The Genetics of Glutamic-Pyruvic Transaminase in Mice: Inheritance, Electrophoretic Phenotypes, and Postnatal Changes

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Received 19 Dec. 1972—Final 6 March 1973

Glutamic-pyruvic transaminase (GPT, E.C. 2.6.1.2) from 18 inbred strains of mice was subjected to starch gel electrophoresis. Two electrophoretic phenotypes were observed: a fast-migrating pattern in 16 strains and a slower-migrating pattern in two strains. A comparison of electrophoretic patterns of F1 and backcross progeny of two strains of mice showed that the inheritance of GPT is autosomal with two codominant alleles. The genetic locus for GPT is designated Gpt-1, and its two alleles are designated Gpt-1a and Gpt-1b to represent the fast-migrating (A) and slow-migrating (B) patterns. The GPT was expressed in 11 tissues with different amounts of enzyme activity. Developmental studies of GPT activity in liver showed that between 5 and 12 days after birth the mean activity was 10 units/g protein. Between 12 and 19 days, a dramatic rise in activity occurred and adult values of 300 units/g protein were reached by 26 days.

INTRODUCTION

Glutamic-pyruvic transaminase (GPT, alanine aminotransferase; E.C. 2.6.1.2)

This research was supported by The National Foundation (CRBS-258) and the National Institutes of Health (GM15253).

1 Preliminary results were reported at the Annual Meeting of the American Society of Human Genetics, October 11–14, 1972, in Philadelphia.

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catalyzes the reversible reaction L-alanine + α-ketoglutarate ⇌ pyruvate + L-glutamate. It plays a pivotal role in the interconversion of carbohydrates and amino acids. The enzyme is widely distributed in animals and human tissues and is particularly abundant in liver and heart (Hopper and Segal, 1964; Gatehouse et al., 1967; Jenkins and Saier, 1970). It has been purified from rat liver and found to have a molecular weight of 114,000 and two identical subunits.

Genetic polymorphism of GPT has recently been described in human populations (Chen and Giblett, 1971; Chen et al., 1972). Three common phenotypes were found, representing the homozygous or heterozygous condition of two autosomal alleles. The identification of three enzyme bands by electrophoresis in human heterozygotes supports the concept of a two-subunit structure for this enzyme.

In this paper, we describe the autosomal codominant transmission, phenotypic variation, tissue distribution, and postnatal activity changes of GPT in the mouse, *Mus musculus*.

**MATERIALS AND METHODS**

Inbred laboratory mice were obtained from The Jackson Laboratory and maintained on Purina laboratory chow. The cage bedding was San-I-Cel. The animals were sacrificed by cervical dislocation. Tissues were rapidly removed, washed in cold saline twice, minced, and then homogenized in a tissue grinder with a teflon pestle in about 5 vol of distilled water. In mice of 5–12 days of age, tissues were homogenized with an equal volume of distilled water. The homogenates were centrifuged twice at 27,000 x g for 30 min and the clear supernatant was used for the enzyme assays.

Starch gel electrophoresis of fresh extracts was performed at 4 C for 18 hr at 7 v/cm in 0.1 M tris–citrate buffer, pH 7.6. The gels were stained for GPT activity as previously described (Chen et al., 1972).

The assay procedure for GPT activity was modified from that of Segal et al. (1962). The incubation mixture contained 100 mM tris–HCl buffer, pH 8.0; L-alanine, 33 mM; α-ketoglutarate, 4 mM; NADH, 0.17 mM; and 4 units/ml of LDH. The reaction was initiated by adding 5–40 µl of tissue extract to 3 ml of reaction solution at room temperature. Decrease of optical density at 340 mµ was measured and recorded against a blank for 15 min using a Gilford 2400S spectrophotometer. Enzyme activity was linear for at least 30 min. Control incubations showed negligible change in optical density. One unit of enzyme activity was defined as the conversion of 1 µmole of substrate per minute. Specific activity was expressed as units per gram of soluble protein. Protein was determined by the method of Lowry et al. (1951).