日本人類遺伝学会第70回大会
The 70th Annual Meeting of the Japan Society of Human Genetics

ランチョンセミナー11
Luncheon Seminar 11

日程 Date
2025年12月20日(土) 12:00～13:00
Saturday, December 20, 2025, 12:00-13:00

会場 Venue
第2会場(パシフィコ横浜 5F 503)
Venue 2, PACIFICO Yokohama 5F 503

フェニルケトン尿症の診断と治療
Diagnosis and Treatment of Phenylketonuria

座長 Chair
新宅 治夫 先生 大阪公立大学大学院医学研究科 名誉教授
Dr. Haruo Shintaku Honorary professor, Graduate School of Medicine, Osaka Metropolitan University

フェニルケトン尿症：病態生理と成人期への影響
Phenylketonuria:Pathophysiology and its impact on adulthood

演者 Speaker
野口 篤子 先生 秋田大学大学院医学系研究科 小児科学講座 講師
秋田大学医学部附属病院 遺伝子医療部
Dr. Atsuko Noguchi Instructor, Department of Pediatrics, GraduateSchool of Medicine, Akita University
Division of Genetic Counselling, Akita University Hospital

古典的フェニルケトン尿症における ペグバリアーゼの臨床経験
Clinical Experience with Pegvaliase in classical Phenylketonuria

演者 Speaker
高野 智圭 先生 日本大学医学部 病態病理学系微生物学分野 助教／小児科学系小児科学分野
Dr. Chika Takano Assistant professor, Division of Microbiology,
Department of Pathology and Microbiology, Nihon University School of Medicine
Department of Pediatrics and Child Health, Nihon University School of Medicine

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事前予約は参加登録マイページより可能です。
This luncheon seminar will require advance reservations and will require numbered tickets.
Advance reservations can be made from your participation registration My Page.

共催：日本人類遺伝学会第70回大会／BioMarin Pharmaceutical Japan 株式会社
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Phenylketonuria：Pathophysiology and its impact on adulthood

Speaker
Dr. Atsuko Noguchi
Instructor, Department of Pediatrics, GraduateSchool of Medicine, Akita University
Division of Genetic Counselling, Akita University Hospital

Phenylketonuria (PKU; OMIM #261600) is an autosomal recessive disorder caused by mutations in the *PAH* gene encoding phenylalanine hydroxylase. More than 500 pathogenic variants have been reported worldwide, with notable ethnic differences. In Japan, p.R111*, p.R241C, p.R408Q, and p.R413P are relatively common, while p.R53H is frequent in both Japanese and Chinese populations. Current diagnostic practice includes plasma phenylalanine measurement, pteridine analysis, dihydropteridine reductase (DHPR) testing, and evaluation of tetrahydrobiopterin (BH4) responsiveness. Genetic data also provide valuable information for predicting the need for dietary treatment and the efficacy of BH4 therapy.
However, long-term outcomes are not determined solely by genotype. Early initiation of treatment and continuous dietary and therapeutic interventions to maintain strict phenylalanine control are critically important.
Recent reports have highlighted that, even in patients who received appropriate treatment during childhood, interruption of therapy in adulthood may result in cognitive impairment, psychiatric symptoms, bone metabolic abnormalities, cardiovascular risk, and change of MRI findings, underscoring the importance of lifelong management.
Since PKU was first described in 1951, dietary therapy was the only treatment for decades. Sapropterin hydrochloride was introduced in 1992, and pegvaliase in 2023, enabling more flexible strategies. Given the marked allelic heterogeneity of PKU, individualized approaches and comprehensive lifelong support systems are desirable to improve outcomes.

Clinical Experience with Pegvaliase in classical Phenylketonuria

Speaker
Dr. Chika Takano
Assistant professor, Division of Microbiology,
Department of Pathology and Microbiology, Nihon University School of Medicine
Department of Pediatrics and Child Health, Nihon University School of Medicine

Pegvaliase (Palynziq®) is a PEGylated phenylalanine ammonia lyase that converts phenylalanine (Phe) to trans-cinnamic acid and ammonia, thereby lowering Phe independently of phenylalanine hydroxylase. It was approved for clinical use in individuals with phenylketonuria (PKU) in Japan in 2023. As an enzyme substitution therapy, pegvaliase enables liberalization of dietary protein intake in responsive individuals.
At our center, more than 20 patients have initiated pegvaliase therapy. Among those who reached a maintenance dose, 60% achieved blood Phe concentrations below 360 µmol/L. Further Phe reductions were observed with dose escalation in some patients, indicating timely up-titration is important for achieving therapeutic efficacy. Subjective improvement in neurocognitive function was reported in several patients. Adverse events are frequent, with nearly all patients developing injection-site reactions. Because of the risk of anaphylaxis, induction must be performed cautiously and requires close monitoring.
Treatment response cannot be predicted from genotype alone and appears to be strongly influenced by immunological factors. Robust pretreatment predictors of efficacy are still lacking.
In summary, pegvaliase is effective for individuals with classical PKU, but substantial inter-individual variability in efficacy and tolerability exists. Personalized dosing and shared decision-making are essential. In this seminar, representative clinical cases and practical strategies to optimize pegvaliase therapy, together with current updates in PKU management will be discussed.

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