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HUMAN AMYLOID-BETA INDUCES ABNORMAL EMBRYONIC DEVELOPMENT AND HIGH EMBRYONIC LETHALITY IN CAENORHABDITIS ELEGANS

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The aggregation of amyloid-β (Aβ) proteins is widely recognized as a key pathological biomarker of Alzheimer's Disease (AD); its physiological function, however, remains largely unknown. Previous research has suggested that Aβ may regulate human brain embryogenesis and embryonic development in zebrafish. In this study, we used a *Caenorhabditis elegans* model of AD to explore the physiological function of human Aβ during embryogenesis. Analysis of embryonic lethality using strains CL2120 (human Aβ expressing) and CL2122 (empty vector control) shows a high embryonic lethality rate (31%), mostly occurring between the end of gastrulation to the 1.5-fold stage. RNAi screening and transcriptome analysis revealed that a key HOX developmental gene, *nob-1*, and its upstream regulator, *elt-1*, are significantly overexpressed in CL2120. As *nob-1* is heavily involved in posterior development at the end of gastrulation, our findings suggest that the elevated levels of ELT-1, induced by human Aβ expression, contribute to the observed high embryonic lethality. Taken together, our results indicate that Aβ proteins influence embryonic development by dysregulating key HOX genes.