THE INFLUENCE OF IN-UTERO SMOKE EXPOSURE ON ATOPIC DISORDERS VIA EPIGENETIC MECHANISM

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Background and Aims: Evidence has shown that in-utero exposure has important effects on DNA methylation. However, how prenatal tobacco smoke exposure affects DNA methylation leading to atopic disorders remains to be addressed. Since most children suffering from atopic dermatitis (AD) continue to develop asthma later in life, we explored whether prenatal smoke exposure may induce aberrant DNA methylation of specific genes that were related to childhood AD.

Methods: We recruited 261 newborns with cord blood in Taiwan birth panel study. At 2 years of age, information about development of AD and environmental exposures were collected. Cord blood cotinine levels were measured by high performance chromatography-mass spectrometry (HPLC-MS/MS) to stand for prenatal smoke exposure. Methylation differences associated with smoke exposure were screened in cord blood DNA of 14 cohort children by whole genome methylation array. CpG loci that demonstrated a statistically significant difference in methylation were validated by SNaPshot. The functions of the candidate genes were also investigated.

Results: Differential methylation of CpG loci in four genes (TSLP, GSTT1, CYB5R3, and KRT6C) was identified through the screen. Of these, thymic stromal lymphopoietin (TSLP) gene exhibited significant increases in methylation in the exposed than non-exposed children after being validated by SNaPshot ($p = 0.001$). TSLP gene was therefore selected for further investigation in a larger sample of 54 cohort children. The degree of TSLP 5-CpG islands methylation was inversely related with TSLP protein levels in cord blood.

Conclusions: The effect of prenatal tobacco smoke exposure on the risk for childhood atopic disorders may be mediated through alterations in DNA methylation.

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