Rewiring of protein interactions between stimulated and unstimulated immune cells

Sudharshini Thangamurugan[1] and Volkhard Helms[2]

Center for Bioinformatics[1] and Center for Bioinformatics[2], Saarland University, Saarbrücken, Germany.

The immune system is a collaboration of diverse cell types performing functions that are in general aimed at defence mechanisms against infection. Each immune cell develops from stem cells in the bone marrow and differentiates into specialised cells with targeted functions. Differentially analysing various immune cell types would capture the hallmark characteristics that distinguish a particular immune cell type from other cell types in certain conditions. Here we retrieved the RNAseq data of 25 stimulated and unstimulated types of immune cells processed by Calderon et al. (2019)[1]. A complete protein interaction network (PPIN) provides a superset of the existing interactome of a cell and but does not contain characteristic information specific to the cell and condition. Hence, the in-house computational tool PPIXpress[2] was used to construct condition-specific PPIN for all 25 immune cells (stimulated and unstimulated) by pruning the global PPIN to those genes/transcripts that are covered by at least a single sequencing read. Subsequently, we used another in-house tool termed. PPICompare[3] to compare and analyze the condition-specific PPINs of immune cells. The results showed the rewired interaction events between various cell types and conditions and the causes of rewiring either due to differential expression (loss or gain of interacting partners) or alternative splicing (isoform-switch of transcript) as large text files. Furthermore, we developed a new tool that can be used downstream of PPICompare. It executes automatic biological interpretation of the PPICompare results based on Gene Ontology and KEGG pathway enrichment analysis. Here, it reported the most enriched annotations of proteins affected in rewirings between unstimulated and stimulated immune cells. The tool has a feature to filter out and perform enrichment analysis on how the PPI rewirings affect certain groups of proteins of interest such as transcription factors, chromatin readers and splicing factors and their binding proteins. When comparing the unstimulated and stimulated versions of an immune cell, the top enriched GO terms showed the characteristics involved in the stimulation of the immune cell. Similarly, by comparing two immune cell types such as CD8 and NK cells, the enriched GO terms suggested the characteristics of CD8 lost or gained in the NK cell.

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