MPRINT Research Thrusts

Molecular Basis of Resistance to Pyrethroids

During the last few years Barry Pittendrigh's work has focused on how insects develop resistance to pyrethroid insecticides, using Drosophila as a genetically tractable insect system to address these issues. One example is his work with temperature-sensitive mutations in the voltage-gated sodium channel. He found that many of the point mutations in the Drosophila gene *para* that caused temperature sensitivity also conferred pyrethroid resistance. One of these mutations was analogous to the knock-down resistance (*kdr*) allele in houseflies and cockroaches. Additionally, a second mutation that has been observed in houseflies, along with the *kdr* amino acid change (on the same allele), confers very high levels of resistance to pyrethroids. This double mutant allele in houseflies is known as *super-kdr*.

Pittendrigh observed a mutant allele in Drosophila carrying only a single amino acid change analogous to the second mutation in *super-kdr*. When he crossed the *kdr* and (the second mutation) *super-kdr* analogous alleles, the resultant heterozygous female progeny contained both mutations found in the *super-kdr* allele in houseflies (but *in trans*) and had much elevated levels of resistance, similar to what is observed in the *super-kdr* houseflies.

In subsequent work in collaboration with Dr. D. Hank's group at the University of Chicago, Pittendrigh and his colleagues were able to show that the *kdr*-like mutation resulted in sodium channels with reduced sensitivity to pyrethroids. This work has also provided new insights into the functioning of the voltage-gated sodium channel.

Pittendrigh has a second ongoing project in Drosophila involving pyrethroid resistance. He is mapping and cloning a metabolic resistance gene in Drosophila that confers resistance to pesticides. He has mapped this gene to a very restricted region in the Drosophila genome. Once this gene is identified and characterized it should provide new insight into how economically important pests develop resistance to insecticides.

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