Complex Genetic Disorders, Genetic Susceptibility to Infections

AB053. *NRG1* rare variant effects in Hirschsprung disease patients

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Background: Hirschsprung disease (HSCR) is a heterogeneous genetic disorder characterized by absence of ganglion cells along intestines resulting in functional bowel obstruction. *NRG1* gene has been implicated in the intestinal ganglionosis. This study aimed to investigate the contribution of *NRG1* gene into the HSCR development in Indonesian population.

Methods: We performed Sanger sequencing to find *NRG1* variants in 54 HSCR patients.

Results: All patients were sporadic non-syndromic HSCR with 53/54 (98%) and 1/54 (2%) were short-segment and long-segment patients, respectively. *NRG1* analysis showed one rare variant, c.397G > C (p.V133L), and three common variants, rs7834206, rs3735774, and rs75155858. The p.V133L was predicted to reside within in a region of high mammalian conservation, overlap with the promoter and enhancer histone marks of relevant tissues such as digestive and smooth muscle tissues and alter AP-4_2, BDP1_disc3, Egr-1_known1, Egr-1_known4, HEN1_2 transcription factor binding motifs. Furthermore, this variant was absent in 92 controls.

Conclusions: This study is the first report of *NRG1* rare variant associated with HSCR patients in South-East Asian ancestry and adds insights into the *NRG1* effect in the molecular pathogenesis of HSCR.

Keywords: Hirschsprung disease (HSCR); Indonesia; *NRG1* rare variant; transcription factor binding motif

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