

C. ELEGANS AS A MODEL HOST FOR INNATE IMMUNITY AGAINST RNA VIRUSES

STEPHANIE COFFMAN⁽¹⁾, ZHIHUAN GAO⁽²⁾, GINA BROITMAN-MADURO⁽³⁾, MORRIS MADURO⁽³⁾, SHOU-WEI DING⁽²⁾
 {SUNDE003, ZHGAO, GINAM, MMADURO, SHOU-WEI.DING}@UCR.EDU

(1) GRADUATE PROGRAM IN GENETICS, GENOMICS AND BIOINFORMATICS, UNIVERSITY OF CALIFORNIA RIVERSIDE, RIVERSIDE 92521

(2) DEPARTMENT OF PLANT PATHOLOGY AND MICROBIOLOGY, UNIVERSITY OF CALIFORNIA RIVERSIDE, RIVERSIDE 92521

(3) BIOLOGY DEPARTMENT, UNIVERSITY OF CALIFORNIA RIVERSIDE, RIVERSIDE 92521



SUMMARY

C. elegans is an ideal model system to study the dynamics of viral infection, because it is transparent and the movement of proteins and organelles can be readily visualized in a living animal. Using video bioinformatics, we aim to gain a better understanding of how the host responds to viral replication, as well as how the virus exploits the host.

Caenorhabditis elegans

C. elegans is a widely used, genetically tractable model organism that has paved the way for numerous discoveries in medicine. To date three nobel prizes have been awarded to *C. elegans*, including one for the discovery of RNA interference (RNAi) and Green Fluorescent Protein (GFP). In 2002, *C. elegans* was shown to be capable of Flock House Virus (FHV) replication and to utilize RNAi as an antiviral mechanism. This system has since been used to uncover other immunity pathways that are homologous to those found in mammals.

Flock House Virus

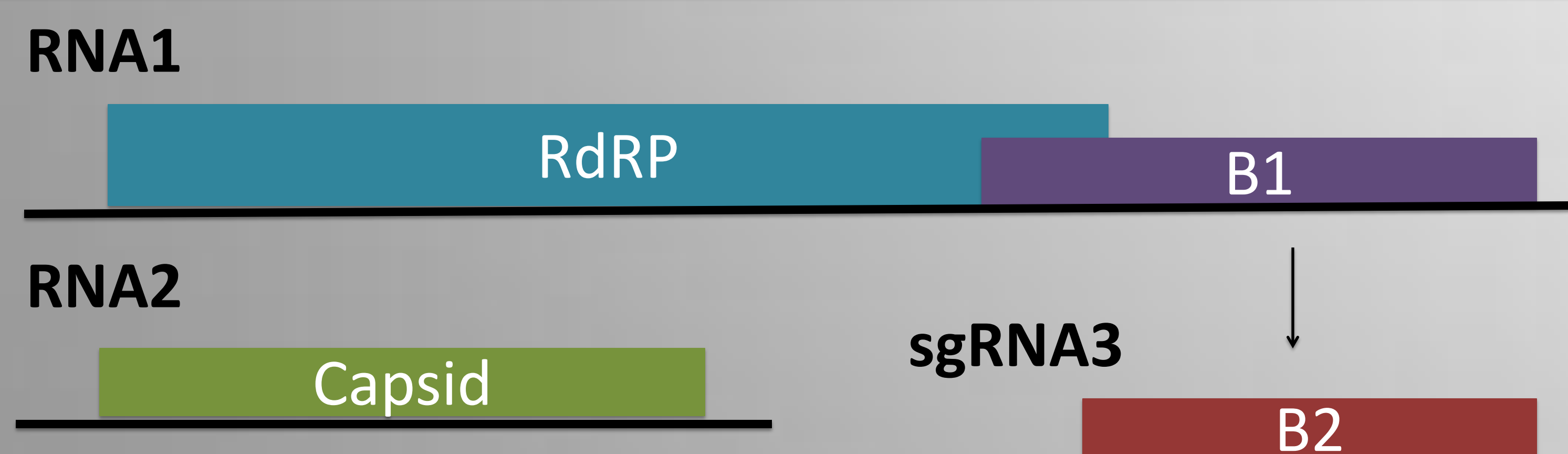


Fig 1. Flock House Virus (FHV) Genome. RdRP encodes an RNA dependent RNA Polymerase and B2 encodes a Viral Suppressor of RNAi from a sub-genomic RNA3 (sgRNA3). RNA2 encodes the capsid protein.

RESEARCH METHODS

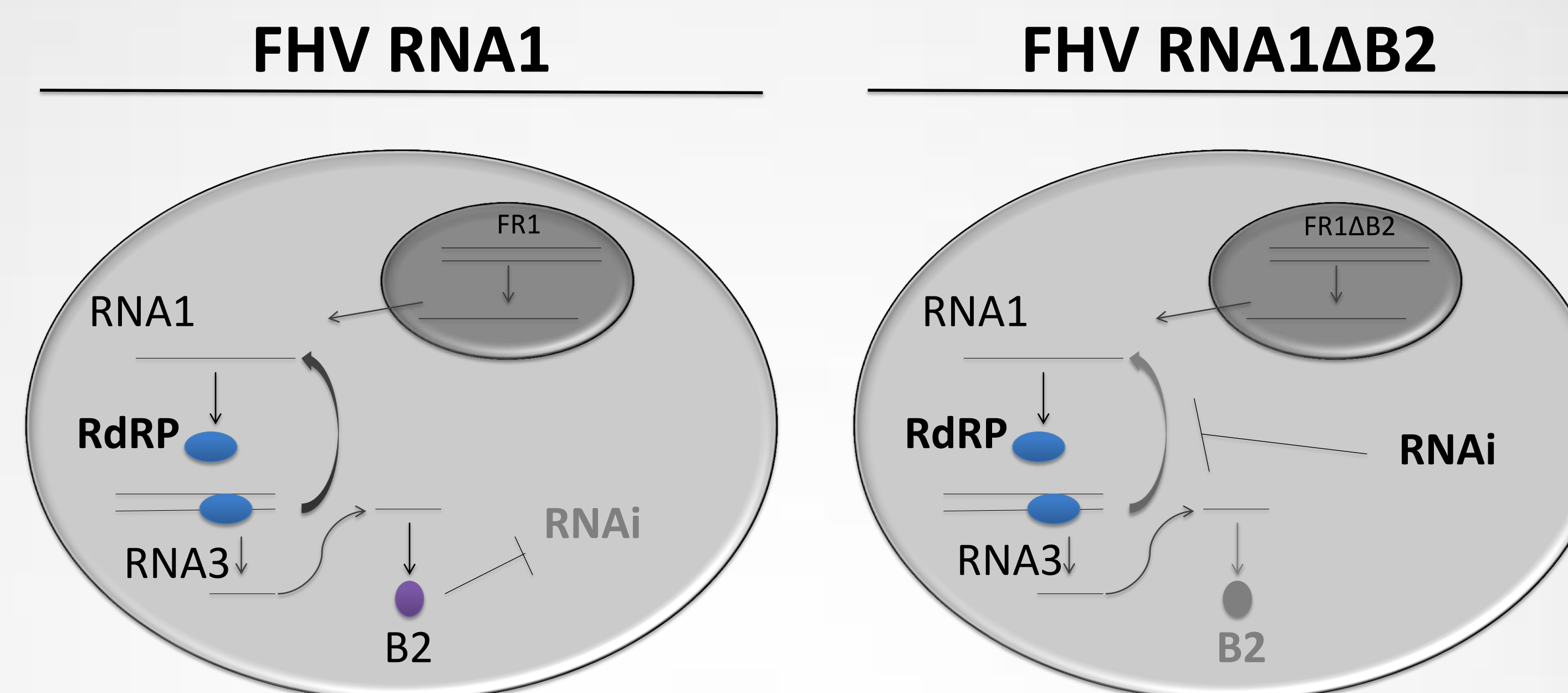


Fig 2. Expression of FHV RNA1 and RNA1ΔB2 from chromosomally integrated transgenes, which are under the control of a heat shock promoter.

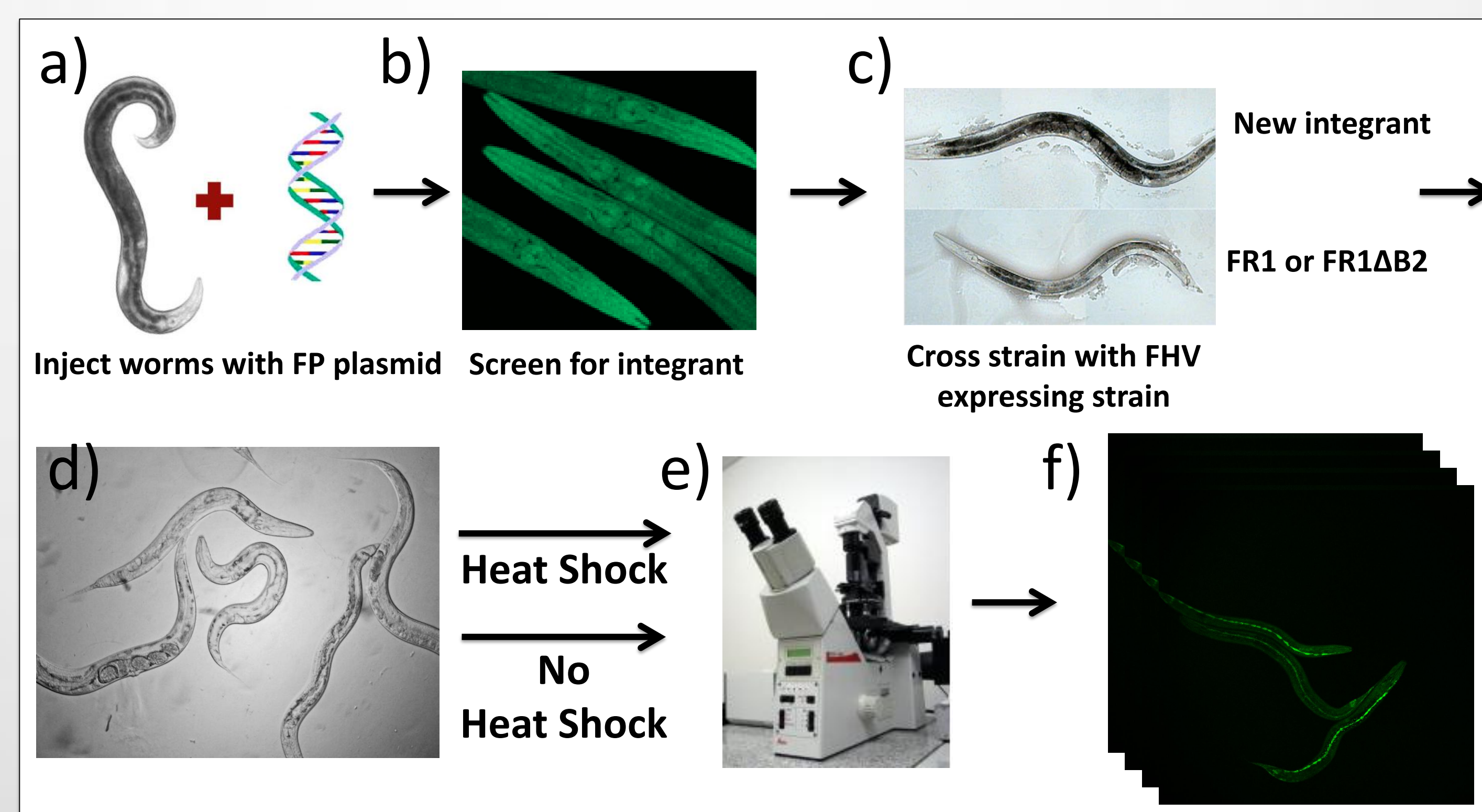


Fig 3. (a-c) The development of new strains expressing a host protein fused with a fluorescent protein (FP). (d-f) Acquisition of time-lapse (scanning confocal) or real-time (spinning disk confocal) imaging data. Automated analysis of videos would allow for measurements of the re-localization, co-localization, or the formation of aggregates after induction of FHV replication from a large sample population.

EXAMPLE: LGG-1::GFP

LGG-1::GFP is a marker for the formation of autophagosomes, which form in response to stress and have been implicated in viral immunity.

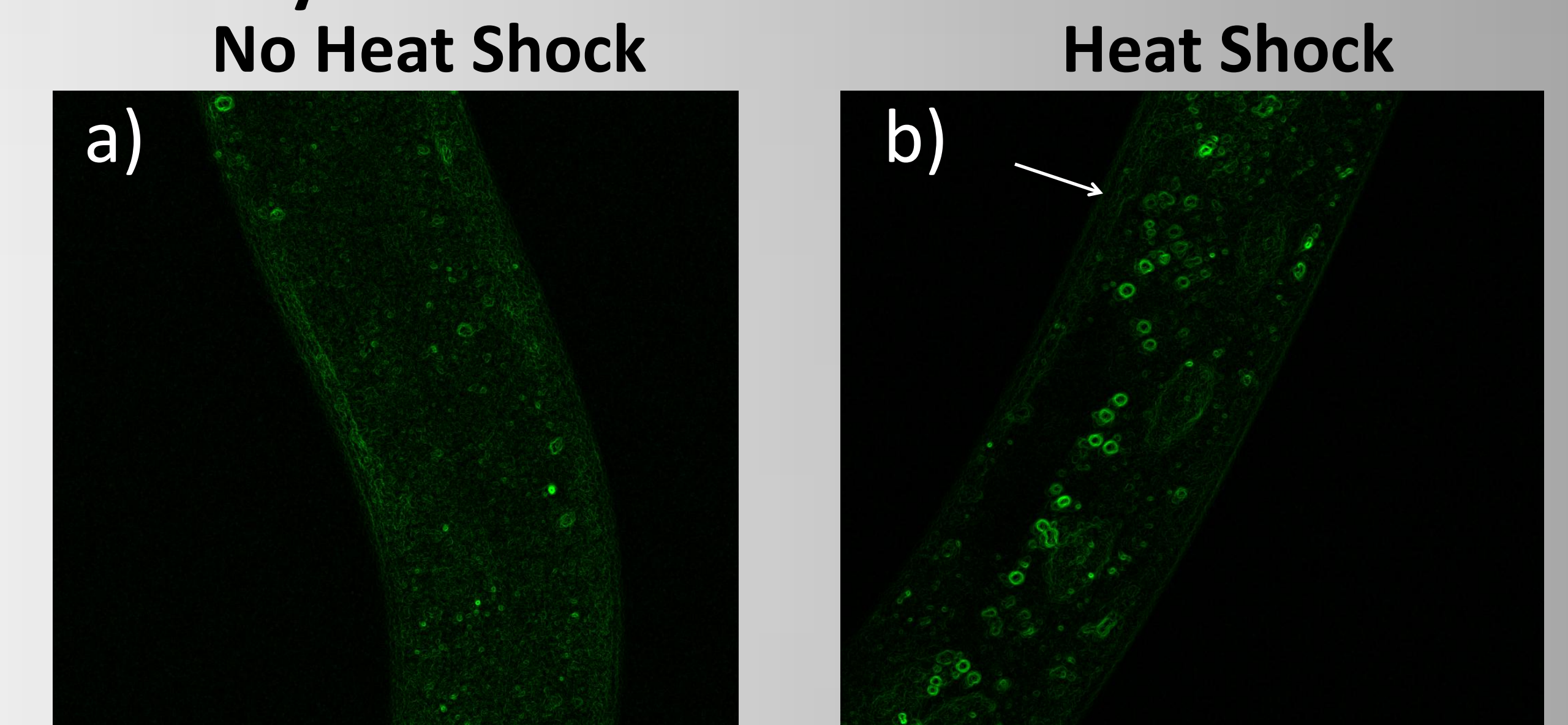


Fig 4. Edge detection of a) LGG-1::GFP b) LGG-1::GFP after the induction of autophagy.

CHALLENGES AND FUTURE WORK

1. Develop methods for visualizing assembly of the virus.
2. Develop a strain expressing the viral RdRP fused with mCherry to determine if replication begins in the cytoplasm before it is re-located to the mitochondria.
3. Automate the analysis of the images.

SIGNIFICANCE

1. Little is known about the earliest steps of viral infection.
2. Could lead to new methods for screening for factors involved in viral immunity.

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