学位論文要約
Extended Summary in Lieu of the Full Text of a Doctoral Thesis

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学位論文題目：
Thesis Title
Development of a system adapted for the diagnosis and evaluation of peroxisomal disorders by measuring bile acid intermediates

学位論文要約：
Summary of Thesis

Objective: Bile acid intermediates, 3α,7α,12α-trihydroxycholestanoic acid (THCA) and 3α,7α-dihydroxycholestanoic acid (DHCA), are metabolized in peroxisomes. Some peroxisomal disorders (PDs), such as Zellweger spectrum disorder (ZSD), show an accumulation of bile acid intermediates. In particular, ABCD3 deficiency and acyl-CoA-oxidase 2 deficiency are characterized by these metabolite abnormalities. In patients with ZSD, levels of bile acid intermediates can be lowered by a primary bile acid supplementation treatment; therefore, measuring their levels could help evaluate treatment effectiveness. Here, we established a method for the quantitative determination of bile acid intermediates (THCA/DHCA) for differentiating PDs and assessing bile acid treatment.

Methods: Serum samples, obtained from patients with several forms of ZSD as well as peroxisomal β-oxidation enzyme deficiencies, were deproteinized and analyzed using liquid chromatography-mass spectrometry.

Results: Levels of the bile acid intermediates increased significantly in patients with Zellweger syndrome (ZS) and slightly in patients with neonatal adrenoleukodystrophy and infantile Refsum disease (IRD), reflecting the severity of these diseases. One patient with ZS treated with primary bile acids for 6 months showed slightly decreased serum DHCA levels but significantly increased serum THCA levels. One patient with IRD who underwent living-donor liver transplantation showed a rapid decrease in serum THCA and DHCA levels, which remained undetected for 6 years. In all controls, THCA and DHCA levels were below the detection limit.

Conclusion: The analytical method developed in this study is useful for diagnosing various PD and validating bile acid treatment. Additionally, it can help predict the prognosis of patients with PD and support treatment strategies.