



The 1st International Forum of Fabry Disease

第1回国際ファブリー病フォーラム

Program & Abstract

プログラム & 抄録集

2026 年 Oct. 2, (FRI) 9:00 - 18:30 | Oct. 3, (SAT) 9:00 - 14:20

東京慈恵会医科大学 1 号館 3 階講堂
Tokyo Jikei University School : Main Auditorium

The 1st International Forum of Fabry Disease

第 1 回国際ファブリー病フォーラム

Program & Abstract

プログラム & 抄録集

President: Yoshikatsu Eto

(Southern Tohoku Institute for Neuroscience/The Jikei Univ. School of Medicine)

Vice President: Masahisa Kobayashi

(The Jikei Univ. School of Medicine)

共催: NPO法人日本ライソゾーム病研究センター、国際ライソゾーム病フォーラム、
厚生労働省難治性疾患行政事業ライソゾーム病小林班、財)脳神経疾患研究所

Welcome Message

It is our great pleasure to announce that the 1st International Fabry Disease Forum 2026 will be held over two days, October 2 (Fri) and 3 (Sat), 2026, at the Auditorium of Jikei University School of Medicine in Tokyo.

Fabry disease is the most common of the lysosomal storage disorders and presents with a wide spectrum of clinical manifestations involving the cardiac, renal, and nervous systems, as well as otolaryngological, ophthalmological, and dermatological domains. Its management therefore spans multiple medical specialties. In recent years, remarkable advances have been made in therapeutic development, leading to significant progress in basic research, diagnosis, and treatment.

This Forum will bring together leading researchers from Europe, the United States, Asia, and Japan to engage in active discussions on the latest findings and future perspectives in areas such as basic science, diagnosis, treatment, and newborn screening for Fabry disease. We are confident that the outcomes of this meeting will greatly contribute to the advancement of Fabry disease research and clinical practice in Japan.

By welcoming participants from around the world, we aim to host a highly productive international conference whose achievements will ultimately lead to improved medical care and enhanced social welfare for individuals living with Fabry disease.

We sincerely appreciate your warm support and cooperation in making this Forum a success.

Yoshikatsu Eto, MD, PhD Chair, Organizing Committee
Director, Institute of Advanced Medical Research,
Southern Tohoku Institute for Neuroscience
& Professor Emeritus, Jikei University School of Medicine
Department of Pediatrics, The Jikei University School of Medicine



Masahisa Kobayashi, MD, PhD Vice Chair,
Organizing Committee
Associate Professor, Department of Pediatrics,
The Jikei University School of Medicine



ご挨拶

この度、私どもは「第1回国際ファブリー病フォーラム2026」を、2026年10月2日（金）・3日（土）の2日間、東京慈恵会医科大学講堂にて開催する運びとなりました。

ファブリー病はライソゾーム病の中で最も頻度が高く、心臓・腎臓・神経系をはじめ、耳鼻科・眼科領域、さらには皮膚症状に至るまで多岐にわたる臨床像を呈し、診療は多領域にまたがります。近年は治療法の開発が進み、基礎研究・診断・治療のいずれにおいても大きな進歩がみられています。

本フォーラムでは、ファブリー病の基礎研究、診断、治療、新生児スクリーニングなどを中心に、欧米・アジア・日本の研究者が一堂に会し、最新の知見と今後の展望について活発な議論を行います。本フォーラムで得られる成果は、わが国におけるファブリー病診療および研究の発展に大きく寄与するものと確信しております。

世界各国から多くの参加者を迎え、充実した国際会議を開催し、その成果がファブリー病患者さんの医療の向上と社会福祉の発展に結びつくことを目指しております。

皆さまの温かいご支援とご協力を賜りますよう、心よりお願い申し上げます。

令和8年10月

実行委員長 衛藤 義勝
財)脳神経疾患研究所先端医療研究センター長 &
東京慈恵会医科大学名誉教授



副実行委員長 小林 正久
東京慈恵会医科大学 小児科学講座 准教授



General Information

Title : The 1st International Forum of Fabry Disease

President :

Yoshikatsu Eto(Southern Tohoku Institute for Neuroscience/The Jikei Univ. School of Medicine)

Vice President: Masahisa Kobayashi (The Jikei Univ.School of Medicine)

Venue: Main Auditorium, The Jikei University

Information for Participants

Registration

Registration Fee : Regular (Medical personnel are eligible to apply) : 5,000 JPY

Company (Pharmaceutical industry) : 20,000JPY

Student (with verification card) : 0

The Patient group and Mass media : 0

Banquet : 5,000 JPY

Banquet

October 2nd (Fri.) 19:00-21:00

The Prince Park Tower Tokyo 33F

(4-8-1, Shibakoen, Minato-ku, Toyo, Japan, 105-8563)

Special Thanks

Sponsorship

Platinum:

JCR Pharmaceuticals Co., Ltd. Sanofi K.K. Chiesi Pharma Japan K.K.

Gold:

Amicus Therapeutics K.K.

Silver:

Sumitomo Pharma Co., Ltd. AnGes, Inc.

Copper:

Ultragenyx Japan

Co-sponsored Seminar

JCR Pharmaceuticals Co., Ltd.

Sanofi K.K.

Amicus Therapeutics K.K.

Sumitomo Pharma Co., Ltd.

Advertisement

Takeda Pharmaceutical Company Limited

Amicus Therapeutics K.K.

JCR Pharmaceuticals Co., Ltd.

Sanofi K.K.

Clinigen K.K.

Novartis Pharma K.K.

PTC Therapeutics K.K.

Sekisui Medical Co., Ltd..

The 1st International Forum of Fabry Disease Program

Friday 2nd, October

9:00–9:30

Chair: Robert J. Desnick (Icahn School of Medicine at Mount Sinai, USA)

A-1 Opening and New proposal of Fabry disease after NBS

Yoshikatsu Eto (Southern Tohoku Institute for Neuroscience / The Jikei University School of Medicine, Japan)

9:30–10:30

Chair: Aya Narita (Iseikai International General Hospital, Japan)

Masahisa Kobayashi (The Jikei University School of Medicine, Japan)

A-2 Unique Case Presentations of Fabry disease (15 min x 4)

1) Rescue from sudden ventricular tachycardia and fibrillation using wearable cardioverter-defibrillator in male late-onset Fabry disease patient

Toraaki Okuyama (The Jikei University School of Medicine, Japan)

2) Reduced recurrence of strokes after switching to agalsidase beta in Fabry disease: two case reports

Yoshimi Fujita (The Jikei University School of Medicine, Japan)

3) Clinical Decision Making for Diagnosis and Treatment Initiation in Late Onset Mild Fabry Disease

Kaoru Eto (Tokyo Women's Medical University Adachi Medical Center, Japan)

4) SGLT2 Inhibitors in Fabry Disease: Evidence of Renoprotection from Case-Based and Clinical Analyses

Hayaki Okamoto (Kobe University Graduate School of Medicine, Japan)

10:30–10:40

Coffee Break

10:40–11:20

Co-Sponsored by Sanofi

Chair: Yoshikatsu Eto (Southern Tohoku Institute for Neuroscience /

The Jikei University School of Medicine, Japan)

A-3 Fabry Disease: Major Advances in Delineation, Diagnosis and Treatment

Robert J. Desnick (Icahn School of Medicine at Mount Sinai, USA)

Chair: Motomichi Kosuga (National Center for Child Health and Development, Japan)

Kazuya Tsuboi (Nagoya Central Hospital, Japan)

A-4 Key Points on Fabry Disease and LysoGb3

1) Biomarkers in Fabry disease: Diagnosis and treatment monitoring

Takahiro Tsukimura (Meiji Pharmaceutical University, Japan)

2) A biochemical and pharmacological comparison of three agalsidases approved and used in Japan

Hitoshi Sakuraba (Meiji Pharmaceutical University, Japan)

12:30–13:10 Luncheon seminar Co-Sponsored by JCR

Chair: Torayuki Okuyama (Saitama Medical University, Japan)

A-5 Fabry Disease: Real World Evidence (RWE) of Treatment Outcomes

Roberto Giugliani (Federal University of Rio Grande do Sul, Brazil)

13:20–13:50

Chair: Dau-Ming Niu (National Yang Ming Chiao Tung University, Taiwan)

A-6 1. New Therapy

Splicing Modulation Therapy for Taiwanese Cardiac Fabry Disease (GLA c.639+919G>A)

Tomonari Awaya (Osaka Metropolitan University Graduate School of Medicine, Japan)

13:50–14:30

Chair: Yukio Yuzawa (Vice Chairman, Fujita Academy, Japan)

2. Second Generation Enzyme Replacement Therapy (ERT) for Fabry Disease

David G. Warnock (The University of Alabama at Birmingham, USA)

14:30–15:40

Chair: David G. Warnock (The University of Alabama at Birmingham, USA)

Ohsume Migita (St. Marianna University School of Medicine, Japan)

A-7 Organ Specific Outcomes - Kidney, Heart and Brain

1. Renal Problems

1) The Evolving Landscape of Fabry Nephropathy

Naoki Nakagawa (Asahikawa Medical University, Japan)

2) Increasing knowledge and tools within Fabry nephropathy

Camilla Tøndel (University of Bergen, Norway)

Chair: Hiroyuki Yamakawa (Keio University School of Medicine, Japan)

Katsuya Nakamura (Shinshu University School of Medicine, Japan)

A-8 2. Cardiovascular / CNS events

1) Cardiac Involvement in Fabry Disease: Clinical and Pathological Insights

Koji Higuchi (National Institute of Fitness and Sports in Kanoya, Japan)

2) Non-invasive Assessment of Cardiac Involvement in Fabry Disease Using Multimodality Imaging

Kenichi Hongo (The Jikei University School of Medicine, Japan)

3) Fabry Disease and Stroke

Alessandro Burlina (St. Bassiano Hospital, Italy)

Chair: Takeo Iwamoto (Southern Tohoku Institute for Neuroscience /The Jikei University School of Medicine, Japan)

Roberto Giugliani (Federal University of Rio Grande do Sul, Brazil)

A-9 LysoGb3 as a Biomarker in Fabry disease

Albina Nowak (University Zurich, Switzerland)

Chair: Hiroyuki Ida (The Jikei University School of Medicine, Japan)

A-10 Antidrug antibodies in Fabry disease: Impact and challenges

Malte Lenders (Interdisciplinary Fabry Center (IFAZ), University Hospital Muenster, Germany)

Saturday 3rd, October

9:00–10:20

Chair: Hiroshi Kobayashi (The Jikei University School of Medicine, Japan)

Toya Ohashi (The Jikei University School of Nursing, Japan)

B-1 1) AAV based Gene therapy for Fabry disease with ST-920 as an exemplar

Robert J Hopkin (Cincinnati Children's Hospital Medical Center, USA)

2) Lentivirus-Mediated Gene Therapy for Fabry Disease: Long-Term Results and New Initiatives

Jeffrey A Medin (Medical College of Wisconsin, USA)

10:20–12:50 Co-Sponsored by JCR

Chair: Kimitoshi Nakamura (Kumamoto University Graduate School of Medical Sciences, Japan)

Yin-Hsiu Chien (National Taiwan University, Taiwan)

B-2 Newborn screening of Fabry disease: Workshop

1) Kimitoshi Nakamura (Kumamoto University Graduate School of Medical Sciences, Japan)

2) Takaaki Sawada (Kumamoto University Graduate School of Medical Sciences, Japan)

3) Yin-Hsiu Chien (National Taiwan University, Taiwan)

4) Dau-Ming Niu (National Yang Ming Chiao Tung University, Taiwan)

5) Barbara K Burton (Northwestern University, USA)

13:00–14:10 Luncheon seminar Co-Sponsored by Amicus Therapeutics

Chair: Derrallynn A. Hughes (University College London and Royal Free London NHS Foundation Trust, UK)

Norio Sakai (ISEIKAI International General Hospital, Japan)

B3 Pharmacological Chaperones: New Frontier

1. Clinical response of migalastat for Fabry disease in Japan

Masahisa Kobayashi (The Jikei University School of Medicine, Japan)

2. Alternative disease mechanisms and targets in Fabry disease

Derrallynn Hughes (University College of London and Royal Free London NHS Foundation Trust, UK)

14:10–14:20 Closing Remarks

Masahisa Kobayashi (The Jikei University School of Medicine, Japan)



A1 Opening and New proposal of Fabry disease after NBS

Yoshikatsu Eto

Advanced Clinical Research Center, Southern Tohoku Institute for Neuroscience/The Tokyo Jikei University School of Medicine

Fabry disease has entered a transformative era. Once regarded primarily as a lysosomal storage disorder, it is now understood as a complex metabolic disease involving sphingolipid dysregulation, cellular stress pathways, inflammation, and progressive organ remodeling. The discovery of lyso-GL-3 as a key pathogenic mediator has reshaped our understanding of disease progression and opened new avenues for therapeutic intervention.

The global expansion of newborn screening has further changed the landscape of Fabry disease. Across many countries, the majority of infants identified through screening harbor late-onset variants, fundamentally altering our perception of disease epidemiology. These individuals typically remain asymptomatic in childhood, later developing organ-specific manifestations such as left ventricular hypertrophy, arrhythmias, heart failure, proteinuria, and renal decline. The absence of classical early symptoms underscores the need for new clinical strategies, particularly regarding the timing of intervention in asymptomatic infants detected by screening.

At the same time, therapeutic innovation is accelerating. Enzyme replacement therapy and pharmacological chaperones have laid the foundation for treatment, but the field is rapidly moving toward next-generation modalities. AAV-mediated gene therapy has demonstrated sustained α -Gal A expression and reductions in lyso-GL-3 in early studies, offering the possibility of long-term disease control with a single administration. mRNA therapy, substrate reduction therapy, and non-inhibitory chaperones represent additional promising approaches, each addressing limitations of current treatments.

The First International Fabry Disease Forum brings together leading clinicians, scientists, and innovators from around the world to share new insights, challenge existing paradigms, and shape the future of Fabry disease research and care. As we open this meeting, we stand at the threshold of a new era—one defined by earlier diagnosis, deeper biological understanding, and transformative therapeutic possibilities

CURRICULUM VITAE

Graduated from Jikei University School of Medicine, M.D.

Research Associate, Department of Neurology, University of Pennsylvania,

Assistant Professor, Department of Pediatrics, University of Bern, Switzerland

Adjunct Professor, Department of Pediatrics, Georgetown University School of Medicine

Professor and Head, Department of Gene Therapy, Institute for DNA Medicine Jikei University

Director, Institute for DNA Medicine, Tokyo Jikei University School of Medicine

Professor and Chairman, Department of Pediatrics, Tokyo Jikei University School of Medicine

Board of Director, Jikei University

Professor and Director, Department of Genetics & Genome Science Jikei University

Director, Advanced Clinical Research Center, Southern Tohoku Institute for Neuroscience, 2008-Present

President, Japan Pediatric Society 2003-2007

President, Japanese Society of Inborn Error of Metabolism 1999-2008

Vice President, Japan Society of Gene and Cell Therapy, 2006-2009

International:

Standing Committee Member of International Pediatric Association (2004-2013)

Standing Committee Member of Asian-Pacific Society of Pediatrics, (2003-2009)

President, International Congress of Inborn Error of Metabolism, 2006

Honorary Member of American Society of Pediatrics (2006-Present).



A2-1 Rescue from sudden ventricular tachycardia and fibrillation using wearable cardioverter-defibrillator in male late-onset Fabry disease patient

Toraaki Okuyama¹, Kenichi Hongo¹, Masahisa Kobayashi², Hiroshi Kobayashi³

¹Division of Cardiology, Department of Internal Medicine, The Jikei University School of Medicine Japan

²Department of Pediatrics, The Jikei University School of Medicine Japan

³Division of Gene Therapy, Research Center for Molecular Sciences, The Jikei University School of Medicine, Japan

Lethal ventricular arrhythmia is the most important cause of sudden death in Fabry disease. We report a case of a 42-year-old Fabry disease patient who had suffered from ventricular fibrillation during enzyme replacement therapy. After recovery from successful cardiopulmonary resuscitation, we recommended him to have implantable cardioverter-defibrillator (ICD), however, he refused to have the implantation at that time. We gave him wearable cardioverter-defibrillator at his discharge and he was successfully rescued from ventricular fibrillation. He finally took ICD.

CURRICULUM VITAE

Education

M.D., Jikei University School of Medicine, Tokyo, Japan | March 2014

Professional Experience

Assistant Professor | April 2021 – Present

Division of Cardiology, Department of Internal Medicine, The Jikei University Hospital, Tokyo, Japan

Staff Cardiologist | April 2019 – March 2021

Division of Cardiology, Department of Internal Medicine, The Jikei University Kashiwa Hospital, Chiba, Japan

Staff Cardiologist | April 2018 – March 2019

Department of Cardiology, Saitama Cardiovascular and Respiratory Center, Saitama, Japan

Senior Resident in Cardiology | April 2016 – March 2018

Division of Cardiology, Department of Internal Medicine, The Jikei University Hospital, Tokyo, Japan

Junior Resident | April 2014 – March 2016

Saiseikai Yokohama-city Eastern Hospital, Kanagawa, Japan



A2-2 Reduced recurrence of strokes after switching to agalsidase beta in Fabry disease: two case reports

Yoshimi Fujita¹, Masahisa Kobayashi¹, Hiroshi Kobayashi², Kimihiko Oishi¹

¹Department of Pediatrics, The Jikei University School of Medicine Tokyo, Japan

²Division of Gene Therapy, Research Center for Molecular Sciences, The Jikei University School of Medicine Tokyo, Japan

Background

Enzyme replacement therapy (ERT) is standard care in Fabry disease, however clinical responses may vary among formulations. We report two males with different cerebrovascular outcomes after switching ERT formulations.

Methods

We retrospectively reviewed the charts of two males with Fabry disease, analyzing treatment history, cerebrovascular events, and plasma lyso-Gb3 levels.

Results

Patient 1 developed juvenile ischemic stroke and was diagnosed with Fabry disease at 35 years of age. Despite treatment with agalsidase alfa, he experienced three recurrent strokes between 38 and 43 years. After switching to agalsidase beta at 43, no further cerebrovascular events occurred over 2 years. Plasma lyso-Gb3 levels were reduced from 40–50 to 30–40 ng/mL.

Patient 2 was diagnosed with Fabry disease at 13 years of age. He was initially treated with agalsidase beta, and then switched to agalsidase alfa at 16 years of age. He had three recurrent strokes between 20 and 21 years of age. After switching back to agalsidase beta at 22 years, no further cerebrovascular events occurred over 9 years. Plasma lyso-Gb3 levels decreased from 30–40 to 15–25 ng/mL.

Conclusion

In both patients, no recurrent cerebrovascular events occurred after switching to agalsidase beta, consistent with previous reports suggesting a possible protective effect. Plasma lyso-Gb3 levels paralleled event occurrence, supporting a potential utility as a biomarker of treatment response.

CURRICULUM VITAE

I graduated from The Jikei University School of Medicine in 2021 and obtained my medical license the same year. I completed my initial clinical residency at The Jikei University Katsushika Medical Center (2021–2023), followed by pediatric residency training at The Jikei University Katsushika Medical Center, The Jikei University West Medical Center, and The Jikei University Hospital (2023–2026). In 2026, I was appointed Assistant Professor in the Department of Pediatrics at The Jikei University Hospital, where I currently practice as a pediatrician. I am a member of the Japanese Society for Inherited Metabolic Diseases, the Society for the Study of Inborn Errors of Metabolism (SSIEM), the Japanese Society for Neonatal Screening, and the Japan Pediatric Society.



A2-3 Clinical Decision Making for Diagnosis and Treatment Initiation in Late Onset Mild Fabry Disease.

Kaoru Eto¹, Miyo Munakata², Yoshikatsu Eto², Hisafumi Matsuoka¹

¹Tokyo Women's Medical University Adachi Medical Center, Department of Pediatrics JAPAN

²Advanced Clinical Research Center & Asian LSD Center, Institute of Neurological disorders. JAPAN

Fabry disease (FD) is an X-linked lysosomal storage disorder with classic and late-onset forms, in which genotype strongly influences disease severity and clinical presentation. Recent nationwide newborn screening has revealed many variants of unknown significance and that late-onset FD accounts for over 90% of screen-positive cases, underscoring its predominance and phenotypic variability. These findings highlight the difficulty of determining the optimal timing of disease-specific therapy in late-onset cases.

We present a 26-year-old male carrying the familial *GLA* c.1208T>C (p.L403S) variant, classified as late-onset. His mother was diagnosed with Fabry disease at 33 years after kidney biopsy for proteinuria and started enzyme replacement therapy at 47 years. Reduced GLA activity was detected in the patient at 10 years. During regular follow-up, no apparent cardiac or renal involvement was observed, and plasma lyso-Gb3 levels were only mildly elevated (3–4 ng/mL). Migalastat was initiated at 20 years; after six years, he remains clinically stable and lyso-Gb3 has decreased to 1–2 ng/mL.

The p.L403S variant is a C-terminal, surface-exposed missense change located away from the catalytic site and is thought to cause a moderate reduction in enzyme activity and stability without markedly altering the substrate-binding pocket. This suggests functional impairment mainly through subtle misfolding, enhanced degradation, and reduced lysosomal trafficking. The predominance of late-onset variants emphasizes the need for detailed genotype–phenotype correlation, biomarker refinement, and protein structural analysis, as well as for evidence-based treatment guidelines for late-onset FD.

CURRICULUM VITAE

Education

1995-2001:	Tokyo Women's Medical University, School of Medicine.
2001-2002:	Tokyo Women's Medical University, Department of Pediatrics, Resident.
2001-2005:	Tokyo Women's Medical University, Postgraduate School of Medicine.
2003-2005:	Keio University, School of Medicine. Research fellow
2005- :	Tokyo Women's Medical University, Department of Pediatrics, Assistant Professor.
2009-2011 :	University of California, Los Angeles(UCLA), Department of Pediatrics, Postdoctoral Fellow.
2011-2019 :	Tokyo Women's Medical University, Department of Pediatrics, Assistant Professor.
2019- :	Tokyo Women's Medical University, Department of Pediatrics, Lecturer.
2022- 2025 :	Tokyo Women's Medical University Adachi Medical Center, Department of Pediatrics, Tokyo Women's Medical University, Department of Pediatrics, Lecturer
2025- :	Tokyo Women's Medical University Adachi Medical Center, Department of Pediatrics, Tokyo Women's Medical University, Department of Pediatrics, Associate Professor

Affiliated academic society

Japan Pediatric Society. Specialist
Japanese Society of Pediatric Neurology, Specialist
Human Genetics Society, Clinical Genetics., Specialist



A2-4 SGLT2 Inhibitors in Fabry Disease: Evidence of Renoprotection from Case-Based and Clinical Analyses

Hayaki Okamoto, Shunsuke Goto, Mika Fujita, Hideki Fujii

Division of Nephrology, Kobe University Graduate School of Medicine, Japan

Despite advances in disease-specific therapies, including enzyme replacement therapy and pharmacological chaperone therapy, progressive kidney function loss remains a major clinical challenge in patients with Fabry disease, underscoring the need for adjunctive renoprotective strategies. Sodium–glucose cotransporter 2 (SGLT2) inhibitors have become a cornerstone of chronic kidney disease management; however, evidence regarding their renoprotective effects in Fabry disease remains limited.

This lecture will begin with illustrative cases demonstrating marked improvement in the estimated glomerular filtration rate (eGFR) slope following initiation of SGLT2 inhibitors in patients with Fabry disease and will then present the findings of a longitudinal clinical analysis evaluating changes in kidney function before and after SGLT2 inhibitor therapy. Particular emphasis will be placed on the attenuation of kidney function decline and the distinctive renal response observed in Fabry disease, including the absence of a pronounced initial eGFR dip. Potential mechanisms underlying these observations, their clinical implications, current evidence, study limitations, and future perspectives, including the potential role of SGLT2 inhibitors as adjunctive therapy alongside disease-specific treatment, will also be discussed.

By integrating representative clinical cases with longitudinal clinical evidence, this lecture aims to provide a comprehensive overview of the emerging role of SGLT2 inhibitors in Fabry nephropathy and their potential to improve long-term renal outcomes.

CURRICULUM VITAE

Current Position:

Assistant Professor (Program-Specific), Division of Nephrology and Kidney Center, Kobe University Graduate School of Medicine

Education:

2026 PhD: Kobe University Graduate School of Medicine, Kobe, Japan

2016 MD: Kanazawa Medical University, Ishikawa, Japan

Professional Training and Employment:

April 2026–Present: Assistant Professor (Program-Specific), Division of Nephrology and Kidney Center, Kobe University Graduate School of Medicine, Kobe, Japan

October 2024–March 2026: Assistant Professor (Special Appointment), Division of Nephrology, Kobe University Graduate School of Medicine, Kobe, Japan

April 2020–September 2024: Clinical Staff, Department of Nephrology, Kobe University Hospital, Kobe, Japan

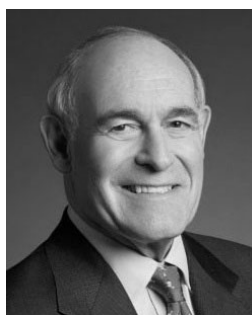
April 2019–March 2020: Clinical Fellow, Department of Internal Medicine, Nishiwaki Municipal Hospital, Hyogo, Japan

April 2018–March 2019: Clinical Fellow, Department of Nephrology, Kita-harima Medical Center, Hyogo, Japan

April 2016–March 2018: Resident, Kobe University Hospital, Kobe, Japan

Membership of Academic Societies:

- The Japanese Society of Internal Medicine
- Japanese Society of Nephrology
- The Japanese Society for Dialysis Therapy
- Japanese Society for Clinical Renal Transplantation
- The Japanese Society of Hypertension
- Japanese Society for Apheresis
- Japanese Society for Peritoneal Dialysis
- American Society of Nephrology
- European Renal Association



A3 Fabry Disease: Major Advances in Delineation, Diagnosis and Treatment

Robert J. Desnick

Icahn School of Medicine at Mount Sinai, USA

Clinical Delineation Advances: First described independently by Dermatologists Johannes Fabry & William Anderson in “classically” affected males (1898). Followed by early reports of systemic manifestations (1900’s), identification of the accumulating substrates GL-3 & GL-2b (1963), classification as a lysosomal storage disease (1965), establishment of X-linked inheritance (1965) demonstration of α -galactosidase deficiency (1967;1970), cloning of the GLA cDNA (1985) & gene (1988), >1250 pathogenic & benign variants (2026), generation of knock-out mice (1996) and distinct “Classic” early-onset and more prevalent “Later-Onset” phenotypes (1981-1991).

Diagnostic Advances: Affected males and heterozygotes diagnosed first by plasma & urinary glycolipid analyses (1970), then by a -Gal A activity (1970f) & definitively by GLA cDNA variants (1985f). Plasma Lyso-Gb3 facilitated diagnosis & provided a disease activity biomarker (2008).

Therapeutic Advances: Intravenous enzyme replacement therapy (ERT) was developed following GLA cDNA cloning (1985), preclinical studies in Fabry knockout mice (1996) & clinical trials in mostly “classic” males (1999-2023). Currently, 3 ERTs are FDA/EMA approved and 3 biosimilars are country specific. Oral chaperone therapy (Migalastat) to increase the activity of residual activity variants was EMA/FDA approved (2016/2018) for residual activity variants. Other therapies in development include substrate inhibition and gene therapy. Successful treatment emphasizes early intervention, dose effectiveness, and monitoring Lyso-Gb3 levels.

CURRICULUM VITAE

Dr. Desnick is Dean for Genetic and Genomic Medicine Emeritus and Professor and Founding Chairman of the Department of Genetics and Genomic Sciences at the Icahn School of Medicine at Mount Sinai in New York City. His main research interests include lysosomal storage diseases (LSDs) and the inherited porphyrias, and in particular their treatment. His LSD research focused on multiple lysosomal disorders. For Fabry disease, his laboratory “firsts” included: developing enzyme and glycosphingolipid diagnostic methods, cloning and characterizing the α -galactosidase A (GLA) cDNA and gene, generating GLA knock-out and transgenic mice, and developing a method to over-express and secrete lysosomal enzymes. These advances led to clinical trials of enzyme replacement therapy (ERT) that resulted in EMA/FDA approval of agalsidase beta (Fabrazyme). His research group similarly developed FDA/EMA-approved ERTs for Niemann-Pick A & B disease (olipidase alfa, Xenpozyme) and for Lysosomal Acid Lipase Deficiency (sebelipase alfa, Kanuma). He co-founded Amicus Therapeutics, which developed FDA/EMA-approved pharmacologic chaperone therapy (migalastat, Galafold) for Fabry disease. In addition, his laboratory developed an FDA/EMA-approved RNAi therapy (givosiran, Givlarri) for the four acute hepatic porphyrias. He has published >615 research papers and >270 chapters in textbooks, and 10 edited books. He is board-certified in Clinical, Biochemical, and Molecular Genetics, and is an elected Member of the National Academies of Sciences, Engineering and Medicine and the National Academy of Inventors.



A4-1 Biomarkers in Fabry disease: Diagnosis and treatment monitoring

Takahiro Tsukimura, Tomoko Shiga, Tadayasu Togawa, Hitoshi Sakuraba

Meiji Pharmaceutical University, Japan

Fabry disease (FD) is an X-linked genetic disorder caused by a deficiency in α -galactosidase A (GLA) activity, leading to the systemic accumulation of globotriaosylceramide (Gb3) and globotriaosylsphingosine (lyso-Gb3). We investigated biomarkers for FD, crucial for diagnosis and monitoring of treatment progress.

In diagnosis of male FD patients, measuring GLA activity and genetic analysis are effective. On the other hand, measuring plasma lyso-Gb3 and urinary Gb3, combined with genetic analysis, is essential for female patients. Furthermore, pathological analyses using biopsy tissues as samples can provide insights. Recently, subjects with *GLA* variants of unknown significance (VUS) have been found through newborn screening. Usually, they are asymptomatic, and their lyso-Gb3 and Gb3 levels remain comparable to those of healthy controls. Therefore, clinical follow-up of them will become very important.

For monitoring of treatment progress, plasma lyso-Gb3 is measured. However, plasma lyso-Gb3 levels at baseline in later-onset type male patients and female patients are only moderately elevated, and their reduction following treatment is often unclear. Additionally, anti-drug antibodies (ADAs) can develop in male patients undergoing enzyme replacement therapy (ERT). As ADAs may cause allergic reactions and reduce therapeutic effectiveness, monitoring of ADA titers during ERT is crucial for these patients.

The results revealed the importance of analyses of biomarkers and ADAs.

CURRICULUM VITAE

Education

2012: Ph.D., Pharmaceutical Sciences
Meiji Pharmaceutical University, Tokyo, Japan

Professional experience

2012-2020: Assistant Professor
Department of Functional Bioanalysis, Meiji Pharmaceutical University, Tokyo, Japan

2018-2019: Postdoctoral Fellow
Department of Genetics and Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, NY, USA.

2020-2025: Lecturer
Department of Functional Bioanalysis, Meiji Pharmaceutical University, Tokyo, Japan

2025-2026: Lecturer
Department of Functional Morphology, Meiji Pharmaceutical University, Tokyo, Japan

2026-present: Associate Professor
Department of Functional Morphology, Meiji Pharmaceutical University, Tokyo, Japan



A4-2 A biochemical and pharmacological comparison of three agalsidases approved and used in Japan

Hitoshi -Sakuraba¹, Takahiro -Tsukimura¹, Tomoko Shiga¹,
Tadayasu Togawa¹, Yasunori Chiba², Youichi Tajima³, Seiji-
Saito⁴

¹Meiji Pharmaceutical University, Japan

²National Institute of Advanced Industrial Science and Technology, Japan

³Tokyo Metropolitan Institute of Medical Science, Japan

⁴Hokkaido Information University, Japan

To compare the biochemical and pharmacological properties of three recombinant human α -galactosidase A drugs (agalsidases) approved and used in Japan, we performed *in vitro*, cell, and animal experiments.

The results revealed that there were no differences in the kinetic parameters and enzyme activity between these agalsidases. But their affinity for domain 9 of cation-independent mannose 6-phosphate receptor (CI-M6PR), which exists in various cells, was higher in the order: agalsidase beta biosimilar 1 (agalsidase beta BS) > agalsidase beta > agalsidase alfa, which almost coincided with the experimental results regarding the efficiency of their incorporation into cultured fibroblasts derived from a Fabry mouse. The animal experiments using Fabry mice revealed that the incorporation of the agalsidases into the kidneys and heart, where CI-M6PRs are widely distributed, was efficient in the order: agalsidase beta/agalsidase beta BS > agalsidase alfa, which reflected the degree of reduction of glycosphingolipids accumulated in the organs/tissues. On the other hand, no differences in the efficiency of their uptake or reduction of the accumulated substances were observed in the liver, probably due to asialoglycoprotein receptors expressed on the surface of hepatocytes.

This information will be useful for developing new recombinant enzymes for enzyme replacement therapy of Fabry disease by modification of the sugar chains and protein portion.

CURRICULUM VITAE

Hitoshi Sakuraba, MD, PhD

Birth: July 25, 1947

2025 Retired from Meiji Pharmaceutical University

2013 Professor, Department of Clinical Genetics, Meiji Pharmaceutical University, Tokyo, Japan.

2007 Professor, Department of Analytical Biochemistry, Meiji Pharmaceutical University, Tokyo, Japan.

1988 Director, Department of Clinical Genetics, The Tokyo Metropolitan Institute of Medical Science, Tokyo Metropolitan Organization for Medical Research, Tokyo, Japan.

1986 Assistant Professor (Visiting), Department of Pediatrics, Mount Sinai School of Medicine, New York, NY, U.S.A.

1981 Research Fellow, National Research Center of Neurology, Tokyo, Japan.

1977 Assistant Professor, Department of Pediatrics, The University of Tokyo, School of Medicine, Tokyo, Japan.

1976 Doctor, Department of Pediatrics, Kanto Rosai Hospital, Kawasaki, Japan.

1975 Doctor, Department of Pediatrics, Tora-no-Mon Hospital, Tokyo, Japan.

1974 Trainee Doctor, Department of Pediatrics, The University of Tokyo Hospital, Tokyo, Japan

1974 Graduated from The University of Tokyo, Faculty of Medicine, School of Medicine, Tokyo, Japan

Specialty: Lysosomal disease.



A5 Fabry Disease: Real World Evidence (RWE) of Treatment Outcomes

Roberto Giugliani

UFRGS, HCPA, DASA and CASA DOS RAROS

Fabry disease is an X-linked condition caused by pathogenic variants in the *GLA* gene, leading to the deficiency of the lysosomal enzyme alpha-galactosidase A and widespread accumulation of its substrate, globotriaosylceramide (Gb3). The disease is progressive and characterized by skin angiokeratomas, neuropathic pain, gastrointestinal disturbances, kidney failure, hypertrophic cardiomyopathy, arrhythmias, stroke and several other manifestations. Both hemizygous males and heterozygous females are affected, being the manifestations in females more variable due to different patterns of X-inactivation, among other factors. The first specific treatment - enzyme replacement therapy - became available in 2001. Therapy with pharmacological chaperones was also approved for patients with amenable mutations, and several other therapeutic strategies are currently in clinical development, including substrate reduction therapy and genetic therapies. Real world evidence generated in the last 25 years by the observation in patients, untreated or treated with different therapeutic strategies, allowed some conclusions about the impact of the therapy on renal, cardiac, CNS and other endpoints. There are many indications about the benefits of early introduction of therapy in symptomatic patients. However, despite neonatal screening programs are in place in several parts of the world, there is still no consensus on the start of therapy in asymptomatic patients. In general, therapy brings several measurable benefits, increasing quality of life and survival. The controversial benefits in patients with advanced disease, the need of regular intravenous infusions or continuous administration of oral medication, associated with the high cost of these therapies, are some of the challenges still to be addressed.

CURRICULUM VITAE

Dr. Roberto Giugliani is a Professor at the Postgraduate Program in Genetics and Molecular Biology of the Federal University of Rio Grande do Sul (UFRGS) and Member of the Medical Genetics Service of Hospital de Clinicas (HCPA), in Porto Alegre, Brazil. He is also Head of Rare Diseases at Dasa Genomics, and Executive Director of "Casa dos Raros", a center of excellence for rare diseases in Brazil. He earned his MSc and PhD Degrees at the University of Sao Paulo (Brazil) and did post-doctoral trainings in London, Genova, Paris, Zurich, Oakland, Sydney, Tokyo and Heidelberg. He was past President of the Brazilian Society of Medical Genetics and Genomics and the Latin American Network of Human Genetics (RELAGH), and former Director of the WHO Collaborating Center for the Development of Genetic Services in Latin America. He is also a member of 13 scientific societies, including the Brazilian Academy of Sciences, and is the current vice-president of the Latin American Society of Inborn Errors of Metabolism and Neonatal Screening. Dr. Giugliani's research interests are in the field of inborn errors of metabolism, particularly in lysosomal disorders and neonatal screening. He was granted with the "Life for MPS Award" by ISMPS and with the "Garrod Award" by ISNS. He has supervised the post-graduate studies of more than 100 MSc/PhD graduates and is author of more than 600 papers indexed in PubMed.



A6-1 Splicing Modulation Therapy for Taiwanese Cardiac Fabry Disease (GLAc.639+919G>A)

Tomonari Awaya, Masatoshi Hagiwara¹

Department of Anatomy and Regenerative Biology, Osaka Metropolitan University

¹Department of Drug Discovery Medicine, Kyoto University

Fabry disease caused by the deep intronic *GLA* variant c.639+919G>A is a common late-onset cardiac form of Fabry disease in Taiwan, resulting from a founder effect. This variant activates a cryptic 57-nucleotide pseudoexon containing a premature termination codon, leading to aberrant RNA splicing, reduced α -galactosidase A expression, and progressive cardiac involvement.

Because the primary pathogenic mechanism is RNA mis-splicing, this disease represents an attractive target for RNA-directed therapies.

We have developed a small-molecule splicing modulation strategy aimed at suppressing pseudoexon inclusion and restoring normal *GLA* expression. Our original compound, RECTAS, corrected aberrant splicing and increased α -galactosidase A activity in patient-derived cells. Subsequent medicinal chemistry optimization led to the development of RECTAS-2.0, a more potent and effective next-generation splicing modulator.

Using patient-derived induced pluripotent stem cell (iPSC)-derived cardiomyocytes, we demonstrated correction of aberrant splicing, restoration of alpha-galactosidase (α -GAL) expression, and recovery of enzyme activity. In addition, a transgenic mouse model carrying the human *GLA* c.639+919G>A variant enabled evaluation of *in vivo* efficacy, demonstrating successful correction of cardiac *GLA* splicing following oral administration of RECTAS-2.0.

This presentation will review the molecular basis of *GLA* c.639+919G>A-associated cardiac Fabry disease, summarize recent advances in small-molecule splicing modulation therapy, and discuss future prospects for RNA-targeted therapeutic development in Fabry disease and other splicing disorders.

CURRICULUM VITAE

Professor Tomonari Awaya is a physician-scientist specializing in rare genetic disorders. He graduated from Kyoto University School of Medicine in 2003. After completing his pediatric residency at Nagoya City University, he returned to Kyoto University for specialty training in pediatric neurology and clinical genetics in the Department of Pediatrics under the mentorship of Professors Tatsutoshi Nakahata and Toshio Heike. He earned his PhD in Medicine in 2013 for his research on skeletal muscle differentiation from embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs), while continuing clinical practice focused on rare genetic disorders, including lysosomal diseases.

In 2016, he joined the Department of Anatomy and Developmental Biology at Kyoto University under Professor Masatoshi Hagiwara, where his research focused on RNA splicing and RNA-targeted therapeutic development. He was appointed Associate Professor at the Center for Anatomical Studies, Kyoto University, in 2024, and became Professor of Anatomy and Regenerative Biology at Osaka Metropolitan University in 2026.

His research interests include disease modeling using patient-derived iPSCs, elucidation of disease mechanisms, development of novel therapeutics for rare genetic disorders, and fundamental studies of RNA splicing mechanisms. In addition to his research activities, he is actively engaged in medical education in histology, embryology, and clinical anatomy.



A6-2 Second Generation Enzyme Replacement Therapy (ERT) for Fabry Disease

David Gene Warnock, MD¹, Rizwana Islam, PhD²

¹University of Alabama at Birmingham, Alabama USA

²Crosswalk Therapeutics, Cambridge Massachusetts USA

ERT has been used for Fabry Disease for over 20 years. Clinical outcomes have improved but anti-drug antibodies (ADA), limited bioavailability, short plasma and intracellular half-lives are important limitations.

Second generation ERTs are available (PEG-Unigalsidase (PG); Chiesi Pharma) or are being developed (CWTx; Crosswalk Therapeutics). These new agents have better biodistribution, and in vivo stability, and are less immunogenic. PG is produced in a plant cell system and the glycosylation lacks terminal mannose-6-PO₄ groups, which reduces liver uptake by 50 % and improves distribution of the enzyme to more relevant target organs. CRTx incorporates a 15 kD single domain antibody fragment that targets the transferrin receptor and greatly enhances ERT uptake into relevant target cells (kidney, heart, GI-tract and brain).

PG is PEGylated, and CWTx has been mutated. These changes improve in vivo stability and prolong plasma and intracellular half-lives compared to first generation ERTs. Longer plasma half-lives permit meaningful PK studies. Longer intracellular half-lives support confocal co-localization of ERT with extra- and intracellular substrate (GB3) accumulation.

Immunogenicity is reduced by PEGylation of epitopes with PG, and mutational deletion with CWTx. These changes blunt immune responses in patients who have pre-formed ADAs against first-generation ERTs, and may also impact on T-cell functions related to antigen recognition and tolerance induced by repeated ERT exposure.

CURRICULUM VITAE

Dr. David Warnock received a BA degree in 1966 from the University of California at Berkeley and received his MD degree in 1970 from the University of California, San Francisco. Following a fellowship at the NIH, his positions included Section Chief at the San Francisco VA Medical Center, Director of Nephrology at the University of Alabama at Birmingham (UAB) from 1988 to 2008, and Director of the Office of Human Research at UAB from 2005 to 2008.

He served as the Marie K Ingalls Professor of Medicine and the Hilda B. Anderson Endowed Professor in Nephrology at UAB, and became an Emeritus Professor of Medicine at UAB in October 2015.

Dr Warnock's focus is on the genetic and environmental factors that contribute to hypertension and chronic kidney disease. The spectrum extends from basic studies of salt and water transport systems to population-based studies of the prevalence of CKD and the association with stroke and heart disease. Additional research interests include acid-base physiology, sodium transport mechanisms, chronic kidney disease, diabetes and kidney disease, and inherited renal diseases.

A major focus has been inherited renal disease, with a current emphasis on Fabry disease. Dr. Warnock was a Founding Member and Chair of the Organizing Committee for the biannual Update on Fabry Disease Conference which began in Bergamo, Italy in 2007, with the 9th Update on Fabry Disease held in Bologna, Italy (June 6-9, 2026).



A7-1 The Evolving Landscape of Fabry Nephropathy

Naoki Nakagawa

Asahikawa Medical University

Fabry disease (FD) is a progressive lysosomal storage disorder in which delayed diagnosis remains a major barrier to timely disease-specific therapy. Pathological studies have shown that globotriaosylceramide accumulation and podocyte injury precede overt proteinuria or decline in kidney function, highlighting the important role of kidney biopsy in detecting early renal involvement. Among emerging non-invasive diagnostic tools, urinary mulberry bodies have gained recognition as biomarkers of renal glycosphingolipid accumulation and can be detected before renal dysfunction develops. Moreover, molecular imaging flow cytometry markedly improves the sensitivity of mulberry body detection compared with conventional microscopy, expanding the role of urinary cytology in early diagnosis and targeted high-risk screening.

In addition, evidence suggests that FD may remain unrecognized among patients receiving dialysis, particularly those with an unknown underlying kidney disease. Identification of these index patients through high-risk screening also enables cascade family screening, facilitating early diagnosis in younger affected relatives.

The diagnostic landscape of Fabry nephropathy is shifting from reliance on established clinical manifestations toward earlier detection through integrated pathology, urinary biomarkers, and targeted high-risk screening. These evolving strategies may facilitate timely therapeutic intervention and improve long-term renal and cardiovascular outcomes.

CURRICULUM VITAE

EDUCATION

M.D., Jichi Medical University, Japan | 1997

PROFESSIONAL EXPERIENCE

Professor | 2024–Present

Division of Cardiology and Nephrology, Department of Internal Medicine, Asahikawa Medical University, Hokkaido, Japan

Visiting Scientist in Nephrology | 2012–2014

Division of Nephrology, University of Washington, Seattle, WA, USA

Clinical Research Fellow | 1997

First Department of Internal Medicine, Asahikawa Medical University, Hokkaido, Japan



A7-2 Increasing knowledge and tools within Fabry nephropathy

Camilla Tøndel

Department of Clinical Science, University of Bergen, Norway

Fabry nephropathy may lead to kidney failure through reduced α -galactosidase A activity, globotriaosylceramide (Gb3) accumulation and increasing tissue damage (1). Rapid advances in experimental modeling and emerging therapeutic strategies have dramatically reshaped understanding and treatment prospects for Fabry nephropathy (2-5). These insights challenge the traditional paradigm by highlighting various contributors, such as lyso-Gb3, α -synuclein accumulation etc as well as cellular dysfunction and may open new doors to track disease course or treatment efficacy and potential targets for adjunct pharmaceutical treatment.

1. Clinical relevance of globotriaosylceramide accumulation in Fabry disease and the effect of agalsidase beta in affected tissues. Tøndel C, Thurberg BL, DasMahapatra P, Lyn N, Maski M, Batista JL, George K, Patel H, Hariri A. *Mol Genet Metab*. 2022 Dec;137(4):328-341. doi: 10.1016/j.ymgme.2022.10.005. Epub 2022 Oct 29.
2. Development of an automated estimation of foot process width using deep learning in kidney biopsies from patients with Fabry, minimal change, and diabetic kidney diseases. Smerkous D, Mauer M, Tøndel C, Svarstad E, Gubler MC, Nelson RG, Oliveira JP, Sargolzaeiaval F, Najafian B. *Kidney Int*. 2024 Jan;105(1):165-176. doi: 10.1016/j.kint.2023.09.011. Epub 2023 Sep 27.
3. Systems analyses of the Fabry kidney transcriptome and its response to enzyme replacement therapy identified and cross-validated enzyme replacement therapy-resistant targets amenable to drug repurposing. Delaleu N, Marti HP, Strauss P, Sekulic M, Osman T, Tøndel C, Skrunes R, Leh S, Svarstad E, Nowak A, Gaspert A, Rusu E, Kwee I, Rinaldi A, Flatberg A, Eikrem Ø. *Kidney Int*. 2023 Oct;104(4):803-819. doi: 10.1016/j.kint.2023.06.029. Epub 2023 Jul 5.
4. Accumulation of α -synuclein mediates podocyte injury in Fabry nephropathy. Braun F, Abed A, Sellung D, Rogg M, Woidy M, Eikrem O, Wanner N, Gambardella J, Laufer SD, Haas F, Wong MN, Dumoulin B, Rischke P, Mühlhig A, Sachs W, von Cossel K, Schulz K, Muschol N, Gersting SW, Muntau AC, Kretz O, Hahn O, Rinschen MM, Mauer M, Bork T, Grahammer F, Liang W, Eierhoff T, Römer W, Hansen A, Meyer-Schwesinger C, Iaccarino G, Tøndel C, Marti HP, Najafian B, Puelles VG, Schell C, Huber TB. *J Clin Invest*. 2023 Jun 1;133(11):e157782. doi: 10.1172/JCI157782
5. Modeling Fabry nephropathy: insights from experimental systems towards precision nephrology. Elsaid H, Furriol J, Eikrem Ø, Tøndel C, Svarstad E. *Dis Model Mech*. 2026 May 1;19(5):dmm052716. doi: 10.1242/dmm.052716. Epub 2026 May 29.

CURRICULUM VITAE

Camilla Tøndel has been following children and adults with Fabry disease since 2001 in a multidisciplinary team with a special focus on functional and structural aspects of Fabry nephropathy. She is professor of paediatrics at the University of Bergen and physician at Haukeland University Hospital, Bergen, Norway. She is heading the hospitals paediatric clinical trials unit and works as senior consultant at the pediatric nephrology and rheumatology unit. Since 18 years she has been national principle investigator of multiple clinical trials on new treatment approaches within Fabry disease.



A8-1 Cardiac Involvement in Fabry Disease: Clinical and Pathological Insights

Koji Higuchi

National Institute of Fitness and Sports in Kanoya

Fabry disease is an X-linked lysosomal disorder caused by deficiency of α -galactosidase A (α -Gal A), resulting in the accumulation of globotriaosylceramide (GL-3) in lysosomes of various cell types throughout the body. Although Fabry disease affects multiple organ systems, cardiac involvement is one of the most important determinants of prognosis.

We have been actively engaged in the diagnosis and investigation of Fabry cardiomyopathy. In this lecture, we will review the historical development of our work on Fabry cardiomyopathy and provide an overview of its clinicopathological characteristics based on our accumulated clinical experience.

Cardiac manifestations of Fabry disease include left ventricular hypertrophy, arrhythmias, and valvular heart disease. The underlying pathology is characterized by the accumulation of GL-3 within vascular endothelial cells and cardiomyocytes. Notably, we have encountered patients in whom GL-3 deposition in myocardial tissue had already progressed before the onset of overt clinical manifestations. These histopathological findings in the preclinical stage provide valuable evidence supporting the importance of early diagnosis and timely therapeutic intervention.

Through these clinical experiences, we will discuss the importance of early diagnosis of Fabry disease, appropriate therapeutic intervention, and continuous long-term follow-up with comprehensive evaluation of multiple organ systems.

CURRICULUM VITAE

2025-present	Associate Professor, Faculty of Sports and Life Science, National Institute of Fitness and Sports in KANOYA, Kagoshima, Japan.
2024-2025	Associate Professor, Department of Cardiovascular Medicine and Hypertension, Kagoshima University, Kagoshima, Japan.
2023-2024	Lecturer, Department of Therapeutic Strategy for Heart Failure, University of Tokyo, Tokyo, Japan.
2022-2023	Lecturer, Department of Cardiovascular Medicine and Hypertension, Kagoshima University, Kagoshima, Japan.
2015-2022	Assistant Professor, Department of Cardiovascular Medicine and Hypertension, Kagoshima University, Kagoshima, Japan.
2014-2015	Chief physician, Department of Cardiovascular Medicine, National Hospital Organization Kagoshima Medical Center, Kagoshima, Japan.
2006-2012	Assistant Professor, Division of Cardiac Repair and Regeneration, Kagoshima university, Kagoshima, Japan.
2003-2006	Research scholar, Ontario Cancer Institute, University Health Network, Toronto, Canada.



A8-2 Non-invasive Assessment of Cardiac Involvement in Fabry Disease Using Multimodality Imaging

Kenichi Hongo

Division of Cardiology, Department of Internal Medicine, The Jikei University School of Medicine

Cardiac involvement is a major determinant of prognosis in Fabry disease, as cardiovascular complications account for more than half of all deaths. We established a non-invasive approach for assessing cardiac involvement using multimodality imaging. On electrocardiography, we found that a shortened PQ interval minus P-wave duration in lead II (Pend-Q) is a specific finding in patients with Fabry disease. In addition, strain pattern in the absence of left ventricular hypertrophy (LVH) was useful for identifying female patients. On echocardiography, the left ventricular mass index was significantly correlated with age in both male and female patients with Fabry disease. Overt LVH developed from the third decade of life in male patients and from the fifth decade in female patients. Speckle-tracking echocardiography demonstrated that longitudinal strain could detect early left ventricular systolic dysfunction. On cardiac magnetic resonance imaging, late gadolinium enhancement (LGE) in the posterolateral wall of the left ventricle reflected myocardial damage in the advanced stage of the disease. Native T1 values effectively differentiated Fabry disease from hypertrophic cardiomyopathy, particularly in male patients. Furthermore, in patients without LGE, native T1 values reflected the degree of glycosphingolipid accumulation in the left ventricle. In conclusion, multimodality non-invasive imaging provides an effective approach for evaluating cardiac involvement in Fabry disease.

CURRICULUM VITAE

Field of Research: Cardiology

Education

1980-1986 MD The Jikei University School of Medicine

1988-1992 PhD The Jikei University School of Medicine

Professional Experience

1986-1988 Medical Intern, The Jikei University School of Medicine

1992-1993 Resident in Internal Medicine, The Jikei University School of Medicine

1993-1995 Post Doctoral Research Fellow, University of Leeds, UK

1995-1996 Resident in Cardiology, The Jikei University School of Medicine

1997-2007 Assistant Professor in Cardiology, The Jikei University School of Medicine

2007-2014 Associate Professor in Cardiology, The Jikei University School of Medicine

2014- Professor in Cardiology, The Jikei University School of Medicine

Recent Related Publications (5 Papers)

1. Nojiri A...**Hongo K.** Role of Longitudinal Strain in the Evaluation of Contractile Dysfunction in Japanese Fabry Disease Patients. *Circ J.* 2024;89(1):53-61.

2. **Hongo K.** Cardiac involvement in Fabry disease - A non-invasive assessment and the role of specific therapies. *Mol Genet Metab.* 2022;137(1-2):179-86.

3. Anan I...**Hongo K.** The role of native T1 values on the evaluation of cardiac manifestation in Japanese Fabry disease patients. *Mol Genet Metab Rep.* 2022;31:100858.

4. Morimoto S...**Hongo K.** Characteristics of the Electrocardiogram in Japanese Fabry Patients Under Long-Term Enzyme Replacement Therapy. *Front Cardiovasc Med.* 2021;7:614129.

5. Nojiri A...**Hongo K.** Clinical findings of gadolinium-enhanced cardiac magnetic resonance in Fabry patients. *J Cardiol.* 2020;75(1):27-33.



A8-3 Fabry Disease and Stroke

Alessandro P. Burlina

Neurology Unit, Dept. of Medicine, St. Bassiano Hospital, Bassano del Grappa, Italy

Stroke is a serious clinical manifestation and the first cause of disability in Fabry disease. We assessed the incidence of stroke among agalsidase beta-treated (1.0 mg/kg every other week) patients compared to untreated patients, enrolled in the Fabry Registry as of October 2024. Agalsidase beta-treated patients who were stroke-free at the time of treatment initiation were 1:1 matched with untreated patients by sex, phenotype, and age. Untreated patients were eligible for matching if they had developed Fabry disease symptoms and were stroke-free by the treatment initiation age of a treated patient. Patients were followed up until the occurrence of a stroke, switch to alternative therapy (if treated), treatment initiation (if untreated), or the end of registry follow-up, whichever occurred first. Cox proportional hazards regression models conditioned on matched pairs were used to estimate hazard ratios (HRs) and 95% confidence intervals (CI) for stroke. The analysis included 1626 matched pairs of patients (51.7% males, 48.3% females, 82.8% classic, 17.2% later-onset). Median age at diagnosis was 30.9 and 33.8 years for treated and untreated patients, respectively. After a median follow-up of 6.0 (3.6, 9.0) years for treated patients and 3.2 (1.8, 5.6) years for untreated patients, 60 treated and 88 untreated patients experienced their first stroke, mainly ischemic strokes. Agalsidase beta-treated patients had a significantly lower risk of stroke compared to untreated patients (HR=0.29; 95% CI: 0.17, 0.48). Results remained consistent after adjusting for history of renal and cardiac events, and use of concomitant drugs (ex. antiplatelets). In conclusion, agalsidase beta-treated patients with Fabry disease may have significantly lower risk of developing stroke compared to untreated patients (71% lower risk in the studied population).

CURRICULUM VITAE

Dr. Alessandro P. Burlina MD, PhD is an adult neurologist. He is Director of the Department of Medicine and the Neurology Unit at St. Bassiano Hospital in Bassano del Grappa, Italy.

Dr. Burlina graduated from the University of Padua in 1985. In 1989 he obtained the specialization in Neurology and in 1995 he obtained his doctorate in Neurological Sciences. Since then, he has held positions at the Center for Neurochemistry of the Nathan S. Kline Institute for Psychiatric Research, New York University, USA; the Department of Neurology at Yale University, School of Medicine, USA; the Department of Biophysical Chemistry, Biozentrum, University of Basel, Switzerland; and the Department of Neurology, University Hospital of Padua, Italy.

His clinical and scientific work focuses on neurological complications of neurometabolic hereditary diseases in adults, especially Fabry disease and phenylketonuria. Dr. Burlina is author and co-author of more than 120 peer-reviewed articles and 12 book chapters in the field of Neurometabolic hereditary diseases, Neurology and Neuroscience. In 2018 he edited the book entitled "Neurometabolic Hereditary Diseases of Adults"



A9 LysoGb3 as a Biomarker in Fabry disease

Albina Nowak

University Hospital of Zurich, Switzerland

Fabry disease (FD) is a rare X-linked glycosphingolipid storage disease and a result of mutations in the α -galactosidase A gene (GLA), which leads to reduced activity of the encoded lysosomal exoglycohydrolase, α -galactosidase A (α -Gal A). The α -Gal A defect causes the progressive accumulation of globotriaosylceramide (Gb3) and other related glycosphingolipids in lysosomes of patients affected with FD.

The deacylated derivative of Gb3, globotriaosylsphingosine (Lyso-Gb3), has been identified as a hallmark of FD. Lyso-Gb3 has been described as a helpful tool for newborn and high-risk group screening, for diagnosis, as a biomarker for phenotypic assignment, a tool reflecting disease severity, therapeutic monitoring and risk predictor for severe clinical events. Further organ-specific biomarkers for kidney and heart function have been identified for the disease progress monitoring.

CURRICULUM VITAE

Since 10.2010	Attending Physician at the University Hospital Zurich at the Departments of Endocrinology, Nephrology and Internal Medicine, 50% workload since January 2018
Since 01.2018	Chief Physician in the Internal Medicine Service, Psychiatric University Hospital Zurich, 50% workload
09.2008 – 11.2010	Resident, Departments of Nephrology and Internal Medicine, University Hospital Basel
04.2009 – 10.2009	Resident Intensive Care Unit Royal Sussex County Hospital Brighton, UK
07.2007 – 06.2008	Resident at the Department of Internal Medicine, Biel Cantonal Hospital
04.2004 – 04.2007	Resident, Departments of Nephrology and Internal Medicine, Inselspital Bern
1997 – 2003	Medical studies at the Universities of Frankfurt am Main Germany, Rostock Germany and King's College London UK
1993 – 1997	Nurse specializing in nephrology and dialysis Villingen-Schwenningen, Germany



A10 Antidrug antibodies in Fabry disease: Impact and challenges

Malte Lenders

University Hospital Muenster

Fabry disease (FD) is a rare X-linked lysosomal storage disorder caused by mutations in the α -galactosidase A (AGAL/GLA) gene. The lysosomal accumulation of the substrates globotriaosylceramide (Gb3) and globotriaosylsphingosine (lyso-Gb3) leads to progressive kidney failure, cardiomyopathy associated with cardiac arrhythmia, and recurrent strokes, significantly reducing life expectancy in affected patients. Current treatment options for FD include recombinant enzyme replacement therapies (ERTs) with intravenous agalsidase alfa (0.2 mg/kg body weight), agalsidase beta (and biosimilars) (1 mg/kg body weight), or pegunigalsidase alfa (1.0 mg/kg body weight) every 2 weeks, facilitating cellular Gb3 clearance and an overall improvement in the disease burden. However, ERT can lead to infusion-associated reactions, as well as the formation of neutralizing anti-drug antibodies (ADAs) in ERT-treated patients, leading to a reduction in therapy efficacy and, consequently, disease progression. Here, we focus on the formation of neutralizing ADAs and anti-PEG antibodies and how they reduce drug efficacy. In addition, we provide an overview of different methods for ADA measurement and characterization and how this may contribute to clinical management.

CURRICULUM VITAE

Malte Lenders (PhD) studied biology at the University of Münster, specializing in genetics and biotechnology. In 2011, he began working as the laboratory head for Prof. Eva Brand at the University Hospital of Münster. Since then, he has been jointly responsible for research projects that have resulted in more than 50 peer-reviewed publications focusing on Fabry disease. In 2025, he was appointed professor of “Experimental Medicine” at the University Hospital of Münster. His research focuses on inflammation, adaptive immune responses, and new therapies, with a particular emphasis on Fabry disease.



B1-1 AAV based Gene therapy for Fabry disease with ST-920 as an exemplar

Robert J Hopkin

Cincinnati Children's Hospital Medical Center Division of Human Genetics

Without treatment Fabry disease leads to progressive life-threatening complications such as progressive renal, heart and cerebrovascular disease. In addition, many patients experience severe GI manifestations, neuropathic pain, and chronic fatigue. There are now several options for treatment, but all have a high burden of care. ST-920 is an investigational gene therapy using a recombinant AAV2/6 vector containing human galactosidase alpha cDNA to produce continuous α -Gal A expression. It is the gene therapy program that currently has the most experience for treatment of Fabry disease.

33 participants (median age: 42 years [range: 18–67]) received ST-920 (up to 2.63×10^{13} vg/kg); Time since treatment ranges from 2-5 years. There were no serious treatment associated with events. Only 1 patient required steroids in the period immediately following treatment. There were several minor transient symptoms reported, but overall the safety profile was excellent. Fabry biomarkers (alpha-galactosidase A activity, and lyso-GB3) showed results comparable to current treatment with ERT, Cardiac parameters of LVMI, ejection fraction, and wall thickness have remained stable. Calculated GFR increased initially and was still at 1.747 ml/min/1.73 m². This was a surprising finding as positive slope has not previously been achieved with any treatment. In addition MSS1, SF-36, and GSRS each demonstrated improvement that was both clinically important and statistically significant.

AAV based gene therapy for Fabry disease appears to be promising as a one-time durable treatment option with safety, positive clinical impact and stable enzyme production for greater than 5 years.

CURRICULUM VITAE

Robert J. Hopkin, MD is a Professor of Clinical Pediatrics at Cincinnati Children's Hospital Medical Center. Dr. Hopkin graduated from the University of Nevada Medical School in 1990. He completed his residency and chief residency in Pediatrics in Phoenix Arizona in 1994. He completed his training in Medical Genetics at Cincinnati Children's Hospital Medical Center in 1997.

The majority of Dr. Hopkin's time is spent caring for patients with genetic disorders. He participates in clinics from Fetal Care to Adult Genetics. He is the Director of the Medical Genetics Residency and Fellowship Program at Cincinnati Children's Hospital. Dr. Hopkin has participated in a number of clinical trials for a variety of genetic conditions. He has participated in, or is currently participating in, clinical studies on Fabry disease, Pompe disease, Niemann Pick C, MPS II, NF1, Prader-Willi syndrome, and other rare diseases. The unifying principle in his research interests is application of scientific knowledge to improve outcomes for patients afflicted with genetic disorders.



B1-2 Lentivirus-Mediated Gene Therapy for Fabry Disease: Long-Term Results and New Initiatives

Jeffrey A. Medin, Aneal Khan¹, Michael L. West², Armand Keating³

Departments of Pediatrics and Biochemistry, Medical College of Wisconsin, Milwaukee, WI, USA

¹M.A.G.I.C. (Metabolics and Genetics in Canada) Clinic, Calgary, AB, Canada

²Division of Nephrology, Department of Medicine, Dalhousie University, Halifax, NS, Canada

³Department of Laboratory Medicine and Pathobiology, University of Toronto and the Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada

We recently published 5-year end-of-study results from our first-in-the-world gene therapy trial for Fabry disease (FD). Five male patients with classical FD were treated by a single infusion of autologous hematopoietic stem/progenitor cells (HSPCs) transduced *ex vivo* by a recombinant lentivector (LV) that engineers expression of alpha-galactosidase A (a-gal A). Patients received a reduced-intensity melphalan treatment to aid in engraftment. By 8 days post-infusion, all patients had increases in circulating a-gal A activity. This expression persisted through the end of the study. Engraftment of the transduced HSPCs was polyclonal and durable in all patients. Lyso-Gb3 levels were significantly lower in the plasma of 4 patients. No adverse events of any grade were attributed to the host conditioning or the gene therapy.

To advance this therapy, a company called AVROBIO, Inc., was formed in the Boston area in 2016. Misguidance from AVROBIO's KOLs led to changes in our original gene therapy protocol. In the end, no engraftment of LV-transduced cells was seen and no circulating a-gal A was made. So AVROBIO dropped their Fabry program. Further fumbling by AVROBIO's management led to a 'reverse-merger' and complete dissolution of the company in 2024.

This presentation will focus on clinical and LTFUS data from our original cohort. It will also discuss Glafabra, Inc., of Park City, Utah, which was formed in 2024 to resurrect our original protocol and treat more Fabry patients.

CURRICULUM VITAE

Professional History:

2016–Present	Professor. Departments of Pediatrics and Biochemistry. MCW
2016–Present	Adjunct Senior Investigator. Blood Research Institute, Milwaukee, WI.
2016–2023	Inaugural MACC Fund Endowed Professor. Vice Chair of Research Innovation, Dept. of Pediatrics. Research Director, Division of Pediatric Hematology/Oncology. Director, GMP Vector Facility, MCW/BRI Joint Initiative. MCW. Milwaukee, WI
2013–2015	Senior Scientist (tenure-level) University Health Network (Ontario Cancer Institute, Toronto General Research Institute, and Toronto Western Research Institute Appointments)
2008–2022	Professor. Department of Medical Biophysics Faculty of Medicine. University of Toronto
2006–2012	Senior Scientist (tenure-level). OCI, UHN
2016	Academic Co-Founder: AVROBIO Inc. Cambridge, MA.
2021	Principal Founder. Tundra Targeted Therapeutics, Inc. Milwaukee, WI.
2024	Co-Founder. Glafabra, Inc. Park City, Utah.
2025	Co-Founder. Athouba Corporation. Toronto, ON

Scientific Contributions:

195 peer-reviewed publications. 14 issued US Patents. 170 Invited Lectures.
2 first-in-human clinical trials.



B2-1 Expanded newborn screening for Fabry Disease in Japan.

Kimitoshi Nakamura

Department of Pediatrics, Kumamoto University

Newborn screening (NBS) for Fabry disease is an important example of expanded screening for lysosomal storage disorders in the era of disease-specific therapy. In Japan, regional pilot programs have introduced enzymatic assays using dried blood spots for conditions such as Fabry disease, Pompe disease, Gaucher disease, and mucopolysaccharidoses.

Fabry disease is an X-linked disorder caused by deficient α -galactosidase A activity. NBS can identify affected newborns before symptoms appear, but clinical manifestations usually develop much later, and treatment is rarely started before late infancy or childhood. Thus, careful long-term follow-up is needed to avoid both delayed intervention and unnecessary anxiety. Because of X-linked inheritance, diagnosis of an infant may also reveal previously unrecognized affected relatives, especially on the maternal side. In heterozygous females, the age of onset and severity vary widely, from childhood to old age, making surveillance complex.

A further challenge is the interpretation of low enzyme activity with genetic variants of uncertain significance. Such cases are difficult to classify and require integration of biochemical data, genotype, family history, biomarkers, and longitudinal clinical findings. Future Fabry disease NBS should therefore be implemented with standardized diagnostic algorithms, expert follow-up systems, and appropriate genetic counseling to maximize clinical benefit while minimizing psychosocial burden.

CURRICULUM VITAE

Professor and Chairman,

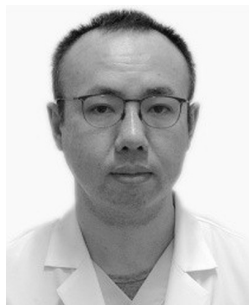
Department of Pediatrics, Graduate School of Medical Sciences, Kumamoto University

Education:

- Mar 1990 Bachelor of Medicine, Kumamoto University School of Medicine
- May 1990 Medical license
- Apr 1994 Pediatrics specialist
- Mar 1996 Doctor of Philosophy, Kumamoto University
- Dec 2002 Clinical Geneticist Employment history
- Apr 1990 Clinical fellow, Kumamoto University Hospital
- Sep 1996 Postdoctoral fellow, Department of Biochemistry, University of Alberta, Edmonton, Canada
- Sep 2000 Research Associate, Institute of Molecular Embryology and Genetics, Kumamoto University
- May 2001 Assistant Professor, Department of Pediatrics, Kumamoto University
- Apr 2014 Associate Professor, Department of Pediatrics, Kumamoto University
- Sep 2017 Professor and Chairman, Department of Pediatrics, Kumamoto University
- Apr 2019 Vice-Director, Kumamoto University Hospital (to Mar 31, 2020)
- Apr 2023 Vice-Director, Kumamoto University Hospital (to Mar 31, 2024)
- Dean, Undergraduate School of Medicine, Kumamoto University

Committee members :

- Apr 2008 Secretary-general, Japanese Society for Inherited Metabolic Diseases (to Mar.31, 2014)
- Executive committee member, Seminar of Japanese Society for Inherited Metabolic Diseases
- Oct 2010 Council of Japanese Society for Inherited Metabolic Diseases
- Apr 2011 Council of Japanese Society for Pediatric Endocrinology
- Apr 2013 Council of Japanese Society for Neonatal Screening
- Nov 2013 Council of Japanese Society for Pediatrics
- Oct 2015 Council of Japanese Society for Human Genetics
- Oct 2016 Board member of Japanese Society for Inherited Metabolic Disease
- Nov 2019 Board member of Japanese Society for Neonatal Screening
- Jul 2022 President of Asian Society of Inherited Metabolic Diseases
- Nov 2022 President of Japanese Society for Inherited Metabolic Diseases
- Sep 2025 President of International Congress of Inborn Errors of Metabolism 2025



B2-2 The Kumamoto and Fukuoka experience in newborn screening for Fabry disease

Takaaki Sawada, Kimitoshi Nakamura¹

Center for Clinical Genetics, Kumamoto University Hospital, Japan

¹Department of Pediatrics, Faculty of Life Sciences, Kumamoto University, Japan

Newborn screening (NBS) for Fabry disease (FD) enables the identification of affected individuals before the onset of clinical symptoms and is increasingly being implemented worldwide. We previously reported the outcomes of the first large-scale NBS program for FD in western Japan, between August 2006 and December 2018, in which 599,711 newborns were screened. The program was subsequently continued in Kumamoto and Fukuoka prefectures, and additional data were collected from January 2019 to September 2022.

Overall, 782,591 newborns were screened during the study period. Among them, 77 newborns, including 57 males and 20 females, were found to carry 29 different *GLA* variants. These included 18 pathogenic variants and 11 variants of uncertain significance (VUS). Pathogenic *GLA* variants were identified in 35 male and 14 female newborns, whereas VUS were detected in 22 male and six female newborns. At the most recent follow-up, five of the 35 hemizygous males with pathogenic variants had developed symptoms or clinical signs of FD and were receiving enzyme replacement therapy.

The estimated frequency of FD, including newborns with either pathogenic variants or VUS, was 1 in 7,730. When limited to newborns with pathogenic variants, the estimated frequency was 1 in 12,436. Because FD-related cardiac and renal tissue damage may occur before typical symptoms, such as limb pain, become apparent, these findings emphasize the clinical value of early diagnosis through NBS and the need for regular long-term monitoring of identified individuals.

CURRICULUM VITAE

2010: Graduated, Faculty of Medicine, Kumamoto University; completed initial clinical training at Kumamoto Red Cross Hospital

2012: Department of Neonatology, Kumamoto City Hospital; Department of Pediatrics, Kumamoto University Hospital

2013: Department of Pediatrics, Kumamoto Red Cross Hospital

2014: Department of Pediatrics, Kumamoto Saishunso Hospital

2015: Department of Pediatrics, Minamata General Medical Center

2018: Assistant Physician, Department of Pediatrics, Kumamoto University Hospital

2019: Kumamoto Ashikita Rehabilitation and Medical Center

2020: Assistant Physician, Department of Pediatrics, Kumamoto University Hospital

2022: Completed Graduate School of Medical Sciences, Kumamoto University (Ph.D. in Medicine)

2022: Assistant Professor (Special Appointment), Southern Kyushu and Okinawa Unit Center of The Japan Environment and Children's Study,

Faculty of Life Sciences, Kumamoto University

2023: Assistant Professor, Department of Pediatrics, Faculty of Life Sciences, Kumamoto University

2023–present: Lecturer (Special Appointment), Center for Clinical Genetics, Kumamoto University Hospital



B2-3 Classical Fabry Males in Taiwan's Newborn Screening Program: Genotypes and Long-Term Outcomes

Yin-Hsiu Nancy Chien

National Taiwan University Hospital

Background: Newborn screening (NBS) enables early identification of Fabry disease (FD), yet risk stratification in asymptomatic infants remains challenging. We evaluated long-term outcomes and biomarker-genotype associations in males at high risk for classic FD identified through one Taiwan's NBS program.

Methods: We retrospectively analyzed 54 males with non-cardiac *GLA* variants identified through NBS (2006–2025). Dried blood spot (DBS) α -galactosidase A activity, plasma lyso-Gb3, genotype, and longitudinal outcomes were assessed.

Results: At a mean follow-up of 9.6 years, six patients (11.1%) developed symptoms and initiated enzyme replacement therapy (ERT), an estimated birth prevalence of 1 in 106,600 males. Birth lyso-Gb3 correlated more strongly with leukocyte enzyme deficiency. All symptomatic individuals had elevated lyso-Gb3 and/or markedly reduced enzyme activity. Truncating variants showed severe biochemical abnormalities, while common missense variants (c.1078G>T, c.1067G>A) remained asymptomatic. Median age at onset was 10 years, most often neuropathic pain, though cardiac involvement may occur earlier. Early ERT was associated with stable outcomes.

Conclusion: Combining DBS enzyme activity, lyso-Gb3, and genotype enables effective early risk stratification and supports timely intervention in NBS-identified males.

CURRICULUM VITAE

Dr Yin-Hsiu Chien is Clinical Professor at the Department of Pediatrics at the National Taiwan University, Taiwan, and Attending Physician of the Department of Medical Genetics and Pediatrics at the National Taiwan University Hospital (NUH). She completed her pediatric residency and fellowship training in Pediatric Allergy, Immunology & Rheumatology, followed by advanced fellowship training in Medical Genetics and Metabolism.

Dr. Chien directs the NTUH Newborn Screening Center, which oversees approximately one-third of all newborns in Taiwan and has served a major national hub for translational research. Her team's pioneering work has shifted the global paradigm for Pompe disease, SMA, and AADC deficiency from late-stage management to early, pre-symptomatic intervention.



B2-4 Newborn Screening for Fabry Disease Enables Earlier Intervention and Better Cardiac Outcomes

Dau-Ming Niu, Chia-Feng Yang², Yann-Jang Chen², Yung-Hsiu Lu², Yun-Ru Chen², Yu-Ting Chiang¹

Institute of Clinical Medicine, National Yang Ming Chiao Tung University

Department of Pediatrics, Taipei Veterans General Hospital

National Health Research Institutes, Institute of Molecular and Genomic Medicine, Taiwan

¹Institute of Clinical Medicine, National Yang Ming Chiao Tung University Taiwan

²Department of Pediatrics, Taipei Veterans General Hospital, Taiwan

Late-onset cardiac Fabry disease is often diagnosed after cardiomyopathy has developed. We evaluated whether newborn screening (NBS)-linked family screening enabled earlier enzyme replacement therapy (ERT) and more favorable cardiac remodeling in a real-world setting. We retrospectively studied 56 adults with the IVS4+919G>A variant who received ERT after NBS-linked cascade screening or clinical diagnosis. At ERT initiation, patients were classified as minimal stage, defined as left ventricular hypertrophy (LVH) without recognized cardiac symptoms, or overt stage, defined as LVH with Fabry-related cardiac symptoms. Outcomes included left ventricular mass index (LVMI), NT-proBNP, high-sensitivity troponin I, and late gadolinium enhancement-defined fibrosis. The cohort included 41 men and 15 women, with a mean age of 57.3 ± 8.1 years and a median follow-up of approximately 10 years. LVMI trajectories differed significantly by stage at ERT initiation (time-by-stage interaction, $p < 0.001$). The minimal-stage group maintained a favorable and stable LVMI response, whereas the overt-stage group showed early improvement followed by long-term deterioration. Elevated NT-proBNP, elevated high-sensitivity troponin I, and fibrosis beyond a minimal extent were associated with unfavorable LVMI progression. In this real-world cohort, the long-term response to ERT was stage-dependent. NBS-linked family screening may identify adults before they recognize cardiac symptoms, enabling earlier ERT and more favorable cardiac outcomes.

CURRICULUM VITAE

Dau-Ming Niu, MD, PhD, is Director of the Rare Disease Research and Treatment Center at Taipei Veterans General Hospital and Distinguished Professor at the Institute of Clinical Medicine, National Yang Ming Chiao Tung University, Taiwan. He received his MD degree from Kaohsiung Medical University, completed advanced training in medical genetics at Duke University, USA, and obtained his PhD from National Yang-Ming University.

Professor Niu has devoted more than three decades to the diagnosis, treatment, and research of rare genetic and inherited metabolic disorders. His major research interests include inherited metabolic diseases, newborn screening, genomic medicine, precision medicine, and gene therapy. He has played a pivotal role in the development of Taiwan's newborn screening and confirmatory diagnostic systems and has made significant contributions to improving the diagnosis, treatment, and long-term outcomes of patients with Pompe disease, Fabry disease, and other rare disorders.

His research team actively promotes the clinical application of next-generation sequencing, whole-genome sequencing, and artificial intelligence technologies to improve the efficiency and accuracy of genetic diagnosis. He has also been deeply involved in translational research on rare diseases, spanning newborn screening, molecular diagnostics, and emerging gene-based therapies.

Professor Niu has published over one hundred influential international scientific papers. His research findings have been widely reported in leading journals in the fields of medical genetics, inherited metabolic disorders, and rare diseases. He has received numerous national awards recognizing excellence in medical research, healthcare quality, and biomedical innovation. He continues to advance precision medicine and genomic technologies to improve patient care and outcomes for individuals with rare diseases worldwide.



B2-5 Newborn Screening for Fabry Disease in the US

Barbara K. Burton

Professor Emerita, Northwestern University Feinberg School of Medicine,
Chicago, Illinois, USA

In this presentation I will review the experience with newborn screening for Fabry disease in the United States and will compare this with reported experience from other countries. We will discuss both laboratory methodology and clinical followup assessment. The incidence of the disease as determined by screening in various geographies will be presented as well as the breakdown between classical and late onset cases. The frequent detection of the variant of unclear significance, A143T, will be added, such as lyso-GB3, in predicting phenotype and in monitoring presymptomatic infants and children will be discussed and the opportunity for diagnosis of disease in affected family members through cascade testing will be emphasized. Finally, pitfalls in newborn screening, including the failure to detect affected females, will be addressed.

CURRICULUM VITAE

Dr. Barbara K. Burton is a Professor Emerita of Pediatrics at the Northwestern University Feinberg School of Medicine and an Emerita Attending Physician in the Edwards Family Division of Genetics and Rare Diseases at the Ann & Robert H. Lurie Children's Hospital of Chicago. Her career has been focused on inborn errors of metabolism and newborn screening. Dr. Burton has been an investigator in numerous natural history studies and clinical trials of new therapies for a wide range of metabolic disorders, including many lysosomal disorders. She has published over 300 peer-reviewed articles, 50 chapters in books and is an editor of two textbooks.

Dr. Burton is active in professional organizations and is a Past-President of the Society for Inherited Metabolic Disorders and the Chicago Pediatric Society. She served as a member of the Secretary's Advisory Committee on Heritable Disorders in Infants and Children, the federal advisory committee that makes recommendations regarding newborn screening in the US and served for many years as Chairman of the Newborn Screening Advisory Committee of the Illinois Department of Public Health. She received a Lifetime Achievement Award from the March of Dimes in 2017. She received the PKU Hero Award from the National PKU Alliance in 2018 and the Legacy Award for Clinical Practice from the National MPS Society in 2024. She is a member of the Scientific Advisory Board of the National MPS Society and serves on the medical advisory board of a number of patient advocacy organizations.



B3-1 Clinical response of migalastat for Fabry disease in Japan

Masahisa Kobayashi

Department of Pediatrics, The Jikei University School of Medicine

Background

The indication of pharmacological chaperone therapy (PCT) for Fabry disease is evaluated based on *in vitro* expression study of the mutant GLA gene, rather than on *in vivo* study using patient samples. We studied the clinical responses of migalastat for Fabry disease.

Subjects and Method

This study included 25 Japanese Fabry patients treated with migalastat (10 males, 15 females). We studied biochemical / physiological parameters (plasma lyso-Gb3, eGFR and LVMI). Additionally, in male patients from whom WBC samples could be available, we assessed the changes of WBC GLA activities.

Results

Five male patients and nine female patients were treatment naïve. In 22 of 25 study patients, their lyso-Gb3 levels showed stable or decreasing trends. In remaining 3 classic male patients, their lyso-Gb3 levels were not reduced. Notably, 2 of these 3 patients showed no elevation of WBC GLA activity (WBC sample was not available in 1 patient). In these 3 cases without lyso-Gb3 reduction, the cardiac hypertrophy and the decline of eGFR progressed.

Conclusions

In this study, some cases showed no GLA activity elevations with migalastat treatment, suggesting that *in vitro* amenability does not always correlate with clinical efficacy. Therefore, the clinical efficacy of migalastat should be evaluated even in patients with amenable variants. Fabry disease who harbor responsive variants. The elevation of WBC GLA activities was correlated with reduction of plasma lyso-Gb3 levels, indicating that plasma lyso-Gb3 serves as a useful biomarker for evaluating clinical efficacy in PCT.

CURRICULUM VITAE

1996, Graduated from The Jikei University School of Medicine

Since 1998, Department of Pediatrics, The Jikei University School of Medicine

2009, Assistant professor, Department of Pediatrics, The Jikei University School of Medicine

2019, Associate professor, Department of Pediatrics, The Jikei University School of Medicine



B3-2 Alternative disease mechanisms and targets in Fabry disease

**Derralynn Hughes, Lucia Lavallo¹, David Moreno Martinez²,
Veronica Lentini¹, Giuseppe Uras¹**

University College London and Royal Free London NHS Foundation Trust,
United Kingdom

¹University College London, UK

²Addenbrookes Hospital, UK

Fabry disease (FD) is an X-linked lysosomal storage disorder caused by α -galactosidase A deficiency, leading to progressive accumulation of globotriaosylceramide (Gb3) and its bioactive deacylated derivative lyso-Gb3. While current disease-modifying treatments, enzyme replacement therapy (ERT) and pharmacological chaperone therapy, have improved patient outcomes, further gains might be achieved by addressing downstream and alternative pathophysiological mechanisms.

Emerging evidence has reframed our understanding of FD pathogenesis beyond substrate accumulation. Gb3 and lyso-Gb3 function as damage-associated molecular patterns, activating Toll-like receptor 4 (TLR4)-mediated innate immunity, dysregulating invariant natural killer T cells, and sustaining chronic cytokine networks involving TNF- α , IL-6, and complement activation. These inflammatory cascades appear self-perpetuating and persist despite substrate reduction. Concurrently, endoplasmic reticulum stress and unfolded protein response activation, mitochondrial respiratory chain dysfunction, impaired autophagic flux through mTOR pathway dysregulation, and lyso-Gb3-mediated voltage-gated calcium channel modulation each contribute independently to cellular injury and organ damage. Recent multi-omics approaches have further identified systemic metabolic reprogramming and gut microbiota dysbiosis as additional, previously underappreciated disease dimensions.

These insights reveal a complex landscape for novel therapeutic targets. Repurposing strategies encompassing TLR4 antagonists, IL-6 and TNF- α inhibitors, antifibrotic agents, autophagy modulators, mitochondrial support strategies, and SGLT2 inhibitors, now supported by emerging real-world data in FD, offer mutation-independent approaches that could complement existing therapies.

This lecture will synthesise these evolving mechanistic insights, evaluate the evidence base for alternative therapeutic targets, and consider how combination strategies addressing both substrate burden and downstream pathophysiology may define the next generation of personalised FD management.

CURRICULUM VITAE

Professor Derralynn Hughes is a leading expert in lysosomal storage disorders (LSDs), rare inherited metabolic conditions including Gaucher, Fabry, Pompe and Mucopolysaccharidosis disorders. She holds the position of Full Professor of Experimental Haematology at University College London and serves as Director of Research and Innovation at the Royal Free London NHS Foundation Trust.

Professor Hughes trained in medicine at Oxford University, where she intercalated a doctorate in macrophage physiology, before completing specialist training in haematology in London. She has led research into Lysosomal Storage Disorders Unit for over two decades, combining clinical care, translational research and clinical trials.

She chairs the International Working Group on Gaucher Disease and serves as co-Clinical Director of the North Central London Cancer Alliance. Her research programme encompasses the pathophysiology of bone disease and malignancy in Gaucher disease, phenotypic variation in Fabry disease, with a particular focus on improving diagnosis in women, and the development of novel therapeutics including gene therapy and the use of data to improve equity in diagnosis and therapy.

Professor Hughes has published more than 250 papers in the areas of macrophage biology and lysosomal storage disorders and has been Principal Investigator on numerous landmark clinical trials evaluating enzyme replacement, chaperone and gene therapies. She has received NIHR Principal Investigator awards and is actively involved in developing next-generation treatments.

海外招聘講演者 (Oversea Speakers)

1. Camilla Tøndel (University of Bergen, Norway)
2. Alessandro Burlina (St. Bassiano Hospital, Italy)
3. Albina Nowak (University of Zurich, Switzerland)
4. Malte Lenders (Interdisciplinary Fabry Center (IFAZ), University Hospital Muenster, Germany)
5. Robert J. Hopkin (Cincinnati Children's Hospital Medical Center, USA)
6. Jeffrey A. Medin (Medical College of Wisconsin, USA)
7. Barbara K. Burton (Northwestern University, USA)

日本人講演者 (Japanese Speakers)

1. Toraaki Okuyama (The Jikei University School of Medicine, Japan)
2. Yoshimi Fujita (The Jikei University School of Medicine, Japan)
3. Kaoru Eto (Tokyo Women's Medical University Adachi Medical Center, Japan)
4. Hayaki Okamoto (Kobe University Graduate School of Medicine, Japan)
5. Takahiro Tsukimura (Meiji Pharmaceutical University, Japan)
6. Hitoshi Sakuraba (Meiji Pharmaceutical University, Japan)
7. Tomonari Awaya (Department of Anatomy and Regenerative Biology, Graduate School of Medicine, Osaka Metropolitan University, Japan)
8. Naoki Nakagawa (Division of Cardiology and Nephrology, Department of Internal Medicine Asahikawa Medical University, Japan)
9. Koji Higuchi (National Institute of Fitness and Sports in Kanoya, Japan)
10. Kenichi Hongo (The Jikei University School of Medicine, Japan)
11. Takaaki Sawada (Kumamoto University Graduate School of Medical Sciences, Japan)

講演者 & 司会者 (Speakers and Chairs)

Overseas

1. Robert J. Desnick (Icahn School of Medicine at Mount Sinai, US)
2. Roberto Giugliani (Federal University of Rio Grande do Sul, Brazil)
3. David G. Warnock (The University of Alabama at Birmingham, USA)
4. Dau-Ming Niu (National Yang Ming Chiao Tung University, Taiwan)
5. Yin-Hsiu Chien (National Taiwan University, Taiwan)
6. Derralynn A. Hughes (University College of London and Royal Free London NHS Foundation Trust, UK)

Japanese

1. Yoshikatsu Eto (Southern Tohoku Institute for Neuroscience / The Jikei University School of Medicine, Japan)
2. Masahisa Kobayashi (The Jikei University School of Medicine, Japan)
3. Kimitoshi Nakamura (Kumamoto University Graduate School of Medical Sciences, Japan)

日本人司会者 (Japanese Chairs)

1. Aya Narita (Iseikai International General Hospital, Japan)
2. Motomichi Kosuga (National Center for Child Health and Development, Japan)
3. Kazuya Tsuboi (Nagoya Central Hospital, Japan)
4. Torayuki Okuyama (Saitama Medical University, Japan)
5. Yukio Yuzawa (Vice Chairman, Fujita Academy, Japan)
6. Ohsuke Migita (St. Marianna University School of Medicine, Japan)
7. Hiroyuki Yamakawa (Keio University School of Medicine, Japan)
8. Katsuya Nakamura (Shinshu University School of Medicine, Japan)
9. Takeo Iwamoto (Southern Tohoku Institute for Neuroscience /The Jikei University School of Medicine, Tokyo)
10. Hiroyuki Ida (The Jikei University School of Medicine, Japan)
11. Hiroshi Kobayashi (The Jikei University School of Medicine, Japan)
12. Toya Ohashi (The Jikei University School of Nursing, Japan)
13. Norio Sakai (ISEIKAI International General Hospital, Japan)