



# Reprogramming Viral Host Specificity To Control Insect Populations

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# Reprogramming Viral Host Specificity To Control Insect Populations



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## 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's health and development...

Such pests have been efficiently controlled using chemical **insecticides**, but the rise of **resistances**, the broadly **untargeted** 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 degree of **specificity**. Their **minute genomes** comprise a handful of genes, which lend themselves to **in-depth molecular dissection** using **synthetic biology** approaches.

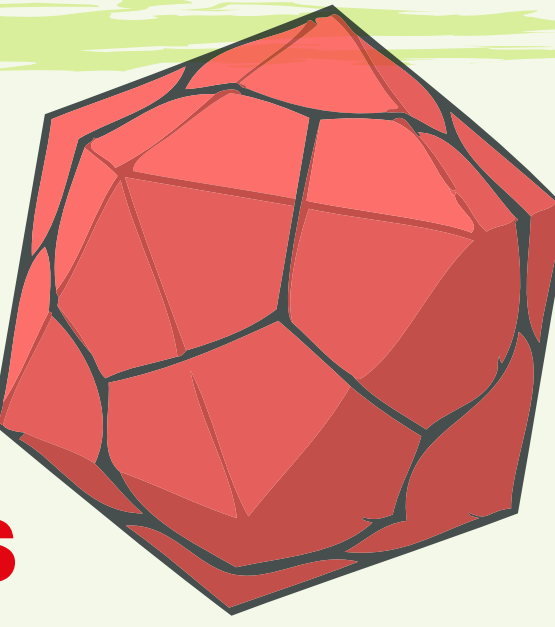
Our goal is to develop the **tools** and **knowledge** necessary to enable the use of **densoviruses** as **safe, specific and efficient biocontrol agents**. We focus on **JcDV**, which infects **crop-devasting caterpillars** and **AaIDV**, which infects **disease-vector mosquitoes**.

Here, I present **early efforts** to systematically **unravel the structural motifs** responsible for **capsid specificity**.

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 capsid proteins. The DNA sequences coding these proteins represent roughly a **third of the genome** and are the **prime determinant of specificity**. I am using the genome of JcDV to setup a the **high-throughput, cost-effective pipeline** to **deconstruct the phenotypic consequences** of many precise **capsid mutations**. This will permit to better understand **natural variations**, to map **evolutionary landscape**, to discover **useful properties** and to learn the rules to **reprogram specificities**.



**Targeting insect pests with densoviruses**



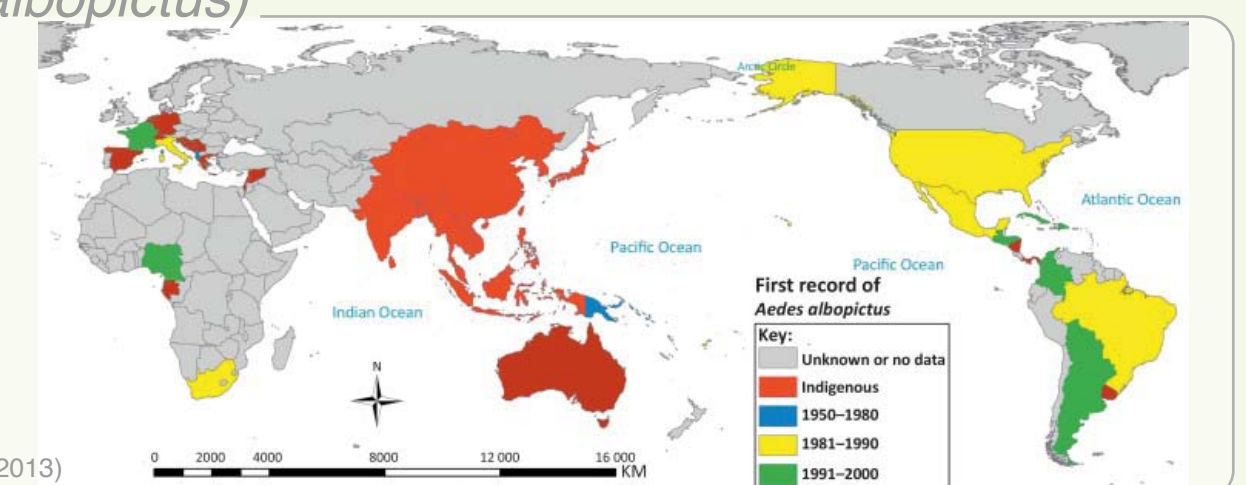
### The fall armyworm (*Spodoptera frugiperda*)

- Crop pest
- Eats >80 plants
- From S. and N. America
- >100 kms / day
- Currently invading Africa at lightning speed



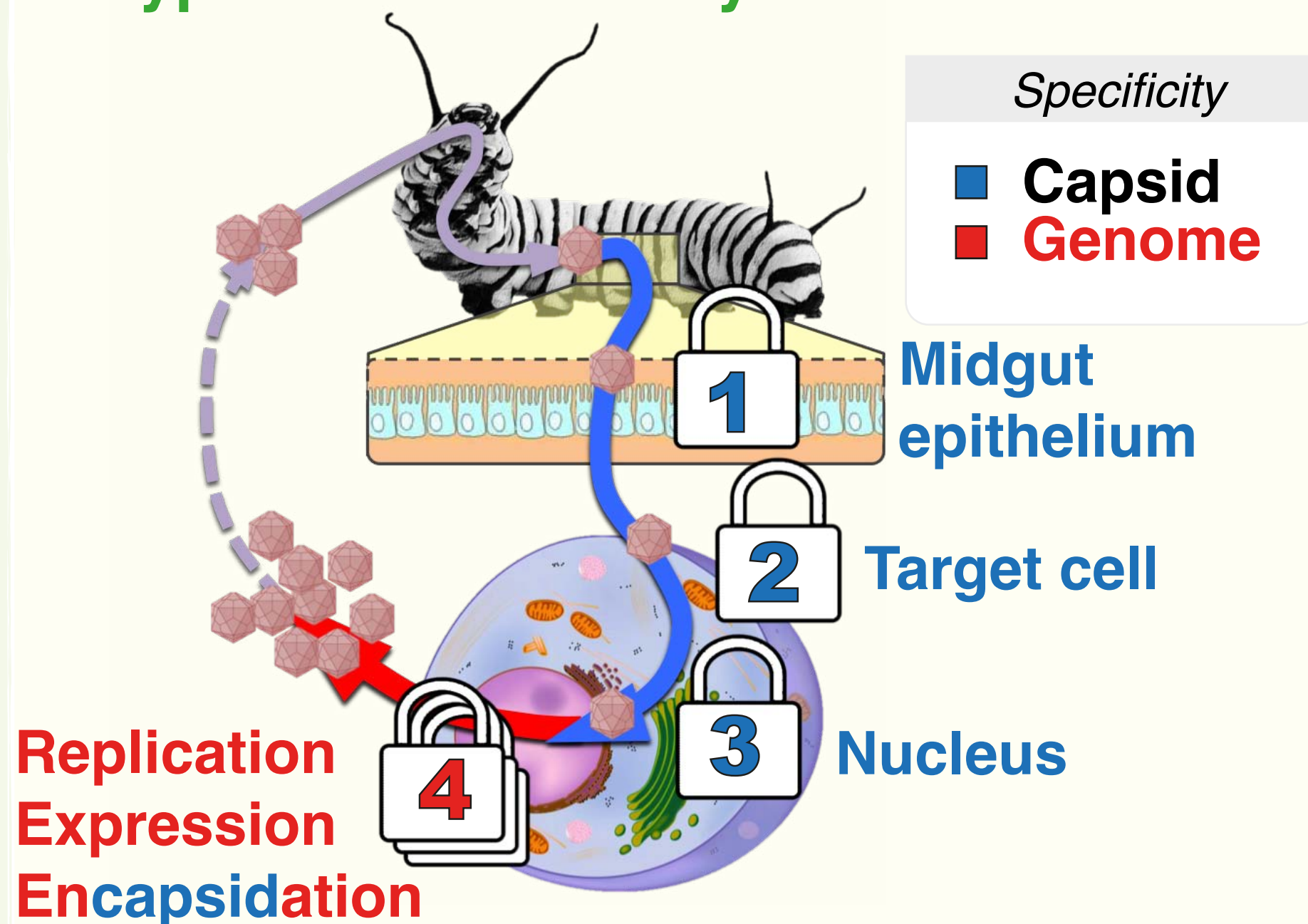
### The tiger mosquito (*Aedes albopictus*)

- Disease vector : Yellow fever, Dengue, Chikungunya, Zika, ...
- Originally from S.E. Asia
- Spreading over the world for decades

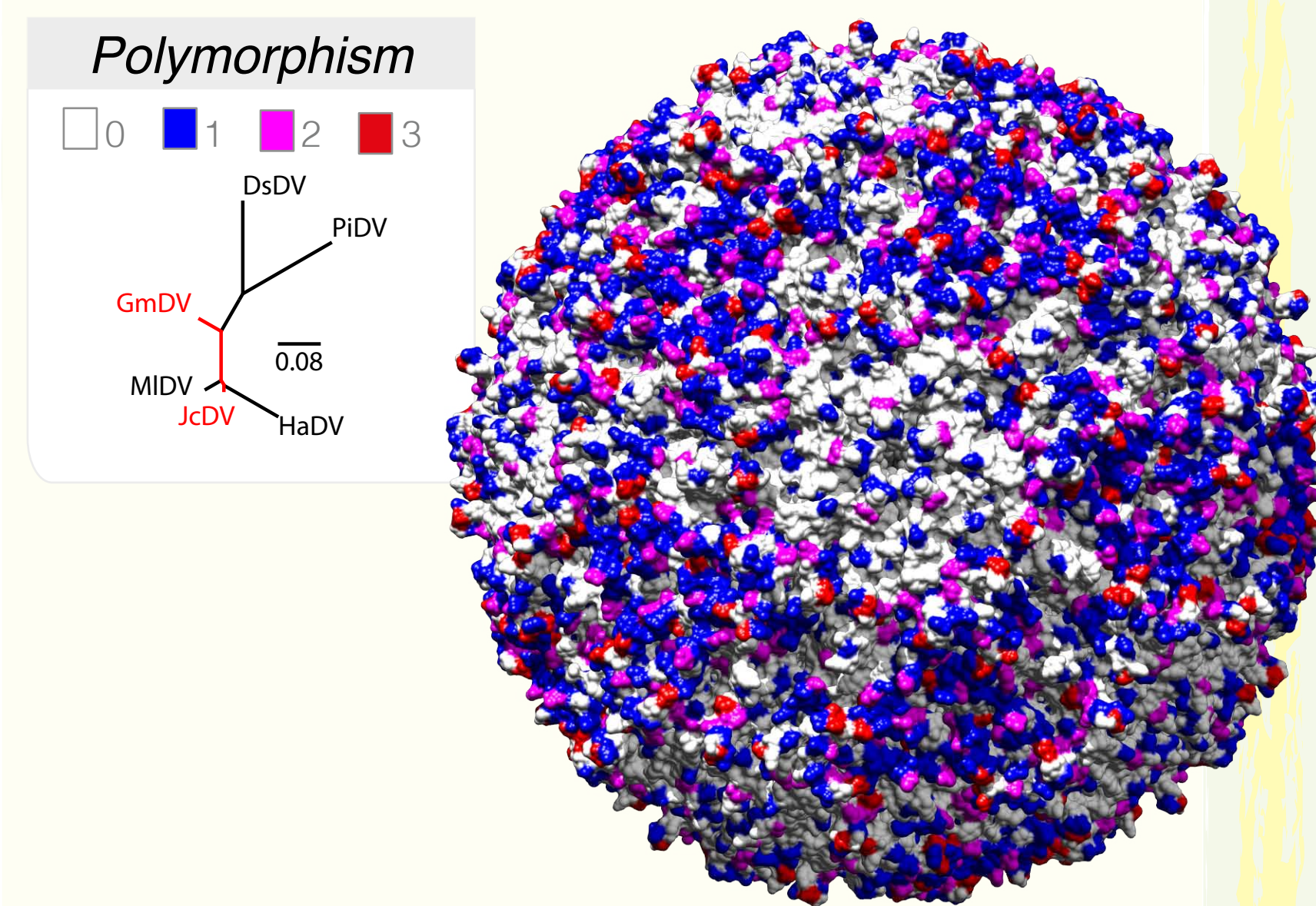


## Molecular Dissection Of A Complex Phenotype

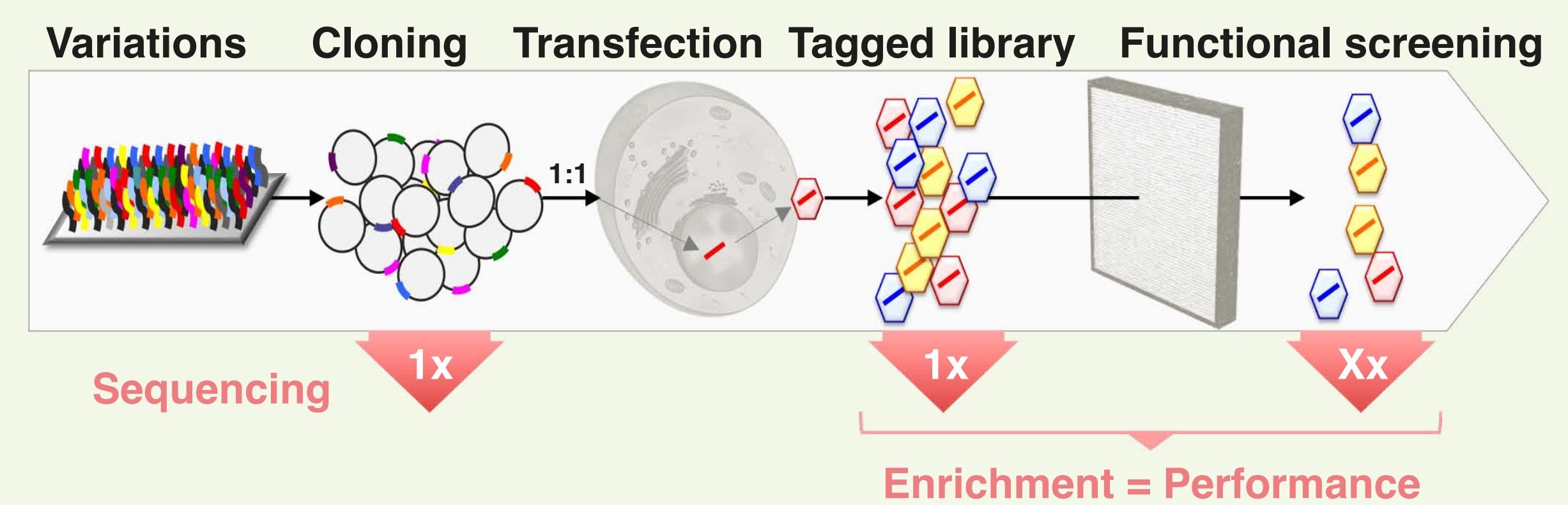
### A typical infectious cycle



### Sequence & Structure

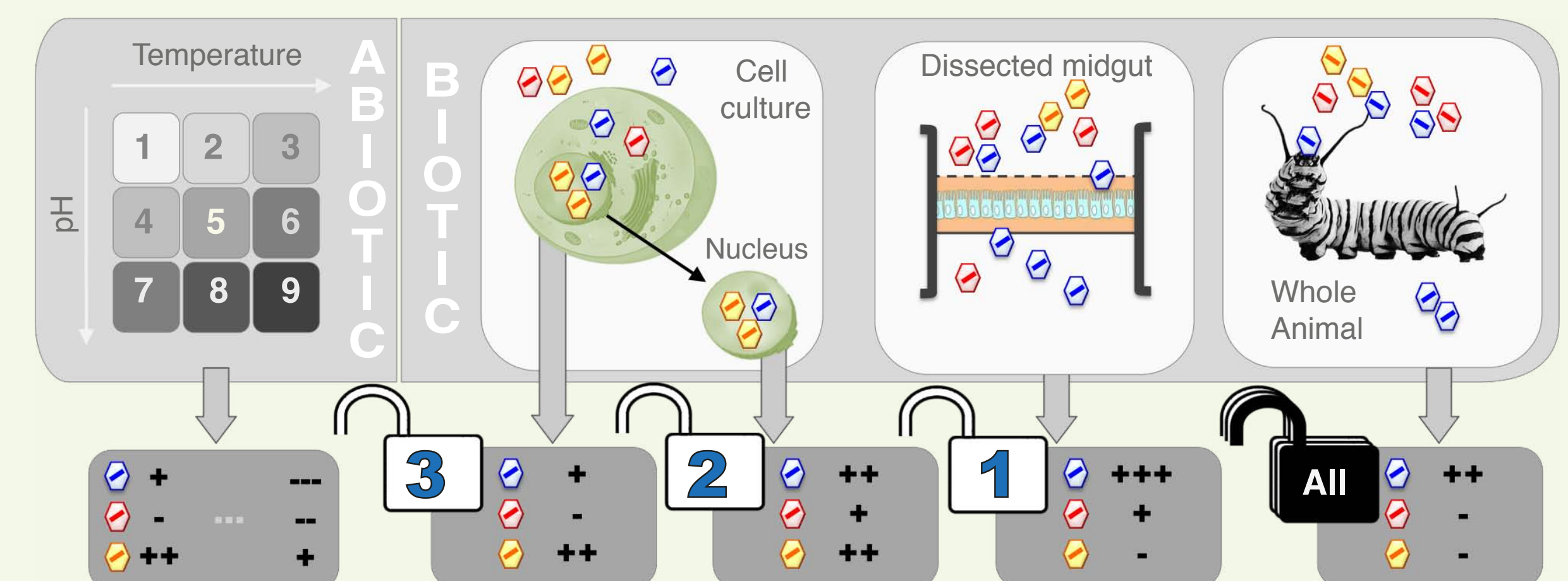


### Sequencing-based phenotyping of designer capsids



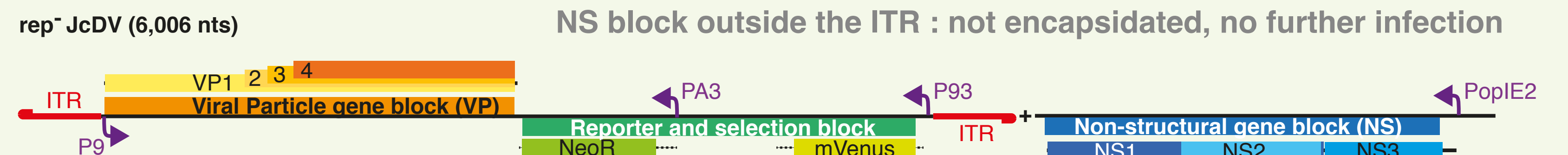
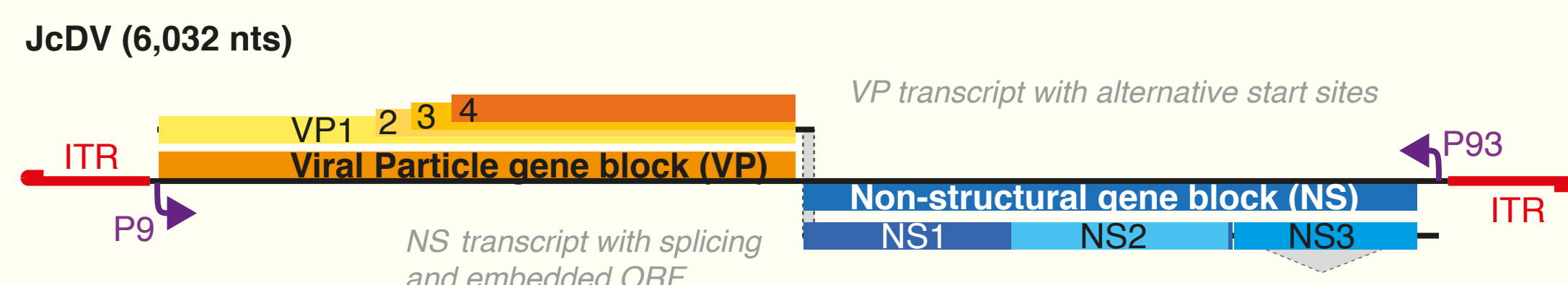
Quantitative characterization of several hundred of thousands precisely designed capsid variants based on high-throughput DNA synthesis and amplicon sequencing. Supports heavy multiplexing to screen many abiotic and biotic conditions.

### Parallel screening



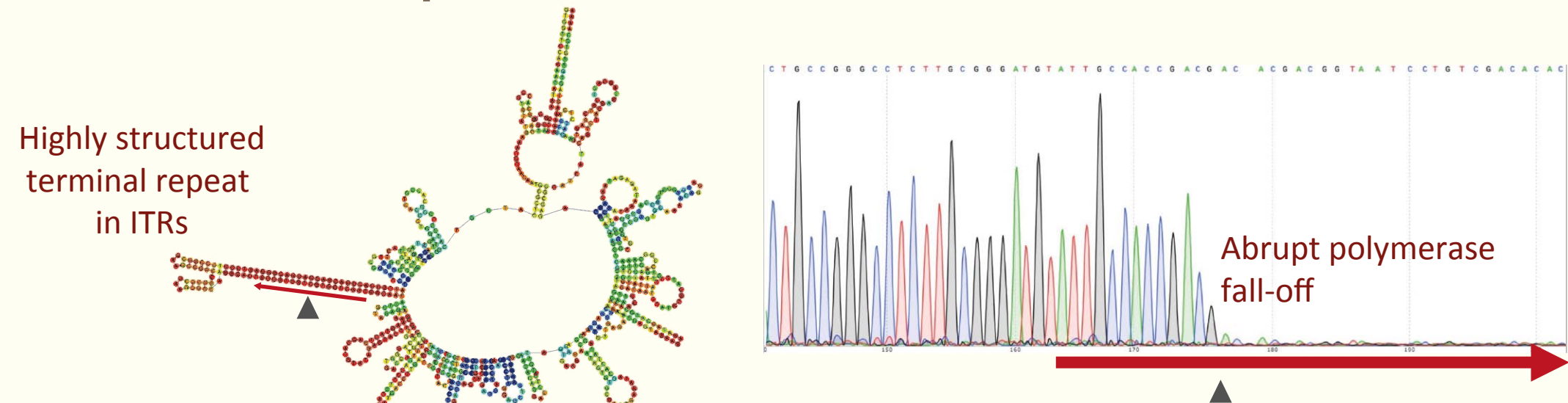
## Small, But Not So Simple : The Price Of Biosafety

### Construction of a mutable non-propagatable JcDV

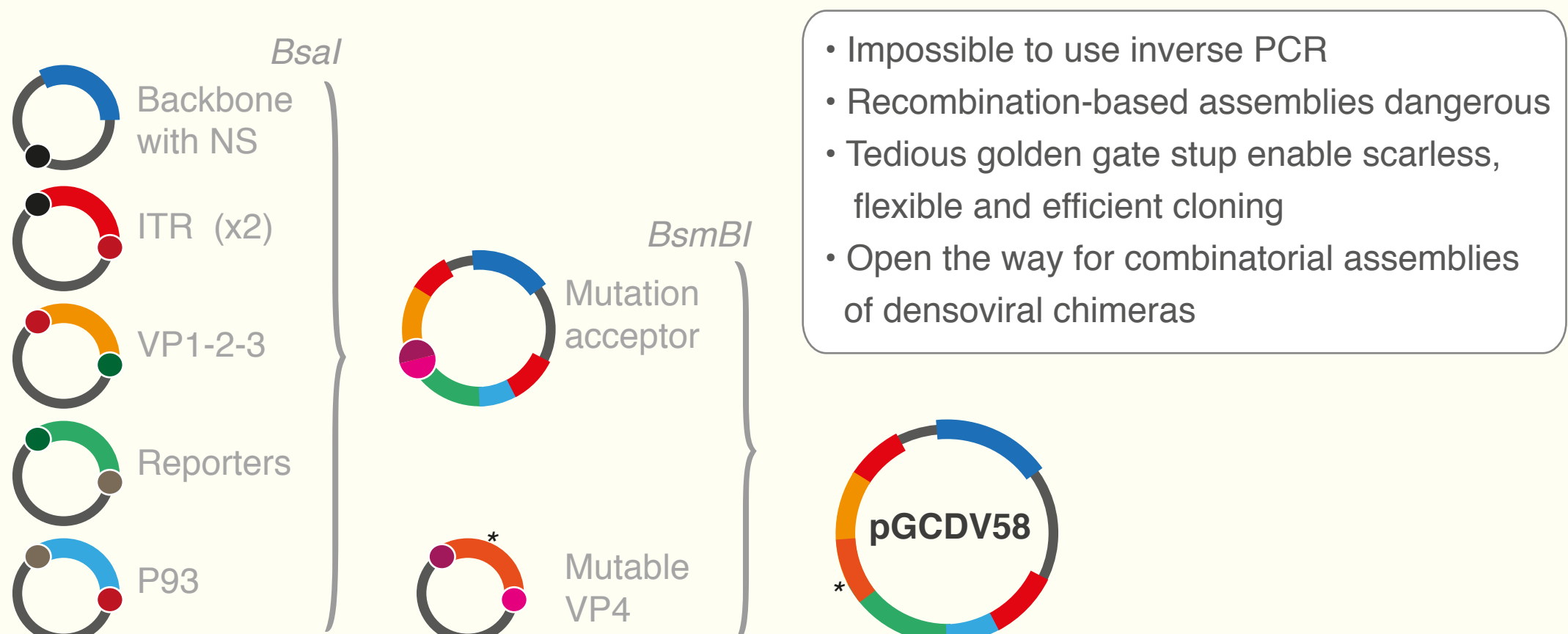


### Roadblock #1 : No PCR through ITRs

#### Of structure and repeats

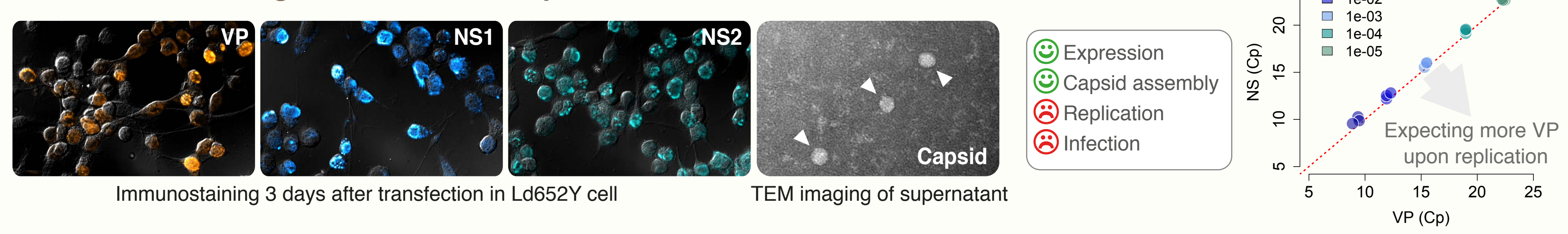


#### A winding detour through the golden gate



### 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

