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The recombination between 3-domain Cry-toxin genes as a mechanism to extend the list of affected hosts

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Motivation and Aim: The application of *Bacillus thuringiensis* (*Bt*) both in form of spores and toxins produced by the bacterium provides a wide range of activities against different pests, including insects and nematodes. Of these pesticidal moieties, crystalliferous Cry toxins, in particular, three-domain Cry toxins represent the most effective insecticides with high host specificity. The exact mechanism driving the evolution of these toxins remains unknown, however, a hypothesis that the emergence of new Cry toxins occurs as a result of domain exchange was proposed. In this work we for the first time performed the large-scale analysis of the recombination events to reveal the role of recombination-driven domain exchange in 3-D Cry toxins' evolution.

Methods and Algorithms: We gathered data from several sources, namely, Genebank, IPG (identical protein database), *Bt* assemblies, and the *Bt*-nomenclature, and retrieved sequences of 3-D cry toxins using our tool developed earlier, CryProcessor [1]. We then reconstructed phylogenies based on the sequences of each domain and the whole toxin. The topologies of the phylogenies were compared afterward. Next, we used RDP (Recombination Detection Protocol) tool to reveal recombination events and filtered raw data based on the similarity between sequences and their position on phylogenetic trees. To collect the data on the specificity of the toxins we used literature and public databases and compared specificity between parents and children in recombination events. Finally, we used the ETE3 utility to reveal how recombination affects evolutionary selection.

Results: After filtration of the toxin sequences, 370 clusters of Cry toxin sequences were obtained. The topologies of the trees differed significantly, and it was especially evident for the third domain. We then revealed more than 70 recombination events. Importantly, the events affected each domain, however, the third domain was exchanged more frequently. Fisher test showed that recombination events lead to significant ($p < 0.01$) changes in host specificity both in terms of orders and species. The analysis of evolutionary selection revealed that recombinatiola exchanges are accompanied by the intensive selection, both positive and negative.

Conclusion: The results clearly support the hypothesis of the role of domain exchanges between toxins in their evolution. Not only are the recombination events widespread, but they also lead to alterations in host specificity and are subjected to evolutionary selection as well. So, they might be considered as large evolutionary events, leading to extending of the list of possible susceptible hosts.

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References

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