The Role of QSER1 During Early Stages of Zebrafish Embryonic Neural Development

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Neurogenesis during early embryonic development is a highly regulated, transcriptional process that establishes the framework for the vertebrate central nervous system (CNS). The QSER1 gene protects DNA methylation valleys (DMVs) from de novo methylation via DNMT3A and DNMT3B by blocking transcription factors and recruiting repressive proteins. This study investigates QSER1's potential role as a regulatory factor in neurogenesis by analyzing the impact of a double KO of the QSER1 allele on the expression of key neural genes during the pharyngula period. This was achieved by comparing Pax2a, Tfap2a, Lhx9, and Lhx2b expression levels in 24 hours post fertilization (hpf) heterozygous and 24 hpf mutant QSER1 embryos using Whole Mount In Situ Hybridization (WISH) and manual quantitative analysis via ImageJ. All analyses showed heterozygous embryos expressing high levels of Pax2a, Tfap2a, Lhx9, and Lhx2b indicating proper neurogenesis. In contrast, QSER1 mutants showed significant drops in expression levels for all four genes. The marked decrease in staining intensity in mutants implies that QSER1 is involved in mediating the transcriptional activity of genes necessary for synthesis of astrocyte proteins, maintaining homeostasis of the CNS and neural development. Moreover, QSER1 is implicated in neural crest patterning, and intra-brain, ophthalmological, and craniofacial development. This study discusses the epigenetics of QSER1's regulatory functions during neurogenesis and explores impacts of maternal mRNA gastrulation failure on gene expression levels. Characterizing QSER1's function in neurogenesis allows researchers to now target QSER1 mutations in neurodevelopmental disorders associated with DNA hypermethylation, such as Rett syndrome, ICF, and imprinting disorders.

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