Journal of Zhejiang University SCIENCE B
ISSN 1673-1581
http://www.zju.edu.cn/jzus
E-mail: jzus@zju.edu.cn

Report:

Human biochemical genetics: an insight into inborn errors of metabolism*

YU Chunli[1], SCOTT C. Ronald[2]

([1]*Laboratory of Biochemical Genetics, Emory University, Decatur, GA 30033, USA*)

([2]*Center on Human Development and Disability, University of Washington, Seattle, WA 98195, USA*)

E-mail: cyu@genetics.emory.edu; crscott@u.washington.edu

Received Nov. 22, 2005; revision accepted Dec. 22, 2005

Abstract: Inborn errors of metabolism (IEM) include a broad spectrum of defects of various gene products that affect intermediary metabolism in the body. Studying the molecular and biochemical mechanisms of those inherited disorder, systematically summarizing the disease phenotype and natural history, providing diagnostic rationale and methodology and treatment strategy comprise the context of human biochemical genetics. This session focused on: (1) manifestations of representative metabolic disorders; (2) the emergent technology and application of newborn screening of metabolic disorders using tandem mass spectrometry; (3) principles of managing IEM; (4) the concept of carrier testing aiming prevention. Early detection of patients with IEM allows early intervention and more options for treatment.

Key words: Inborn errors of metabolism (IEM), Newborn screening (NBS), Disease phenotype and therapy
doi:10.1631/jzus.2006.B0165 **Document code:** A **CLC number:** Q342

Advances in human genome project and related research have been the driving force for detecting and understanding genetic disorders. This is especially true in the area of inborn errors of metabolism. From Garrod's understanding of alkaptonuria to today's ability to detect single nucleotide changes, we have had a century of technology-driven discoveries. In the last 30 years, we have seen the utilization of bacterial mutants for the early detection of pehnylketonuria (PKU) (Guthrie, 1969) and the development of amino acid analyzers, gas chromotography/mass spectrometers (Hoffmann and Sweetman, 1987), and tandem mass spectrometers (Chace and Kalas, 2005) for the detection of analytes related to disorders of amino acids, organic acids, and fatty acids. The utilization of these technologies has led to the early detection of metabolic diseases. This early detection has allowed for the development of normal therapies that have included simple dietary alterations, enzyme inhibitors, enzyme replacement therapy, or bone marrow transplantation.

Examples of the technology used for detection or confirmation of phenylketonuria, medium chain acyl-CoA dehydrogenase deficiency, and tyrosinemia-1 will be presented. Clinical and biochemical phenotypes of representative disorders from amino acids, organic acids, fatty acids and carbohydrate metabolism will be illustrated. Each disorder represents unique clinical approaches and insights to metabolic disorders. Concept of carrier testing will also be introduced as example for disease prevention.

In all cases, the early identification of persons affected with genetic disorders by new technology has led to unexpected discoveries related to the natural history of the disorder or options for therapy.

* Special topic report in the First Hangzhou International Symposium on the Medical and Laboratory Applications of Medical Genetics and Genomics held in Hangzhou, China, 2005

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