Volume 12

Washington University
Undergraduate Research Digest

Spring 2017

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Christian Leung
Washington University in St. Louis

Identification of Genes Essential for Orsay Virus Infection in *C. elegans*

Christian Leung

Mentor: David Wang

The host factors responsible for viral infections remain poorly characterized, in part, due to a lack of systematic approaches that identify such factors in a whole organism. The model organism, *C. elegans*, has proven invaluable in dissecting many biological processes conserved from worms to humans. Study of host-virus interaction was limited in *C. elegans* due to the lack of a natural infecting virus. The Wang Lab has discovered the Orsay virus, a single-stranded, positive sense RNA virus that infects and replicates in a subset of the twenty intestinal cells of the host *C. elegans*.

Through a forward based genetic screen, we have identified three mutant lines that block or inhibit Orsay virus infection. Out of these three, we focus on *viro-133* and *viro-116*, which identify a premature stop codon in the gene *sid-3* and *B0280.13*, respectively. Genome annotation showed that *sid-3* encodes a non-receptor tyrosine kinase and *B0280.13* encodes an ortholog of the human WAS (Wiskot-Aldrich Syndrome) gene. We examine the mechanism of these genes in the context of Orsay virus infection.

To understand these genes, we first confirm that loss of function in *sid-3* or *B0280.13* blocks viral infection by confirming that an independently generated null allele of either *sid-3* or *B0280.13* causes the same phenotype. Second, we assess whether the mutation in these genes block viral entry by examining *viro-133* or *viro-116* worms that possess a heat inducible integrated viral genome. In these mutant worms, exogenous viral infection is blocked, but viral infection through heat induction is successful. Bypassing the entry step allows the Orsay virus to complete its lifecycle, suggesting that *sid-3* and *B0280.13* are involved in an early stage of the viral lifecycle, such as virus entry. These results begin to elucidate the nature and mechanism of these two host factors in Orsay virus infection.