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The method of using many electrophoretic conditions to study enzyme variation in natural populations has led to a significant increase in the amount of variation when compared to that detected by only a single electrophoretic condition (Singh et al. 1976; Coyne and Felton 1977; Coyne et al. 1979a). This increase in variation is most dramatic for loci which are already known to be polymorphic under a single electrophoretic condition. Loci which are monomorphic under one electrophoretic condition, however, remain monomorphic even when studied under several conditions.

It is possible that some of the observed enzyme variation may not be due to changes at the structural locus but rather to modifier genes which influence enzyme mobility. It is thus important to investigate the genetic basis of variation whenever possible.

Such genetic studies have been done in our laboratory for the loci xanthine dehydrogenase, esterase-5, and alcohol dehydrogenase-6 in D. pseudoobscura and D. persimilis. Our investigations have always shown codominant segregation of mobility variation with no evidence of inheritance patterns suggesting modification elsewhere in the genome. However, it is possible that modifiers of enzyme mobility exist in addition to the variation which has been so far discovered. The way to search for such variation would be to hold the structural locus constant while varying the genetic background to investigate possible changes in mobility of the enzyme. We have done this for the xanthine dehydrogenase locus in D. pseudoobscura and have found no such modifiers in a sample of 52 X chromosomes from 12 geographic populations (Coyne et al. 1979b).

Esterase loci are generally highly polymorphic in species of Drosophila. Cochrane and Richmond (1979) have reported segregation at a locus on the 3rd chromosome of D. melanogaster which modifies the mobility of the esterase-6 enzyme produced by a structural locus elsewhere on this chromosome. Although this allele is not common in natural populations of the species (a search of 50 lines from nature failed to reveal it), these authors suggest that such modifier genes may account for esterase polymorphisms in other drosophilids.

We report here the initial results of a search for modifier loci on the major autosomes of D. pseudoobscura which might modify electrophoretic mobility of the esterase-5 protein produced by a locus on the X chromosome. In this study we have used a wide variety of isochromosomal lines which were constructed in this laboratory. Such lines homozygous for a given autosome derive their X chromosomes entirely from the marker stock used to construct them (see Coyne et al. 1979b). If the marker stock happens to be homogeneous for one electrophoretic allele at an X-linked locus, then the isochromosomal lines all share the same allelic form of this locus while differing in genes on the isochromosome. These isochromosomal lines can then be examined for possible mobility effects of the X-linked enzyme induced by the autosomes. Our marker stocks for the 2nd, 3rd and 4th autosomes of D. pseudoobscura have all proven to be homogeneous for different esterase-5 alleles when investigated under the five electrophoretic conditions of Coyne et al. (1978).

We have studied 51 isochromosomal-2 lines of D. pseudoobscura from 11 geographic populations. The Delta-cardinal marker stock used to make these lines was homozygous for the 1.06 allele of the esterase-5 locus, and no variation in mobility of this allele was seen in any of the 51 lines tested at the same five electrophoretic conditions. Initial analysis was also done for six isochromosomal-3 lines constructed with an orange-Blade-scute stock, and these lines showed no variation of the esterase-5 allele carried by that stock.

We conclude from this and previous studies that while secondary modification of protein structure may exist for certain proteins, it is probably of little importance in accounting for allozyme polymorphisms detected by differences in electrophoretic mobility. Rather, this observed variation is due to either allelic variation at the structural locus or closely linked cis-dominant modifiers of mobility (Coyne et al. 1979b).

References: Cochrane, B. and R. Richmond 1979, Biochem. Genetics in press; Coyne, J. and A. Felton 1977, Genetics 87:285; Coyne, J., A. Felton and R. Lewontin 1978, Proc. Nat. Acad. Sci. 75:5090; Coyne, J., W. Eanes, J. Ramshaw and R. Koehn 1979a, Syst. Zool. in press; Coyne, J., W. Eanes and R. Lewontin 1979b, Genetics in press; Singh, R., R. Lewontin and A. Felton 1976, Genetics 84:609.