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AB097. Combined effects of *RET* transcriptional enhancer variants in Hirschsprung disease

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Background: Hirschsprung disease (HSCR) is a complex genetic disorder, which characterized by absence of ganglion cells along variable lengths of the intestines in neonates, with the *RET* was identified as a major locus involved in HSCR. In this study, we investigated the joint effects of common variants within the *RET* transcriptional enhancer, rs2435357 and rs2506030, for development of HSCR in Indonesia.

Methods: Sixty HSCR patients and 122 non-HSCR controls was involved in this study. Two genetic markers of the *RET* were examined using TaqMan assay. We analyzed the case-control association tests between two genetic markers and HSCR using the statistic. A P value <0.025 is considered significant given that two tests (markers) were performed in the analysis.

Results: There was high correlation between *RET* rs2435357 marker and HSCR either by case-control analysis (OR =4.46, $P=2.5\times10^{-8}$) or transmission disequilibrium test (TDT, $P=4.2\times10^{-6}$), but not *RET* rs2506030 (OR =1.68, P=0.042 and P=0.034, respectively). Two locus analyses of variants revealed that *RET* rs2435357 (TT), in combination with rs2506030 (GG), were associated with the increased disease risks of HSCR (OR =5.42, $P=3.9\times10^{-6}$) compared with a single variant of rs2506030.

Conclusions: Our study shows that *RET* rs2435357 variant is a strong genetic risk factors for development of HSCR in Indonesia. In addition, the disease effects of *RET* rs2506030 genotypes are crucially dependent on the effects of rs2435357 genotypes.

Keywords: Hirschsprung; RET; rs2506030; rs2435357

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