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Identification of co-expressed genes during macrophage polarization and reconstruction of their regulatory mechanisms using artificial intelligence methods

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Motivation and Aim: Macrophages play a key role in maintaining homeostasis of the body and its protection from damage and infections, being the central controlling element of immune responses [1, 2]. In response to incoming signals, macrophages are able to provide phenotypic adaptation from a pro-inflammatory phenotype (M1) to wound healing and tissue regeneration (group of M2 phenotypes), thus exhibiting plasticity [3]. In publications there are observations about the relationship between individual macrophage phenotypes and certain pathologies, or the relationship between the outcome of a disease and a certain macrophage phenotype. For example, studies have shown that patients with high-grade serous papillary ovarian cancer who have a higher M1/M2 macrophage ratio had significantly better overall survival [4]. Investigation of the molecular mechanisms underlying the functions of different macrophage phenotypes may allow the manipulation of immune responses. The goal of our work was to identify groups of co-expressed genes in different macrophage phenotypes and their subsequent analysis.

Methods and Algorithms: To analyze transcriptomic data, publicly available single cell RNA-seq data obtained on macrophages under different experimental conditions were taken. To detect co-expressed genes, a software package based on artificial intelligence methods was developed and applied.

Results: Single cell RNA-seq transcriptomic data was analyzed and differentially expressed genes were identified in macrophages under different conditions corresponding to the phenotype M1 (after adding LPS or IFN-γ+LPS), M2a (after adding IL-4+IL-13) and M2c (after adding IL-10), as well as M0 (macrophages without inducers), used as a control. Next, using the developed software package using artificial intelligence methods, groups of co-expressing genes characteristic of each phenotype were found. The resulting groups of coexpressed genes were analyzed and compared with genes accepted in the scientific literature as markers of each phenotype, similarities and differences were found. Biological processes and pathologies associated with the co-expressing groups of genes were found.

Conclusion: A new approach to the study of co-expressed genes based on artificial intelligence has revealed differences in the molecular mechanisms that provide different functions of different macrophage phenotypes.

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