Séminaire DYNAMOP (ouvert à tous)
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Engineering Insecticidal Bacterial Protein Synthesis for Improving Efficacy and Knowledge of their Mode of Action

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Two bacteria, *Bacillus thuringiensis* (Bt) and *Lysinibacillus sphaericus* (Ls) are the active ingredients of commercial insecticides used to control the larvae of many agricultural insect pests and vectors of important diseases such as malaria, filariasis, Dengue and Zika fever. These bacteria synthesize several different types of proteins during sporulation that form natural crystals, which have evolved to dissolve in the alkaline midgut upon ingestion by larvae. After dissolution, these proteins are activated by proteolysis and bind to midgut microvillar proteins or lipids, causing lysis of midgut epithelial cells and larval death. We improved the efficacy of these bacteria by recombining genetic elements including promoters, chaperone-like proteins, a mRNA stabilizing sequence, and stem-loop structures to significantly increase the size of the crystals produced by each bacterial cell from 8-10 fold, which resulted in similar increases in efficacy. In addition to improving efficacy, these increased yields have enabled us to synthesize large amounts of individual proteins for studies of their structure and mode of action. In this presentation, I will focus on molecular methods we developed to produce large crystals of Bt Cry3A, Cry11B, and the Ls heterodimer binary toxin, BinAB, which have benefitted structural studies of these proteins. In addition, whereas all of these bind to protein receptors on midgut microvilli, I will also discuss how we used the same techniques to synthesize and study the mode of action of Cyt1A, a Bt lipophilic protein that causes large lesions in midgut microvilli without the aid of a protein receptor. Cyt1A is especially important because it synergizes the potency of other Bt proteins and delays the evolution of resistance to these and Ls BinAB in mosquito larvae. Finally, I will briefly discuss recent studies in which we made a Cyt1A-BinA chimera with high efficacy against larvae of a wide range of mosquito vectors.