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Multiple 'omics'-analysis reveals the role of prostaglandin E2 in Hirschsprung's disease

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The etiology and pathogenesis of Hirschsprung's disease (HSCR) remain largely unknown. Here we employed a multiple 'omics'-analysis to explore the important pathway related to the development of HSCR. We examined colon tissues from three independent populations with a combined analysis of metabolomics, transcriptomics and proteomics to understand HSCR. Mouse model was used for examining PGE2 induced clinical presentation of HSCR. SH-SY5Y and SK-N-BE(2) cell lines were used for examining PGE2 inhibited cell migration through EP2.The integrated analysis suggests that the level of PGE2, the expression of the genes encoding its receptor (EP2) (PTGER2) and PGE2 synthesis enzyme genes (PTGS1 and PTGES) increased in HSCR colon tissues, together with a decreased synthesis of PGE2-related byproducts. In animal study, the pregnant mice treated with PGE2 gave birth to offspring with the lack of gangliocytes in colon and gut mobility. *In vitro* study, we confirmed that, when EP2 was blocked, the PGE2-inhibited migration of neural cell was recovered. Our study identified a novel pathway linking expression of PTGS1 and PTGES, level of PGE2, expression of PTGER2, and neural cell migration in HSCR, providing a novel avenue for the future diagnosis and prevention of HSCR.

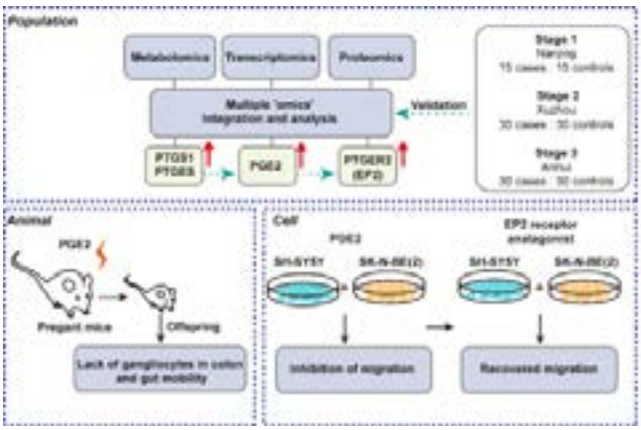

Figure: Multiple 'omics'-analysis reveals the role of PGE2 in HSCR pathogenesis. In HSCR, the expression of PTGS1 upregulates accompanied with the increased expression of PTGES, inducing the increased production of PGE2. With up-regulated expression of PGE2 receptor 2 (EP2) genes, PTGER2, the neuron cell migration is inhibited, causing the absence of gangliocytes in lesion colon.

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Biography

Yankai Xia is the Dean of the School of Public Health, Nanjing Medical University, Vice Director of Center for Global Health and the PI of State Key Laboratory of Reproductive Medicine and Key Laboratory of Modern Toxicology of the Ministry of Education. His current research interests are Systems Biology and Environmental Health. He has been using high-throughput techniques to profile human environmental exposure and biological responses to exogenous chemicals. He has presided over more than ten national and ministerial projects, including the State Key Program of National Natural Science Foundation of China and the National Outstanding Youth Science Foundation. He has been the committee member of several domestic and international academic organizations. He has published over 110 peer-reviewed articles, and got 7 national invention patents. He also serves as the editor and reviewer of more than 20 international journals.

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