The Effects of cisd Gene Family Disruption in Caenorhabditis elegans Fertility

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Up to 30% of the 50 million infertile people worldwide are affected by unexplained infertility, which could result from a CISD gene mutation. The CDGSH iron sulfur domain (CISD) family consists of three mammalian genes: CISD1, CISD2 and CISD3. Others have shown through in vivo cell culture experiments that CISD genes have a role in regulating iron and reactive oxygen species homeostasis and that CISD mutations cause irregular free iron levels. Free iron is similar to the elevated iron caused by the human disease hemochromatosis, as both can cause bodily harm. Excess iron is deposited into organs and glands, often leading to infertility in both sexes. Given the similarities in iron levels between cisd mutations and hemochromatosis, this project hypothesizes that cisd gene mutations display an infertility phenotype. To test this, the model organism Caenorhabditis elegans was utilized as its genome contains three cisd genes that code for proteins homologous to human CISD genes: cisd-1, homologous to CISD1 and CISD2, and cisd-3.1 and cisd-3.2, homologous to CISD3. The control strain N2 wild-type and mutant strains cisd-1(tm4993), cisd-3.1(pn24) and cisd-3.2(pn64) were used to test for infertility. After worm growth synchronization, three experiments were conducted: sterility assays, embryo lethality assays, and fecundity assays. Compared to N2, the assays found the following results: cisd-1(tm4993) and cisd-3.2(pn64) display low sterility percentages, cisd-3.2(pn64) animals have significant quantities of embryo lethality, and cisd-1(tm4993) and cisd-3.2(pn64) have significantly reduced offspring numbers. Together, these results suggest the cisd genes may have a role in fertility in C. elegans.

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