Takeda invites you to the Satellite Symposium

Understanding Phenotypic Variability in Lysosomal Diseases – Gaining a Foothold in Precision Medicine

23 February

Thursday, February 23, 2023
5:15 – 6:15 PM EST

ADD to your CALENDAR

Florida Ballroom
Hilton Orlando, FL, USA

JOIN US!

DESCRIPTION

This symposium will employ a combination of case studies and didactic presentations to explore approaches being undertaken to establish genotype-phenotype correlations in rare diseases, particularly lysosomal diseases, and the significant difficulties involved in defining these relationships.[1,2]

It will also focus on the importance of close monitoring for patients identified prior to symptom onset (e.g., by newborn screening) who may not require immediate intervention at the time of identification, but who may benefit from treatment when symptoms emerge.[3]

In addition, the symposium will consider the potential benefits of rapid whole genome sequencing for supporting diagnosis and treatment decisions in acutely ill patients with who require immediate intervention.[4]

1. Santhanakumaran V, Groeschel S, Harzer K, et al. *Mol Genet Metab*. 2022;137(3):273-82.
2. Davidson BA, Hassan S, Garcia EJ, et al. *Hum Mutat.* 2018;39(12):1739-51.
3. Saich R, Brown R, Collicoat M, et al. *Int J Neonatal Screen.* 2020;6(1):1.
4. Kingsmore SF, Henderson A, Owen MJ, et al. *NPJ Genom Med.* 2020;5:49.

OBJECTIVES

Attending this symposium will enable you to:

- **Summarize** approaches to establishing genotype-phenotype relationships in rare diseases and challenges to establishing a prognosis for patients with these conditions
- **Describe** the importance of close patient monitoring to detect emergence of signs and/or symptoms that may signal the need for treatment initiation
- **Review** results supporting the benefits of rapid genomic sequencing for achieving an etiologic diagnosis and potentially improve outcomes in acutely ill neonates and infants with rare diseases

The Satellite Symposium is open to all registered participants and will be of special interest to clinicians involved in the diagnosis and management of patients with rare diseases, particularly lysosomal diseases.

Three presentations, multiple clinical case studies, and a Q&A session will be delivered by:

DID YOU KNOW?

Welcome & introduction Clinical case studies

Dawn Laney
(USA)

Patients with a given lysosomal disease and the same pathogenic variant may have dramatically different phenotypes

Study of rare diseases, including lysosomal diseases, might be expected to greatly simplify establishment of genotype-phenotype relationships.[1] Most of these conditions are attributed to a single defective gene, i.e., they have Mendelian inheritance, and the identity of this gene and specific disease-associated variants are known in thousands of patients.[1,2]

However, there is phenotypic discordance with respect to involvement of specific organs, severity, and time of onset in individuals with the same genotype, including siblings and monozygotic twins.[3,4]

1. Posey JE, O'Donnell-Luria AH, Chong JX, et al. *Genet Med.* 2019;21(4):798-812.
2. Chung BHY, Chau JFT, Wong GK. *NPJ Genom Med.* 2021;6(1):19.
3. Samadzadeh S, Kruschel T, Novak M, et al. *Genes (Basel).* 2022;13(7):1217.
4. Parenti I, Rabaneda LG, Schoen H, et al. *Trends Neurosci.* 2020;43(8):608-21.

DID YOU KNOW?

Genomic analysis and prediction: Implications for precision medicine

Charlotte Hobbs
(USA)

Precision medicine is now advancing to the bedside to guide treatment of rare diseases

Precision medicine uses information about a person's own genes to treat disease.[1] Genetic diseases are a leading cause of neonatal and infant mortality,[2] and disease progression in these children may be very rapid.[3] Early etiologic diagnosis is needed to decrease the risks for morbidity, and mortality.[4] Rapid genomic sequencing has the potential to improve outcomes in seriously ill infants with suspected genetic disorders.[5] A review of the literature published in 2020 indicated that over the prior 5 years, rapid genomic sequencing showed consistent effectiveness, revealing a genetic disease diagnosis in over one-third of patients.[5]

Changes in outcomes were reported for over one-fourth of these patients and included avoidance of both infant mortality by therapeutic interventions and palliative care decisions.[5] Rapid genome sequencing, with a turn-around time <14 hours, is now available in neonatal intensive care units.[6] Widespread implementation of this approach to patient diagnosis has the potential to improve outcomes for critically ill newborns while decreasing the cost of their care.[6]

1. National Cancer Institute. Precision Medicine. 2022. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/precision-medicine, accessed January 2023.
2. Wojcik MH, Schwartz TS, Yamin I, et al. *Genet Med.* 2018;20(11):1396-404.
3. Saunders CJ, Miller NA, Soden SE, et al. *Sci Transl Med.* 2012;4(154):154ra135.
4. Kingsmore SF, Cakici JA, Clark MM, et al. *Am J Hum Genet.* 2019;105(4):719-33.
5. Kingsmore SF, Henderson A, Owen MJ, et al. *NPJ Genom Med.* 2020;5:49.
6. Kingsmore SF, Cole FS. *Annu Rev Genomics Hum Genet.* 2022;23:427-48.

DID YOU KNOW?

Establishing genotype-phenotype correlations in lysosomal diseases

Melissa Wasserstein
(USA)

New approaches are being developed to follow patients with lysosomal diseases to identify first symptoms and guide treatment initiation

Newborn screening (NBS) has the potential to support prompt initiation of treatment prior to symptom onset in infants with lysosomal diseases.[1] However, some individuals identified by NBS may only develop symptoms in adulthood or perhaps not at all.[1] Deciding when to start treatment is an important consideration in many patients with lysosomal diseases, particularly those in which there may be late symptom onset.[2,3] Close monitoring and timely initiation of therapy is essential for patients identified by NBS who do not require immediate intervention.[4]

ScreenPlus is a consented, multi-disorder pilot NBS program involving long-term follow-up for infants who are confirmed to have a disorder.[5,6] They will be closely monitored for signs and symptoms and referred for treatment when indicated.[6] A systematic approach, such as the one initiated in ScreenPlus, may provide guidance for future management of patients with lysosomal diseases.[4]

1. Beck M. *Dev Med Child Neurol.* 2018;60(1):13-8.
2. Pastores GM, Weinreb NJ, Aerts H, et al. *Semin Hematol.* 2004;41(4 Suppl 5):4-14.
3. Kronn DF, Day-Salvatore D, Hwu WL, et al. *Pediatrics.* 2017;140 (Suppl 1): S24–S45.
4. Saich R, Brown R, Collicoat M, et al. *Int J Neonatal Screen.* 2020;6(1):1.
5. ScreenPlus: A comprehensive, flexible, multi-disorder newborn screening program (ScreenPlus). 2022. https://clinicaltrials.gov/ct2/show/NCT05368038, accessed January 2023.
6. ScreenPlus. Goals of ScreenPlus. 2022. https://www.einsteinmed.edu/research/screenplus/, accessed January 2023.