第６回生命科学セミナー

演題：

Queuine in eukaryotic metabolism: You are what you eat!

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日時：2011 年 7 月 21 日（木）17:00-18:00

会場：生命科学動物資源センター 発生工学棟２階
リフレッシュコーナー

要旨：

Queuosine is a modified pyrrolopyrimidine nucleoside found in the anticodon loop of transfer RNA acceptors for the amino acids tyrosine, asparagine, aspartic acid, and histidine. Because it is exclusively synthesized by bacteria, higher eukaryotes must salvage queuosine or its nucleobase queuine from food and the gut microflora. Previously, animals made deficient in queuine died within 18 days of withdrawing tyrosine, a nonessential amino acid, from the diet (Marks, T., and Farkas, W. R. (1997) Biochem. Biophys. Res. Commun. 230, 233-237). Here, we show that human HepG2 cells deficient in queuine and mice made deficient in queuosine-modified transfer RNA, by disruption of the tRNA guanine transglycosylase enzyme, are compromised in their ability to produce tyrosine from phenylalanine. This has similarities to the disease phenylketonuria, which arises from mutation in the enzyme phenylalanine hydroxylase or from a decrease in the supply of its cofactor tetrahydrobiopterin (BH4). Immunoblot and kinetic analysis of liver from tRNA guanine transglycosylase-deficient animals indicates normal expression and activity of phenylalanine hydroxylase. By contrast, BH4 levels are significantly decreased in the plasma, and both plasma and urine show a clear elevation in dihydrobiopterin, an oxidation product of BH4, despite normal activity of the salvage enzyme dihydrofolate reductase. Our data suggest that queuosine modification limits BH4 oxidation in vivo and thereby potentially impacts on numerous physiological processes in eukaryotes.

Rakovich T, Boland C, Bernstein I, Chikwana VM, Iwata-Reuyl D, Kelly VP (2011) Queuosine Deficiency in Eukaryotes Compromises Tyrosine Production through Increased Tetrahydrobiopterin Oxidation. J Biol Chem. 86(22):19354-63.

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