A Quantitative Genetic Analysis of Tissue-Specific Catalase Activity in *Mus musculus*

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Tissue-specific catalase activity in 3-week-old animals from inbred mouse strains 129/ReJ, BALB/c, C3H/HeAnl/Cas-1, C3H/HeSnJ, C3H/S, C57BL/6J, and Swiss–Webster was found to be highly variable by analysis of variance ($P = 0.01$). Appropriate crosses were made among strains which were classified as normal (BALB/c, C3H/HeSnJ, C3H/S), hypocatalasemic (129/ReJ, C57BL/6J), and acatalasemic (C3H/HeAnl/Cas-1) with respect to blood catalase activity to study the inheritance of the blood, kidney, liver, and lung catalase activity levels in a number of generations (reciprocal $F_1$s, $F_2$, two backcrosses —BC$_1$ and BC$_2$— and some RI lines). Segregation analysis and statistical methods which tested different models of inheritance as well as calculations of heritability were used in an effort to assess and evaluate genetic parameters that affect catalase activity. Results indicate that the inheritance of blood catalase activity in the cross involving acatalasemic and normal (BALB/c, C3H/HeSnJ) strains is compatible with the single-locus difference between the parental strains; however, the difference between the acatalasemic and the hypocatalasemic strain (C57BL/6J) would require additional genetic interaction for a satisfactory explanation. A similar pattern of generalization also applies to the inheritance of kidney catalase activity. The segregation pattern for the liver and lung catalase activity in most crosses is significantly different from the expectations of the single locus model. These results are compatible with the concept that a number of genes must affect tissue-specific catalase activity in mice. These may include previously described (e.g., Ce-1 and Ce-2) or novel genetic regulators/modifiers which interact with a single structural gene (Cas-1) or its product to produce the catalase phenotype characteristic of specific tissues in each strain.

KEY WORDS: catalase; mouse; quantitative genetics; segregation.

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INTRODUCTION

Oxygenation of the biosphere imposed stringent evolutionary pressure on organisms accustomed to an anaerobic existence. The most facile route of oxygen reduction releases reactive metabolites including superoxide (O$_2^-$), hydrogen peroxide (H$_2$O$_2$), and hydroxyl radicals (OH') into the cellular milieu (Britton et al., 1978), where they may cause lipid peroxidation, depolymerization of polysaccharides, DNA damage, enzyme inactivation, membrane damage, and cytotoxicity (Fridovich, 1978). Defense mechanisms mitigate these effects and include simple chemical compounds such as ascorbic acid, tocopherol, uric acid, and glutathione and the enzymes superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GSH-Px) (Fridovich, 1978), which function through the pathway

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O_2 \overset{SOD}{\longrightarrow} H_2O_2 \overset{CAT/GSH-Px}{\longrightarrow} H_2O + O_2
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We have assessed the relative variability of these three enzymes in inbred strains of mice during development and aging and have shown that CAT, a tetrameric, ferrirriprotoporphyrin enzyme (MW 240,000), displayed the highest overall level of variation (Schisler and Singh, unpublished). This is not surprising since it is well established that CAT is variable among species (Feinstein, 1970; Holmes and Masters, 1972), strains (Hoffman and Rechcigl, 1971; Hoffman and Grieshaber, 1976; Novak et al., 1978), tissues (Holmes and Masters, 1972; Novak et al., 1978), and developmental stages (Holmes, 1971). Previous investigations have shown that a single structural gene (Cas-1) located on chromosome 2 is responsible for coding the primary structure of this enzyme (Dickerman et al., 1968; Holmes and Duley, 1975) and epigenetic modification (Masters et al., 1986) yields two distinct subunits that combine to produce five tetrameric isozymes (Holmes and Masters, 1970). This gene starts transcription with somite formation (day 8) in developing embryos in vivo, and the processing of the primary transcript may be delayed until birth (El-Hage and Singh, 1989). Further, the 2.4-kb mature message may not be effectively translated during in vivo development and differentiation and accumulate (El-Hage and Singh, 1990) in a tissue-specific manner (Reimer and Singh, 1990). Several alleles, which seem to affect blood and kidney CAT activity primarily, account for normal (Cas-1$^a$), acatalasemic (Cas-1$^b$), and hypocatalasemic (Feinstein et al., 1966, 1967) enzyme activity. Investigations by Feinstein (1970) have shown that acatalasemic mouse erythrocytes have normal levels of catalase protein but the enzyme is abnormally labile, resulting in low levels of activity in mature cells, a result he attributed to a mutation in the structural gene. Other loci that affect the CAT phenotype, distinct from the structural gene, have been