Combatting Familial Alzheimer's Disease by Comparing Calcium Retention of Mutated Presenilin Genes and Assessing the Restorative Potential of Parathyroid Hormone in a Caenorhabditis elegans Model

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Endoplasmic reticulum calcium dysregulation caused by mutations in the presenilin has been implicated in neuronal death and in Familial Alzheimer's Disease (FAD) pathology. The purpose of this experiment was to determine the individual and combined effect of the presenilin genes on abnormal calcium retention levels in the endoplasmic reticulum implicated in familial Alzheimer's Disease (FAD) as well as to determine the restorative ability of parathyroid hormone in cellular calcium homeostasis. It was hypothesized that if C.elegans mutants possessing the genes sel-12, hop-1, and sel-12 and hop-1 respectively are tested to observe which has the highest endoplasmic reticulum(ER) calcium retention, then the sel-12 and hop-1 mutant will have the highest retained ER calcium. The sel-12 and hop-1 genes are C. elegans homologs to the presenilin genes. RNA interference was used to obtain a mutant with both sel-12 and hop-1 mutations. Paralysis assays, oxidative stress assays, and levamisole assays were conducted to observe phenotypic manifestations of calcium retention indirectly through accompanying pathways. The data supported($p<0.05$) that sel-12 and hop-1 combined caused the largest degree of calcium retention. Additionally, parathyroid hormone had an alleviative effect($p<0.05$) by decreasing retained calcium concentration in each mutant strain. The supported restorative potential of parathyroid hormone in alleviating excess calcium retention will open a new avenue of research into slowing FAD progression beyond the scope of a model organism, indicating a potential mechanism for a multi-targeted cure for Alzheimer's Disease.

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