Kinetic Analysis of Primate and Ancestral Alcohol Dehydrogenases

Kinetic Analysis of Primate and Ancestral Alcohol Dehydrogenases

Myers, Candace R.

Name: MYERS FINAL 04.17 ...
Size: 3.907Mb
Format: PDF
Description: MYERS, C.R. THESIS ...
View/Open

Permanent Link:	http://hdl.handle.net/1805/3168
Date:	2012-11-29
Committee Chair:	Hurley, Thomas D., 1961-
Committee Members:	Goebl, Mark G. Mosley, Amber L.
Degree:	M.S.
Degree Year:	2012
Department:	Department of Biochemistry & Molecular Biology
Grantor:	Indiana University
Keywords:	alcohol dehydrogenase, ADH, primate evolution
LC Subjects:	Alcohol -- Physiological effect ; Alcoholism -- Nutritional aspects ; Cell metabolism ; Ethanol -- Metabolism ; Alcohol dehydrogenase -- Analysis ; Alcohol dehydrogenase -- Regulation ; Isoenzymes ; Human evolution ; Primates -- Genetics ; Enzymes ; Catalysis ; Nutrition ; Liver -- Metabolism ; Drug-nutrient interactions ; Brown lemur -- Behavior ; Marmosets -- Behavior

Abstract:

Seven human alcohol dehydrogenase genes (which encode the primary enzymes involved in alcohol metabolism) are grouped into classes based on function and sequence identity. While the Class I ADH isoenzymes contribute significantly to ethanol metabolism in the liver, Class IV ADH isoenzymes are involved in the first-pass metabolism of ethanol. It has been suggested that the ability to efficiently oxidize ethanol occurred late in primate evolution. Kinetic data obtained from the Class I ADH isoenzymes of marmoset and brown lemur, in addition to data from resurrected ancestral human Class IV ADH isoenzymes, supports this proposal--suggesting that two major events which occurred during primate evolution resulted in

major adaptations toward ethanol metabolism. First, while human Class IV ADH first appeared 520 million years ago, a major adaptation to ethanol occurred very recently (approximately 15 million years ago); which was caused by a single amino acid change (A294V). This change increases the catalytic efficiency of the human Class IV enzymes toward ethanol by over 79-fold. Secondly, the Class I ADH form developed 80 million years ago--when angiosperms first began to produce fleshy fruits whose sugars are fermented to ethanol by yeasts. This was followed by the duplication and divergence of distinct Class I ADH isoforms--which occurred during mammalian radiation. This duplication event was followed by a second duplication/divergence event which occurred around or just before the emergence of prosimians (some 40 million years ago). We examined the multiple Class I isoforms from species with distinct dietary preferences (lemur and marmoset) in an effort to correlate diets rich in fermentable fruits with increased catalytic capacity toward ethanol oxidation. Our kinetic data support this hypothesis in that the species with a high content of fermentable fruit in its diet possess greater catalytic capacity toward ethanol.

Description:

Indiana University-Purdue University Indianapolis (IUPUI)

This item appears in the following Collection(s)

- Biochemistry & Molecular Biology Department Theses and Dissertations (/handle/1805/1663)

Show Statistical Information (#)