ASSOCIATION OF POLYMORPHISMS IN WNT9B AND PBX1 WITH MAYER-ROKITANSKY-KÜSTER-HAUSER SYNDROME IN CHINESE HAN

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Background: Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome is a rare disease characterized by congenital aplasia of uterus and the upper portion (2/3) of vagina. Some studies designed to identify MRKH syndrome causal mutations have mostly resulted in negative outcomes. With a relatively large sample size, we discussed if these reported variants associate with MRKH syndrome in Chinese Han, and if any gene-gene epistatic interaction exists among them for MRKH syndrome.

Methods: This study was performed on 182 unrelated Chinese women with pure MRKH syndrome and 228 randomized female controls. Seventeen candidate loci in AMH, PBX1, WNT4, WNT7A, WNT9B, HOXA10, HOXA11, LHXA1 and GALT genes were genotyped with the Sequenom MassARRAY iPLEX platform. Single-marker association analysis was performed using logistic regression. Additive and multifactor interactions were also investigated.

Results: The rs34072914 of WNT9B was associated with MRKH syndrome (P=0.024, OR=2.65, 95%CI=1.14-6.17). And the dominant models of rs34072914 and rs2275558 in WNT9B and PBX1 showed significant association with MRKH syndrome risk in Chinese Han. In addition, additive gene-gene interaction analysis indicated significant synergetic interaction between WNT9B and PBX1 (RERI=1.397, AP=0.493, SI=4.204). With Multifactor Dimensionality Reduction (MDR), we found novel dimensional four-gene epistatic effects (AMH, PBX1, WNT7A and WNT9B) in MRKH syndrome.

Conclusions: This association study succeeded in identifying two susceptibility SNPs (WNT9B, PBX1) associated with MRKH syndrome risk separately and interactively. The discovery of four-gene epistatic effect (AMH, PBX1, WNT7A and WNT9B) in MRKH syndrome will provide a new entrance to unravel the genetic mechanism underlying etiology of MRKH syndrome.