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Aberrant expression of histone homocysteinylation: Implications for neural tube defects

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Neural tube defects (NTDs) are serious congenital malformations. Excessive maternal homocysteine (Hcy) increases the risk of NTDs, while its mechanism remains elusive. In this study, we evaluated the role of histone homocysteinylation in neural tube closure (NTC). A total of 39 histone homocysteinylation sites were identified in samples from human embryonic brain tissue using mass spectrometry. Elevated levels of histone KHcy and H3K79Hcy were detected at increased cellular Hcy levels in human fetal brains. Using ChIP-seq and RNA-seq assays, we demonstrated that an increase in H3K79Hcy level down-regulated the expression of selected NTC-related genes including Cecr2, Smarca4, and Dnmt3b. In human NTD brain tissues, decrease in expression of Cecr2, Smarca4, and Dnmt3b was also detected along with high levels of Hcy and H3K79Hcy. Our results suggest that higher levels of Hcy contribute to the onset of NTDs through up-regulation of histone H3K79Hcy, leading to abnormal expression of selected NTC-related genes

Biography

QinZhang worked in capital institution of pediatrics. Her work focus on the role of histone modifications in nural tube defects, especially the application of mass spectrometry in histone modification idendification and validation. Her current work is concerned with the role of histone homocysteinylation in nural tube defects.

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