Is 5-Hydroxymethylcytosine a Suppressor or Activator in Epigenetic Marks?

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Alcohol has been observed to have teratogenic effects on humans and mice during different stages of embryonic development. These effects can be condensed under fetal alcohol spectrum disorder (FASD), exhibiting a variety of signs from growth retardations to neurobehavioral aberrations. Despite better understanding of several potential mechanisms, the question of how alcohol, as an environmental factor leads to brain growth delay in FASD remains elusive. DNA methylation is key to development and tissue specification. Studies have suggested that alcohol may alter gene expression by affecting DNA and histone methylation. Previous studies have demonstrated that 5-methylcytosine (5mC), a DNA methylation mark, is associated with histone 3 lysine-9me3, (H3K9me3) to play a role in gene repression. Recently another methylation mark, 5hydroxylmethylcytosine (5hmC), was found to prevail in the nervous system. However, its function has not been clear. Global analysis suggests that it is a transition of demethylation leading to transcription. The study will first identify its association with histone 3 lysine-4me3, (H3K4me3) a transcriptional activator in gene expression, and then study the 5hmC under influence of alcohol exposure. This study will utilize both an in vivo model—the vapor chamber, and an in vitro model—the embryonic culture system to address this question. Embryos were exposed to alcohol (400mg/dL, 88mM) from the beginning of embryonic day (E) 8 for 6hrs, harvested at E10, and processed for immunohistochemistry. Compare the DNA methylation marks, and histone modification marks to see if the spatial and/or temporal distribution has been affected by alcohol exposure. It is expected that in the alcohol-treated embryos, an overall retardation of embryonic growth, delayed neural tube formation, and altered expression of epigenetic markers will be observed. This study could indicate that alcohol, through alteration of DNA and histone methylation is a potential mechanism underpinning brain growth delay in FASD.

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