Precise gene regulation is pivotal for proper development. Dosage compensation, a specialized mechanism of chromosome-wide gene regulation, is the process by which the expression of genes on the X chromosome are equalized between males, which have a single X chromosome and females or hermaphrodites, which have two. This process is essential in all organisms where there are two sexes and the two sexes have different sex chromosomes, or the same sex chromosomes, but different numbers of sex chromosomes. For example, humans and flies both exist as two sexes that have different sex chromosomes. Males have an X and an Y chromosome, whereas, females have two X chromosomes. Similarly, worms, such as *C. elegans* also exist as two sexes. *C. elegans* exist as males and self-fertile hermaphrodites (modified females that make sperm for a short period of time before switching to egg production). While each of these organisms (humans, flies, and worms) uses dosage compensation to equalize the amounts of gene expression between the one X chromosome in males and the two X chromosomes in females/hermaphrodites, they have each co-opted a different module of genes for dosage compensation which has resulted in three very different dosage compensation mechanisms (Plath, et al., 2003; Meller, et al., 2003; Meyer and Casson, 1986).

To better understand how this essential chromosome-wide gene regulation process has evolved, characterization and comparison of this process in more closely related species is required. An excellent platform for comparison are the two *Caenorhabditis species, Caenorhabditis briggsae* and *Caenorhabditis elegans*. *C. elegans* and *C. briggsae* diverged ~15-30 million years ago and their sequence divergence is about 0.3 substitutions per site slightly greater than human and mouse (Cutter, 2008). These characteristics make these two species an ideal choice. The level of divergence is such that you would not necessarily predict complete conservation or complete divergence of dosage compensation mechanisms. Rather, you would expect the presence of enough differences such that it would further our understanding of dosage compensation evolution.

In *C. elegans*, dosage compensation has been well characterized. *C. elegans* dosage compensation is mediated by the developmental switch gene *xol-1* (Rhind, et al., 1995). The function of *xol-1* is conserved between *C. elegans* and *C. briggsae*. In both species, loss of *xol-1* results in male-specific lethality and overexpression results in hermaphrodite specific lethality. To further understand the evolution of *xol-1* function, we performed a *C. briggsae xol-1* suppressor screen. *C. briggsae xol-1* suppressors will be identified based on their ability to suppress the *xol-1* male lethality phenotype. We are currently characterizing eight newly identified suppressors and have determined the ability of each suppressor to rescue the *xol-1* male lethality phenotype. Male rescue percentages for the eight suppressors range from 8% to 30%, suggesting that the eight

newly identified suppressors are likely to be different. Next, we will use whole genome sequencing to determine the genetic identity of these suppressors.

We predict that these suppressors will belong to one of two classes: (1) *C. briggsae* homologs of a known *C. elegans* dosage compensation pathway component or (2) novel suppressors. Novel suppressors will represent components of the *C. briggsae* dosage compensation pathway that we are currently unaware of and further our understanding of the *C. briggsae* dosage compensation pathway. Furthermore, comparison of the dosage compensation pathways in *C. elegans* and *C. briggsae* will provide novel insights into the evolution of dosage compensation, an important chromosome-wide gene regulation mechanism.

Works Cited


1. Cutter, A.D. Divergence Times in Caenorhabditis and Drosophila Inferred from Direct Estimates of the Neutral Mutation Rate. *Mol Biol Evol* **25,** 778 - 786 (2008).
2. Katherine Plath, Susanna Mlynarczyk-Evans, Dimitri A. Nusinow, and & Panning, B. Xist RNA and the Mechanism of X Chromosome Inactivation. (2003).
3. Meller, V. H. & Kuroda, M. I. Sex and the single chromosome. *Adv. Genet.* **46**, 1-24 (2002).
4. Meyer, B.J. & Caason, L. P. Caenorhabditis elegans compensates for the difference in X chromosome dosage between the sexes by regulating transcript levels. *Cell* **47**, 871 - 881 (1986).
5. Rhind, N. R., Miller, L. M., Kopczynski, J.B. & Meyer, B. J. xol-1 acts as an early switch in the C. elegans. *Cell* **80**, 71-82 (1995).