Genetics of Cytochrome P450 in Two Insecticide-Resistant Strains of the Housefly, *Musca domestica* L.¹

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A susceptible strain of *Musca domestica* containing visible mutant markers on chromosomes II, III, and V was crossed with multiresistant R-Fc and R-diazinon strains. F₁ flies were backcrossed to the mutant parent, resultant progenies were isolated according to phenotype, and substrains were established. The level of resistance to diazinon, aldrin epoxidase activity, and cytochrome P450 difference spectra of microsomes from each substrain were measured. Titers of cytochrome P450, measured as CO spectra, as well as type I, type II, and type III cytochrome P450 substrate difference spectra were compared in microsomal preparations obtained from phenotypes containing various resistant chromosome combinations. In both resistant strains, high levels of cytochrome P450 were controlled by a gene(s) on chromosome II. In R-diazinon, qualitative spectral changes were also controlled by chromosome II, whereas in R-Fc both chromosomes II and V contributed to qualitative changes in cytochrome P450. Both quantitative and qualitative characteristics were intermediate in heterozygous flies, suggesting incomplete dominance for their inheritance. Findings are discussed in relation to known genetics of microsomal resistance to insecticides.

KEY WORDS: cytochrome P450; microsomes; binding spectra; *Musca domestica* L.; mixed-function oxidases.

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INTRODUCTION

Increased levels of microsomal mixed-function oxidase are characteristic of many organophosphate- and carbamate-resistant strains of the housefly, *Musca domestica* (Schonbrod *et al.*, 1968; Hodgson and Plapp, 1970). In resistant houseflies, high oxidase activity is conferred by genes on either chromosome II or chromosome V (Hodgson and Plapp, 1970). High oxidase activity segregates with the second chromosome in Isolan-R (Schonbrod *et al.*, 1968; Khan and Terriere, 1968; Khan, 1969), Carbaryl-R (Schonbrod *et al.*, 1968), Dimetilan-R (Khan *et al.*, 1970), and Baygon-R (Plapp and Casida, 1969; Plapp, 1970) strains. Chromosome V controls levels of oxidase activity in R-Fc (Oppenooorth and Houx, 1968; Plapp and Casida, 1969) strains. SKA and *R*<sub>Hokota</sub> strains have mixed-function oxidase factors on both chromosomes II and V (Sawicki and Farnham, 1967; Tsukamoto *et al.*, 1968). Resistance in these strains is generally controlled by the same chromosomes as high oxidase activity.

Although the genetics of resistance in the housefly with respect to oxidative metabolism is well established, no information is available on the genetics of any single component of the mixed-function oxidase system. The carbon monoxide and substrate spectra of cytochrome P450, the terminal electron acceptor of the mixed-function oxidase system (Estabrook *et al.*, 1970), differ both qualitatively and quantitatively among several resistant strains from the cytochrome P450 spectra of susceptible housefly strains (Philpot and Hodgson, 1971; Tate *et al.*, 1973). Cytochrome P450 titers in microsomes of several resistant strains are higher than in the susceptible strains (Matthews and Casida, 1970; Georghiou, 1971; Perry *et al.*, 1971; Philpot and Hodgson, 1971, Tate *et al.*, 1973). Microsomes from the R-Diazinon<sup>4</sup> (Philpot and Hodgson, 1971; Perry *et al.*, 1971) as well as R-Fc and Dimethoate-R strains (Tate *et al.*, 1973) form cytochrome P450-CO difference spectra which have an absorption maxima 2-4 nm lower than in other strains. Also comparisons of type I, type II, and type III substrate difference spectra of microsomes from these strains with those of susceptible strains show several major qualitative differences (Philpot and Hodgson, 1971; Tate *et al.*, 1973). Since at this time insect cytochrome P450 has not been solubilized, qualitative differences could possibly reflect differences in the microsomal environment rather than in the cytochrome itself.

The presence of quantitative and qualitative differences in cytochrome P450 from several housefly strains makes possible a genetic analysis when such strains are crossed to obtain specific combinations of resistant chromosomes.

<sup>4</sup> Previously referred to in communications from this laboratory as the Rutgers diazinon-resistant strain (Folsom *et al.*, 1970; Philpot and Hodgson, 1971).