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Identification of altered pathways in Down syndrome-associated congenital heart defects using an individualized pathway aberrance score

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ABSTRACT. The aim of this study was to identify disrupted pathways related to Down syndrome (DS), and DS-associated congenital heart defects (DS-CHD). The gene expression profile and pathway data of 10 human DS patients and 5 control samples in E-GEOD-1789 were recruited and analyzed by the individualized pathway aberrance score (iPAS) method, consisting of the data processing, gene-level statistics, pathway-level statistics, and significant measurement steps. The pre-processing step identified 12,493 genes and 1022 pathways (4269 genes). The pathway significant analysis identified eight pathways (adjusted P value <0.1) that differed between the disease and control samples. The cross-presentation of particulate exogenous antigen (phagosomes) and methionine salvage pathways showed the most significant differences among these. The gene expression levels of key pathway genes, such as *CYBB* and *ADI1*, were higher in disease samples than in normal controls. Based on our results, we predicted that the cross-presentation of particulate exogenous

antigens (phagosomes) and the methionine salvage pathway could be good indicators of DS-CHD.

Key words: Down syndrome; Congenital heart defect; Individualized pathway aberrance score (iPAS)

