INVESTIGATION ON THE EFFECT AND MECHANISM OF ABNORMALLY ACTIVATED CD8+ T CELLS FROM BONE MARROW ON HEMATOPOIETIC STEM CELLS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: SLE is an autoimmune disease characterized by the abnormal function of lymphocytes. The impairment of hematopoietic function of bone marrow participates in its pathogenesis, in which T cells play an important role. However, study on bone marrow T cells in SLE patients is very limited.

Objectives: This study aims to characterize the phenotype and molecular characteristics of abnormally activated CD8+ T cells in bone marrow of SLE patients and explore the mechanism of hematopoietic stem cells (HSCs) reduction caused by the abnormally activated CD8+ T cells in bone marrow of patients with SLE.

Methods: A total of 8 SLE patients and 5 age- and sex-matched controls were recruited in our study. Among them, 3 SLE patients and 4 donors were collected based on blood origin. The CD8+ T cells from peripheral blood samples for Single-cell RNA sequencing (scRNA-seq) and functional studies. BM and peripheral T cell subsets were measured by flow cytometry. Plasma cytokines and secreted immunoglobulins were detected by Luminex. Disease activity of SLE patients was measured using the SLE Disease Activity Index (SLEDAI). All analyses were performed using R language and Flowjo 9.

Results: In the present study, SLE patients had increased CD8+ T cell numbers in peripheral blood samples compared to controls. CD8+ T cells in bone marrow were reduced number of HSCs, and with a downward trend of the numbers of peripheral red blood cells. Those patients also showed reduced number of HSCs, and with a downward trend of the numbers of peripheral red blood cells, white blood cells, neutrophils, hemoglobin, and platelets. By scRNA-seq, the expression of killer cell lectin-like receptor subfamily K member 3 (KLRK3), a marker of killer natural killer cells, was increased in SLE patients. A large number of CD38+HLADR+CD8+ T cells existed in the bone marrow and peripheral blood of SLE patients. Those patients also showed increased number of HSCs, and with a downward trend of the numbers of peripheral red blood cells, white blood cells, neutrophils, hemoglobin, and platelets. By scRNA-seq, the CD38+HLADR+CD8+ T cells contained high levels of GZMK, GZMA, PRF1, IFNG, and TNF in the bone marrow of SLE patients. The CD38+HLADR+CD8+ T cells exhibited significant relationship with HSCs, white blood cells, neutrophils, and platelets.

Conclusion: These findings demonstrated that the abnormal activation of CD8+ T cells in bone marrow can reduce the number of HSCs by the expression of killer molecules, which contributes to the impairment of hematopoietic function and the development of SLE. This project focuses on the specific bone marrow T cell subset in SLE. The completion of this project provides information for exploring the mechanism of hematopoiesis involvement.

REFERENCES:

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The correlations between the ACR/EULAR 2019 Criteria global score, and activity and damage indexes were recorded. In addition, activity and damage indexes were recorded in the group with SLE.

Three SLE experts, blinded to the diagnosis determined, for every individual if the patient had SLE or another rheumatological disease. An interrater agreement (kappa 0.72) for the 3 evaluations was considered “defined SLE” and used as gold standard. In all cases, ACR 1997/SLICC 2012/ACR/EULAR 2019 criteria were applied and compared with the gold standard. Sensitivity, specificity, positive and negative LR of the criteria were determined. The association between the final score based on the scorings and expert opinion. (Fig.1) Adherence to the final set of QIs related to monitoring to 88% for treatment-related QIs. Regarding targets of therapy, sustained remission or low disease activity were achieved, had a lower risk of experiencing a flare (OR=0.23 and 0.46 respectively). On average, SLE patients received 54% (95%CI 52–56%) of the indicated care during follow-up (monitoring QIs) was associated with reduced toxicity; therapy and targets of therapy; fertility and pregnancy; and adjunct therapy. On October 21, 2023 by guest. Protected by copyright. http://ard.bmj.com/ Ann Rheum Dis: first published as 10.1136/annrheumdis-2021-eular.3162 on 19 May 2021. Downloaded from http://ard.bmj.com/