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Sulforaphane-mediated epigenetic modulation of ethanol-induced apoptosis and birth defects

Sulforaphane (SFN) is an isothiocyanate derived from cruciferous vegetables. SFN's cytoprotective properties have been demonstrated in several models associated with a variety of disorders. Previous studies from our laboratory have shown that SFN protects against ethanol-induced oxidative stress and apoptosis in neural crest cells (NCCs), an ethanol-sensitive cell population implicated in Fetal Alcohol Spectrum Disorders (FASD). More recently, it was discovered that SFN can regulate gene expression through epigenetic mechanisms, specifically by decreasing the activities of histone deacetylase (HDAC) and DNA methyltransferase (DNMT). Our studies have shown that exposure to ethanol resulted in a significant increase in the activities of HDAC and DNMT in NCCs. Ethanol exposure also increased the methylation of the Bcl2 promoter. In addition, ChIP-qPCR assay revealed that ethanol exposure significantly decreased acetyl-histone H3 binding to the Bcl-2 promoter and the expression of Bcl-2. Supplementing with SFN reversed the ethanol-induced hypermethylation of Bcl-2 promoter and reduction in acetyl-histone H3 binding to the Bcl-2 promoter. Treatment with SFN also restored the expression of Bcl-2 in ethanol-exposed NCCs. Furthermore, supplementing with SFN diminished ethanol-induced apoptosis in NCCs and in mouse embryos exposed to ethanol *in vivo*. These results demonstrate that SFN can epigenetically restore the expression of Bcl-2 and attenuate ethanol-induced apoptosis by decreasing methylation and increasing histone acetylation at the Bcl-2 promoter. These findings support the potential of dietary consumption of SFN or SFN-rich broccoli sprouts to attenuate ethanol-induced apoptosis and confer *in vivo* protection against FASD through epigenetic regulation of the expression of anti-apoptotic genes.

Biography

Shao-yu Chen, PhD, is a tenured Professor and University Scholar at the Department of Pharmacology and Toxicology at the University of Louisville. He received his PhD degree in 1991 in China and was trained as a postdoctoral associate in the University of North Carolina at Chapel Hill. He joined the University of Louisville in 2014. He has conducted alcohol-related birth defects research for more than 20 years. His research program, funded by multiple NIH R01 grants, focuses on elucidation of cellular and molecular mechanisms of Fetal Alcohol Spectrum Disorders. He has published a number of papers in high profile journals, including PNAS, Nat Commun, and EMBO Journal. He has been serving as an editorial board member of the Oxidative Medicine and Cellular Longevity and other journals. He has also served as a grant reviewer for NIH and other international agencies.

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