4H Leukodystrophy Disease Model in Zebrafish

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Leukodystrophies, rare genetic disorders that cause abnormal myelin development or destruction, have recently been discovered to be associated with the polr3a gene. This experiment aimed to observe the effects of a polr3a knockout gene in zebrafish. Zebrafish were used because of their genetic similarity to humans, transparent embryos, rapid development and growth, and ease of genetic manipulation. There are currently no animal models representing early onset 4H leukodystrophy, and pathophysiological mechanisms are unclear. Because humans and zebrafish share many genes and biological processes, inferences about the possible effects of a mutation in humans can be made from what is observed in zebrafish. 136 embryos were collected, and sixty-eight were microinjected with the polr3a knockout sequence. Behavior tests, performed by gently poking zebrafish on top of concentric circles and recording their touch-response movement distances, were conducted on both control and knockout groups at three and five days post fertilization across three different cohorts of fish. It was found that the average distances of the control and knockout groups were significantly different, with each T-test resulting in a p-value less than 0.05. The statistics revealed that this polr3a mutation most likely affects motor function. The results also emphasize the severe impact of the polr3a mutation on zebrafish and suggest its potential implications for human health. Using zebrafish offered a novel opportunity to study the genetic and molecular mechanisms that present from this disease, reinforced zebrafish as a valuable model for leukodystrophy, and can aid in further studies to develop effective treatments.

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