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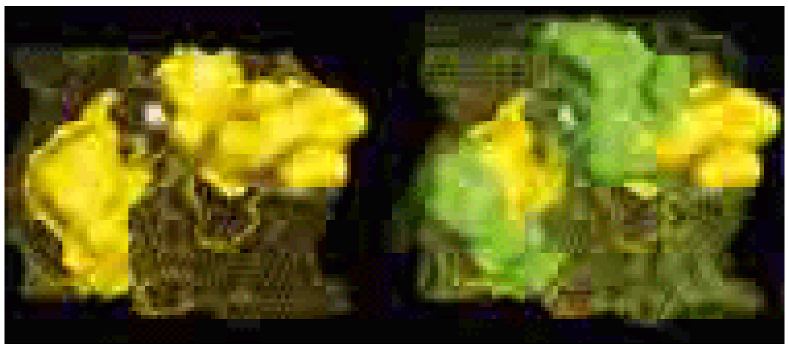
Insect pests and plants, struggling for survival



In nature we can see many examples of adaptable evolution. On of these mechanisms may be seen in the co-evolution of herbivorous insects and the plants they feed on: while prey develop biological defences, the predators react to make themselves insensitive to attack. Researchers at the UAB have studied this process in depth in the case of a nocturnal lepidopteron insect of the genre *Helicoverpa, H. zea*.

One of the defence mechanisms developed by plants consists of the expression of proteins which act as enzyme inhibitors in the insects' digestive system. These inhibitors are usually very resistant and effective molecules and are designed to cause problems in the absorption of nutrients thereby affecting development, reducing fertility and even causing death in the insects.

For their part, certain insects have developed what can be called a counter-response, consisting of the adaptation to the arsenal of inhibitors synthesised by the host plants. Examples of proteases, enzymes in the digestive system which degrade proteins so they can be absorbed by the intestine are well known. We also know that some of these proteases, specifically those which digest proteins by producing internal breaks in their sequence, are resistant to inhibitors of a vegetal origin, but we do not know well the underlying molecular mechanisms in this phenomenon. It is thought that the appearance of resistance is one of the main factors which allow an insect species to develop into a devastating pest.

There is a family of protease inhibitors, specifically those that, rather than digesting proteins by means of internal breaks, do so by excision of amino acids from their ends, which are well known and studied: these are the carboxypeptidase protein inhibitors which can be found in such common sources as potatoes and tomatoes. However, until quite recently we did not have any experimental evidence on the adaptation of insects to this specific type of inhibitors.

When studying the behaviour of a nocturnal lepidopteron of the genre *Helicoverpa, H. zea*, probably the most important pest affecting corn in the whole American continent, when faced with protease inhibitors present in their diet, we observed that the insects' carboxipeptidases were insensitive to the inhibitors and, moreover, the larvae showed perfectly normal growth. The isolation of the resistant enzyme allowed us to obtain the recombined protein, its crystallization and to determine its three-dimensional structure by means of X-ray diffraction.

The structure of this protein, shown in the figure allows us to explain its resistance to attack on the part of the inhibitor: Subtle variations produced by mutations in the gene which codifies the protein and which are expressed as isolated modifications in its sequence also cause subtle changes in the surface of the protein which, nevertheless, are enough to impede the inhibitor from accessing the active centre of the enzyme: the protease has changed the lock on the door and the stranger cannot enter. Understanding the essence of these mechanisms may help us to design molecular strategies to fight crop pests.

The surface of the proteins may be represented as a three-dimensional map. At the top we can see a specific region (the entrance to the active centre, where the reaction catalysed by the enzyme takes place) of the forms which are sensitive (in yellow) and insensitive to inhibitors (in green, overlaid) of a single digestive enzyme. At the bottom: while the inhibitor (in magenta) matches perfectly with the structure on the left and can, therefore, block its activity, it is not able to do so with the molecule on the right because both enzyme and protein occupy identical spatial zones, in a molecularly unviable structural game.

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