Childhood obesity interacts with the HIF3A variant on plasma ALT mediated by DNA methylation

Shuo Wang¹, Jieyun Song¹, Haijun Wang¹ and Jun Ma¹
¹Peking University, China
²University of Notre Dame, USA

Hypoxia Inducible Factor 3 Alpha Subunit (HIF3A) DNA methylation has been demonstrated to be associated with obesity, and also reported to have a Body Mass Index (BMI)-independent association with plasma alanine aminotransferase (ALT). To further examine the relation among obesity, ALT and HIF3A, the genotype of the HIF3A rs3826795 polymorphism was tested in a case-control study including 2030 Chinese children aged 7-18 years old (705 obese cases and 1,325 non-obese controls), and furthermore the HIF3A DNA methylation of the peripheral blood was measured in 110 severely obese children and 110 age- and gender- matched normal-weight controls. A significant interaction between obesity and the HIF3A rs3826795 polymorphism in relation with ALT was found ($P_{inter}<0.050$), with rs3826795 G-allele number elevating ALT significantly only in obese children ($\beta'=0.075$, $P=0.037$), but not in non-obese children ($\beta'=-0.009$, $P=0.741$). Additionally, a complete mediation effect of HIF3A methylation was indicated in the association between the HIF3A rs3826795 polymorphism and ALT among obese children ($\beta'=0.242$, $P=0.014$). This is the first study to report the interaction between obesity and HIF3A gene in relation with plasma ALT, and also the first to reveal a complete mediation effect among the HIF3A polymorphism, methylation and plasma ALT. This study could provide new clues to the function of HIF3A gene and its relation with obesity and ALT, which would be useful for future risk assessment and personalized treatment of liver diseases.

Biography
Shuo Wang has majored in Public Health and is pursuing PhD degree at Peking University (Sep 2013). She is now a visiting PhD student at University of Notre Dame (Oct 2015). Her research focus is on the genetic risk factors of obesity in children and adolescents, including single nucleotide polymorphisms, gene-behavior interaction and DNA methylation. She has published more than 10 papers in reputed journals including PLoS One, Chinese Journal of Child Health Care, Chinese Journal of Epidemiology, etc.

swang16@nd.edu

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