ZC4H2 Deficiency
RESEARCH FOUNDATION
hope through science

# 1st International Scientific Meeting on ZC4H2 Deficiency

## 20TH-21ST September
Dubai, United Arab Emirates

In partnership with

the orphan disease center

Penn Medicine

Hosted by

Al Jalila Children's Specialty Hospital
الجليلة للأطفال المستشفى التخصصي

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**ZC4H2 Deficiency Research Foundation**

hope through science

# Participants

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**Michael J. Bamshad, MD, FACMG**
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**Professor Bing-Yu Mao**
Assistant Director
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Chinese Academy of Sciences
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**Dr. Thomas Voets**
Full professor at the KU University of Leuven, Department of Cellular and Molecular Medicine, Chairman of the Laboratory of Ion Channel Research, Group Leader at the VIB Center for Brain & Disease Research, Leuven, Belgium

**Laura Vangeel, MSc**
PhD Student, Laboratory of Ion Channel Research, Department of Cellular and Molecular Medicine, KU University of Leuven
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**John W. Paul**
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Dubai, United Arab Emirates

**Catherine Paul-Fijten**
Co-Founder
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Dubai, United Arab Emirates



# Foreword

Dear Participants,

With great pleasure and gratitude we welcome all the participants to the 1st International Scientific Meeting on ZC4H2 Deficiency. Welcome to our home, Dubai.

A journey of a thousand miles begins with a single step. This meeting is that single first and most important step towards significant and valuable research into the condition that affects our dear daughter Marie-Louise and all other children with ZC4H2 Deficiency worldwide. It is our hope to eventually find therapies that will improve our children's quality of life.

We as parents of a child with ZC4H2 Deficiency, cannot begin to express the appreciation we feel for all the participants to have travelled from all over the world despite their busy schedules to be present here.
The journey that today has started will be a long, but undoubtedly very satisfactory one. There are several aspects which will need to be addressed -such as patient identification, establishing of a patient registry, understanding the clinical aspects, conducting basic research and translational research- to eventually form a homogenized and harmonious plan for the future success of ZC4H2 Deficiency treatment.

Together with the Orphan Disease Center we have tried to come up with an agenda that we feel bests contributes to the most pressing initial stages of understanding of *ZC4H2* and related research. We hope to make this meeting a recurring event and we look forward to the steps that will stem from this first meeting, and that will lead us through those thousand miles of hope.

We would like to specially thank the Orphan Disease Center, under the leadership of Dr. Jim Wilson, for their continued support, to the Al Jalila Children's Hospital for so generously hosting this meeting and believing in our cause, and to the Loulou Foundation for their inspiration, advice and guidance.

We wish you all a successful meeting and a memorable stay in Dubai.

With warm regards,

**John and Cathy Paul**
ZC4H2 Deficiency Research Foundation

# Agenda

## Day 1 - Thursday, September 20th. Basic Biology and Therapeutic Focus

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| 8:45am – 9:00pm | Arrival and Coffee |

Welcome and Introductions

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|---|---|
| 9:05am – 9:15am | ZC4H2 Foundation Welcome<br>John and Cathy Paul |
| 9:15am - 9:20am | Orphan Disease Center Welcome<br>James M. Wilson, MD, PhD |
| 9:20am – 9:30am | Al Jalila Children's Hospital Welcome<br>Dr. Ahmad Abou Tayoun, PhD, FACMG |
| 9:30am – 9:45am | Loulou foundation: inspiration from the parent community<br>Majid and Lynn Jafar |
| 9:45am – 9:55am | Meeting Objectives<br>Vera Kalscheuer, PhD<br>Ashley Winslow, PhD |

Session 1: Overview of ZC4H2 Deficiency and ZC4H2 Genetics/Locus/Mutations
Chair: Vera Kalscheuer, PhD

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| 9:55am – 10:10am | Living with ZC4H2 Deficiency: a brief summary of different phenotypes<br>Cathy Paul, ZC4H2 Foundation |
| 10:10am – 10:30am | Genetic findings on 20 novel families and simplex cases with ZC4H2 deficiency disorder and review of the literature<br>Vera Kalscheuer, PhD |
| 10:30am – 10:50am | The Genetic Basis of Mendelian Conditions: Discoveries, Challenges and Opportunities<br>Michael Bamshad, MD, FACMG |
| 10:50am – 11:00am | BREAK |
| 11:00am – 11:20am | X-inactivation in affected and unaffected female carriers<br>Charles E. Schwartz, PhD |
| 11:20am – 11:50am | Discussion |
| 11:50am – 12:20pm | *Tour of Al Jalila Children's Specialty Hospital* |



Agenda

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| 12:20pm – 1:20pm | LUNCH |

Session 2: Summary of ZC4H2 basic biology
Chair: Dr. Thomas Voets

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| 1:20pm – 1:40pm | ZC4H2 regulates neural patterning through RNF220, an ubiquitin E3 ligase involved in Gli signaling<br>Professor Bing-Yu Mao |
| 1:40pm – 2:00pm | ZC4H2/RNF220 complex is involved in DBX2 degradation, V2-interneuron specification, and movement disorders<br>Cheol-Hee Kim, PhD |
| 2:00pm – 2:20pm | Potential link between TRP channelopathies and ZC4H2<br>Laura Vangeel, MSc<br>Dr. Thomas Voets |
| 2:20pm – 2:50pm | Discussion |
| 2:50pm – 3:05pm | BREAK |

Session 3: Group Discussion: Basic and Translational Research Tools
Chair: Vera Kalscheuer, PhD

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| 3:05pm – 3:25pm | Rapid validation of new patient mutations by rescue experiment using ZC4H2 KO zebrafish; Phenotype-based screen of 2,200 plant extracts using ZC4H2 KO zebrafish<br>Cheol-Hee Kim, PhD |
| 3:25pm – 4:00pm | Discussion |

Session 4: Group Discussion: Therapeutic Discovery
Chair: Ashley Winslow, PhD

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| 4:00pm – 5:15pm | Group Discussion of Therapeutic Opportunities |

# Agenda

## Day 2 - Friday, September 21st. Clinical Focus and Future Steps in ZC4H2 Research

8:45am – 9:00pm — Arrival and Coffee

### Session 5: Clinical Spectrum and Data Collection
Chair: Michael J. Bamshad, MD, FACMG

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|---|---|
| 9:05am – 9:20am | Clinical presentation of child believed to have ZC4H2 mutation/natural history/identify functional differences based on gene mutation<br>Maureen Donohoe, PT, DPT, PCS |
| 9:20am - 9:40am | ZC4H2 deletions in females: Clinical presentation and response to current care and options<br>Michael Binet, PT, DPT, PCS, CFMT, BSPTS |
| 9:40am – 9:55am | Miles–Carpenter Syndrome<br>Charles E. Schwartz, PhD |
| 9:55am – 10:10am | “Wieacker-Wolff Syndrome” controversy - Nomenclature<br>Cathy Paul, ZC4H2 Foundation |
| 10:10am – 10:25am | Patient data collection and sharing: MyGene2<br>Michael Bamshad, MD, FACMG |
| 10:25am – 10:40am | BREAK |

### Session 6: Conclusions
Chair: Vera Kalscheuer, PhD

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|---|---|
| 10:40am – 11:40am | Discussion, Conclusions, and Next Steps<br>Vera Kalscheuer, PhD |
| 11:40am – 11:50am | Meeting Summary<br>James M. Wilson, MD, PhD |
| 11:50am – 12:00pm | Thank You<br>John and Cathy Paul |

# About the Foundation

The ZC4H2 Deficiency Research Foundation was started by John and Catherine Paul, the parents of Marie-Louise, a wonderful little girl who is one of the very few diagnosed cases of ZC4H2 Deficiency, an ultra-rare and often severely affecting genetic condition.
John and Catherine are originally from The Netherlands but they have been calling Dubai home for the last 12 years. It is there where both their daughters were born.

Soon after her birth in 2015, Marie-Louise, was diagnosed as having a de-novo partial deletion of the *ZC4H2* gene. Like most rare diseases, her condition is unfortunately not enough studied and not well understood.

With limited information about Marie-Louise's condition, full of unanswered questions and in desperate need of inexistent effective treatments, the Pauls decided to find the answers by themselves. In 2017, the Pauls were introduced to the Orphan Disease Center (ODC) by their dear friends, the founders of the Loulou Foundation, who also have a little daughter with a rare genetic condition. This family was able to start an incredible movement in the scientific world to bring the condition of their daughter to the forefront of scientific and clinic research. Inspired by the extraordinary research efforts started by their friends and encouraged by the ODC, the Pauls decided to create a formal body to support research on *ZC4H2*: The ZC4H2 Deficiency Research Foundation.

The main purpose of the ZC4H2 Deficiency Research Foundation is to promote and support relevant basic and translational scientific research to find and develop viable therapies for the treatment of ZC4H2 Deficiency.

For this purpose, the Foundation is committed to fund relevant scientific research projects.
Besides the necessary fundraising activities, the Foundation will support the establishment and continuation of those research efforts, identify patients and promote early diagnosis, support the dissemination of information between the patient community and the scientific & medical communities and create general awareness about ZC4H2 Deficiency.
The Foundation partnered with the Orphan Disease Center as its main advisory body for this first event.

In the next 3 years, the Foundation strives to achieve its goals through establishing fundraising activities for allocation of grants to relevant research projects, creating an informative website, funding an open patient registry, organizing scientific and patient meetings and carrying out activities within the community to increase general awareness about ZC4H2 Deficiency.



the orphan disease center

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# About The Orphan Disease Center

The Orphan Disease Center (ODC) at the University of Pennsylvania aims to develop transformative therapies using platform technologies that can be deployed across multiple rare diseases. ODC emphasizes disorders with substantial unmet need independent of their incidence and strives to assure access to patients of all populations.

Each type of orphan disease affects such a small subset of the population, so the need for research and funding in this area is largely unmet. The Orphan Disease Center, the first of its kind, works closely with patient groups and foundations, pharma and biotech, and the academic community. ODC brings a unique set of programs to the table, adding value at any stage - from building the initial knowledge base to enabling therapeutic development. Through grants, Programs of Excellence, International Patient Registries, Jump Start programs, and a number of new initiatives, the ODC seeks to drive therapeutic development for rare diseases. ODC helps to identify and fund the most promising therapeutics while also tackling obstacles present in rare disease drug development.

# About Al Jalila Children's Specialty Hospital

Our meeting's host, Al Jalila Children's Specialty Hospital, is the first and only paediatric hospital in UAE. It caters for children and adolescents up to the age of 18. Inaugurated on November 1, 2016, Al Jalila Children's is an ultramodern hospital with world-class teams of highly qualified healthcare experts that employs SMART technology and designed to enhance patient care and outcomes. The hospital also aims to foster clinical innovations, astute learning and development programmes, and host cutting-edge research facilities. It is a 200-bed facility in a child and family friendly environment.

As the only children's hospital in the United Arab Emirates, Al Jalila Children's aims to be at the forefront of innovation in paediatric healthcare in the region. Medical research is a main pillar within the overall strategy of Al Jalila Children's Specialty Hospital, and hosting the ZC4H2 deficiency falls perfectly within its endeavor to push the boundaries of paediatric medical research to benefit all children.

Al Jalila Children's Specialty Hospital
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# What is ZC4H2 Deficiency?

*ZC4H2* stands for "Zinc finger C4H2-type". *ZC4H2* is a protein-coding gene located on the X-chromosome. This gene encodes a protein which is a member of the so-called zinc finger domain-containing protein family. There is currently very limited understanding about the ZC4H2 gene and its protein function. We refer to any pathogenic variant of *ZC4H2* which is associated with a clinical phenotype as "ZC4H2 Deficiency"*.

The limited research published to date indicates that *ZC4H2* is expressed at various developmental stages and is subject to X-inactivation in females. There are a few families and singletons (males and females) with pathogenic variants of *ZC4H2* described in the medical literature [1,2,5-8]. In the families the variants can be transmitted as an X-linked recessive trait, which means that the disorder is fully expressed predominantly in males, while their carrier female siblings are unaffected or much less severely affected. In contrast to these females, heterozygous de novo variants in *ZC4H2* in singleton females can result in a specific phenotype.

It is believed that the pathogenic variants of *ZC4H2* may result in impairment of the central and peripheral nervous system through the impairment of neurologic development and/or synaptic plasticity[1]. Studies in zebrafish showed that the homologue of human *ZC4H2* is associated with the generation of a specific subset of central nervous system interneurons[2].

Besides the cases described in the current literature, we currently know of 46 additional diagnosed cases of males and females with ZC4H2 Deficiency worldwide, constituting this an ultra-rare orphan disorder.

There is no clear prediction of the phenotypic expression but we know that the disorder can be fully expressed in males, while the clinical presentation in singleton females who have a *de novo* variant can be very variable.

Patients with this condition can have several disabilities and health concerns, including a large array of (neuro) muscular and neurological manifestations. These can include:

- Arthrogryposis Multiplex Congenita (AMC)
- Muscular atrophy of pelvis and lower extremities
- Trunk hypotonia and decreased trunk stability
- Dysphagia
- Respiratory distress
- Joint dislocations of mainly hips
- Elevated muscular tone in lower extremities
- Spasticity
- Dystonia
- Autonomic storms
- Camptodactyly
- Apraxia of speech
- Oculomotor apraxia
- Cortical Visual Impairment
- Epilepsy
- Global developmental delay

There is currently no cure or effective treatment for this condition. Current approach is limited to supportive therapies and interventions.

**The expression of the ZC4H2 mutation is referred by some as "Wieacker-Wolff Syndrome" [3] (in other publications appearing as "Miles-Carpenter Syndrome" [4]). These nomenclatures describe the phenotypes observed in some individuals with a deleterious mutation on the ZC4H2 gene but they do not accurately define the highly varied clinical presentations found among the affected population. Therefore we prefer referring to the condition by its cause, as ZC4H2 Deficiency.*



What is ZC4H2 Deficiency?

## References:


[1] Hirata H, et al. *ZC4H2 mutations are associated with arthrogryposis multiplex congenita and intellectual disability through impairment of central and peripheral synaptic plasticity*. Am. J. Hum. Genet. 2013; 92: 681–695.

[2] May M, et al. *ZC4H2, an XLID gene, is required for the generation of a specific subset of CNS interneurons*. Hum. Mol. Genet. 2015; 24: 4848–4861.

[3] Wieacker P, Wolff G, Wienker TF, et al. *A new X-linked syndrome with muscle atrophy, congenital contractures, and oculomotor apraxia*. Am. J. Med. Genet. 1985; 20:597-606.

[4] Miles JH, Carpenter NJ, et al. *Unique X-linked mental retardation syndrome with fingertip arches and contractures linked to Xq21.31*. Am. J. Med. Genet. 1991; 38:215–223.

[5] Zanzottera C, et al. *ZC4H2 deletions can cause severe phenotype in female carriers*. Am J Med Genet A. 2017; 173(5):1358-1363.

[6] Godfrey ND, et al. *Wieacker-Wolff syndrome with associated cleft palate in a female case*. Am J Med Genet A. 2018;176(1):167-170.

[7] Okubo Y, et al. *A severe female case of arthrogryposis multiplex congenita with brain atrophy, spastic quadriplegia and intellectual disability caused by ZC4H2 mutation*. Brain Dev. 2018;40(4):334-338.

[8] Kondo D, et al. *A novel ZC4H2 gene mutation, K209N, in Japanese siblings with arthrogryposis multiplex congenita and intellectual disability: characterization of the K209N mutation and clinical findings*. Brain Dev. 2018;40(9):760-767.

# Meeting hosts

## John W. Paul

Co-founder
ZC4H2 Deficiency Research Foundation
Dubai, United Arab Emirates

John is the father of Marie-Louise, a ZC4H2 Deficiency patient. He was born in The Netherlands and spent his youth between Florida, USA, and his native Holland. He studied Law at Leiden University, the Netherlands, where he obtained his Master's Degree in Business Law. Following graduation he moved to Saudi Arabia in 1995 where he started his career in the field of hydraulics and industrial equipment and continued working in managerial positions for the trading & contracting industry, and executed, most notably, several projects in the offshore Oil & Gas Industry in Iraq. In 2009 he moved to Dubai where he is now the GM and majority shareholder in the region's largest marine equipment distributor.

John loves spending his free time with his wife Catherine and his little daughters Philippa and Marie-Louise.

## Catherine Paul-Fijten

Co-founder
ZC4H2 Deficiency Research Foundation
Dubai, United Arab Emirates

Catherine Paul-Fijten is the co-founder of the ZC4H2 Deficiency Research Foundation, a private, non-profit foundation created to support research on the condition which affects her 3 years-old daughter, Marie-Louise. Catherine was born in Colombia. She studied Biology at the Leiden University, The Netherlands, where she obtained a double Masters of Science in both Medical Biology and Science-Based Business. She started her career in science working as fellow researcher at the Institute for Applied Sciences in Leiden, The Netherlands, and subsequently at the Laboratory for Molecular Genetics at the National University Hospital, Singapore. She continued her career in the private sector, where she worked for the medical communications and the medical devices businesses in South East Asia, the Middle East and North Africa. There she was involved in marketing, sales and managerial positions.

Catherine has lived in Dubai for the past 12 years. Since 2015, Catherine is full-time mother to her two wonderful daughters, Philippa and Marie-Louise.





# Meeting chair

## Vera Kalscheuer, PhD

Group Leader
Max Planck Institute for Molecular Genetics
Berlin, Germany

Dr. Kalscheuer's expertise, training, knowledge and motivation focuses on the identification of novel genes for intellectual disability (ID) and related disorders as well as on the molecular and functional characterization of genes and proteins for which her research group have established the genetic cause for a better understanding of the underlying pathomechanisms. The group has so far discovered or contributed to the discovery of numerous genes for various forms of ID and their function in the brain, thereby establishing a molecular diagnosis for the patients and their families, and resulting in >85 publications to date. Dr. Kalscheuer's functional work on newly identified ID genes, partly in close collaboration with experts in the respective scientific fields, contributed to understanding the pathological processes and provided new insights into the disease mechanisms. The results will eventually help developing therapeutic interventions. Dr. Kalscheuer's recent publications and contributions to publications in high impact journals reflect the significant impact of her research findings in this important field. Each of these was a major contribution to its respective area of research such as ID, epilepsy and autism.

Dr. Kalscheuer is the principal author of the 2013 paper *"ZC4H2 mutations are associated with arthrogryposis multiplex congenita and intellectual disability through impairment of central and peripheral synaptic plasticity"*

# Meeting co-chair

## Ashley R. Winslow, PhD

Senior Director, Portfolio Development
Orphan Disease Center
University of Pennsylvania
Philadelphia, USA

Ashley Winslow is Senior Director of Translational Research & Portfolio Development at the Orphan Disease Center (ODC) at the University of Pennsylvania. In her current role, Ashley focuses on strategies to address critical gaps in drug development for rare disease by developing innovative solutions and partnerships with international rare disease communities to build and share critical resources. Primary areas of focus for the Center are international patient registries, enabling access to disruptive technologies, funding promising research, and helping foundations and families jump-start their own research portfolio.

Ashley received her PhD in Medical Genetics from the University of Cambridge and completed her postdoctoral work at Massachusetts General Hospital and Harvard Medical School. Before joining the ODC, Ashley was Associate Director of Neurogenetics in the Human Genetics and Computational Biomedicine group at Pfizer where she oversaw use and interpretation of human-derived data across R&D, from early target discovery to clinical development.

## James M. Wilson, MD, PhD

Director, Gene Therapy Program
Rose H. Weiss Professor and Director, Orphan Disease Center
Professor of Medicine and Pediatrics, Department of Medicine
University of Pennsylvania
Philadelphia, USA

James M. Wilson MD, PhD, is a Professor in the Perelman School of Medicine at the University of Pennsylvania where he has led an effort to develop the field of gene therapy. Dr. Wilson began his work in gene therapy during his graduate studies at the University of Michigan over 30 years ago. He then moved to Boston to do a residency in Internal Medicine at the Massachusetts General Hospital and continued his work in gene therapy at MIT. Dr. Wilson has been at the nexus of this emerging therapeutic area from its birth. He created the first and largest academic-based program in gene therapy after being recruited to Penn in 1993. He initially focused on the clinical translation of existing gene transfer technologies but soon redirected his efforts to the development of second and third generation gene transfer platforms; the first of which was licensed to a biotechnology company he founded that resulted in the first, and only, commercially approved gene therapy in the western hemisphere.

More recently, his laboratory discovered a family of viruses from primates that could be engineered to be very effective gene transfer vehicles. These so called "vectors" have become the technology platform of choice and have set the stage for the recent resurgence of the field of gene therapy. Dr. Wilson has also been active in facilitating the commercial development of these new gene therapy platforms through the establishment of several biotechnology companies. He is currently leading a national dialogue on the challenges of commercializing these potentially lifesaving treatments due to the disruptive nature they will have on traditional business models. Throughout his career, the focus of Dr. Wilson's research has been rare inherited diseases, ranging from cystic fibrosis to dyslipidemias to a variety of metabolic disorders.

Dr. Wilson has published over 550 papers, reviews, commentaries and editorials in the peer-reviewed literature and is an inventor on over 117 patents. He was the second President of the American Society of Gene Therapy. Dr. Wilson was the 2014 recipient of the William Osler Patient Oriented Research Award of the University of Pennsylvania and received the 2015 Scientific Achievement Award from Pennsylvania Bio. Dr. Wilson was noted by the journal Nature Biotechnology to be the "second most productive bio-entrepreneur in life sciences." Dr. Wilson is a Trustee at Albion College and founder of a 501(c)3 called Health Through Fitness in Orphan Diseases. He is also the Director of a bicycle team called Rare Disease Cycling, whose participants compete at a national level and help raise money for rare disease research.





## Charles E. Schwartz, PhD

Senior Research Scholar
Greenwood Genetic Center
Greenwood, SC, USA

Dr. Schwartz joined the Greenwood Genetic Center (Greenwood, SC) as the Director of their newly created Molecular Genetics Laboratory in 1985. With the completion of the J.C. Self Research Institute, he became the Director of the Center of Molecular Studies and then Director of Research. After 13 years in that tenure, Dr. Schwartz stepped down as Director of Research and became a Senior Research Scholar at the Center in 2018.

Dr. Schwartz's research interests focuses on the causes of intellectual disabilities and birth defects. For the former, his laboratory concentrated on identifying genes responsible for X-linked intellectual disabilities (XLID) for which his lab cloned 27 XLID genes.

For the past two decades, the laboratory has conducted research into the genetic causes of Autism Spectrum Disorder (ASD), identifying genes being responsible for X-linked syndromes in which autism was a major component.
Currently, Dr. Schwartz is finalizing studies on two novel XLID genes, developing genome wide methylation profiles for various rare genetic syndromes and exploring the utilization of the interconnectivity of various 'omics' to unravel the secrets behind genetic disorders.

Dr. Schwartz holds a PhD in biochemistry from Vanderbilt University.
Together with Prof. Cheol-Hee Kim, Dr. Schwartz made equal senior contribution to the 2015 paper "ZC4H2, an XLID gene, is required for the generation of a specific subset of CNS interneurons".

## Cheol-Hee Kim, PhD

Professor
Department of Biology
Chungnam National University
Daejeon, South Korea

Professor Kim obtained his PhD in neural development from the Osaka University Medical School in Japan. Since 2001, Professor Kim is affiliated to the Chungnam National University in Daejeon, Korea. He has co-authored 140 papers in the fields of developmental genetics and neural development. His group cloned the first ZC4H2 zebrafish model.

Currently, his group is conducting a systematic zebrafish knockout project to validate candidate genes for mental disorders, including intellectual disability and autism.

Together with Dr. Charles Schwartz, Prof. Cheol-Hee Kim made equal senior contribution to the 2015 paper *"ZC4H2, an XLID gene, is required for the generation of a specific subset of CNS interneurons"*.

## Michael J. Bamshad, MD, FACMG

Professor and Chief, Division of Genetic Medicine
Allan and Phyllis Treuer Endowed Chair in Genetics and Development
Department of Pediatrics, University of Washington & Seattle
Children's Hospital
Seattle, USA

Dr. Michael Bamshad is Professor and Chief of Genetic Medicine in the Department of Pediatrics at the University of Washington School of Medicine and Seattle Children's Hospital. He also holds the Allan and Phyllis Treuer Endowed Chair in Genetics and Development. He has studied rare genetic conditions for more than 25 years and he and his colleagues at the University of Washington were the first scientists to use exome sequencing to discover the genetic basis of a rare condition: "Exome sequencing identifies the cause of a mendelian disorder" (2010). He is a principal investigator of the University of Washington Center for Mendelian Genomics, part of a NIH program to identify the genes underlying all rare, Mendelian conditions and has developed innovative ways to share data (i.e., MyGene2) and manage return of genetic testing results (i.e., My46) from exome and whole genome sequencing in both research and clinical settings. He co-authors a popular textbook entitled Medical Genetics.

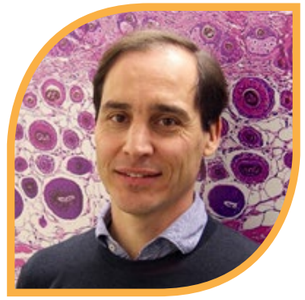
## Professor Bing-Yu Mao

Assistant Director
Kunming Institute of Zoology
Chinese Academy of Sciences
Kunming, China

Dr. Mao's group has been focusing on the molecular mechanisms of neural patterning using mice and Xenopus as animal models. They have identified an ubiquitin E3 ligase, RNF220, as a key regulator of ventral neural patterning through regulation of the nuclear exportation of Gli -the transcriptional effector of Sonic hedgehog signaling (Shh)- (Shh signal gradient plays a key role in the patterning of the neural tube). Loss of RNF220 leads to unique ventral neural patterning defects in mice embryos. Interestingly the group identified ZC4H2 as a regulator of RNF220 stability. Loss of ZC4H2 in both mouse and zebrafish produces similar ventral neural defects to that of RNF220. The group proposes that ZC4H2 regulates neural patterning through RNF220 and Gli signaling.







## Dr. Thomas Voets

Full professor at the KU University of Leuven, Department of Cellular and Molecular Medicine
Chairman of the Laboratory of Ion Channel Research
Group Leader at the VIB Center for Brain & Disease Research
Leuven, Belgium

Since 2010, Prof. Voets is full professor and chairman of the Laboratory of Ion Channel Research within the Department of Cellular and Molecular Medicine at the University of Leuven. Since 2017, he combines this professorship with a group leader position within the VIB-KU Leuven Center for Brain and Disease Research. He has published more than 200 papers in international biomedical research journals. His recent research focuses on Transient Receptor Potential (TRP) ion channels, molecular gateways for ions in the membranes that surround the cells in the human body. The opening and closing of these TRP channels initiates calcium signals and electrical impulses that underlie key processes in various cells and tissues, including the central and peripheral nervous system, the heart, the musculoskeletal system and kidneys. Dysregulation of TRP channel function is the cause of a various severe inherited and acquired human diseases. The central aim of the research team of Prof. Voets is to provide better insight in the aetiology of TRP-related diseases and to use this knowledge to develop novel therapeutic strategies for patients.

## Laura Vangeel, MSc

PhD Student, Laboratory of Ion Channel Research, Department of Cellular and Molecular Medicine
KU University of Leuven
VIB Center for Brain & Disease Research
Leuven, Belgium

Laura Vangeel is a researcher in the field of ion channel research. After an education in biomedical sciences, she enrolled a PhD considering TRP channels under the supervision of Prof. Thomas Voets. These cation channels dominate several signal transduction processes all over the human body, and their electrophysiological activity is studied in every possible aspect. Her personal project focusses on TRPV4, a channel interestingly linked to multiple diseases. Despite the broad and fundamental character of the research, she is convinced it is necessary for the understanding and eventually treatment of diseases. Currently, Laura is finishing her PhD in the laboratory of ion channel research.

## Maureen Donohoe, PT, DPT, PCS

Clinical Specialist, Arthrogryposis Group
Nemours/ Alfred I duPont Hospital for Children
Wilmington, DE, USA

Dr. Donohoe's expertise lies in paediatric orthopaedics. She has been working with contracture disorders for 30 years, as the primary physical therapist in the hospital's Arthrogryposis Program and Osteogenesis Imperfecta Program. She is also Ponseti trained and is the lead physical therapist in the clubfoot clinic.
Dr. Donohoe authored the chapters on arthrogryposis and osteogenesis imperfecta in all five editions of Physical Therapy for Children, authored the Relapsed Clubfoot in Paediatric Clinical Case Studies, and Sports and Recreation in Children with Osteogenesis Imperfecta: Strategies to Enhance Performance. She has lectured nationally and internationally.

Through her extensive clinical exposure with arthrogryposis, Dr. Donohoe has treated and evaluated a number of (possible and diagnosed) cases of ZC4H2 Deficiency in her practice. Together with Prof. Judith Hall, Dr. Donohoe recognized the clinical presentation of ZC4H2 Deficiency as being a separate entity from the thus-far under that group diagnosed classical presentation of arthrogryposis (amyoplasia).

## Michael Binet, PT, DPT, PCS, CFMT, BSPTS

Head of Physical Therapy
High Hopes Pediatric Therapy Center
Dubai, United Arab Emirates

Dr. Binet began practicing as a doctor of physical therapy in 2003 at The Children's Hospital of Colorado, USA where, over an 11-year tenure, he developed expertise in providing care for children with complex medical presentations. He co-founded multiple pediatric subspecialty clinics including The Rett Syndrome Clinic and went on to complete manual therapy certification through The Institute of Physical Arts. In 2014, Mike moved to Delhi, India, where he spent two years training developing manual therapists in an intensive residency format at the Vardan Center. He went on to add certifications in the BSPTS Schroth approach to scoliosis-specific exercise and ABPTS Pediatric specialty certification.





## Dr. Ahmad Abou Tayoun

Director, Genetics Laboratory
Al Jalila Children's Specialty Hospital
Dubai, United Arab Emirates

Dr. Abou Tayoun completed his doctoral studies at Dartmouth College in the USA followed by a fellowship in molecular diagnostics at Dartmouth Medical School. In 2013, he joined Harvard Medical School where he completed his clinical molecular genetics fellowship and in 2015, he became board-certified by the American Board of Medical Genetics and Genomics (ABMGG). Dr. Abou Tayoun is a fellow of the American College of Medical Genetics and Genomics.

Prior to joining Al Jalila Children's, he was a director in the Division of Genomic Diagnostics at the Children's Hospital of Philadelphia, and also an assistant professor of Pathology and Laboratory Medicine at the University Of Pennsylvania Perelman School Of Medicine. To support clinicians in various specialties at CHOP, Dr. Abou Tayoun developed genomic sequencing-based diagnostic tests for a range of pediatric disorders. He also developed and published several tools and assays involving next generation sequencing and variant interpretation. Dr. Abou Tayoun is a co-chair of the Clinical Genome Resource (ClinGen) Hearing Loss Expert Group, and is a member of the ClinGen Sequence Variant Interpretation group. In both capacities, Dr. Abou Tayoun is working with international experts to establish guidelines and recommendations for sequence variant interpretation in general, and in the hearing loss disease area specifically.

## Majid Jafar

Co-founder
Loulou Foundation
Dubai, United Arab Emirates

Majid is CEO of Crescent Petroleum, active in the oil & gas business in the Middle East, and Vice-Chairman of the Crescent Group of Companies, a diversified family business group headquartered in Sharjah in the UAE. Educated at Eton, Cambridge University, and Harvard Business School, Majid is committed to philanthropy in medical research and an active parent advocate and co-founder with his wife Lynn of the Loulou Foundation, a UK private non-profit foundation dedicated to tackling CDKL5 Deficiency Disorder, which affects their eldest daughter Alia. He is a member of the Academy of the University of Pennsylvania and a member of the Board of Fellows of Harvard Medical School, and has been named a Young Global Leader by the World Economic Forum.

## Lynn Barghout Jafar

Co-founder
Loulou Foundation
Dubai, United Arab Emirates

Lynn is the co-founder of Loulou Foundation, a private non-profit UK foundation dedicated to advancing research into the understanding and development of therapeutics for CDKL5 Deficiency, a rare condition. Lynn is a mother of two wonderful girls, one of them with CDKL5 Deficiency. Lynn is also the founder and Managing Mum of High Hopes Pediatric Therapy Center, a leading therapeutic non-profit facility in Dubai where children with moderate to severe special needs are supported through an integrative approach to maximize their potential.

She was selected among the 100 Arab Youth Pioneers in 2018 for the work she achieved at her center, High Hopes, in Dubai. The Arab Youth Pioneers is a prestigious initiative launched under the patronage of His Highness Sheikh Mansour bin Zayed Al Nahyan, Deputy Prime Minister and Minister of Presidential Affairs of the United Arab Emirates. Lynn holds a BA in Business Marketing from the American University of Beirut (AUB) and an MSc in Management and Marketing from CASS Business School in London.

## Samantha M. Charleston

Assistant Director, Orphan Disease Center
University of Pennsylvania
Philadelphia, USA

Samantha Charleston is the Assistant Director of the Orphan Disease Center (ODC) at the University of Pennsylvania. Samantha oversees program development for the Center's grants program, Million Dollar Bike Ride fundraiser, patient advocacy initiatives, scientific symposia and advisory board/KOL meetings. Samantha manages a portfolio of over 50 international grants annually and is chiefly responsible for managing partnerships and communications with patients, foundations and academia. Samantha oversees the Center's marketing and outreach efforts, and interfaces with key stakeholders, caregivers and patients in over 30 rare disease areas to facilitate collaboration that drives research and drug development. Samantha's background is in nonprofit fundraising and program development. She graduated from the Pennsylvania State University with a Bachelor of Arts in Sociology.





## Monique R. Molloy

Executive Director, Orphan Disease Center
Executive Director, Research Administration, Gene Therapy Program
University of Pennsylvania
Philadelphia, USA

Monique Molloy serves as the Executive Director of the Orphan Disease Center at Penn Medicine, a role she took on in 2014. The mission of the Orphan Disease Center is to apply novel therapeutic platforms across a broad array of rare diseases focusing on those with substantial unmet need. The team at the Orphan Disease Center works with over 30 rare disease patient advocacy groups to raise money, advance translational research, and partner programs with biotech/pharma. In addition, Monique serves as the Executive Director of Research Administration for the Gene Therapy Program at Penn, which is capable of translating discoveries into proof-of-concept first in human studies. She has over 20 years of experience providing administrative support to this research effort which currently includes 5 biopharmaceutical alliances and is largely focused on orphan diseases. Monique has a BS in Biology from Villanova University.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