A gene pathway analysis highlights the role of cellular adhesion molecules in multiple sclerosis susceptibility.

Genome-wide association studies (GWASs) perform per-SNP association tests to identify variants involved in disease or trait susceptibility. However, such an approach is not powerful enough to unravel genes that are not individually contributing to the disease/trait, but that may have a role in interaction with other genes as a group. Pathway analysis is an alternative way to highlight such group of genes. Using SNP association P-values from eight multiple sclerosis (MS) GWAS data sets, we performed a candidate pathway analysis for MS susceptibility by considering genes interacting in the cell adhesion molecule (CAMs) biological pathway using Cytoscape software. This network is a strong candidate, as it is involved in the crossing of the blood-brain barrier by the T cells, an early event in MS pathophysiology, and is used as an efficient therapeutic target. We drew up a list of 76 genes belonging to the CAM network. We highlighted 64 networks enriched with CAM genes with low P-values. Filtering by a percentage of CAM genes up to 50% and rejecting enriched signals mainly driven by transcription factors, we highlighted five networks associated with MS susceptibility. One of them, constituted of ITGAL, ICAM1 and ICAM3 genes, could be of interest to develop novel therapeutic targets.