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Guillaume Cambray

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Reprogramming Viral Host Specificity To Control Insect Populations

Guillaume Cambray
UMR 1333 DGIMI, INRA-University of Montpellier, France
guillaume.cambray@inra.fr

Abstract

One of the most diverse and successful group of animals, Insects are an integral part of ecosystems. Yet, some represent great nuisances for human health and development. Such pests have been efficiently controlled using chemical insecticides, but the rise of resistances, the broadly targeted environmental impacts and the increasing recognition of chronic toxicity call for the urgent development of safer and cleaner alternatives. Biological control strategies that take advantage of natural antagonistic relationships between existing organisms and a target pest have been around for millennia. In spite of the inherent risks of unintended side effects, these approaches have recently gained renewed interest. Perhaps because they evoke greater fears, surprisingly few microorganisms have been used in that perspective. Densoviruses are small viruses capable—as a group—of infecting a broad range of insects with various degrees of specificity. Their minute genomes comprise a handful of genes, which lend themselves to deep-molecular dissection using synthetic biology approaches. Our goal is to develop these tools and knowledge necessary to enable the use of densoviruses as safe, specific and efficient biocontrol agents. We focus on JcDV, which infects crop-devasting caterpillars and is the prototype of densoviruses. The capsid of densoviruses are small (19-24 nm) non-enveloped icosahedrons (T=1) resulting from the self-assembly of 60 identical or highly similar proteins. Here, I present an in-depth molecular dissection of JcDV, which infects crop-devesting caterpillars JcDV and AalDV, which infects disease-vector mosquitoes. Several surface polymorphism between JcDV and GmDV are an integral part of ecosystems. Reprograming Viral Host Specificity To Control Insect Populations

Molecular Dissection Of A Complex Phenotype

A typical infectious cycle

Non-enveloped capsid:
- maintains genome integrity
- essential for early infectious steps
- JcDV’s capsid:
  - lossofshell: T=1, Ø=24 nm
  - 60 capsomers (1 VP1 : 3 VP2 : 4 VP3 : 41 VP4)
  - Structural model based on 94% identical GmDV (Bålden et al. 1974)

Some surface polymorphism between JcDV and GmDV impacts host specificity

Sequence & Structure

Phenotypic consequences of many precise capsid mutations. This will permit to better understand natural variation, to map evolutionary landscapes, to discover useful properties and to learn the rules to reprogram specificity.

Sequencing-based phenotyping of designer capsids

Quantitative characterization of several hundred of thousands precisely designed capsid variants based on high-throughput DNA synthesis and amplicon sequencing.

Supports heavy multiplexing to screen many abiotic and biotic conditions.

Parallel screening

The reconstructed genome does not replicate

Construction of a mutable non-propagatable JcDV

Roadblock #1 : No PCR through ITRs

Of structure and repeats

A winded detour through the golden gate

Roadblock #2 : Unexpected loss of function

The reconstructed genome does not replicate

Complementation reveals NSs regulatory function and the role of VP transcript’s tail in replication

Small, But Not So Simple : The Price Of Biosafety

The fall armyworm (Spodoptera frugiperda)
- Originally from S.E. Asia
- Spreading over the world for decades
- Currently invading North America and Europe

The tiger mosquito (Aedes albopictus)
- Disease vector: Yellow Fever, Dengue
- Chronically ingesting Africa
- Spreading over the world for decades

JcDV (6,032 nts)
Highly structured ITR
ITR
- Essential for early infectious steps
- Maintains genome integrity

Non-structural gene block (NS)

VP transcript with alternative start sites

5-fold axis motifs:
- pGCDV73
- pGCDV77
- pGCDV79
- pGCDV90
- pGCDV92

5-fold-axis tunnel:
- pGCDV73
- pGCDV77
- pGCDV79
- pGCDV90
- pGCDV92

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