Appreciation & Acknowledgment	42

Deciphering Challenging Conditions : New Insights into Diagnosis

 April 12nd, 2026 (Sunday)

 3F, NTUH International Convention Center

TIME	TOPIC	SPEAKER	MODERATOR	POSTER WALL
08:30-08:50	Registration			Poster Set up 3F Lobby
08:50-09:00	Opening Remark	Fuu-Jen Tsai, MD, PhD President, Taiwan Human Genetics Society		
09:00-12:00 <Session I> Precision Medicine				
09:00-09:45 (including 10 minutes for Q&A)	The Taiwan Precision Medicine Initiative: Building the Largest non-European Cohort for Precision Health	Jer-Yuarn Wu, PhD Research Fellow, Institute of Biomedical Sciences, Academia Sinica	Fuu-Jen Tsai, MD, PhD Vice Superintendent, China Medical University Hospital	Poster Viewing 3F Lobby
09:45-10:30 (including 10 minutes for Q&A)	Spatial Biomarkers in Ovarian Cancer	Yun-Ju Huang, MD, PhD Professor, School of Medicine, National Taiwan University	Shih-Feng (Peter) Tsai, MD, PhD Honorary Investigator, Institute of Molecular and Genomic Medicine, National Health Research Institutes	
10:30-11:00 Coffee Break				
11:00-11:30 (including 10 minutes for Q&A)	Navigating Clinical Genomics Test: When Panel Is Not Enough	Seung Woo Ryu, PhD Lead Clinical Genomics Scientist, 3billion, Inc., Seoul, Korea	Shuan-Pei Lin, MD Professor, College of Medicine, MacKay Medical University, and Department of Infant and Early Childhood Care, National Taipei University of Nursing and Health Sciences	Poster Session 3F Lobby
11:30-12:00	2026 THGS General Assembly	Yin-Hsiu Chien, MD, PhD Secretary-General, Taiwan Human Genetics Society		
12:00-13:00 Lunch Break				
13:00-15:55 <Session II> Tackling Difficult Cases				
13:00-13:10 (including 10 minutes for Q&A)	Afternoon Program Opening Remarks	Yueh-Ping Liu, MD Director-General, Department of Medical Affairs, Ministry of Health and Welfare Hung-Yi Chiou, PhD Distinguished Investigator and Director, Institute of Population Health Sciences, National Health Research Institutes		Poster Viewing 3F Lobby
13:10-13:55 (including 10 minutes for Q&A)	DNA Methylation Episignatures: Clinical Biomarkers for Rare Diseases and Beyond	Bekim Sadikovic, PhD Professor, Departments of Pathology and Laboratory Medicine and Pediatrics Western University, London, Canada	Hung-Yi Chiou, PhD Distinguished Investigator and Director, Institute of Population Health Sciences, National Health Research Institutes	
	Experience sharing - Part I The Pitfalls of Whole Exome Sequencing Analysis in Clinical: A Single Medical Center Experience	Chen-Hao Lee, MD Attending Physician, Division of Genetics and Endocrinology, Department of Pediatrics and Genetic Counseling Center, Kaohsiung Chang Gung Memorial Hospital	Shao-Yin Chu, MD Director, Department of Medical Education, Buddhist Tzu Chi Medical Foundation Hualien Tzu Chi Hospital	
13:55-14:40 (15 min/part, including 3 minutes for Q&A)	Experience sharing - Part II Genetic Testing and Rare Disease: The CGMH Experience	Po-Jung Lai, MD Attending Physician, Division of Pediatric Endocrinology and Genetics Linkou Chang Gung Memorial Hospital	Ju-Li Lin, MD Senior Attending Physician, Division of Genetics and Endocrinology, Department of Pediatrics, Chang Gung University College of Medicine and Linkou Chang Gung Memorial Hospital	
	Experience sharing - Part III Copy Number Variant Calling in Whole Exome Sequencing	Yu-Ming Chang, MD Attending Physician, Department of Genomic Medicine and Department of Pediatrics, National Cheng Kung University	Yen-Yin Chou, MD Attending Physician, Department of Pediatrics, Division of Pediatric Endocrinology, Genetics and Metabolism, National Cheng Kung University Hospital	
14:40-15:10 Coffee Break				
				Poster Removal 3F Lobby

**Continued on next page*

Deciphering Challenging Conditions : New Insights into Diagnosis

📅 April 12nd, 2026 (Sunday)

📍 3F, NTUH International Convention Center

TIME	TOPIC	SPEAKER	MODERATOR	POSTER WALL	
13:00-15:55 <Session II> Tackling Difficult Cases					
	Experience sharing - Part IV Hypophosphatasia: A Case Report	Hsin-Ru Wu, MD Attending Physician, Division of Pediatric Genetics, Endocrinology and Metabolism, China Medical University Children's Hospital	Chung-Hsing Wang, MD Director, Division of Pediatric Genetics, Endocrinology and Metabolism, China Medical University Children's Hospital		
15:10-15:55 (15 min/part, including 3 minutes for Q&A)	Experience sharing - Part V Beyond Familial Hypercholesterolemia: A Diagnostic Reconsideration of Childhood Xanthomas	Hsu-Heng Lin, MD Attending Physician, Division of Pediatric Genetics and Metabolism, Department of Pediatrics, Changhua Christian Hospital	Tung-Ming Chang, MD, PhD Director, Department of Pediatrics, Changhua Christian Children's Hospital		
	Experience sharing - Part VI Prenatal Non-Immune Hydrops Fetalis with Unexplained Structural Anomalies on Chromosomal Microarray: Postnatal Diagnosis of Cardiofaciocutaneous Syndrome by Whole Genome Sequencing	Chung-Lin Lee, MD, PhD Attending Physician, Division of Pediatric Genetics Mackay Memorial Hospital, Tamsui Branch	Hsiang-Yu Lin, MD, PhD Director, Division of Genetics and Metabolism, Department of Pediatrics, MacKay Memorial Hospital		
13:00-15:55 <Session III> Tackling Difficult Cases					
	Oral presentation I Genetic and Neurodevelopmental Investigation of Microcephaly Using a Drosophila Model	Kai-Hung Chen PhD Student, Graduate Institute of Physiology, National Taiwan University College of Medicine			
15:55-16:55 (15 min/part, including 3 minutes for Q&A)	Oral presentation II The m ⁶ A Epitranscriptome Unravels: m ⁶ A Dysregulation in ALS Motor Neuron Degeneration	Ya-Ping Yen Postdoctoral Research Fellow, Institute of Molecular Biology, Academia Sinica	Wuh-Liang Hwu, MD, PhD Distinguished Research Fellow, China Medical University Hospital		
	Oral presentation III Homozygous Variant in <i>TOMM7</i> Leads to Metabolic Reprogramming and Microcephalic Osteodysplastic Dwarfism with Moyamoya Disease	Chia-Yi Li Postdoctoral Researcher, Institute of Clinical Medicine, National Cheng Kung University, Taiwan/ Laboratory of Molecular Genetics			
	Oral presentation IV Investigating the Cellular and Molecular Mechanisms of <i>MAST1</i> Mutations in Cortical Malformation	Agnes Dwi Ariyanti Postdoctoral, Institute of Brain Science, College of Medicine, National Yang Ming Chiao Tung University			
16:55-17:10	Closing Ceremony	Fuu-Jen Tsai, MD, PhD President, Taiwan Human Genetics Society			

Deciphering Challenging Conditions : New Insights into Diagnosis

PRESIDENT

MODERATOR

09:00-09:45

The Taiwan Precision Medicine Initiative: Building the Largest non-European Cohort for Precision Health



Fuu-Jen Tsai, MD, PhD

- President, Taiwan Human Genetics Society
- Vice Superintendent, China Medical University Hospital

PRESENT POSITION

- 2020/07-Present: President, Taiwan Human Genetics Society
- 2023-Present: President, Taiwan Foundation for Rare Disorders
- 2015/08-Present: Distinguished Professor of Pediatrics, China Medical University
- 2013/08-Present: Vice President, China Medical University
- 2009/08-Present: Chief, Department of Medical Research and Medical Genetics, China Medical University Hospital

EDUCATION

- PhD, Institute of Chinese Medicine, China Medical University
- MD, China Medical University, Taichung, Taiwan

BRIEF CHRONOLOGY OF EMPLOYMENT

- 2009/08-2015/08: Dean, Office of Research and Development, China Medical University
- 2003/10-2009/10: Dean, College of Chinese Medicine, China Medical University
- 2002/03-2005/03: President, Taiwan Human Genetics Society
- 2001/03-2003/10: Chief, Department of Pediatrics, China Medical University Hospital

SELECTED PUBLICATIONS

1. Diversity and longitudinal records: Genetic architecture of disease associations and polygenic risk in the Taiwanese Han population. Liu TY, Lu HF, Chen YC, Liao CC, Lin YJ, Yang JS, Liao WL, Lin WD, Chen SY, Huang YC, Lin WY, Liu YH, Hsu KC, Chang SS, Chen HD, Chou YP, Chang JG, Wang CH, Chang CT, Huang CM, Yeo KJ, Wang TY, Yeh CC, Chen JH, Huang CP, Lai HC, Chen RH, Lin HJ, Wu PY, Wang JY, Kuo CC, Cho DY, Tsai CH, Tsai FJ*. Sci Adv. 2025 Jun 6;11(23):eadt0539.
2. Discovery and prioritization of genetic determinants of kidney function in 297,355 individuals from Taiwan and Japan. Chen HL, Chiang HY, Chang DR, Cheng CF, Wang CCN, Lu TP, Lee CY, Chattopadhyay A, Lin YT, Lin CC, Yu PT, Huang CF, Lin CH, Yeh HC, Ting IW, Tsai HK, Chuang EY, Tin A, Tsai FJ*, Kuo CC. Nat Commun. 2024 Oct 29;15(1):9317. (Impact factor: 14.7)
3. Utility of polygenic scores across diverse diseases in a hospital cohort for predictive modeling. Sun TH, Wang CC, Liu TY, Lo SC, Huang YX, Chien SY, Chu YD, Tsai FJ*, Hsu KC. Nat Commun. 2024 Apr 12;15(1):3168. (Impact factor: 14.7)

*Due to space constraints, some experiences could not be included. Apologies for any inconvenience.

Deciphering Challenging Conditions : New Insights into Diagnosis

SPEAKER

09:00-09:45

The Taiwan Precision Medicine Initiative: Building the Largest non-European Cohort for Precision Health



Jer-Yuarn Wu, PhD

- Research Fellow, Institute of Biomedical Sciences, Academia Sinica

PRESENT POSITION

- 2023-Present: Principle Investigator, Taiwan Precision Medicine Initiative
- 2016-Present: Research Fellow, Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan
- 2011-Present: Director, National Center for Genome Medicine, Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan

EDUCATION

- 1985-1992: PhD, Department of Biochemistry, Duke University, Durham, USA
- 1977-1981: B.S., Department of Agricultural Chemistry, National Taiwan University, Taipei, Taiwan

BRIEF CHRONOLOGY OF EMPLOYMENT

- 2005-2017: Professor, College of Chinese Medicine, China Medical University, Taichung, Taiwan
- 2006-2016: Research Scientist, Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan
- 1996-2005: Associate Professor, Department of Medicine, China Medical University, Taichung, Taiwan
- 1992-1996: Research Associate, Department of Pediatrics, Duke University Medical Center, Durham, North Carolina, USA

SELECTED PUBLICATIONS

1. Chen HH, Chen CH, Hou MC, Fu YC, Li LH, Chou CY, Yeh EC, Tsai MF, Chen CH, Yang HC,....., Lin YH, Lee JY, Lu HJ, Lu CH, Feng AC, Liu JS, Chiang CP, Chu NF, Lin JC, Yeh YW, Meng E, Huang CY, Li CC,, Kwok PY, Sheu WH*, Yang SF*, Liou JM*, Wang JY*, Chiou JF*, Wu JY*, Fann CSJ*. Population-specific polygenic risk scores for people of Han Chinese ancestry. Nature. 2025 Dec;648(8092):128-137. doi: 10.1038/s41586-025-09350-y. Epub 2025 Oct 15. PMID: 41094136 (*: These authors jointly supervised this work.)

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Deciphering Challenging Conditions : New Insights into Diagnosis

ABSTRACT

09:00-09:45

The Taiwan Precision Medicine Initiative: Building the Largest non-European Cohort for Precision Health

Data from the national biobanks, especially those from the UK Biobank, show that disease risk prediction based on genetic profiles is feasible but the prediction models created with European data do not translate to other ethnic groups. The current bottleneck is therefore a large dataset which consists of genetic profiles and matching clinical information from many individuals in Taiwan. Equally important is the analysis of this large dataset to produce disease risk models that predict an individual's disease risk for all the major diseases. To establish this large dataset, we collaborated with 16 major hospital systems across Taiwan and launched Taiwan Precision Medicine Initiative (TPMI) in 2019.

We produced a reference panel against which anyone of Han Chinese ancestry can use to assess his/her own disease risk for precision health management. Leveraging the whole genome sequencing data produced by the Taiwan Biobank and the genome reference assemblies produced by the Kwok group, we have designed and validated a custom single nucleotide polymorphism (SNP) array that can produce the genetic profile of a person and test all known clinically useful genetic variants at the same time. We have genotyped ~500,000 participants enrolled (as of December 31, 2023). All participants have agreed to contribute their clinical data (EMR, electronic medical record) to the database, allowing us to analyze not just their current disease state, but also their treatment response and long term disease progression.

Our result showed that 327 diseases have more than 10,000 participants. 37 of those diseases have polygenic risk scores with high accuracy (AUC value larger than 0.6). We anticipate the established TPMI dataset will advance the promise of "Precision Medicine" for individuals in Taiwan.

Deciphering Challenging Conditions : New Insights into Diagnosis

MODERATOR

09:45-10:30 Spatial Biomarkers in Ovarian Cancer



Shih-Feng (Peter) Tsai, MD, PhD

- Honorary Investigator, Institute of Molecular and Genomic Medicine, National Health Research Institutes

PRESENT POSITION

- 2025-Present: Honorary Investigator, Institute of Molecular and Genomic Medicine, National Health Research Institutes, Taiwan
- 1997-Present: Professor, Department of Life Sciences and Institute of Genomic Sciences (Formerly Institute of Genetics), National Yang-Ming University, Taiwan

EDUCATION

- 1987: PhD, Division of Human Genetics, Mt. Sinai School of Medicine, City University of New York, USA
- 1981: MD, Taipei Medical College, Taiwan

BRIEF CHRONOLOGY OF EMPLOYMENT

- 2010-2025: Distinguished Investigator, Institute of Molecular and Genomic Medicine (Formerly Division of Molecular and Genomic Medicine), National Health Research Institutes, Taiwan
- 2020: Acting director, Institute of Molecular and Genomic Medicine, National Health Research Institutes, Taiwan
- 2017-2021: Director, Department of Research Planning and Development, National Health Research Institutes, Taiwan
- 2017-2020: Principle Investigator, Flagship Program of Precision Medicine for AsiaPacific Biomedical Silicon Valley, Taiwan

SELECTED PUBLICATIONS

1. Tsai CY, Lu YS, Chiang YT, Lo MY, Lin PH, Tsai SF, Hsu CJ, Chen PL, Hsu JSJ, Wu CC. Comprehensive genetic analysis of STRC variants in hereditary hearing impairment using long-read sequencing 2024.11.05.24316795
2. Huang YJ, Lim JQ, Hsu JS, Kuo MC, Wang PN, Kao HW, Wu JH, Chen CC, Tsai SF, Ong CK, Shih LY. Next-Generation Integrated Sequencing Identifies Poor Prognostic Factors in Patients with MYD88-Mutated Chronic Lymphocytic Leukemia in Taiwan. Pathobiology. 2024 Oct 2:1-13.

*Due to space constraints, some experiences could not be included. Apologies for any inconvenience.

Deciphering Challenging Conditions : New Insights into Diagnosis

SPEAKER

09:45-10:30 Spatial Biomarkers in Ovarian Cancer



Yun-Ju Huang, MD, PhD

- Professor, School of Medicine, National Taiwan University

PRESENT POSITION

Director, SMART MHI Program, International College, National Taiwan University, Taiwan
 Professor, School of Medicine, College of Medicine, National Taiwan University
 Professor, Graduate Institute of Oncology, College of Medicine, National Taiwan University, Taiwan
 Professor, Department of BioMedical Engineering, College of Engineering, National Taiwan University, Taiwan
 Visiting Professor, IRCMS, Kumamoto University, Japan
 Visiting Professor, National University of Singapore, Singapore
 Visiting Professor, IQB, University of Tokyo

EDUCATION

2004/09-2008/06: PhD Institute of Anatomy and Cell Biology, College of Medicine, National Taiwan University
 1992/09-1999/06: MD, School of Medicine, College of Medicine, National Taiwan University

SELECTED PUBLICATIONS

1. Lin CY, Chao AS, Chao A, Wu RC, Yu AL, Fu CH, Teng YC, Huang RY, Lai CH. Combined targeting poly (ADP-ribose) polymerase and receptor tyrosine kinase inhibits ovarian clear cell carcinoma progression through disrupted ribosome biogenesis. J Mol Med (Berl). 2026 Jan 24;104(1):33.
2. Davidson B, Hauladen S, Holth A, Huang RY. Grainyhead-Like 2 Expression Is Associated with Disease Progression, Chemoresistance and Poor Survival in Tubo-Ovarian High-Grade Serous Carcinoma. Pathobiology. 2025 Oct 24:1-13.
3. Berrell N, Kilgallon A, Donovan ML, Lawler C, Tan CW, Embaye KS, Tubelleza R, Monkman J, Fraser JF, O'Byrne K, Huang R, Kulasinghe A. Proximity and metabolic activity proxies in the tumor microenvironment as predictors of survival in high grade serous ovarian cancer. iScience. 2025 Sep 15;28(10):113572.
4. Ismagulov G, Takahashi Y, Ishiyama E, Ogasawara K, Sakai K, Chan YN, Huang RY, Fukuda T, Sheng G. Morphogenetic maturation of chicken chorioallantoic membrane (CAM) and its disruption by tumor xenografts. Dev Biol. 2026 Jan;529:154-166.

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Deciphering Challenging Conditions : New Insights into Diagnosis

ABSTRACT

09:45-10:30 Spatial Biomarkers in Ovarian Cancer

Biomarker discovery has been one of the driving forces in modern precision oncology. Biomarker strategies have been applied in both forward and reverse translation research studies. In the era when spatial omics technologies have been nominated as “Method of the Year” in 2020 and 2024, the development spatial biomarkers in precision oncology have emerged in concepts such as “spatial oncology”. This talk will give examples of different potential spatial biomarkers in ovarian cancer.

Deciphering Challenging Conditions : New Insights into Diagnosis

MODERATOR

11:00-11:30 Navigating Clinical Genomics Test: When Panel Is Not Enough



Shuan-Pei Lin, MD

- Professor, College of Medicine, MacKay Medical University, and Department of Infant and Early Childhood Care, National Taipei University of Nursing and Health Sciences

● PRESENT POSITION

Senior Attending Physician, Department of Pediatric Genetics, MacKay Children's Hospital, Founding Director, Rare Disease Center, Director of Division of Biochemical Genetics, Department of Medical Research, MacKay Memorial Hospital, Taipei, Taiwan
Professor, College of Medicine, MacKay Medical University, and Department of Infant and Early Childhood Care, National Taipei University of Nursing and Health Sciences

● EDUCATION

Researcher, Yale University, School of Medicine, Division of Human Genetics
MD, Kaohsiung Medical University, Kaohsiung, Taiwan

● BRIEF CHRONOLOGY OF EMPLOYMENT

- | | |
|------------------|---|
| 2013/01-Present: | Co-founder and Board Director, Asia Pacific MPS Network (APMN) |
| 2010/03-Present: | Board Member, Asian Congress of Inherited Metabolic Diseases (ACIMD) |
| 2008/10-Present: | Honorary President, Taiwan MPS Society, Taipei, Taiwan |
| 2005/11-Present: | Committee Member, Committee of Academic Affairs, Taipei Medical Association, Taipei, Taiwan |
| 2000/07-Present: | Committee Member, Committee of Early Intervention Program, MacKay Memorial Hospital, Taipei, Taiwan |

● SELECTED PUBLICATIONS

1. Lee CL, Chang YH, Chuang CK, Chiu HC, Tu YR, Lo YT, Wu JY, Lin HY, Lin SP. Skipping the Biopsy: Real-World Experience of Whole-Exome Sequencing as First-Tier Testing in Pediatric Muscular Disorders. *Int. J. Mol. Sci.* 2026, 27(5), 2446.
2. Lee CL, Chang YW, Lin HY, Lee HC, Yeh TC, Fang LC, Lee NC, Tsai JD, Lin SP. Multisystem disorder associated with a pathogenic variant in CLCN7 in the absence of osteopetrosis. *Mol Genet Genomic Med.* 2024 Jul;12(7):e2494. doi: 10.1002/mgg3.2494.
3. Lee CL, Chuang CK, Chiu HC, Chang YH, Tu YR, Lo YT, Lin HY, Lin SP. Application of whole exome sequencing in the diagnosis of muscular disorders: a study of Taiwanese pediatric patients. *Front Genet.* 2024 May 15;15:1365729. doi: 10.3389/fgene.2024.1365729. eCollection 2024.

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Deciphering Challenging Conditions : New Insights into Diagnosis

SPEAKER

11:00-11:30 Navigating Clinical Genomics Test: When Panel Is Not Enough



Seung Woo Ryu, PhD

- Lead Clinical Genomics Scientist, 3billion, Inc., Seoul, Korea.

● PRESENT POSITION

2025-Present Lead Clinical Genomics Scientist, 3billion, Inc., Seoul, Korea

● EDUCATION

2015-2021: PhD Biochemistry, University of Texas at Austin, Austin, TX

2010-2014: B.S. Biochemistry, University of Illinois at Urbana-Champaign, Urbana, IL

● BRIEF CHRONOLOGY OF EMPLOYMENT

2021-2024: Clinical Genomics Scientist, 3billion, Seoul, South Korea

2015-2021: Graduate Research Assistant, University of Texas at Austin, Austin, TX. United States of America

Advisor: Professor Tanya Paull

2012-2015: Staff Research Assistant, University of Illinois at Urbana-Champaign, Urbana, IL. United States of America

Advisor: Professor Richard H. Perry

2012 Summer: Intern Research Assistant, National Cancer Center, Ilsan dong-gu, GyeongGi Province. Republic of Korea

Advisor: Professor Sun Young Kong

● SELECTED PUBLICATIONS

1. Research Articles

<https://scholar.google.com/citations?user=CXgoHekAAAAJ&hl=en&authuser=1&oi=ao>



*Due to space constraints, some experiences could not be included. Apologies for any inconvenience.

Deciphering Challenging Conditions : New Insights into Diagnosis

ABSTRACT

11:00-11:30 Navigating Clinical Genomics Test: When Panel Is Not Enough

Targeted gene panel testing is widely used as a first-line diagnostic approach in clinical genetics due to its efficiency, cost-effectiveness, and high analytical performance. However, a significant proportion of patients with a strong clinical suspicion of a genetic disorder remain undiagnosed after panel testing, creating diagnostic uncertainty in routine clinical practice. Selecting the appropriate genomic test is therefore critical in difficult cases.

This session will review clinical scenarios in which panel testing is insufficient and illustrates how exome sequencing has enabled diagnosis in challenging cases. The clinical strengths and inherent limitations of panel-based testing are examined, followed by discussion of exome sequencing as a practical next step after negative panel results. Particular emphasis is placed on the broader gene coverage of exome sequencing and its ability to support reanalysis as gene–disease associations, variant classifications, and patient phenotypes evolve over time. Clinical situations in which genome sequencing should be considered are also outlined.

Understanding the complementary roles of panel, exome, and genome sequencing supports more informed diagnostic decision-making and improved outcomes in challenging clinical cases.

Deciphering Challenging Conditions : New Insights into Diagnosis

MODERATOR

13:10-13:55

DNA Methylation Episignatures: Clinical Biomarkers for Rare Diseases and Beyond



Hung-Yi Chiou, PhD

- Distinguished Investigator and Director, Institute of Population Health Sciences, National Health Research Institutes

● PRESENT POSITION

Distinguished Investigator and Director, Institute of Population Health Sciences, National Health Research Institutes, Taiwan

● EDUCATION

1996: PhD in Epidemiology of National Taiwan University
1989: MS in Public Health of National Taiwan University
1985: BS in Public Health of National Taiwan University

● BRIEF CHRONOLOGY OF EMPLOYMENT

2025/10-Present: President, APACPH, Asia-Pacific Academic Consortium for Public Health
2020/09-Present: Distinguished Investigator and Director, Institute of Population Health Sciences, National Health Research Institutes, Taiwan
2020/07-Present: Board Director, International Cooperation and Development Fund ICDF
2019/10-Present: Supervisor, Taiwan Public Health Association
2017/10-Present: Finance Vice President, APACPH, Asia-Pacific Academic Consortium for Public Health
2017/04-Present: Distinguished Professor, Master program in Applied Molecular Epidemiology, Taipei Medical University
2017/02-Present: President, Taiwan Society for Development of Long-Term Care and Senior Health Management

● SELECTED PUBLICATIONS

1. Sung, Y. F., Lee, J. T., Hu, C. J., Jeng, J. S., Chiou, H. Y., & Peng, G. S. (2025). Impact of ALDH2 genotypes and alcohol consumption on age at first-ever ischemic stroke: A cohort study in Taiwan. Alcohol, clinical & experimental research, 10.1111/acer.70217. Advance online publication. <https://doi.org/10.1111/acer.70217>
2. Lin, Y. C., Hung, Y. P., Tian, Y. C., Wu, M. J., Lin, H. C., Chen, S. Y., Wu, M. S., & Chiou, H. Y. (2025). Real-World Data as External Control in Assessing the Efficacy of Allogeneic Adipose-Derived Stem Cells Therapy for Advanced Chronic Kidney Disease. Clinical and translational science, 18(12), e70415. <https://doi.org/10.1111/cts.70415>

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Deciphering Challenging Conditions : New Insights into Diagnosis

SPEAKER

13:10-13:55

DNA Methylation Episignatures: Clinical Biomarkers for Rare Diseases and Beyond



Bekim Sadikovic, PhD

- Professor, Department of Pathology and Laboratory Medicine and Department of Pediatrics, Western University, London, Canada

PRESENT POSITION

LHSC Research Chair in Clinical Genomics and Epigenomics, London Health Sciences Centre
Professor, Department of Pathology and Laboratory Medicine and Department of Pediatrics, Western University

Division Head, Molecular Diagnostics, Pathology and Laboratory Medicine, London Health Sciences Centre

Scientific and Clinical Director, Verspeeten Clinical Genome Centre, London Health Sciences Centre

EDUCATION

2007: PhD, Biochemistry, Western University

2002: BSc, Genetics, Western University

BRIEF CHRONOLOGY OF EMPLOYMENT

2023-Present: Chief Scientific Officer, EpiSign Inc., London, Ontario, Canada

2023-Present: Endowed Professorship in Epigenetics of Disease, Amsterdam University, Netherlands

2022-Present: London Health Sciences Research Chair in Clinical Genomics and Epigenomics, Department of Pathology and Laboratory Medicine, London Health Sciences Centre, London, Ontario, Canada

2021-Present: Program Head, Molecular Diagnostics Program; Department of Pathology and Laboratory Medicine, London Health Sciences Centre, London, Ontario, Canada

SELECTED PUBLICATIONS

1. Evaluation of DNA methylation episignatures for diagnosis and phenotype correlations in 42 Mendelian neurodevelopmental disorders E Aref-Eshghi, J Kerkhof, VP Pedro, M Barat-Houari, N Ruiz-Pallares, ...The American Journal of Human Genetics 106 (3), 356-370
2. Clinical epigenomics: genome-wide DNA methylation analysis for the diagnosis of Mendelian disorders B Sadikovic, MA Levy, J Kerkhof, E Aref-Eshghi, L Schenkel, A Stuart, ... Genetics in Medicine 23 (6), 1065-1074

*Due to space constraints, some experiences could not be included. Apologies for any inconvenience.

Deciphering Challenging Conditions : New Insights into Diagnosis

ABSTRACT

13:10-13:55

DNA Methylation Episignatures: Clinical Biomarkers for Rare Diseases and Beyond

Rare genetic disorders remain a significant diagnostic challenge, with approximately 60–70% of affected individuals lacking a definitive molecular diagnosis despite widespread use of genome sequencing. This gap underscores the need for complementary biomarkers that capture disease-associated biology beyond DNA sequence variation. DNA methylation episignatures are recurring epigenomic patterns detectable in peripheral blood of individuals sharing a common genetic or environmental etiology. These DNA methylation biomarkers provide a systems-level view of epigenomic states.

This presentation will introduce the conceptual framework of DNA methylation episignatures and discuss their clinical applications in rare disease evaluation, including disease stratification, variant interpretation, and identification of clinically relevant subtypes. Recent advances in reference datasets, analytical methods, and international clinical testing networks will be highlighted, illustrating how episignatures complement existing genomic technologies and expand the diagnostic landscape.

Deciphering Challenging Conditions : New Insights into Diagnosis

MODERATOR

13:55-14:10

Experience sharing-Part I

The Pitfalls of Whole Exome Sequencing Analysis in Clinical: A Single Medical Center Experience



Shao-Yin Chu, MD

- Director, Department of Medical Education, Buddhist Tzu Chi Medical Foundation Hualien Tzu Chi Hospital

PRESENT POSITION

- 2024-Present: Director, Department of Medical Education, Buddhist Tzu Chi Medical Foundation Hualien Tzu Chi Hospital
- 2020-Present: Associate Professor, School of Medicine, Tzu Chi University
- 2019-Present: Director, Genetic Counseling Center, Hualien Tzu Chi Hospital
- 2019-Present: Teaching Attending Physician, Hualien Tzu Chi Hospital
- 2002-Present: Attending Physician, Department of Pediatrics, Hualien Tzu Chi Hospital

EDUCATION

- 2002-2005: MS in Human Genetics, Tzu Chi University
- 1988-1995: MD, National Taiwan University

BRIEF CHRONOLOGY OF EMPLOYMENT

- 2007-2014: Deputy Director, Department of Medical Education, Hualien Tzu Chi Hospital
- 2007-2014: Director, Faculty Development Center, Hualien Tzu Chi Hospital

SELECTED PUBLICATIONS

1. Lin, C. W., Kuo, B. Y., Wang, H. C., Lin, M. J., & Chu, S. Y. (2026). Developing a patient narrative interview guide using the Delphi method. BMC Medical Education, 26:444.
2. Chu, S. Y., Wang, H. C., Kuo, B. Y., Lin, M. J., Chang, Y. C., & Lin, C. W. (2026). Development and Validation of Narrative Competence Scale for Medical Students. Perspectives on medical education, 15(1), 150.
3. Wang, H. C., Lin, C. W., Kuo, B. Y., Lin, M. J., Chang, Y. C., & Chu, S. Y. (2026). The impact of patient narrative interview training on medical students' narrative competence—A randomized controlled trial. Tzu Chi Medical Journal, 10-4103.
4. Tseng, T. C., Kuo, P. Y., Lin, M. J., & Chu, S. Y. (2025). Narrative medicine in pediatric medical education and patient care: A scoping review. Tzu Chi Medical Journal, 37(2), 167-174.
5. Yi, L. Y., Tseng, T. C., & Chu, S. Y. (2024). Exploring medical humanities from heterogeneous focus groups: A thematic analysis. Tzu Chi Medical Journal, 36(4), 460-468.

*Due to space constraints, some experiences could not be included. Apologies for any inconvenience.

Deciphering Challenging Conditions : New Insights into Diagnosis

SPEAKER

13:55-14:10

Experience sharing-Part I

The Pitfalls of Whole Exome Sequencing Analysis in Clinical: A Single Medical Center Experience



Chen-Hao Lee, MD

- Attending Physician, Division of Genetics and Endocrinology, Department of Pediatrics and Genetic Counseling Center, Kaohsiung Chang Gung Memorial Hospital

● PRESENT POSITION

2022/04-Present: Division of Genetics and Endocrinology, Department of Pediatrics and Genetic Counseling Center, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan

● EDUCATION

2001/09-2009/06: MD, China Medical University, Taichung, Taiwan

● BRIEF CHRONOLOGY OF EMPLOYMENT

2016/09-2022/03: Attending Physician, Department of Pediatrics, E-Da Hospital, Kaohsiung, Taiwan

2015/07-2016/06: Attending Physician, Division of Pediatric Emergency and Critical Care Medicine, Department of Pediatrics, MacKay Children's Hospital, Taipei, Taiwan

2013/07-2015/06: Clinical Fellow, Division of Genetics and Metabolism, Department of Pediatrics, Mackay Memorial Hospital, Taipei, Taiwan

2013/07-2014/06: Resident, Department of Pediatrics, Mackay Memorial Hospital, Taipei, Taiwan

● SELECTED PUBLICATIONS

1. Hsi-Yun Liu+, Chen-Hao Lee+, Chien-Ning Hsu, You-Lin Tain. Maternal High-Fat Diet Controls Offspring Kidney Health and Disease. *Nutrients*, 2023 Jun 9;15(12):2698.
2. Rai-Hseng Hsu+, Chen-Hao Lee+, Yin-Hsiu Chien, Shuan-Pei Lin, Miao-Zi Hung, Nai-ChiChen, Yi-Lin Lin, Wuh-Liang Hwu1, Ni-Chung Lee. Utility of whole-exome sequencing for patients with multiple congenital anomalies with or without intellectual disability/developmental delay in East Asia population. *Molecular Genetics & Genomic Medicine*, 2023 Jun;11(6):e2160.
3. Chung-Lin Lee+, Chen-Hao Lee+, Chih-Kuang Chuang, Huei-Ching Chiu, Yen-Jiun Chen, Chao-Ling Chou, Peih-Shan Wu, Chih-Ping Chen, Hsiang-Yu Lin, Shuan-Pei Lin. Array-CGH increased the diagnostic rate of developmental delay or intellectual disability in Taiwan. *Pediatrics and Neonatology*, 2019 Aug;60(4):453-460

*Due to space constraints, some experiences could not be included. Apologies for any inconvenience.

Deciphering Challenging Conditions : New Insights into Diagnosis

ABSTRACT

13:55-14:10

Experience sharing-Part I

The Pitfalls of Whole Exome Sequencing Analysis in Clinical: A Single Medical Center Experience

Whole exome sequencing (WES) is not only a massive parallel but also a high-throughput DNA sequencing for all coding regions in an individual's genome. As a result, WES has emerged as a powerful diagnostic tool to detect gene variants associated with disease in clinical. However, pitfalls can still occur during the annotation and interpretation of gene variants in WES data. In this discussion, we share the common but important perspectives that are often overlooked. One was a three-year-eight-month-old girl presenting with hypokalemia and metabolic alkalosis. Initially diagnosed with Bartter syndrome by the nephrologist and WES identified only the heterozygous pathogenic variant SLC12A3 c.179C>T (p.Thr60Met). Subsequent analysis of the BAM file revealed a copy number variant, specifically a deletion at 16q13 (56879064-56880251), encompassing the SLC12A3 gene. This finding confirmed the diagnosis of Gitelman syndrome, illustrating the importance of considering both single nucleotide variants and copy number variants in autosomal recessive disease. Another was a three-year-eight-month-old girl with strong suspicion of neurofibromatosis. At first, WES did not reveal any pathogenic variant in the NF1 or NF2 gene. Examination of the BAM file revealed absence of reads in the regions c.2326-5 to c.2409+5 and c.2991-5 to c.3113+5 of the NF1 gene. Sanger sequencing of these regions identified the heterozygous pathogenic variant NF1 c.2352 G>C (p.Trp784Cys). This is a technical limitation in WES due to ineffective capture and amplification. In conclusion, our experience demonstrates that the paramount importance of phenotype in diagnosis, even initial whole exome sequencing analysis fails to align with the observed phenotype. Additionally, BAM files represent valuable data resources that can assist to identify genetic variations beyond single nucleotide variant in WES.

Deciphering Challenging Conditions : New Insights into Diagnosis

MODERATOR

14:10-14:25

Experience sharing-Part II

Genetic Testing and Rare Disease: The CGMH Experience



Ju-Li Lin, MD

- 新北市立土城醫院及林口長庚醫院兒童內分泌暨遺傳科顧問級主治醫師

● PRESENT POSITION

新北市立土城醫院及林口長庚醫院兒童內分泌暨遺傳科顧問級主治醫師

● EDUCATION

中國醫藥大學醫學系畢業

● BRIEF CHRONOLOGY OF EMPLOYMENT

台北馬偕醫院小兒科住院醫師
台北馬偕醫院新生兒科研究員
嘉義基督教醫院小兒科主治醫師
林口長庚醫院兒童內科部新生兒科主治醫師
美國杜克大學小兒遺傳科研究員
林口長庚醫院兒童內科部遺傳科主任
林口長庚醫院兒童內科部內分泌暨遺傳科主任

● SELECTED PUBLICATIONS

1. Ma YT, Lin JL, Lai MW, Chou IJ, Hwang MS. A Case of Infantile Reversible Cytochrome C Oxidase Deficiency Myopathy in Taiwan: A 4-Year Follow-Up. Case Rep Med. 2025 Feb
2. Lin J, Wang S, Hou JW (2002): Evaluating clinical efficacy and safety of palmidronate in patients with osteogenesis imperfecta. American Society of Human Genetics, 52nd Annual Meeting, Oct 15-19, 2002, Baltimore, USA. [Am J Hum Genet 71 (suppl): 255.]
3. 洪嘉穗, 林如立, 李燕晉, 林炫沛, 趙美琴, 羅福松. Mutational analysis of ptpn11 gene in taiwanese children with noonan syndrome. Journal of the formosan medical association. 2007, 106: 169-172.
4. Lin JL, Muenzer J, Weston BW, Chen YT. New mutations of glycogen storage disease type Ia and an unusual type Ib phenotype in a patient. Am J Hum Gen 1996;59(4):A203

Deciphering Challenging Conditions : New Insights into Diagnosis

SPEAKER

14:10-14:25

Experience sharing-Part II

Genetic Testing and Rare Disease: The CGMH Experience



Po-Jung Lai, MD

- Attending Physician, Division of Genetics and Endocrinology, Department of Pediatrics, Linkou Chang Gung Memorial Hospital

● PRESENT POSITION

Attending Physician, Division of Genetics and Endocrinology, Department of Pediatrics, Linkou Chang Gung Memorial Hospital, Taoyuan, Taiwan

● EDUCATION

MD, School of Medicine, Chung Shan Medical University

● BRIEF CHRONOLOGY OF EMPLOYMENT

- 2018/05-2019/05: Internship, National Taiwan University Hospital
- 2019/08-2020/07: Post-Graduate Year, National Taiwan University Hospital
- 2020/08-2023/07: Pediatric Resident, National Taiwan University Children's Hospital
- 2023/08-2025/07: Medical Genetics Fellow, National Taiwan University Children's Hospital

● SELECTED PUBLICATIONS

1. Lai PJ, Tseng WC, Chen HA, Hsu RH, Chien YH, Hwu WL, Lee NC. Double-outlet right ventricle in a patient with Takenouchi-Kosaki syndrome. *Pediatrics & Neonatology* 2025;66(2): 176–177.

Deciphering Challenging Conditions : New Insights into Diagnosis

ABSTRACT

14:10-14:25

Experience sharing–Part II

Genetic Testing and Rare Disease: The CGMH Experience

Chang Gung Memorial Hospital (CGMH) is a medical center in Linkou offering genetic evaluation and testing for children with various congenital anomalies. Through collaboration with the Lo-Hui-Fu Craniofacial Foundation, many children with craniofacial differences are referred to the department. The department provides standard genetic tests including karyotype, aCGH, and whole exome sequencing (WES), as well as specialized single-gene tests such as Achondroplasia mutation detection for the FGFR3 gene and KMT2D gene analysis for Kabuki syndrome. These services support accurate diagnosis, early intervention, and personalized care planning, helping families manage rare or complex conditions affecting growth, development, and craniofacial features.

We present a case of a preterm neonate with congenital agnathia, characterized by complete absence of the mandible, microstomia, and low-lying ears. Prenatal care was irregular, with polyhydramnios as the only finding. Genetic testing through the Pediatric Undiagnosed Disease Platform identified a heterozygous pathogenic OTX2 variant, also detected in the mother. This rare case of severe mandibular agenesis expands the OTX2 phenotypic spectrum and highlights the importance of specialized genetic evaluation and multidisciplinary management, including airway support and family counseling.

Deciphering Challenging Conditions : New Insights into Diagnosis

MODERATOR

14:25-14:40

Experience sharing-Part III

Copy Number Variant Calling in Whole Exome Sequencing



Yen-Yin Chou, MD

- Attending Physician, Department of Pediatrics, Division of Pediatric Endocrinology, Genetics and Metabolism, National Cheng Kung University Hospital

PRESENT POSITION

- 2007-Present: Attending physician of Genetics and Metabolism, NCKUH
2004-Present: Attending physician of Pediatric Endocrinology, NCKUH

EDUCATION

MD, National Cheng Kung University Medical College

BRIEF CHRONOLOGY OF EMPLOYMENT

- 2007-2009: Academic visitor of Department of Molecular Endocrinology, Imperial College London
2005-2007: Genetics and Metabolism Fellow in National Cheng Kung University Hospital
2002-2004: Endocrinology Fellow in National Cheng Kung University Hospital
1999-2002: Resident in Department of Pediatrics in National Cheng Kung University Hospital

SELECTED PUBLICATIONS

1. Kang TY, Chou YY, Chang YM, Pan YW, Tsai MC. Novel Variants and Clinical Heterogeneity in Pediatric Calcium Metabolism Disorders Identified Through High-Yield Tiered Genetic Testing in a Taiwanese Cohort. *Medicina (Kaunas)*. 2025 Oct 16;61(10):1861.
2. Shen CF, Chang PD, Chou YY, Wang SW, Pan YW, Chen CA, Lin CW, Tsai BY, Tsai PJ, Liu CC, Cheng CM, Ko WC, Shieh CC; Taiwan Pediatric Infectious Disease Alliance (TPIDA). BNT162b2 mRNA vaccine elicits robust virus-specific antibodies but poor cross-protective CD8+ memory T cell responses in adolescents with type 1 diabetes. *J Microbiol Immunol Infect*. 2025 Jun;58(3):294-303.
3. Khoo WS, Chen YC, Chou YY, Pan YW, Weng YH, Tsai MC. Cross-Sectional and Longitudinal Associations Among Weight Stigma, Psychological Distress, and Eating Behaviors in Youth with Obesity: A Clinical Sample. *Medicina (Kaunas)*. 2025 Mar 7;61(3):466.
4. Yang YN, Chou YY, Cheng CN. Luspatercept for non-deletional hemoglobin H disease. *Pediatr Blood Cancer*. 2024 Oct;71(10):e31224.
5. Tsai CC, Chang YM, Chou YY, Chen SY, Pan YW, Tsai MC. Identification of southern Taiwan genetic variants in thyroid dyshormonogenesis through whole-exome sequencing. *Kaohsiung J Med Sci*. 2024 Aug;40(8):744-756.

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Deciphering Challenging Conditions : New Insights into Diagnosis

SPEAKER

14:25-14:40

Experience sharing-Part III

Copy Number Variant Calling in Whole Exome Sequencing



Yu-Ming Chang, MD

- Attending Physician, Department of Genomic Medicine and Department of Pediatrics, National Cheng Kung University Hospital

● PRESENT POSITION

Attending physician, Department of Genomic Medicine and Department of Pediatrics, National Cheng Kung University Hospital

● EDUCATION

MD, Department of Medicine, College of Medicine, National Cheng Kung University Hospital, Taiwan

● BRIEF CHRONOLOGY OF EMPLOYMENT

- 2022/08-2024/07: Clinical fellow, Division of Genetics, Metabolism and Endocrinology, Department of Pediatrics, National Cheng Kung University Hospital
- 2019/08-2022/07: Resident, Department of Pediatrics, National Cheng Kung University Hospital

● SELECTED PUBLICATIONS

1. Chang YM, Huang YT, Lai PC. Genetic testing for diagnosing neurodevelopmental disorders and epilepsy: a systematic review and meta-analysis. Syst Rev. 2025 Jul 28;14(1):155. doi: 10.1186/s13643-025-02896-y. PMID: 40722196.
2. Tsai CC, Chang YM, Chou YY, Chen SY, Pan YW, Tsai MC. Identification of southern Taiwan genetic variants in thyroid dysmorphogenesis through whole-exome sequencing. Kaohsiung J Med Sci. 2024 Aug;40(8):744-756. doi: 10.1002/kjm2.12871. Epub 2024 Jun 25. PMID: 38923290.
3. Chang YM, Pan YW, Chou YY, Yu WH, Tsai MC. A boy with a progressive neurologic decline harboring two coexisting mutations in KMT2D and VPS13D. Brain Dev. 2023 Nov;45(10):603-607. doi: 10.1016/j.braindev.2023.08.001. Epub 2023 Aug 18. PMID: 37599126.
4. Chang YM, Chen CC, Lee NC, Sung JM, Chou YY, Chiou YY. PAX2 Mutation-Related Renal Hypodysplasia: Review of the Literature and Three Case Reports. Front Pediatr. 2022 Jan 11;9:765929. doi: 10.3389/fped.2021.765929. PMID: 35087773

Deciphering Challenging Conditions : New Insights into Diagnosis

ABSTRACT

14:25-14:40

Experience sharing-Part III

Copy Number Variant Calling in Whole Exome Sequencing

Whole-exome sequencing (WES) is increasingly expected to resolve challenging germline diagnostic cases beyond single-nucleotide variants and small indels. WES-based CNV calling leverages read-depth signals across captured targets and can be complemented by additional sequencing signatures, including discordant read-pair orientation/insert size, split-read evidence at breakpoints, and allele-balance shifts across heterozygous variants. Modern callers compare each sample against a well-matched reference cohort and apply segmentation or probabilistic frameworks to infer deletions and duplications from single-exon events to multi-gene CNVs.

Compared with chromosomal microarray (CMA), WES CNV analysis can offer higher resolution within coding regions, enabling detection of single-gene and even single-exon CNVs that may fall below array probe density, and integrates CNV, SNV/indel, and phenotype-driven prioritization within a single test. However, performance remains limited by uneven coverage, breakpoint imprecision, and reduced sensitivity in poorly captured or highly repetitive regions, so careful cohort construction, quality control, and orthogonal confirmation remain central to clinical implementation.

Large-cohort benchmarking studies in germline WES provide an evidence base for comparing tools such as GATK-gCNV, ExomeDepth,XHMM, and CoNIFER. These evaluations demonstrate trade-offs between recall and precision, the impact of reference cohort size and composition, and the substantial benefits through downstream filtering and visual review of read depth profiles. Complementary signals can further strengthen CNV interpretation, including run-of-homozygosity profiling (e.g., AutoMap), allele-balance deviations across heterozygous variants, and family-based segregation checks. A robust WES CNV pipeline can therefore improve diagnostic yield while maintaining clinically acceptable false-positive rates.

Deciphering Challenging Conditions : New Insights into Diagnosis

MODERATOR

15:10-15:25

Experience sharing-Part IV

Hypophosphatasia: A Case Report



Chung-Hsing Wang, MD

- Director, Division of Pediatric Genetics, Endocrinology and Metabolism, China Medical University Children's Hospital

PRESENT POSITION

- 2025/08-Present: Promotion to Associate Professor, China Medical University
- 202/03-Present: Surveyor of Laboratory Developed Test(LDTs)Review Program.
- 2020/07-Present: Vice Chairperson of division of medical genetics/metabolism of the Taiwan Pediatric Association
- 2018/01-Present: Director of the Genetics and Rare Disease Center, China Medical University Children's Hospital, Taichung, Taiwan
- 2013/01-Present: The expert committee member of the Human Genetics Society's rare disease case report review standard mechanism of Republic of China
- 2011/04-Present: Director of the Division of Medical Genetics and Pediatric Endocrinology/Metabolism, China Medical University Children's Hospital, Taichung, Taiwan
- 2011/02-Present: Assistant professor, School of Medicine, China Medical University
- 2003/07-Present: Attending Physician of the Division of Medical Genetics and Pediatric

EDUCATION

- 1988-1995: Bachelor Degree of Medical Science Conferred in June 1995 Major in Medicine, China Medical College, Taichung, Taiwan.

BRIEF CHRONOLOGY OF EMPLOYMENT

- 2001/08-2011/01: Clinical Lecturer, China Medical University
- 2000/07-2003/06: Research Fellow of the Division of Medical Genetics and Pediatric Endocrinology/Metabolism, China Medical University Hospital, Taichung, Taiwan
- 2007/07-2001/06: Chief Resident of the Department of Pediatrics, China Medical University Hospital, Taichung, Taiwan

SELECTED PUBLICATIONS

1. Liu TY, Lu HF, Chen YC, Liao CC, Lin YJ, Yang JS, Liao WL, Lin WD, Chen SY, Huang YC, Lin WY, Liu YH, Hsu KC, Chang SS, Chen HD, Chou YP, Chang JG, Wang CH, Chang CT, Huang CM, Yeo KJ, Wang TY, Yeh CC, Chen JH, Huang CP, Lai HC, Chen RH, Lin HJ, Wu PY, Wang JY, Kuo CC, Cho DY, Tsai CH, Tsai FJ*. Diversity and longitudinal records: Genetic architecture of disease associations and polygenic risk in the Taiwanese Han population. Sci Adv. 2025 Jun 6; 11(23): eadt0539.

*Due to space constraints, some experiences could not be included. Apologies for any inconvenience.

Deciphering Challenging Conditions : New Insights into Diagnosis

SPEAKER

15:10-15:25

Experience sharing-Part IV

Hypophosphatasia: A Case Report



Hsin-Ru Wu, MD

• 中國附醫兒童醫院主治醫師

● PRESENT POSITION

中國附醫兒童醫院主治醫師

● EDUCATION

中興大學生命科學系博士班
長庚大學醫學系

● BRIEF CHRONOLOGY OF EMPLOYMENT

中山附醫兒科部住院醫師
彰化基督教醫院兒童遺傳新陳代謝科研究醫師

Deciphering Challenging Conditions : New Insights into Diagnosis

ABSTRACT

15:10-15:25

Experience sharing–Part IV

Hypophosphatasia: A Case Report

Hypophosphatasia is a rare genetic disease characterized by low serum alkaline phosphatase activity and defective bone mineralization. It is caused by mutations in the ALPL gene and is inherited in an autosomal recessive pattern.

Here we report a case of infantile hypophosphatasia. This female infant presented with failure to thrive and hypercalcemia. A series of low serum alkaline phosphatase levels was noted during the investigation, which raised clinical suspicion of hypophosphatasia. Molecular analysis established the diagnosis of hypophosphatasia. She was treated with asfotase alfa at a dose 6mg/kg/week but hypercalcemia persisted. After the addition of calcitonin, her hypercalcemia was under control. We keep monthly surveillance to evaluate her clinical outcome.

Deciphering Challenging Conditions : New Insights into Diagnosis

MODERATOR

15:25-15:40

Experience sharing-Part V

Beyond Familial Hypercholesterolemia: A Diagnostic Reconsideration of Childhood Xanthomas



Tung-Ming Chang, MD, PhD

• 彰基兒童醫院兒科部部主任

● PRESENT POSITION

彰基兒童醫院兒科部部主任
彰基兒童發展中心主任

● EDUCATION

陽明交通大學生物科技學系博士
台北醫學大學學士

● BRIEF CHRONOLOGY OF EMPLOYMENT

台中榮總兒童醫學部住院醫師, 小兒神經研究醫師
台北榮總新竹分院小兒科主任

● SELECTED PUBLICATIONS

1. Chou IJ, Fan PC, Wu CT, Yeh TH, Chiu NC, Liu YL, Liao YH, Lee MJ, Huang CC, Lu CY, Chang TM, Hung PL, Lin RL, Hung KL, Wang HS, Lin KL; Taiwan Child Neurology Society (TCNS). A consensus on the diagnosis and management of neurofibromatosis type 1 in Taiwan. J Formos Med Assoc. 2025 Aug 22:S0929-6646(25)00438-3
2. Chang TM, Chen Y, Yang KD, Wang JY, Lin CY, Chang YJ, Chen CH, Tsai YG. Asthma control associated with anxiety and depression in asthmatic children following post-acute COVID-19. Pediatr Allergy Immunol. 2024 Jun;35(6):e14168.
3. Chang TM, Lin HL, Tzang CC, Liang JA, Hsu TC, Tzang BS. Unraveling the Role of miR-200b-3p in Attention-Deficit/Hyperactivity Disorder (ADHD) and Its Therapeutic Potential in Spontaneously Hypertensive Rats (SHR). Biomedicines. 2024 Jan 10;12(1):144
4. Li SP, Lin LC, Yang RC, Ouyang CS, Chiu YH, Wu MH, Tu YF, Chang TM, Wu RC. Predicting the therapeutic response to valproic acid in childhood absence epilepsy through electroencephalogram analysis using machine learning. Epilepsy Behav. 2024 Feb;151:109647.
5. Hsu RH, Lee NC, Chen HA, Hwu WL, Chang TM, Chien YH. Late-onset symptomatic hyperprolactinemia in 6-pyruvoyl-tetrahydropterin synthase deficiency. Orphanet J Rare Dis. 2023 Nov 10;18(1):351

*Due to space constraints, some experiences could not be included. Apologies for any inconvenience.

Deciphering Challenging Conditions : New Insights into Diagnosis

SPEAKER

15:25-15:40

Experience sharing-Part V

Beyond Familial Hypercholesterolemia: A Diagnostic Reconsideration of Childhood Xanthomas



Hsu-Heng Lin, MD

- Attending Physician, Division of Pediatric Genetics and Metabolism, Department of Pediatrics, Changhua Christian Hospital

● PRESENT POSITION

Attending Physician, Division of Pediatric Genetics and Metabolism, Department of Pediatrics, Changhua Christian Hospital, Taiwan

● EDUCATION

MD, School of Medicine, Taipei Medical University, Taiwan

● BRIEF CHRONOLOGY OF EMPLOYMENT

Pediatric Resident, Changhua Christian Hospital, Taiwan

Fellow, Division of Pediatric Genetics and Metabolism, National Taiwan University Hospital, Taiwan

Attending Physician, Department of Pediatrics, Changhua Christian Hospital, Taiwan

● SELECTED PUBLICATIONS

1. Lin HH, Chen HA, Lin SJ, et al. Pathogenic variants and olipudase alfa treatment of patients with acid sphingomyelinase deficiency in Taiwan. Mol Genet Genomic Med. 2026;14(2):e70204. doi:10.1002/mgg3.70204.
2. Lin HH, Tsai MM, Chen HA, et al. Pharmacogenomic calling from whole-exome sequencing in the Taiwanese population: A real-world experience. Mol Genet Genomic Med. 2026;14(1):e70201. doi:10.1002/mgg3.70201.

Deciphering Challenging Conditions : New Insights into Diagnosis

ABSTRACT

14:25-14:40

Experience sharing-Part III

Copy Number Variant Calling in Whole Exome Sequencing

A nine-year-old girl developed multiple yellowish nodules from age three. Initial biopsy suggested a benign condition, yet the lesions progressed. Her younger brother had similar findings, while both parents were asymptomatic, suggesting autosomal recessive inheritance. LDL cholesterol was elevated (~297 mg/dL), but the degree of elevation was inconsistent with classical autosomal recessive familial hypercholesterolemia. Statin therapy showed limited response. Owing to discordant pathology, clinical severity, treatment response, and family pattern, whole-exome sequencing identified a homozygous ABCG5 c.1336C>T (p.Arg446*) variant, confirming sitosterolemia. Treatment was shifted to ezetimibe with dietary modification. This case underscores the importance of re-evaluating the working diagnosis and pursuing genetic testing when clinical and therapeutic findings are incongruent.

Deciphering Challenging Conditions : New Insights into Diagnosis

MODERATOR

15:40-15:55

Experience sharing-Part VI

Prenatal Non-Immune Hydrops Fetalis with Unexplained Structural Anomalies on Chromosomal Microarray: Postnatal Diagnosis of Cardiofaciocutaneous Syndrome by Whole Genome Sequencing



Hsiang-Yu Lin, MD, PhD

• 馬偕兒童醫院兒童遺傳學科主任

● PRESENT POSITION

馬偕兒童醫院兒童遺傳學科主任
馬偕紀念醫院罕見疾病中心主任
馬偕兒童醫院醫學研究室主任
馬偕醫學大學醫學系部定教授

● EDUCATION

國立陽明大學臨床醫學研究所博士
臺北醫學大學醫學系醫學士

● BRIEF CHRONOLOGY OF EMPLOYMENT

行政院衛生福利部中央健康保險署西醫醫院醫療服務審查醫藥專家
行政院衛生福利部國民健康署「罕見疾病及藥物審議委員會」醫師級專家審查小組評審委員
中華民國人類遺傳學會第七屆、第八屆秘書長
中華民國人類遺傳學會第九屆理事

● SELECTED PUBLICATIONS

1. Lee CL, Chuang CK, Chiu HC, Chang YH, Tu YR, Lo YT, Wu JY, Hsiang-Yu Lin* (co-corresponding author), Lin SP*. Novel ADAMTSL2 Compound Heterozygous Mutations in Geleophysic Dysplasia with Bilateral Glaucoma and Keratoconus-like Corneal Ectasia. Front Genet. 2026; 17:1751809. (SCI)
2. Lee CL, Chuang CK, Chiu HC, Chang YH, Tu YR, Lo YT, Wu JY, Hsiang-Yu Lin* (co-corresponding author), Lin SP*. From Overgrowth to Complex Malformations: A Novel EZH2 Variant Reveals the Expanding Clinical Spectrum of Weaver Syndrome. Children. 2025; 12(11):1487. (SCI)
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*Due to space constraints, some experiences could not be included. Apologies for any inconvenience.

Deciphering Challenging Conditions : New Insights into Diagnosis

SPEAKER

15:40-15:55

Experience sharing-Part VI

Prenatal Non-Immune Hydrops Fetalis with Unexplained Structural Anomalies on Chromosomal Microarray: Postnatal Diagnosis of Cardiofaciocutaneous Syndrome by Whole Genome Sequencing



Chung-Lin Lee, MD, PhD

- Attending Physician, Division of Genetics and Metabolism, Department of Pediatrics, Mackay Memorial Hospital

PRESENT POSITION

- 2021-Present: Attending Physician, Division of Genetics and Metabolism, Department of Pediatrics, Mackay Memorial Hospital, Taipei, Taiwan
- 2021-Present: Lecturer, School of Medicine, Mackay Medical University, New Taipei City, Taiwan
- 2021-Present: Lecturer, Department of Nursing, Mackay Junior College of Medicine, Nursing and Management, New Taipei City, Taiwan

EDUCATION

- 2019-2025: PhD, Institute of Clinical Medicine, National Yang-Ming Chiao-Tung University, Taipei, Taiwan
- 2005-2012: MD, School of Medicine, Chang-Gung University, Taoyuan, Taiwan

BRIEF CHRONOLOGY OF EMPLOYMENT

- 2018-2021: Attending Physician, Division of Pediatric Emergency, Department of Pediatrics, Mackay Memorial Hospital, Hsinchu, Taiwan
- 2016-2018: Chief Resident, Division of Genetics and Metabolism, Department of Pediatrics, Mackay Memorial Hospital, Taipei, Taiwan
- 2013-2018: Resident, Department of Pediatrics, Mackay Memorial Hospital, Taipei, Taiwan

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1. Chung-Lin Lee, Chih-Kuang Chuang, Huei-Ching Chiu, Ya-Hui Chang, Yuan-Rong Tu, Yun-Ting Lo, Jun-Yi Wu, Hsiang-Yu Lin, Shuan-Pei Lin (2026, Jan). Case Report: Novel ADAMTSL2 compound heterozygous mutations in geleophysic dysplasia with bilateral glaucoma and keratoconus-like corneal ectasia. *Frontiers in Genetics*, 17, 1751809.
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Deciphering Challenging Conditions : New Insights into Diagnosis

ABSTRACT

15:40-15:55

Experience sharing-Part VI

Prenatal Non-Immune Hydrops Fetalis with Unexplained Structural Anomalies on Chromosomal Microarray: Postnatal Diagnosis of Cardiofaciocutaneous Syndrome by Whole Genome Sequencing

A 29-year-old woman had increased nuchal translucency (2.8 mm) on first-trimester screening. Subsequent ultrasound showed progressive hydrops fetalis, ventricular septal defect, and hydrocephalus. Amniocentesis revealed a normal 46,XX karyotype; SNP array detected only a paternally inherited 7q22.2q22.3 microduplication, which could not explain the phenotype. The neonate expired on the second day of life. Postnatal whole genome sequencing identified a de novo pathogenic BRAF variant (c.1406G>A, p.Gly469Glu), confirming cardiofaciocutaneous syndrome. This case underscores the limitations of microarray in monogenic disorders and the importance of prenatal exome sequencing when array results are uninformative.

Deciphering Challenging Conditions : New Insights into Diagnosis

MODERATOR

15:55-16:55

Experience sharing-Part V

Beyond Familial Hypercholesterolemia: A Diagnostic Reconsideration of Childhood Xanthomas



Wuh-Liang Hwu, MD, PhD

- Distinguished Research Fellow, China Medical University Hospital

● PRESENT POSITION

Distinguished Research Fellow, Center for Precision Medicine, China Medical University Hospital
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Adjunct Attending Physician, Department of Medical Genetics, National Taiwan University Hospital

● EDUCATION

1992-1997: PhD, Institute of Molecular Medicine, National Taiwan University, Taipei, Taiwan
1978-1984: MD, College of Medicine, National Taiwan University, Taipei, Taiwan

● BRIEF CHRONOLOGY OF EMPLOYMENT

1990-2023: Attending Physician, Department of Medical Genetics and Pediatrics, National Taiwan University Hospital, Taipei, Taiwan
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2018-2021: Deputy Director, Department of Pediatrics, National Taiwan University Hospital, Taipei, Taiwan
2006-2012: Director, Department of Medical Genetics, National Taiwan University Hospital, Taipei, Taiwan
2005-2010: Associated Professor, Department of Pediatrics, National Taiwan University Hospital, Taipei, Taiwan

● SELECTED PUBLICATIONS

1. Wang SY, Weng TI, Chen JY, Lee NC, Lee KC, Lai ML, Chien YH, Hwu WL, Chen GY. An automated workflow on data processing (AutoDP) for semiquantitative analysis of urine organic acids with GC-MS to facilitate diagnosis of inborn errors of metabolism. Clin Chim Acta. 2023 Feb 1;540:117230.
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*Due to space constraints, some experiences could not be included. Apologies for any inconvenience.

Deciphering Challenging Conditions : New Insights into Diagnosis

SPEAKER

15:55-16:10

Oral presentation I

Genetic and Neurodevelopmental Investigation of Microcephaly Using a Drosophila Model



Kai-Hung Chen

• 國立臺灣大學醫學院 生理學研究所 博士生

● PRESENT POSITION

國立臺灣大學醫學院 生理學研究所 博士生

● EDUCATION

國立臺灣大學醫學院 生理學研究所 碩士

國立成功大學 生物科技與產業科學系 學士

● SUPERVISOR

詹智強教授

● RESEARCH INTERESTS

- 神經遺傳學及疾病研究
- 細胞生物學

Deciphering Challenging Conditions : New Insights into Diagnosis

ABSTRACT

15:55-16:10
Oral presentation I

Genetic and Neurodevelopmental Investigation of Microcephaly Using a Drosophila Model

Microcephaly is a clinically and genetically heterogeneous neurodevelopmental disorder characterized by a congenitally reduced brain size and frequently accompanied by intellectual disability, developmental delay, and epilepsy. Among the genes implicated in autosomal recessive primary microcephaly, SMPD4, which encodes neutral sphingomyelinase-3 (nSMase-3), has recently emerged as a disease-associated gene. Biallelic SMPD4 variants have been linked to congenital and progressive microcephaly, but the underlying pathogenic mechanisms remain poorly understood.

SMPD4 is localized to the nuclear envelope and hydrolyzes sphingomyelin into ceramide, suggesting that sphingolipid metabolism may play an important role in neural development. To investigate this, we studied CG6962/dSMPD4, the Drosophila homolog of human SMPD4, as an in vivo model for SMPD4-related microcephaly. We found that CG6962/dSMPD4 is expressed in a cell-type-specific manner during larval development, with enrichment in the neural lineage. Loss of CG6962/dSMPD4 caused microcephaly, which could be rescued by overexpression of human SMPD4 or a ceramide synthesis enzyme, supporting an evolutionarily conserved role of SMPD4-dependent sphingolipid regulation. Additionally, CG6962/dSMPD4 deficiency resulted in developmental delay, reduced neuronal density, and impaired cell proliferation.

Mechanistically, CG6962/dSMPD4-deficient neuroblasts exhibited abnormal localization of polarity proteins and defects in asymmetric cell division, indicating that disruption of neuroblast polarity and mitotic regulation may underlie defective brain growth. These findings support a model in which CG6962/SMPD4 regulates ceramide homeostasis to maintain proper asymmetric division in neural stem cells, thereby safeguarding brain development. Our work establishes a Drosophila platform for in-depth mechanistic dissection of SMPD4-related microcephaly, enabling investigation of how altered sphingolipid homeostasis disrupts neural stem cell division and providing a foundation for evaluating potential therapeutic interventions.

Deciphering Challenging Conditions : New Insights into Diagnosis

SPEAKER

16:10-16:25

Oral presentation II

The m⁶A Epitranscriptome Unravels: m⁶A Dysregulation in ALS Motor Neuron Degeneration



Ya-Ping Yen

- Postdoctoral Research Fellow, Institute of Molecular Biology, Academia Sinica

● PRESENT POSITION

Postdoctoral Research Fellow, Institute of Molecular Biology, Academia Sinica

● EDUCATION

- | | |
|------------|--|
| 2010-2018: | PhD, Institute of Molecular Biology, Academia Sinica, Taipei, Taiwan
Institute of Biotechnology, National Taiwan University, Taipei, Taiwan |
| 2008-2010: | M.S., Department of Animal Science and Technology, National Taiwan University, Taipei, Taiwan |
| 2001-2005: | B.S., Department of Animal Science, National Chung Hsing University |

● SUPERVISOR

Dr. Jun-An Chen

● RESEARCH INTERESTS

My research interests focus on neurodegenerative diseases, with an emphasis on the roles of long non-coding RNAs, epigenetics, and the epitranscriptome in motor neuron development and degeneration.

Deciphering Challenging Conditions : New Insights into Diagnosis

ABSTRACT

16:10-16:25

Oral presentation II

The m⁶A Epitranscriptome Unravels: m⁶A Dysregulation in ALS Motor Neuron Degeneration

Amyotrophic lateral sclerosis (ALS) is a devastating, rapidly progressive neurodegenerative disease characterized by selective degeneration of motor neurons (MNs), culminating in paralysis and premature death. The molecular mechanisms underlying MN vulnerability—particularly in the predominant sporadic form—remain poorly understood. Here, we establish N⁶-methyladenosine (m⁶A), the most prevalent internal mRNA modification deposited by the METTL3/METTL14 methyltransferase complex, as a pivotal epitranscriptomic regulator of ALS pathogenesis. Conditional knockout of Mettl14 specifically in mouse MNs recapitulates hallmark ALS features, including progressive MN loss, motor dysfunction, neuromuscular junction defects, and shortened lifespan. Mechanistically, widespread m⁶A hypomethylation disrupts expression of ALS-associated risk genes and, strikingly, reduces chromatin accessibility, thereby impairing transcriptional programs essential for MN survival and identity. In human disease models, induced pluripotent stem cell-derived MNs (iPSC-MNs) from both familial and sporadic ALS patients exhibit conserved m⁶A reduction, reinforcing a shared epitranscriptomic signature across ALS subtypes. To explore therapeutic potential, we deployed small-molecule activators of m⁶A and AAV-mediated gene therapy to restore m⁶A levels. These interventions markedly protected MNs from degeneration, rescued motor deficits in iPSC-MN cultures, and attenuated disease progression in ALS mouse models. Collectively, our findings position m⁶A dysregulation as a central driver of MN degeneration in ALS and highlight epitranscriptomic restoration—via pharmacological or genetic means—as a promising, translatable therapeutic avenue. This work also underscores the power of iPSC-based platforms for elucidating epigenetic contributions to neurodegeneration and broadens our understanding of RNA modifications in disease-relevant human stem cell models.

Deciphering Challenging Conditions : New Insights into Diagnosis

SPEAKER

16:25-16:40

Oral presentation III

Homozygous Variant in *TOMM7* Leads to Metabolic Reprogramming and Microcephalic Osteodysplastic Dwarfism with Moyamoya Disease



Chia-Yi Li

- Postdoctoral Researcher, Institute of Clinical Medicine, National Cheng Kung University / Laboratory of Molecular Genetics

● PRESENT POSITION

2025/08-Present: Postdoctoral Researcher, Institute of Clinical Medicine, National Cheng Kung University, Taiwan/ Laboratory of Molecular Genetics

● EDUCATION

2019/09-2025/07: PhD, Institute of Clinical Medicine, National Cheng Kung University, Taiwan

2015/09-2019/06: B.S., Department of Molecular Biology and Human Genetics, Tzu Chi University, Taiwan

● SUPERVISOR

Peng-Chieh Chen, PhD

● RESEARCH INTERESTS

- CRISPR/Cas gene editing
- Mitochondrial biology

Deciphering Challenging Conditions : New Insights into Diagnosis

ABSTRACT

Oral presentation III

16:25-16:40

 Homozygous Variant in *TOMM7* Leads to Metabolic Reprogramming and Microcephalic Osteodysplastic Dwarfism with Moyamoya Disease

Nearly all mitochondrial proteins are synthesized in the cytosol and subsequently imported in-to the mitochondria via the translocase of the outer membrane (TOM) complex, in which TOM7 acts as a crucial regulatory subunit. Disruption of this import machinery can cause mitochondrial diseases with highly heterogeneous clinical phenotypes. Through whole-exome sequencing, we identified nine patients from seven unrelated Taiwanese families carrying *TOMM7* p.P29L variant. All patients exhibited microcephaly, short stature, facial dysmorphism, and macular scarring; importantly, five of these patients developed moyamoya disease (MMD) at an average age of seven, explicitly establishing an association between the *TOMM7* variant and human cerebrovascular defects. To delineate the pathology, a *tomm7*-knockout zebrafish model generated by CRISPR/Cas9 exhibited microcephaly, cranio-facial abnormalities, and cerebral vessel loss, closely mirroring the patient phenotypes. Furthermore, in CRISPR/Cas9-edited homozygous *TOMM7* p.P29L endothelial cells (ECs), we observed elevated TOM7 protein levels, increased cellular senescence, and impaired tube formation. Mitochondria were abnormally enlarged and round. Proteomic analysis revealed a significant reduction in mitochondrial proteins involved in ATP synthesis and β -oxidation. Despite a modest decline in mitochondrial respiration, the ECs underwent significant metabolic reprogramming, shifting energy reliance to glycolysis, evidenced by the upregulation of HK2 gene and protein expression. This metabolic shift and structural defects, including loss of cristae structure and decreased respiratory function, were consistently validated in patient-derived ECs. Importantly, correction of *TOMM7* p.P29L variant in patient ECs restored partial mitochondrial morphology and respiratory function. In conclusion, we demonstrated the essential role of TOM7 in balancing cellular energy sources and elucidated the molecular mechanism by which the *TOMM7* p.P29L variant leads to autosomal recessive microcephalic osteodysplastic dwarfism with MMD. Our findings provide critical molecular and translational insights into how defects in mitochondrial protein import cause aberrant endothelial metabolism and contribute to cerebrovascular disease.

Key words: TOM complex, moyamoya disease, iPSC-derived endothelial cells, mitochondrial protein import, metabolic reprogramming

Deciphering Challenging Conditions : New Insights into Diagnosis

SPEAKER

16:40-16:55

Oral presentation IV

Investigating the Cellular and Molecular Mechanisms of *MAST1* Mutations in Cortical Malformation



Agnes Dwi Ariyanti

- Postdoctoral Fellow, Institute of Brain Science, National Yang Ming Chiao Tung University

● PRESENT POSITION

Postdoctoral Fellow, Institute of Brain Science, National Yang Ming Chiao Tung University

● EDUCATION

- | | |
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| 2020-2026: | PhD in Interdisciplinary Neuroscience, National Yang Ming Chiao Tung University & Academia Sinica, Taiwan |
| 2018-2019: | Professional Pharmacist Degree, Widya Mandala Catholic University Surabaya, Indonesia |
| 2015-2018: | Master of Engineering in Biomedicine, Department of Bioengineering, Chongqing University, China |
| 2010-2014: | Bachelor of Pharmacy, Widya Mandala Catholic University Surabaya, Indonesia |

● SUPERVISOR

Prof. Jin-Wu Tsai

● RESEARCH INTERESTS

Neurodevelopment and neuronal migration, stem cell biology, and the development of small-molecule therapeutics for neurodevelopmental and age-related diseases.

Deciphering Challenging Conditions : New Insights into Diagnosis

ABSTRACT

Oral presentation IV

16:40-16:55

Investigating the Cellular and Molecular Mechanisms of *MAST1* Mutations in Cortical Malformation

Lissencephaly is a brain development malformation disease caused by aberrant neuronal migration. Disruption of post-mitotic neuronal migration could be affected by the failure of the microtubules to guide neurons to reach their destination. Using whole exome sequencing, we identified a novel missense *MAST1* variant from a lissencephaly patient. Recently, mutations in *MAST1* were found to cause mega-corpus-callosum syndrome with cerebellar hypoplasia and cortical malformations (MCC-CH-CM). By using in-utero electroporation, we found that the knockdown of *Mast1* caused neuronal migration delay but not cell differentiation and maturation. *Mast1* knockdown also disrupts the corpus callosum arrangement compared to control. Interestingly, we did not observe any migration delay in the *MAST1* mutations group, but those variants were not able to rescue and compensate for the loss of *Mast1* induced by shRNA. We found that lissencephaly-related mutations in cell culture promote protein degradation, whereas microcephaly-related mutations showed stable protein expression. However, all the variants decreased the ability of microtubules to polymerize. Moreover, we showed that *MAST1* could interact with Pten and further promote Pten phosphorylation, raising the prospect that phosphorylated Pten might regulate microtubule function through *MAST1*. We propose that *MAST1* mutations caused a haploinsufficiency effect that further delayed post-mitotic neuronal migration through interaction with PTEN-regulating microtubule function.

Appreciation & Acknowledgement

感謝有您與我們一起，為遺傳與罕見疾病的診斷與治療共同努力！

Thank you for being with us and working together for the diagnosis and treatment of genetic and rare diseases!

*按英文字母排序 Arrange in alphabetical order

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衛部罕藥輸字第000091號 健保代碼: VC00091209

適應症：治療成人急性肝臟型紫質症 (AHP, acute hepatic porphyria)

用法用量：每月一次2.5 mg/kg，以皮下注射給藥

紫福拉利Givlaari健保給付規定

限用於確診為衛生福利部國民健康署認定之罕見疾病紫質症 (porphyria)中屬急性肝紫質症 (acute hepatic porphyria, AHP)，且符合下列全部條件者：

- 年滿18歲以上
- 基因診斷報告 (具HMBS(PBGD)、ALAD、CPOX、PPOX 致病基因變異者)
- 經過適當醫療處置 2 年
- 1年內，發生 4 次含以上急性發作，急性發作時需急診或住院治療且使用靜脈輸注血基質(hemin)藥品治療反應不佳^{註1}或耐受性不良^{註2}或無效者。
- 1年內尿液的胺基酮戊酸 (aminolevulinic acid, ALA) 與膽色素原 (porphobilinogen, PBG) 大於等於正常值之 4 倍以上 (需檢附報告)

限由神經內科、血液科、肝膽腸胃科、遺傳科醫師處方。

詳細給付規定與申請所需文件細則請參閱 Givlaari 藥品健保給付規定 (健保代碼: VC00091209)

註1：反應不佳定義：使用hemin治療後，每年平均發作次數仍大於4次，且每次發作都需連續使用hemin

註2：耐受性不良定義：使用hemin後，造成與hemin相關之嚴重且具有臨床顯著意義，會限制生活、對健康有立即或長期影響，或必須住院或延長住院處理的不良反應，例如：反覆人工血管感染或菌血症、敗血症、其他感染、鐵質沉積、靜脈炎等

References

1. 衛部核准仿單_紫福拉利注射劑 Givlaari solution for injection 衛部罕藥輸字第000091號
2. 全民健康保險藥物給付項目及支付標準共擬會議第72次會議紀錄修訂藥品給付規定附表 3.3. page 23~26
3. 全民健康保險藥品新收載品項明細表_Givlaari (2)
4. <https://www.givlaari.com/what-is-givlaari/how-givlaari-works>

紫福拉利注射劑 Givlaari Solution for Injection 衛部罕藥輸字第 000091 號 限由醫師使用

1. 藥品名稱 紫福拉利注射劑 2. 組成與劑型 每毫升溶液中含有200mg givosiran sodium，相當於189mg的givosiran。每個小瓶中含有200mg givosiran sodium，相當於189mg的givosiran。劑型：注射液。3. 臨床特性 3.1 適應症 適用於治療成人急性肝臟型紫質症(AHP, acute hepatic porphyria)。3.2 劑量及給藥方法 應在有紫質症治療經驗的醫療專業人員的監督下開始治療。用法用量 Givlaari 的建議劑量為每月一次2.5 mg/kg，以皮下注射給藥。劑量依實際體重計算。給病人的劑量(mg)和體積(mL)應按以下方式計算：病人體重(kg) × 劑量(2.5 mg/kg) = 要給予的藥物總量(mg)。總量(mg)除以小瓶濃度(189mg/mL) = 要注射的藥品總體積(mL)。漏打 如果漏打，應盡快給藥，並在給予漏打的劑量後恢復每月間隔給藥。對不良反應的劑量調整 對於有臨床相關轉氨酶升高的病人，若給藥中斷後有改善，則可以考慮以每月一次1.25 mg/kg 的劑量恢復使用。特殊族群 老年 65 歲以上的病人無需調整劑量。肝功能不全 輕度肝功能不全(膽紅素 ≤ 1xULN (Upper Limit of Normal)、天門冬氨酸轉氨酶(AST) > 1 × ULN 或膽紅素 > 1 × ULN - 1.5 × ULN)的病人無需調整劑量。尚未對中度或重度肝功能不全病人進行Givlaari的試驗。腎功能不全 對於輕度、中度或重度腎功能不全(預估腎小球濾過率[eGFR] ≥ 15至<90 mL/min/1.73m²)的病人，無需調整劑量。尚未對患有終末期腎病的病人或接受透析的病人進行Givlaari的試驗。小兒 尚未確立Givlaari在小兒的安全性和有效性。3.3 禁忌症 對主成分或所列的任何賦形劑嚴重過敏(例如過敏反應[anaphylaxis])。3.4 特殊警告和使用注意事項 患有急性間歇性紫質症(AIP, acute intermittent porphyria)以外的 AHP 亞型的病人 除AIP以外的AHP亞型(遺傳性黃紫質症(HCP)、異位型紫質症(VP)和ALAD缺乏紫質症(ADP))病人的療效和安全性數據有限。在評估這些罕見的AHP亞型的風險利益時，應列入考量。過敏反應(anaphylactic reaction) 在臨床試驗中，過敏反應發生於一名有過敏性哮喘史和異位性體質的病人。應監測過敏反應的徵象和症狀。如果發生過敏反應，應立即停藥，並應採取適當的醫療措施。轉氨酶升高 曾在 givosiran 治療的病人中觀察到轉氨酶升高。轉氨酶升高主要發生在開始治療後3到5個月之間。在開始治療之前應進行肝功能檢查。在治療的前 6 個月應每月重複進行這些檢查，此後依臨床需要進行。對於臨床相關的轉氨酶升高，應考慮中斷或終止治療。如果轉氨酶數值在中斷治療後有所改善，可以考慮以1.25mg/kg的劑量恢復治療。較低劑量的療效和安全性方面的數據有限，尤其是對於轉氨酶已升高之病人。在轉氨酶升高中斷給藥後，尚無關於將1.25mg/kg劑量增加至2.5mg/kg的數據。對腎功能的影響 曾有接受givosiran 治療期間血清肌酸酐升高和 eGFR 降低的報告。在安慰劑對照試驗中，第3個月肌酸酐升高的中位數6.5mol/L(0.07mg/dL)，繼續接受每月2.5mg/kg givosiran 治療後，在第 6 個月得到解決或穩定。在接受 givosiran 治療期間建議依臨床需要進行腎功能監測。曾在部份已有腎臟疾病的病人中，觀察到腎功能進一步的惡化；對這類病人，需要在治療期間仔細監測腎功能。血中同半胱氨酸(homocysteine)升高 AHP 病人、維生素缺乏或慢性腎病病人可能有血中同半胱氨酸濃度升高。在givosiran治療期間，曾觀察到血中同半胱氨酸濃度較治療前升高(請參閱第8節)。治療期間的血中同半胱氨酸濃度升高與 givosiran 的臨床關聯仍未知。然而，同半胱氨酸濃度升高於先前被認為與增加血栓性(thromboembolic)事件風險有關。建議在治療開始前檢測血中同半胱氨酸濃度以及在 givosiran 治療期間監測其變化。對於血中同半胱氨酸濃度升高的病人，可考慮補充維生素B6。3.5 交互作用 在一個臨床藥物交互作用試驗中，givosiran導致肝臟中某些CYP450酶的活性微弱至中度降低，從而增加了血漿暴露：CYP1A2: caffeine 的Cmax增加1.3倍，AUC0-∞增加3.1倍，CYP2D6: dextromethorphan 的Cmax增加2.0倍，AUC0-∞增加2.4倍，CYP2C19: omeprazole 的Cmax增加1.1倍，AUC0-∞增加1.6倍，CYP3A4: midazolam 的Cmax增加1.2倍，AUC0-∞增加1.5倍，CYP2C9: 對 losartan 的暴露無影響 在進行Givlaari 治療期間時使用為 CYP1A2 或 CYP2D6 受質的藥物時，建議謹慎使用，因為本品可能會增加或延長其治療效果，或改變其不良反應。應考慮依據核准的藥品仿單減少CYP1A2或CYP2D6受質的劑量。3.6 特殊族群注意事項 懷孕 目前缺乏或僅有有限的孕婦使用 givosiran 的數據。動物研究顯示在有母體毒性時會產生生殖毒性。在已考量到對婦女的預期健康益處和對胎兒的潛在風險的情況下，可考慮在懷孕期間使用本品。哺乳 尚不清楚givosiran 是否會分泌到乳汁。不能排除對新生兒/嬰兒的風險。已知的動物藥效學/毒理學顯示givosiran會分泌到乳汁(請參閱第10節)。必須考慮哺育母乳對孩子的益處和治療對婦女的益處，來決定是否停止哺乳或中斷/放棄Givlaari 治療。有生育能力的女性與男性 在大鼠試驗中，未觀察到givosiran對生育力具顯著影響。3.7 不良反應 安全性摘要 使用givosiran治療的病人中最常被回報的不良反應是注射部位反應(ISR)(36%)、噁心(32.4%)和疲倦(22.5%)。導致治療中斷的不良反應是轉氨酶升高(0.9%)和過敏反應(0.9%)。TFDA PI: 2025-02-07 此為簡易仿單，完整產品資訊，請參照完整仿單。

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VOXZOGO™
vosoritide

軟骨發育不全症 Achondroplasia

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https://mcp.fda.gov.tw/im_detail_1/衛部罕菌疫輸字第000049號
https://mcp.fda.gov.tw/im_detail_1/衛部罕菌疫輸字第000050號

VOXZOGO在第3期安慰劑對照研究中顯著提高年增長速度(AGV) 並在開放標籤的第2期延伸研究中顯著提升病人的累積身高¹⁻³



年增長速度

+1,57 公分 / 年

在為期 1 年的第三期研究中，在 5 至 15 歲的病人中
VOXZOGO 使用組相較於安慰劑 年增長速度(AGV)有顯著改善
(n= 60; P< 0,0001)



累積生長

+9,08 公分

相較於未接受治療的病人
VOXZOGO對於累積生長有顯著增加
(n=10; P=0,0002)

AGV, Annualized growth velocity: 年增長速度

參考資料: 1. 產品特性摘要 2. Savarirayan R, Tofts L, Irving M, et al. Once-daily, subcutaneous vosoritide therapy in children with achondroplasia: a randomised, double-blind, phase 3, placebo-controlled, multicentre trial. Lancet. 2020;396(10252):684-692. doi:10.1016/S0140-6736(20)31541-5 3. Savarirayan R, Irving M, Bacino CA, et al. C-type natriuretic peptide analogue therapy in children with achondroplasia. N Engl J Med. 2019;381(1):25-35. doi:10.1056/NEJMoa1813446

扶佐高™ 凍晶注射劑 2 毫克 / 毫升、0.8 毫克 / 毫升 (VOXZOGO™ powder and solvent for solution for injection 2 mg/ml, 0.8 mg/ml)
衛部罕菌疫輸字 第 000049 號、第 000050 號

【適應症】Voxzogo 用於改善 2 歲以上患有軟骨發育不全症 (achondroplasia) 且骨骺未閉合病人之身高。
禁忌：對有效成分或所列之任何賦形劑過敏者。

【用法用量】應在具有治療生長障礙或骨骼發育不全資格的醫師指示下開始使用 vosoritide 進行治療。劑量：兒童治療應越早開始越好。vosoritide 建議劑量係依據病人體重和 vosoritide 濃度。劑量一般為每公斤體重 15 微克。

【警語 / 注意事項】可追溯性：為提高藥品的可追溯性，應清楚記錄使用的藥品名稱和批號。血壓之影響：重大心血管疾病的病人和使用抗高血壓藥物的病人被排除在上市前臨床試驗之外。為了減少血壓降低的風險及相關症狀（頭暈、疲倦及 / 或噁心），病人應在注射時已補充足夠水份。鈉：本藥品的鈉含量低於 1mmol (23 毫克)，因此基本是「無鈉」。操作機械能力：Voxzogo 對病人駕駛和使用機械的能力有中度影響 Vosoritide 可能會導致暫時的輕度血壓降低，曾接獲通報暈厥、暈厥前期和頭暈以及其他血壓降低的跡象和症狀為 VOXZOGO 的不良反應。應考量病人對治療的反應，建議在注射後至少 60 分鐘內不要開車、騎腳踏車或操作機器。其他注意事項：本藥品不應與其他藥品混合。

【副作用 / 不良反應】- 臨床重要副作用 / 不良反應：下列重要不良反應在本仿單其他部分有相關描述：血壓降低 (見「警語及注意事項」與參考仿單「特定不良反應之說明」)。注射部位反應 (請參考仿單「特定不良反應之說明」)。- 臨床試驗經驗：安全性資料摘要：vosoritide 最常見的不良反應為注射部位反應 (85%)、嘔吐 (27%) 和血壓降低 (13%)。不良反應列表清單：使用 vosoritide 治療病人的不良反應如表 2 所示。不良反應係依據 MedDRA 系統器官分類和頻率列示。頻率定義如下：極常見 (≥ 1/10)、常見 (≥ 1/100 至 < 1/10)、不常見 (≥ 1/1,000 至 < 1/100)、罕見 (≥ 1/10,000 至 < 1/1,000)、非常罕見 (< 1/10,000)、頻率未知 (從現有數據中無法估計)。依頻率列示的分組中，各組的不良反應係按照嚴重程度由大到小的順序排列。【北市衛藥廣字第 114020128 號】

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表 2: 病人使用 Voxzogo 治療後產生的不良反應

系統器官分類	極常見	常見
神經系統病變：		暈厥 暈厥前期 頭暈
血管疾病	血壓降低 ^a	
腸胃疾病	嘔吐	噁心
一般疾病和注射部位症狀	注射部位反應 ^b	疲倦
調查 (Investigations)		鹼性磷酸酶升高

a. 血壓降低包括無症狀和有症狀的不良反應。

b. 注射部位反應包括注射部位紅疹、反應、腫脹、蕁麻疹、疼痛、瘀血、搔癢、出血、變色，以及硬結。

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在法布瑞氏症 amenable mutation 患者使用後

達到心臟 LVMi 顯著降低、腎臟功能維持穩定等多重器官臨床指標*

加厲伏藥品處方資訊摘要：藥品名稱：加厲伏膠囊 123 毫克（衛部藥輸字第 000060 號）。**主要成分：**每粒膠囊內含 migalastat hydrochloride，相當於 migalastat 123 毫克。**治療適應症：**加厲伏適用於已確認為法布瑞氏症且於體外試驗確定為可符合性基因突變（amenable mutation）的 12 歲（含）以上病人。**用法與用量：**加厲伏應由具有診治法布瑞氏症經驗的專科醫師監督給藥。加厲伏不適合與酵素替代療法同時給藥。**劑量：**加厲伏建議劑量為每間隔 1 日 1 次，每次在固定的時間服用 migalastat 123 毫克（1 粒）。**遺漏劑量：**不可以連續兩天服用加厲伏，若一整天都忘記服用該日劑量，卻在正常服藥時間的 12 小時內想到，可以立即補服該次劑量；但如果想到時，已經超過應服藥時間 12 小時以上，則應等到下次用藥日與用藥時間，再恢復規則給藥。**給藥方式：**口服給藥。加厲伏與食物併用時，在體內的暴露量大約減少 40%，而當與咖啡併用時體內的暴露量減少 60%。在服用加厲伏前至少 2 小時和服用 2 小時不應攝入食物和咖啡因，確保至少禁食 4 小時，在 4 小時的禁食期間可以飲用水（原味、調味、加糖）、無果肉果汁和不含咖啡因的碳酸飲料。加厲伏膠囊每間隔 1 日 1 次，並在同一時間服用，以確保為病人帶來最佳益處。加厲伏膠囊應整粒吞服，不可切開、碾碎或咀嚼。**禁忌：**對主成分或對賦形劑過敏者禁用。**警告與注意事項：**已開始使用或改用加厲伏的病人應定期（每 6 個月）監測腎功能、心電圖與生化檢驗。當臨床狀況明顯惡化時，應再度作臨床評估或考慮停用加厲伏。加厲伏不適用於具有非可符合性突變的病人。嚴重腎功能不全（腎絲球過濾率小於 30 mL/min/1.73 m²）的病人，不建議使用加厲伏。有少數資料顯示加厲伏單次劑量與一次輸注標準酵素替代療法併用會造成 agalsidase 在體內動態濃度最多增加達到 5 倍。該試驗也指出 agalsidase 不影響 migalastat 的藥品動力學。加厲伏不適合與酵素替代療法同時給藥。**操作機械能力：**加厲伏對駕駛或操作機具的能力無影響或影響極小。**特殊族群注意事項：****懷孕：**孕婦服用加厲伏的資料很少。在兔子試驗中觀察到，只有達到對雌兔有中毒性劑量時才出現生長發育毒性。懷孕期間不可服用加厲伏。**哺乳：**尚不清楚加厲伏是否會排放於人類乳汁中。不過，曾發現 migalastat 出現於正在哺乳的大量乳汁中，因此，喝母乳的嬰兒也可能暴露於 migalastat 的風險。應衡量母親接受加厲伏治療的效益與哺乳帶給嬰兒的風險何者重要，來決定應停止哺乳或停用加厲伏。**有生育能力的女性與男性：**可能懷孕的女性病人/男性與女性病人的避孕：有可能懷孕且未受孕的女性病人不可以使用加厲伏。**生育：**未曾研究加厲伏對人類生育力的影響。實驗顯示雄性大鼠接受所評估的各劑量之 migalastat 後，出現短暫不孕。藥物停用 4 週後可以完全恢復生育能力。其他 iminosugars 治療的前臨床實驗也有類似的結果（參見第 10.3 章節）。加厲伏不影響雌性大鼠的生育能力。**小兒：**加厲伏不適用於 12 歲以上但體重低於 45 公斤的兒童。**腎功能不全：**未曾看到以加厲伏治療的病人有蛋白尿減少的情形。嚴重腎功能不全（腎絲球過濾率小於 30 mL/min/1.73 m²）的病人，不建議使用加厲伏。**交互作用：**依據體外實驗資料，migalastat 不是 CYP1A2、2B6 或 3A4 的誘導劑。而且，migalastat 也不是 CYP1A2、2A6、2B6、2C8、2C9、2C19、2D6、2E1 或 3A4/5 的受質或抑制劑。Migalastat 不是 MDR1 或 BCRP 的受質，也不是 BCRP、MDR1 或 BSEP 等人類外排轉運蛋白的抑制劑。此外，migalastat 不是 MATE1、MATE2-K、OAT1、OAT3 或 OCT2 的受質，也不是 OATP1B1、OATP1B3、OAT1、OAT3、OCT1、OCT2、MATE1 或 MATE2-K 等人類攝入轉運蛋白的抑制劑。**其他藥品對加厲伏的影響：**加厲伏與咖啡因合併用藥會降低加厲伏的全身性暴露量（AUC 和 C_{max}），可能會降低加厲伏療效。在服用加厲伏前至少 2 小時和服用後 2 小時，應避免同時服用加厲伏和咖啡因。**副作用/不良反應：****安全性摘要：**加厲伏最常見的副作用是頭痛，大約有 10% 病人出現頭痛。**副作用列表：**發生頻次類別的定義為：極常見（≥1/10）、常見（≥1/100 到 <1/10）、少見（≥1/1,000 到 <1/100）、罕見（≥1/10,000 到 <1/1,000）、極罕見（<1/10,000）以及不明（現有資料無法估算）。在各種頻次類別中，依據系統器官分類將副作用發生率由高至低順序排列。（請參見仿單表一、完整的不良反應列表。）**兒科族群：**依據 AT1001-020 開放性研究，其中受試者接受與成人相同的給藥方案的一年安全性數據，對 21 名青春前期病人（12 歲以上至 18 歲以下且體重大於 45 公斤以上）進行安全性評估。在青春期和成年病人受試者之間未觀察到不良反應的年齡特異性差異。根據這些數據，預計青春前期病人的不良反應頻率、類型和嚴重程度與成年病人相同。**疑似副作用的通報：**藥品批准上市後的疑似副作用通報相當重要，如此可持續監測該藥品的效益/風險平衡。專業醫護人員必須將所有疑似副作用透過全國藥物不良反應通報系統進行通報。**過量：**若發生過量中毒，應給予一般性醫療處置。當加厲伏用量達到 1250mg 或 2000 mg 時，最常出現的副作用報告分別是頭痛與頭暈。**詳細處方資料備索、僅供專業醫療人員參考**

* References: Galafold 藥品仿單。

衛部藥輸字第 000060 號 北市衛藥廣字第 115030247 號



藥商名稱：台灣大昌華豐股份有限公司 DKSH Taiwan Ltd.
藥商地址：臺北市內湖區堤頂大道 2 段 407 巷 20 弄 1、3、5、7 樓 10 樓，
及 22、24、26 樓 10 樓及 22 樓 10 樓之 1
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創新 Dravet syndrome 適應症藥物

- ✓ 71.4% 病患癲癇發作頻率降低超過50%
- ✓ 42.9% 病患無癲癇發生
- ✓ 戴克癲組21位病患產生輕微的副作用(嗜睡、食慾不振)，安慰劑組則有13位，病患耐受性佳。



* 參考資料：DIACOMIT[®] 戴克癲產品仿單，採法國研究數據計算，處方資訊摘要如下：

【品名】戴克癲膠囊 250 毫克、500 毫克 DIACOMIT Hard Capsules 250 mg、500 mg

【適應症】用於嬰兒期嚴重肌痙攣性癲癇（SMEI, Dravet's syndrome）病人，僅服用 clobazam 及 valproate 無法充分控制癲癇發作時，併 DIACOMIT 作為輔助治療難治的全身性強直陣攣性發作（generalized tonic-clonic seizure）。

【用量】

Stiripentol 劑量以每公斤體重用量（mg/kg）計算。每日總劑量應分成 2 或 3 次服用。最高建議總劑量為 3000mg/day。

一開始 Stiripentol 併用 clobazam 與 valproate 的輔助療法應逐步增加劑量至建議劑量 50 mg/kg/day。Stiripentol 的劑量應逐漸增加，從 20 mg/kg/day 開始一個星期，接著 30 mg/kg/day 一個星期，之後的劑量調升應依據年齡。

【其他抗癲癇藥物劑量調整】

其他抗癲癇藥物與 stiripentol 併用時之劑量調整關於潛在的藥物交互作用，雖然目前沒有充分的藥理學資料，但基於臨床經驗，其他抗癲癇藥物與 stiripentol 併用時，建議以下調整劑量及服藥時間。

Clobazam：在樞紐性試驗中，開始併用 Stiripentol 時，clobazam 每日劑量為 0.5 mg/kg/day，通常分成 2 次使用。當產生不良反應或 clobazam 過量之臨床徵兆時（如：嗜睡、肌張力減退或幼兒煩躁），每日總劑量應每週減少 25%。

Valproate：一般認為 stiripentol 與 valproate 潛在代謝性交互作用不大，因此，當併用 stiripentol 時，不需調整 valproate 劑量，除非有臨床安全性的考量。在樞紐性試驗中，開始併用 stiripentol 時，valproate 每日總劑量不超過 30 mg/kg/day，當腸胃方面發生不良反應時（如：食慾不振、體重減輕）valproate 每日總劑量應每週減少 10 mg/kg/day。

展世達™ Upstaza™

AADC 缺乏症基因治療



AADC 缺乏症是一種先天性神經傳導物質合成障礙，多數病人未能發展出坐、站、走等動作里程碑。

Upstaza™ 一次基因治療，使病人動作功能得以發展，並持續獲得動作里程碑。

展世達 輸注溶液 (Upstaza 2.8×10^{11} vector genomes (vg)/0.5 mL solution for infusion), 衛部罕菌疫輸字第 000051 號

適應症：治療年齡在18個月以上，且經臨床、分子和基因證實確診為具有嚴重表現型的芳香族L-胺基酸類脫羧基酶 (Aromatic L-amino acid decarboxylase, AADC) 缺乏症的病人。用量與用法：應該在專精立體定位神經外科手術的醫學中心治療，並由合格的神經外科醫師在無菌條件下進行給藥。劑量：病人接受總劑量 1.8×10^{11} 個載體基因體 (vg)，以四次0.08毫升(0.45×10^{11} 個載體基因體(vg))輸注，每邊殼核各兩次。給藥方法：殼核內使用。**禁忌：**對本品的活性物質eladocogene exuparvovec或下列出的任何賦形劑過敏：氯化鉀、氯化鈉、磷酸二氫鉀、磷酸氫二鈉、泊洛沙姆 188、注射用水。**警語及注意事項：**Upstaza 的製備和輸注應始終使用適當的無菌技術。監測：應於手術中及手術後密切監測接受基因治療的病人是否發生手術相關併發症、與其本身疾病相關的併發症，以及全身麻醉相關的風險。病人可能會因手術及麻醉使其本身 AADC 缺乏症的疾病症狀惡化。以eladocogene exuparvovec 治療後，AADC 缺乏症的自主神經和血清素相關症狀可能持續存在。可追溯性：為提高生物醫藥產品的可追溯性，應明確記錄給藥產品的名稱和批號。免疫原性：沒有治療前抗AAV2 抗體濃度 $>1:50$ 的病人使用 eladocogene exuparvovec 的經驗。腦脊髓液滲漏：腦脊髓液(CSF)滲漏發生在當大腦或脊髓周圍的腦膜有出現撕裂或孔洞時，使得腦脊髓液溢出。Upstaza透過鑽孔由雙側核殼內輸注給藥，因此術後可能發生腦脊髓液滲漏。接受eladocogene exuparvovec 治療的病人在給藥後應仔細監測是否發生腦脊髓液滲漏，特別是與腦膜炎和腦炎風險相關的情況。異動症 (Dyskinesia)：由於長期多巴胺缺乏，AADC 缺乏症病人可能對多巴胺的敏感性增加。以eladocogene exuparvovec 治療後，曾被報導有26/30名病人異動症發生(見第8節)。異動症的發生是由於多巴胺敏感性所引起，且通常在基因治療給藥後1個月開始，並在數個月內逐漸減少。異動症事件以常規醫療照護來處理，例如：抗多巴胺治療 (例如，risperidone)。病毒脫落風險：由於eladocogene exuparvovec 的全身分佈非常有限，脫落的風險被認為很低。作為預防措施，應建議病人/照護人員適當處理敷料和/或任何分泌物 (例如：淚液、血液、鼻腔分泌物、尿液和腦脊液) 產生的廢棄物，其中包括在處置之前將廢棄物儲存在密封袋中，以及 病人/照護人員戴上手套以更換敷料和處置廢棄物。這些處理預防措施應在eladocogene exuparvovec 給藥後遵循14 天。建議病人/照護人員在換藥和廢棄物處理時戴上手套，尤其是在照護人員懷孕、哺乳或有免疫缺陷的情況下。血液、器官、組織和細胞捐贈：接受Upstaza治療的病人不得捐獻血液、器官、組織和細胞以進行移植。鈉和鉀含量該藥品每劑含有少於1毫摩爾 (mmol) 的鈉 (23毫克)，含有少於1毫摩爾 (mmol) 的鉀 (39毫克)，也就是說基本上“不含鈉”、“不含鉀”。不良反應 (僅列出發生頻率 $\geq 1/10$)：臨床試驗中病人發生的不良反應：初期失眠、異動症。神經外科相關不良反應：貧血、腦脊液滲漏(可能包括假性腦脊膜膨出)。給藥後 ≤ 2 週內發生的麻醉和術後相關不良反應：肺炎、低鉀血症、易怒、低血壓、上消化道出血、腹瀉、褥瘡、發熱、呼吸聲音異常。

其他詳細產品資訊。請參考衛生福利部核准之產品說明

https://mcp.fda.gov.tw/im_detail_1/衛部罕菌疫輸字第000051號?no=1120701840&token=yjBelsizsVWd3j0

吉帝藥品股份有限公司

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Upstaza™
(eladocogene exuparvovec)



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新一代氮清除劑 RAVICTI oral liquid



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涵蓋年紀由新生兒至成人包含短期及長期研究

有效性

- 2月齡以下小兒病人，以苯丁酸甘油酯長期治療，其的平均歸一化靜脈血氮值落在正常限值範圍內。
- 2月齡至17歲病人，短期試驗匯總分析，由苯丁酸鈉轉換為苯丁酸甘油酯後的血漿氮顯著降低，在苯丁酸甘油酯的長期治療期間，平均空腹靜脈血氮值落在正常範圍內。
- 成人病人，以苯丁酸甘油酯長期治療，平均空腹靜脈血氮值落在正常限值。

瑞維安口服液 RAVICTI oral liquid

本藥限由醫師處方使用，此為簡易仿單，完整產品資訊，請參閱完整仿單，衛部藥輸字第 000095 號。

學名：Glycerol phenylbutyrate

適應症：本品用於不能藉由限制蛋白質的攝入和/或單純補充氨基酸控制的尿素循環代謝異常（Urea Cycle Disorders; UCDs）病人的長期輔助治療，包括carbamoyl phosphate synthetase (CPS) I 缺乏症、鳥氨酸氨甲酰基轉移酶 (ornithine carbamoyltransferase (OTC)) 缺乏症、argininosuccinate synthetase (ASS) 缺乏症、argininosuccinate lyase (ASL) 缺乏症、arginase (ARG) I 缺乏症和ornithine translocase缺失引起之高鳥氨酸血症-高氨血症-高瓜氨酸血症症候群 (hyperornithinaemia-hyperammonaemia homocitrullinuria syndrome; HHH)。

使用限制：

1. 服用本品時，必須限制飲食中的蛋白質，某些情況下還應添加膳食補充劑（例如必需氨基酸、精氨酸(arginine)、瓜氨酸(citrulline)、無蛋白熱量補充劑）。

2. 本品不得用於急性高氨血症 (acute hyperammonemia) 之控制。

用法用量：本品必須配合膳食蛋白限制，有時候必須配合飲食補充劑（例如必需氨基酸、精氨酸(arginine)、瓜氨酸(citrulline)、無蛋白熱量補充劑），這取決於促進生長發育所需的每日膳食蛋白攝入量，應根據個別病人蛋白質耐受性和所需的每日膳食蛋白攝入量來調整日劑量。

未進行原位肝移植的病人可能需要終身使用本品治療，每日推薦總劑量需根據體表面積計算，範圍為4.5 ml/m²/天至11.2 ml/m²/天，詳見藥品仿單說明書。

禁忌：對Glycerol phenylbutyrate過敏者禁用。禁用於治療急性高氨血症，因為採取更快速降低血氨濃度的干預措施對於急性高氨血症治療至關重要。

副作用：常見（≥1/100且<1/10）不良反應：食慾增加或減退、厭食、頭暈、頭痛和震顫、胃腸脹氣、腹瀉、嘔吐、噁心、腹痛、消化不良、腹脹、便秘、口腔不適、乾嘔、皮膚氣味異常、瘙癢、子宮出血、疲乏、周邊水腫、天門冬氨酸氨基轉移酶升高、丙氨酸氨基轉移酶升高、陰離子間隙升高、淋巴細胞計數下降、維生素D下降。

注意事項：有些病人即使正在接受苯丁酸甘油酯治療，也會出現急性高氨血症(包括高血氨腦病變)；胰腺功能不全或腸吸收不良病人的苯丁酸吸收下降，應密切監測氮濃度；氮濃度正常或偏低的病人（特別是<2月齡的兒童）有不明原因嗜睡、意識模糊、噁心和困倦，應懷疑PAA濃度高；如果合併使用皮質類固醇和苯丁酸甘油酯，如果UCDs病人必須使用Valproicacid與haloperidol，需密切監測氮濃度；Probenecid可能會抑制苯丁酸甘油酯代謝物（包括PAGN）的腎排泄；本品可能會嚴重影響病人開車和使用機器的能力；每日劑量應根據個別病人的尿素合成能力估計值（如有）、氨基酸特徵、蛋白耐受性和促進生長發育所需的每日膳食蛋白攝入量個別調整，再依據血漿氨、穀氨酸酯、U-PAGN及/或血漿PAA和PAGN以及血漿PAA/PAGN比值的監測作進一步的劑量調整。

RAVICTI®
(glycerol phenylbutyrate) Oral Liquid

審批號碼 202407170011

北市衛藥廣字第114080175號



利甫蓋素 濃縮注射液 REPLAGAL[®]

本藥品已由台灣衛生福利部食品藥物管理署依『罕見疾病防治及藥物法』審查通過，列入罕見疾病用藥品項中，用於治療 α -galactosidase A缺乏病人(即法布瑞氏症)提供長期酵素補充治療。

Replagal 三大產品特點



目前市面上唯一人類細胞來源
 α -Gal A enzyme之ERT治療選項^{1,2}



低免疫原性
(Low potential for immunogenicity)²



每兩週一次, 40分鐘即可完成輸注
(every other week)^{1,3}

利甫蓋素濃縮注射液REPLAGAL治療原則



透過手部靜脈緩慢注射至血液中，
稱為「靜脈注射」(或簡稱IV注射)。



靜脈注射至少40分鐘。



一次劑量為每公斤體重0.2mg，
每2週注射一次。



利甫蓋素濃縮注射液REPLAGAL用於
治療法布瑞氏症，提供長期酵素補充治療。



利甫蓋素濃縮注射液REPLAGAL必須經由治療法布瑞氏症病人的醫師
或其他有遺傳代謝疾病相關經驗之專科醫師開立處方。

產品名稱：利甫蓋素濃縮注射液1毫克/毫升 Replagal 1mg/ml Concentration for Solution for Infusion
衛署平苗疫輸字第000004號

組成：1毫升濃縮注射液含1毫克 α -agalsidase，每支3.5毫升濃縮注射液小瓶含3.5毫克 α -agalsidase。
藥商名稱：台灣武田藥品工業股份有限公司

藥商地址：台北市信義區松高路1號17樓

【處方資訊摘要】

適應症：用於治療 α -galactosidase A 缺乏患者 (即 Fabry Disease)，提供長期酵素補充治療。

用法用量：Replagal 一次劑量為每公斤體重 0.2 mg，以靜脈輸注至少 40 分鐘，隔週注射一次。

禁忌症：對主成分或任何賦形劑產生過敏反應者，不可使用。

警語及注意事項：

- 為了增進生物藥品的可追溯性，施用產品的名稱和批號都應被清楚地記錄。
- 在臨床試驗中，13.7% 成人病人對 Replagal 產生特異輸注反應。最常見的症狀有惡寒、頭痛、噁心、發熱、潮紅及疲勞。嚴重的輸注反應並不常見。
- 已有過敏反應之案例報告。假如嚴重過敏或過敏型反應發生，應迅速停止注射 Replagal，並應立即給予適當的處理。
- 所有蛋白質藥品製劑，病人可能會產生對抗此蛋白質之抗體。
- 大範圍的腎臟損傷由於有潛在不可逆的病理變化，可能限制酵素取代療法在腎臟的療效反應。
- 本藥品每瓶含有 14.2 毫克鈉，等同於 WHO 建議最高每日劑量 2 公克鈉的 0.7%。

藥物交互作用：Replagal 不可與 chloroquine、amiodarone、benoquin 或 gentamicin 等藥物一起使用，它們可能會抑制細胞內 α -galactosidase 的活性。

特定的不良反應：在 Fabry disease 病人中，可能包括與心臟結構有關之臨床事件：心律不整 (心房顫動、心室期外收縮、頻脈心律不整)、心肌缺氧、心臟衰竭。最常見的輸注相關反應都屬輕微，包括：寒顫、發熱、(臉) 潮紅、頭痛、噁心、呼吸困難、震顫、搔癢。輸注相關症狀也可能包括：眩暈、多汗、低血壓、咳嗽、嘔吐、疲累。

曾有過敏反應(包括過敏性反應)之案例報告。

<詳細內容請參閱本品核定仿單> Ref: EU202011TW01

References:

1. REPLAGAL EU Summary of Product Characteristics, January 2018.
2. Bekri S. Importance of glycosylation in enzyme replacement therapy. In: Mehta A, et al. editors. Fabry disease: perspectives from 5 years of FOS, Oxford: Oxford PharmaGenesis Ltd. 2006. Chapter 5.
3. Schiffmann R, et al. Nephrol Dial Transplant. 2006;21(2):345-354.

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讓我們能收集更多寶貴的意見與建議。
感謝您為活動提供寶貴的回饋，
期待您的下次參與！



一劑治療， 改寫 SMA 病程

ZOLGENSMA 是治療兩歲以下，經基因確診之 SMA 脊髓性肌肉萎縮症病人，其 SMN2 為 2 或 3 套，只需單劑 1 小時的靜脈注射。

諾健生® 靜脈懸液注射劑 (Zolgensma® Suspension for Intravenous Infusion)，衛部罕菌疫輸字第 000029 號

本藥限由醫師處方使用

適應症治療 兩歲以下，經基因確診之 SMA 脊髓性肌肉萎縮症病人，其 SMN2 為 2 或 3 套，但不適用於已使用呼吸器每天 12 小時以上且連續超過 30 天者。**用量與用法** 應在臨床中心啟動並執行治療，並由具 SMA 病人治療經驗的醫師負責監督。在給予 Zolgensma 前，需要進行基期實驗室檢測，包含：使用經適當驗證的檢測法對 AAV9 抗體進行測試、丙胺酸轉胺酶 (ALT)、天門冬胺酸轉胺酶 (AST)、總膽紅素、白蛋白、凝血酶原時間、部分凝血活酶時間 (PTT) 和國際標準化比值 (INR)、肌酸酐、全血細胞計數 (包括血紅素和血小板計數) 及肌鈣蛋白 I。在確定 Zolgensma 治療的時機時，必須考量在給藥後是否需要密切監測肝臟功能、血小板計數和肌鈣蛋白 I，以及是否需要皮質類固醇治療。在發生急性或慢性未獲控制的活動性感染時，應延遲治療直到感染緩解或得到控制。**用量**：僅適用於單劑靜脈輸注。病人將接受一劑名義劑量為 1.1×10^{14} vg/kg 的 onasemnogene abeparvovec。**免疫調節療程**：第 9 血清型腺相關病毒載體 (AAV9) 殼體的免疫反應會在給予 Zolgensma 後產生。這可能導致肝臟轉胺酶上升、肌鈣蛋白 I 上升、或是血小板計數降低。為了抑制免疫反應，建議使用皮質類固醇進行免疫調節。在可行的情況下，在給予 Zolgensma 輸注前後，應適當調整病人疫苗接種的時程，以因應同時給予的皮質類固醇治療。**禁忌症** 對下列活性物質或任一賦形劑過敏者：氨基三醇、氯化鎂、氯化鈉、泊洛沙姆 188、鹽酸 (調整 pH)、注射用水。**警語及注意事項/不良反應** 追朔性：為改善生物醫療產品追朔性，應明確記錄給藥產品的名稱及批號。對抗 AAV9 的既有免疫力：在 Zolgensma 輸注前，應檢測病人體內是否存在 AAV9 抗體。若 AAV9 抗體效價通報高於 1:50，則可能需要重新檢測。晚期 SMA：Zolgensma 對病人症狀的效益，取決於在接受治療時的疾病負擔程度，早期治療可能會帶來較高的效益。儘管晚期症狀性 SMA 病人將無法達到與未受影響的健康同齡人相同的粗大動作發展，但他們可能會依照治療時疾病的進展，在臨床受益於基因替代療法。免疫原性：輸注 Zolgensma 後，將發生對於第 9 血清型腺相關病毒載體 (AAV9) 殼體的免疫反應，包含生成對抗 AAV9 殼體的抗體，和以 T 細胞為媒介的免疫反應。肝毒性：施用 AAV 載體可能導致轉胺酶上升，其可能是嚴重反應。在接受輸注後，應監測肝臟功能 (AST、ALT、總膽紅素) 至少 3 個月，在其他時間則視臨床指示而定。如果懷疑肝臟損傷，則建議進一步檢查 (例如：白蛋白、凝血酶原時間、PTT 以及 INR)。免疫媒介型肝毒性可能需要調整皮質類固醇的治療療程，包括更長的治疗時間、劑量增加，或將皮質類固醇逐漸減少的時間延長。其他可能會發生以下不良反應：血小板減少症、血栓性微血管病變、肌鈣蛋白 I 上升。載體嵌入 (vector integration) 可能導致致瘤性的理論風險：重組 AAV 有可能發生載體隨機嵌入人類 DNA 中的罕見情況。有關嵌入事件之整體臨床相關性尚不清楚，但理論上可能有導致致瘤性之風險。免疫調節療程：不應在具活動性感染的同時展開免疫調節治療，無論是急性 (例如急性呼吸道感染或急性肝炎) 或未獲控制慢性感染。脫離：發生暫時 Zolgensma 脫離，主要經由身體排泄物排出。應告知照護者及病人家屬下列對於適當處理病人糞便的說明。鈉含量：此藥品每 mL 含有 4.6 mg 的鈉。每瓶 5.5 mL 的小瓶含有 25.3 mg 的鈉，且每瓶 8.3 mL 小瓶含有 38.2 mg 的鈉。不良反應 (僅列出發生頻率 $\geq 1/10$)：肝臟酵素升高。NOVARTIS