PB and SF cells were collected from each RA patient, whereas only PB cells were collected from HSSs. The expression of CD14 and CD16 surface markers allowed to identify the monocyte population and the monocyte subsets: “classical”(CD14+CD16−), “intermediate”(CD14+CD16+), and “non-classical”(CD14−CD16+). The M1 phenotype (M1 monocytes) was identified by the evaluation of CD80, CD86, TLR2 and TLR4, whereas the M2 phenotype (M2 monocytes) was identified evaluating CD204, CD163 and CD206 surface markers. Results were expressed as percentage of positive cells over total leukocytes from PB and SF. Statistical analysis was carried out by Mann-Whitney non-parametric test.

Results: In RA patients, the percentage of CD14+CD16+ monocytes was significantly higher in PB compared to that in HS (p<0.001), and it was higher in SF compared to PB (p<0.05). The percentage of CD14−CD16+ monocytes was significantly increased in RA-PB compared to HS-PB and RA-SF (p<0.01; p<0.05). RA patients were characterized by an increased percentage of M1 monocyte (CD80+CD86+TLR2+TLR4+CD204+CD163+CD206+cells) in PB compared to HSs and compared to RA-SF. The percentage of M2 monocytes (CD204+CD163+CD206+CD80−CD68−TLR2TLR4−cells) was also increased in RA-PB compared to HS-PB and to RA-SF, but this increase was lower and not significant than that observed for M1 monocytes. Moreover, the M1-M2 monocyte ratio was 8:1 in RA-PB. Therefore, in RA patients, circulating M1 monocytes belonged to the “non-classical” subset, whereas M2 monocytes belonged to the “classical” subset. The percentage of circulating mixed M1/M2 monocytes (CD80+CD86−TLR2+TLR4−CD204+CD163−CD206+cells) was higher in RA patients compared to HSs. Moreover, in RA patients, the percentage of these cells was higher in SF than in PB and they primarily belonged to the “intermediate” monocyte subset. Interestingly, the highest percentage of M2 and mixed M1/M2 monocytes was observed in PB and SF of RA patients receiving a higher daily (25mg) and cumulative glucocorticoid dosages.

Conclusion: The results confirm that RA is an immune-inflammatory disease mainly mediated by both M1 monocytes and macrophages, as demonstrated by the increase in the percentage of circulating M1 monocytes. Glucocorticoids might contribute to the M1 to M2 transition, which characterizes RA patients under remission by increasing mixed M1/M2 and M2 monocyte percentage. REFERENCES:  

Disclosure of Interests: NIL.

AB0081 GLUTATHIONE PEROXIDASE 3 IS A NOVEL CLINICAL DIAGNOSTIC BIOMARKER AND POTENTIAL THERAPEUTIC TARGET FOR NEUTROPHILS IN RHEUMATOID ARTHRITIS

Keywords: Biomarkers, Rheumatoid arthritis, -omics

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Background: Neutrophils have a critical role in the pathogenesis of rheumatoid arthritis (RA) with immune system dysfunction. However, the molecular mechanisms of this process mediated by neutrophils still remain elusive.

Objectives: The purpose of the present study is to identify hub genes in neutrophils for diagnosis and treatment of RA utilizing publicly available datasets.

Methods: Gene expression profiles were downloaded from the Gene Expression Omnibus (GEO) database and normalized using the ComBat package. Gene Ontology and Kyoto Encyclopedia of Genes and Genomes enrichment analysis were used to conduct significantly functional analysis and crucial pathways. The resulting co-expression genes modules and crucial pathways. The resulting co-expression genes modules and Genomes enrichment analysis were used to conduct significantly functional enrichment analysis (GO and KEGG). Gene expression data were obtained from GEO and DGE screening. Agmat, ARG2, OMD, USP2, LI41, and ISQ15 were obtained by construction of molecular interaction regulatory networks. After verification by GEO validation set and our own RA synovial samples, only two genes, USP2 and ARG2, were still upregulated in EPROA after verification (Figure 1) and ARG2 and USP2 could effectively distinguish YPRA and EPROA and potential as biomarkers.

Conclusion: In conclusion, this study is the first to systematically analyze changes in immune cell infiltration between younger and older RA patients and to obtain hub age-related genes, which may provide the basis for illuminating the pathogenesis of RA and informing treatment strategies.

ABC0082 AGE-RELATED GENES USP2 AND ARG2 ARE INVOLVED IN THE REDUCTION OF IMMUNE CELL INFILTRATION IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Biomarkers, Rheumatoid arthritis, -omics

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Background: As the prevalence of rheumatoid arthritis (RA) in the elderly is increasing, rheumatologists are increasingly concerned about this group of patients. There is a large gap between the clinical manifestations and biological markers of elderly patients with RA (EPRA) and younger patients with RA (YPRA, age ≤ 60) in part from the differences in the immune system in different age groups. The current understanding of EPROA remains insufficient.

Objectives: For better understanding of the mechanism of RA disease progression and subsequent treatment options, we focused our attention on the immune cell infiltration in YPRA and EPROA.

Methods: R package “ssGSEA” and “GSEA” were used to identify the changes in immune cell infiltration and immune-pathways. R package “WGCNA” and “DSEq2” were used to screening and verifying age-related differentially expressed genes (DEGs). Hub genes were identified by Cytoscape and cytoHubba. ROC (receiver operator characteristic) analysis was performed to determine the prediction and value of biomarkers. Spearman correlation analysis was conducted to evaluate the correlation between hub age-related genes and immune cells.

Results: In early RA patients (defined as within 12 months of onset of symptoms), there were no differences in the infiltration of 28 types of immune cells between younger and older patients. However, in established RA patients, several immune cells were markedly decreased in older patients, including activated B cells, immature B cells, natural killer cells, CD56dim natural killer cells, MDSCs, monocytes, effector memory CD8+T cells, regulatory T cells, type 1 T helper cells, type 17 T helper cells and T follicular helper cells. Moreover, 78 age-related DEGs related to amino acid and glycosphingolipid synthesis and metabolism were identified by CNV screen and DGE screening. Agmat, ARG2, OMD, USP2, LI41, and ISQ15 were obtained by construction of molecular interaction regulatory networks. After verification by GEO validation set and our own RA synovial samples, only two genes, USP2 and ARG2, were still upregulated in EPROA after verification (Figure 1) and ARG2 and USP2 could effectively distinguish YPRA and EPROA and had potential as biomarkers.

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cles were divided into CD14+CD90+ and non-CD14+CD90+ cell groups and were sorted using flow cytometry. Subsequently, the CD14+CD90+ cells had a higher percentage of cells expressing CD83 and HLA-DR than the group of non-CD14+CD90+ cells.

Conclusion: CD14+ dendritic-shaped cells detected in RA synovial tissues are considered to be derived from CD14+CD90+ cells in the perivascular areas, which may be involved in RA inflammation as dendritic cells.

REFERENCES:


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