CD14+CD90+ cells were divided into CD14+CD90+ and non-CD14+CD90+ cell groups and cultured in dendritic cell differentiation medium. The populations of cells expressing CD83 and HLA-DR were examined by flow cytometry to determine their differentiation potential into dendritic cells.

Results: AMPK day 7 after dendritic cell differentiation culture, the group of 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 peripheral areas, which may be involved in RA inflammation as dendritic cells.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1045

AB0084 EVALUATING THE IMPACT OF METFORMIN TARGETS ON THE RISK OF RHEUMATOID ARTHRITIS: A MENDELIAN RANDOMIZATION STUDY

Keywords: Rheumatoid arthritis

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Background: Metformin is a first-line therapeutic agent for the treatment of type 2 diabetes, and despite its widespread long-term use in type 2 diabetes, the A variety of specific mechanisms of action of metformin are still being elucidated. Metformin is able to regulate cellular metabolism, proliferation, growth and autophagy, so it may have disease-modifying effects under a variety of other conditions. Metformin has been reported to improve a number of autoimmune diseases. Metformin has anti-inflammatory effects through a variety of mechanisms, including inhibition of tumour necrosis α (TNF-α) induced synovial cell inflammation and angiogenesis[1]. Previously, observational studies have demonstrated the ability of metformin to ameliorate the pathogenesis of rheumatoid arthritis (RA). However, the causality from metformin related targets on the risk of RA remains unknown.

Objectives: The aim of this study was to assess the causal effect of metformin related targets (AMPK, MCI, MG3, GDF15 and GLP1/GCG) on the risk of RA using a two-sample Mendelian randomization (MR) study.

Methods: Genetic proxies for the effects of metformin drug targets were identified as variants in the gene for the corresponding target that associated with HbA1c level. We selected genetic variants within 1 megabase pairs downstream and upstream of the genes encoding the five targets, and low-linkage disequilibrium (r2 < 0.3) variants associated with HbA1c at a nominal level of statistical significance (p ≤ 0.05) in the Meta-Analyses of Glucose and Insulin-related traits Consortium (MAGIC), restricted to people of European ancestry to minimise population stratification (n = 88355). Data on RA have been obtained from the NHGRI-EBI Catalog of human genome-wide association studies (14361 cases and 42923 healthy controls)[2]. Two-sample Mendelian randomization (MR) study was conducted to examine the association of metformin related targets and the risk of RA, including the inverse-variance weighted (IVW) method, MR-Egger, and Weighted median (WM), which was followed by sensitivity analyses. In addition, we also performed Cochran’s Q test, MR pleiotropy residual sum and outlier (MR-PRESSO), leave-one-out sensitivity test to test for heterogeneity, horizontal multiplicity and stability of results.

Results: Genetically predicted 5 targets were not associated with RA with odds ratio (OR) [95% CI] = 0.97, 0.80, 1.48, p = 0.20]. M3G[OR=1.76, 95% CI=0.49, 6.31, p = 0.14], GDF15 [OR=0.63, 95% CI=0.19, 2.05, p = 0.31], GLP1/GCG [OR=0.97, 95% CI=0.80, 1.16, p = 0.78](Figure 1). In addition, no apparent heterogeneity and no horizontal pleiotropy were observed in the sensitivity analysis.

Conclusion: Our study using MR herein indicated that the metformin related targets is not causally associated with the risk of RA. Future studies shall further systematically explore other potential pathways that metformin may affect to explore the association.

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