Epigenetic Mechanisms in Perinatal Hypoxic-Ischemic Brain Injury

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Perinatal hypoxic-ischemic encephalopathy (HIE) is associated with high neonatal mortality and severe long-term neurologic morbidity. The molecular mechanisms and the pathway of brain injury in infants with HIE remain largely elusive. Although therapeutic hypothermia is the current standard of care for newborns with moderate to severe HIE, nearly half of affected infants treated with hypothermia still die or suffer significant neurologic disability. Thus, there is an urgent need to further investigate the underlying mechanisms and to develop additional treatment strategies. It has been shown that epigenetic mechanisms are of critical importance in impacting hypoxic-ischemic sensitive phenotype in the developing brain. Our recent studies reveal an important role of epigenetic regulation of the glucocorticoid receptor and microRNA 210 in perinatal hypoxic-ischemic brain injury and provide new insights and proof of concept in novel targets of epigenetic regulation in potential therapeutic strategies that may be beneficial for the treatment of infants with hypoxic-ischemic brain injury. This is of critical importance given the extreme limit of effective therapeutic intervention currently available other than hypothermia for this important clinical problem in newborns.

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