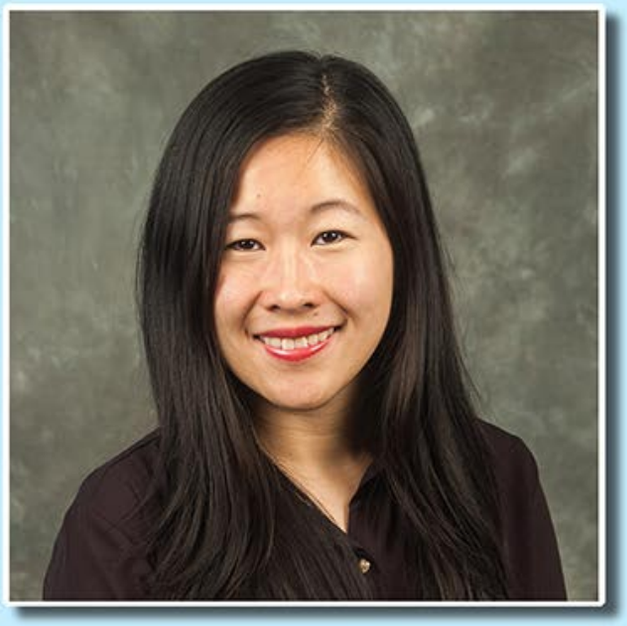

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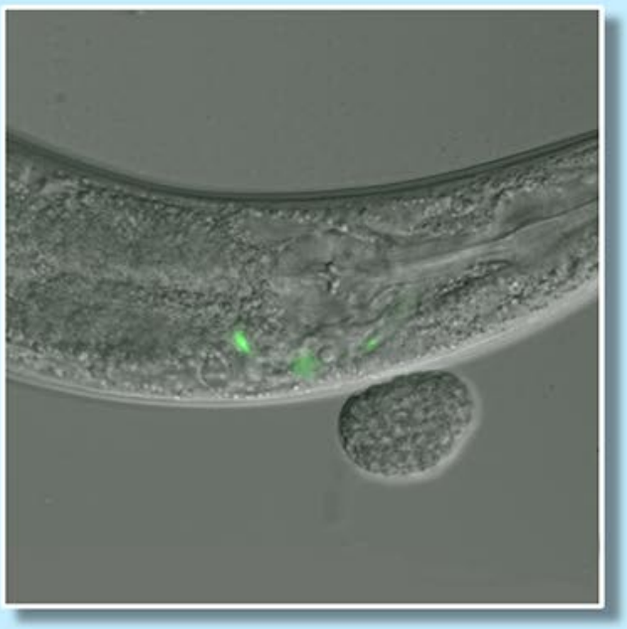

Expression of GS3582 in a neuron
of *Caenorhabditis elegans*

Insertion of Transgene arIs92 Promotes Progressive Sterility in *C. elegans* Strain GS3582

Organismal aging can be caused by epigenetic changes whose ultimate cause is various types of stress. *Caenorhabditis elegans* offers several advantages as a model organism for the study of the effect of epigenetic alterations on aging. With evolutionary conservation of basic genes that control development, *C. elegans* has already provided valuable insight into the genetic basis of age-related diseases in humans. Progressive sterility in *C. elegans* is the result of germline apoptosis from genomic or epigenomic stresses. In wild type *C. elegans*, the germline is an immortal cell lineage that is passed and maintained from generation to generation. A particular strain of *C. elegans* mutants, strain GS3582, which possesses an integrated transgene arIS92, causes progressive sterility. It is not known whether the transgene is the cause of the sterility phenotype. This study aimed to classify whether the key genetic lesion in GS3582 belongs to the signaling pathway of Piwi mutant *prg-1* or that of the nuclear RNAi defective mutant *nrde-1*. *prg-1* and *nrde-1* are two related, but distinct, mutant types that result in an epigenomic transgenerational sterility phenotype. Double mutant analysis, as well as high resolution fluorescence microscopy, was performed to show that strain GS3582 is related to, but not identical, to *prg-1* mutants. It was found that co-suppression, or silencing of high copy number germline genes, contributes to the transgenerational sterility of GS3582. We attenuated co-suppression with a loss-of-function allele of *mut-7*, and found that combining the GS3582 background and a *mut-7* allele had a strong synthetic effect on sterility. This implies that cosuppression represses the epigenomic toxicity of GS3582. The findings from this study could contribute to the understanding of germline maintenance in *C. elegans* and further influence the study of aging regulation in humans.