Host/Pathogen Interactions Discovered In C. Elegans Germ Cells

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EM Scherer

Retrotransposons have been found in all animal and plant genomes analyzed and make up a large fraction of the human genome. Retrotransposons form virus-like particles, or VLPs, in the host cytoplasm before entering the nucleus and can cause enormous damage by inserting into host genes. When retrotransposons infect germ cells, such insertions can be inherited. The nematode*Caenorhabditis elegans* is one of the best understood experimental systems for development, but VLPs have never been observed in nematode germ cells.

To understand possible *Caenorhabditis* defenses against retrotransposons, graduate student Shannon Dennis, her advisor Dr. James Priess, and other members of the Priess Lab in the Basic Sciences Division used electron microscopy to screen over 17,000 germ cells in 21 different *Caenorhabditis* strains for the presence of VLPs. They found VLPs at a very low frequency in a few strains, including the standard laboratory strain N2. With available genetic tools for *C. elegans*, the authors knocked down the expression of different retrotransposons present in the genome, and found that N2 VLPs derive from the Cer1 (*C. elegans*retrotransposon 1) retrotransposon. There is only a single, apparently intact, copy of Cer1 in N2, which encodes for the Gag and Pol polyproteins, similar to a retrovirus.

In the course of evaluating different conditions that affect Cer1 Gag expression, Dennis *et al.* found that culturing adult nematodes at 15°C increased the number of Gag particles expressed compared to the standard laboratory temperature of 20-23°C. Moreover, no Gag particles were observed at 25°C. This result was confirmed by electron microscopy and positively correlated with the level of intact Gag/Pol polyprotein transcript within the gonad cytoplasm. Since Cer1 expression levels are low at standard laboratory culture temperatures, it is perhaps no surprise that retrotransposon replication in nematode germ cells has eluded scientific discovery. The challenge remains to understand how temperature regulates Cer1 production.

The identification of an active retroelement in *C. elegans* further expands the utility of *C. elegans* to analyses of host/pathogen interactions and may lead to new insights in development. It has also stimulated a flurry of research on retrotransposon replication in the Priess Lab. For example, the

authors discovered new aspects of microtubule architecture that accompany different stages of oogenesis and embryonic cell development in the process of tracking Cer1 VLP localization. They are also pursuing studies on the regulation of retrotransposon nuclear import/export and host defense mechanisms that silence Cer1 expression in different *Caenorhabditis* strains or stages of development.

Dennis S, Sheth U, Feldman JL, English KA, Priess JR. 2012. *C. elegans* germ cells show temperature and age-dependent expression of Cer1, a Gypsy/Ty3-related retrotransposon. *PLoS Pathogens* 8:e1002591.

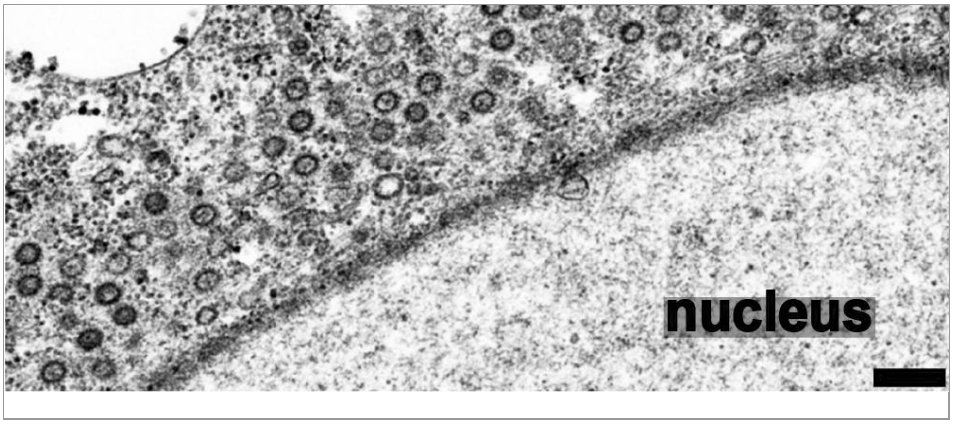

Image courtesy of the authors

Electron micrograph of Cer1 retrotransposon virus like particles (VLPs) approaching the nucleus of a C. elegans germ cell (scale bar is 0.2 µm). Cer1 VLPs are more abundant at temperatures that approximate their native habitat (15°C, shown), than at the standard laboratory culture temperature (20-23°C).