Viral resistance in *Drosophila melanogaster*

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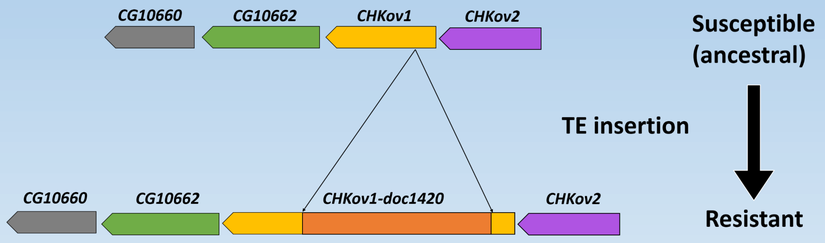
Introduction

In most organisms there is a lot of genetic variation in the susceptibility of individuals to parasitism. Our lab is identifying the genes and mutations that cause variation in resistance to viruses in *Drosophila melanogaster*. This will help us to understand both the mechanisms of resistance and the evolutionary reasons why this variation is maintained in populations. We have identified several genes and polymorphisms that are involved in resistance to *Drosophila melanogaster*'s natural viruses: Sigma virus and Drosophila C Virus (DCV).

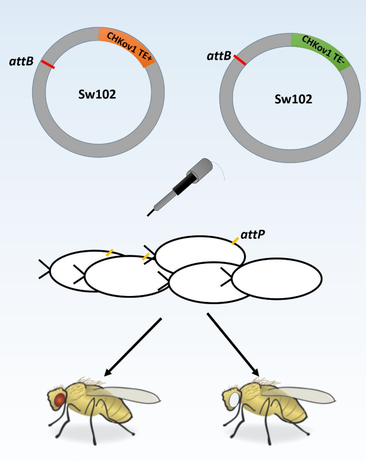
CHKov genes and Sigma Virus

Chkov are a series of paralogous genes located on Chromosome 3. Previous studies found a Transposable element (TE) insertion in *CHKov1* is associated with an increase in resistance to Sigma virus in flies [ǂ]. Transgenic flies carrying *CHKov1* either with or without the TE insertion has been generated through recombineering and embryo injection. Resistance assay indicates that the TE insertion has led to a dramatically increase in viral resistance. RT-qPCR showed that the insertion has changed the expression level of one transcript of *CHKov1*, but not the expression of neighbouring paralogous genes.

- **The evolution of *CHKov* genes [ǂ]**



- **Transgenic flies**

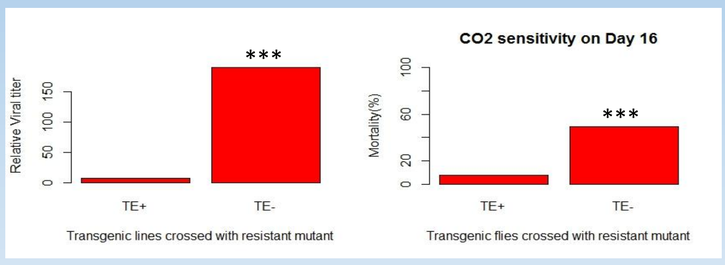


BAC recombineering using *galk* selection to excise TE from BAC [ǂǂ]

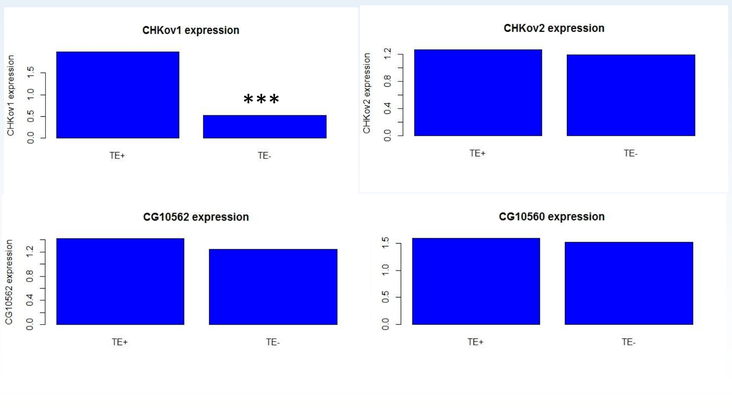
Inject BAC into fly embryo

Transformants carrying resistant or susceptible allele

- **TE insertion in *CHKov1* has increased resistance to Sigma virus in flies.**



- **TE insertion has changed the expression of one transcript of *CHKov1* gene, but not the expression of neighbouring paralogous genes.**



Future Work:

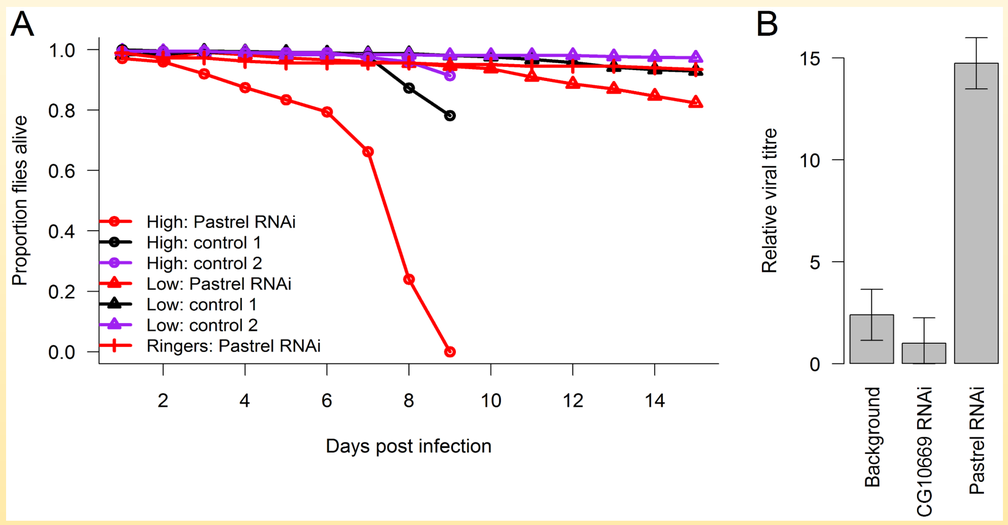
1. Find out whether the TE insertion causes 1) a loss of function of original *CHKov1* (used by virus) or 2) a gain of function of new *CHKov1* transcripts (antiviral) by knock out *CHKov* genes.

2. Investigate how has natural selection acted on *CHKov1* with the TE insertion.

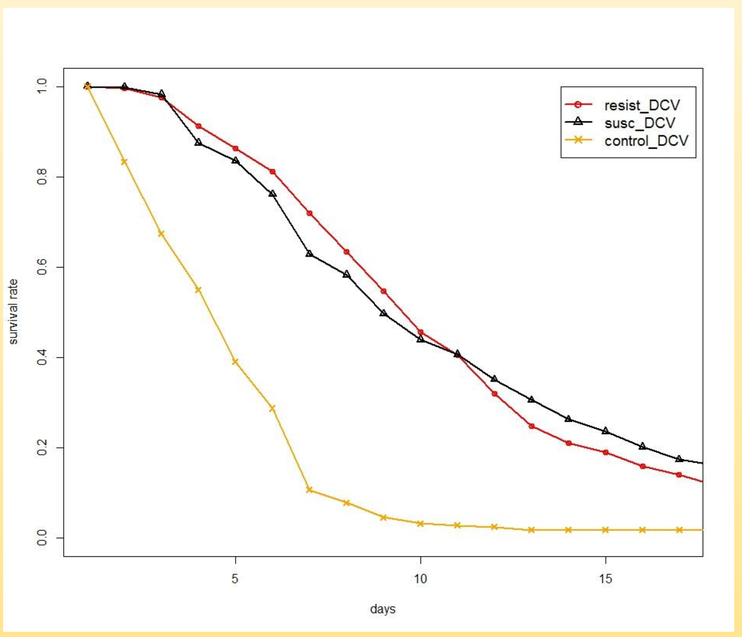
Pastrel (pst) and Drosophila C Virus

Pst is a gene identified by GWAS to be involved in DCV resistance. 6 SNPs are associated with resistance, but it is unclear which if any of these are causing flies to be resistant [ǂǂǂ]. We also found duplications and deletions of *pst* in a North American population.

- **RNAi confirmed that Knock down expression of *pst* increased the sensibility to DCV in flies [ǂǂǂ]**

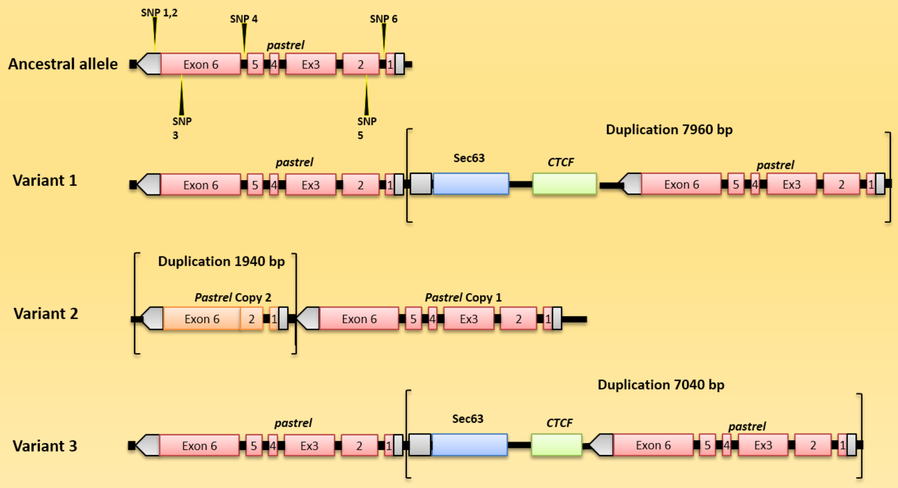


- **Over expression of *pst* led to increased resistance against DCV, however there is no significant difference between over-expressing resistant/susceptible alleles of *pst*.**

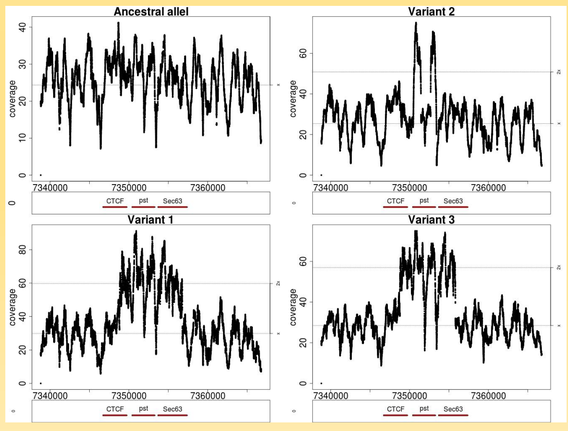


- **Rearrangement of *pst* and important SNPs**

1) 6 SNPs in *pst* are associated with DCV resistance [ǂǂǂ].
2) Duplications and deletions of *pst* are found.



- **Coverage plots of *pst* alleles, x is the average coverage counts and 2x means there is a duplication.**



Future work:

1. Identify the causative variants of *pst* regarding DCV resistance.
2. Study how natural selection acted on variants of *pst*.

ǂ Magwire MM *et al.* 2011 *PLoS Genetics.* 7: e1002337
ǂǂ Søren Warming *et al.* 2005 *Nucleic Acids Research*. Vol. 33, No. 4 e36
ǂǂǂ Magwire MM *et al.* 2012 *PLoS Genetics*. 8: e1003057
ǂǂǂǂ Mackay T *et al.* 2012 *Nature.* 482, 173-178

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