CHARACTERIZING THE ROLE OF NET-DERIVED IL-33 IN SLE PATHOGENESIS

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Background: Interleukin (IL)-33 is a cell necrosis-derived alarmin with immunosurveillance properties which depend on the context of immune cells and the inflammatory milieu (1). In Systemic Lupus Erythematosus (SLE), extracellular DNA (as in extracellular chromatin traps [NETs] or immune complexes [ICs]) combined with alarmins stimulate innate immunity receptors (such as Toll-like receptors [TLRs]) and the production of IFNα by plasmacytoid dendritic cells (pDCs) (2, 3, 4).

Objectives: We hypothesize that NET-derived IL-33 might enhance the interferogenic capacity of NETs. We want to investigate its pro-inflammatory properties. Additionally, NETs could also be crucial in regulating the bioactivity of IL-33.

Methods: Peripheral blood polymononuclear cells (PMNs) were isolated from patients with SLE and healthy controls. In order to form IL-33-decorated NETs, PMNs were assessed by confocal microscopy. Serum sections from active lupus nephritis patients were immunostained to observe any IL-33 decorated NETs. NET-superinjected PMNs were administrated to healthy pDCs and type I IFN production was determined by qPCR. IL-33 receptor blockade significantly decreased the interferogenic capacity of IC-SLE NETs in an IL-33-dependent manner.

Conclusion: NET-derived IL-33 is a novel mediator of the nucleic acid-driven aberrant type I IFN response which exacerbates SLE disease. NET structure may be crucial in regulating the bioactivity of IL-33.

REFERENCES


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REDDUCED FCTR IIB AND ENHANCED FCTR III EXPRESSION ON MONOCYTES IN PATIENTS WITH BEHÇET DISEASE

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Background: Behcet’s disease (BD) is a systemic inflammatory disease without clear pathogenesis. Previous studies have shown the association between FcγR gene polymorphisms and BD (1-2). FcγRs, the receptor of IgG, has both activatory and inhibitory subtypes, and the imbalance of them on monocytes has been illustrated to have significant pathogenetic roles in many autoimmune diseases (3-4).

Objectives: This study aimed to investigate the potential abnormal expression of FcγR in BD patients

Methods: We recruited 27 newly-onset treatment-naive BD patients (according to 2014 International Criteria for BD) and 23 gender-and age-matched healthy controls (HC). Flow cytometry was used for detecting the expression of the inhibitory receptor FcγRIIB and activating receptors (FcγRI and FcγRIII) on the neutrophils, monocytes, B cells, natural killer cells, dendritic cells, and T cell from the whole blood of BD and HC. The correlation between the expression of FcγR and disease activity index of BD was evaluated.

Results: BD patients had increased numbers of monocytes (60.14±3.387% vs 47.56±4.923%, p=0.0365) compared with HC. FcγRIIB expression on monocytes, rather than other subtypes (p>0.05), was significantly lower in BD patients (4.87±0.61% vs 7.67±1.10%, p=0.0199). FcγRIIB expression on monocytes was negatively correlated to ESR (r=−0.576, p=0.031) and CRP (r=−0.539, p=0.047), positively correlated to serum IgA (r=0.785, p=0.001) and uncorrelated to serum IgG, IgM, and PLT (p>0.05). FcγRIII expression on monocytes was higher in BD patients (19.61±3.046% vs 9.349±1.107%, p=0.0091). FcγRIII expression on monocytes was positively correlated to esr (r=0.2551, p=0.0274) and CRP (r=0.2354, p=0.0352), and uncorrelated to serum IgG, IgM, IgA and PLT (p=0.05).

Conclusion: Our research demonstrated, for the first time, that the decreased expression of inhibitory receptor FcγRIIB and increased expression of activatory receptor FcγRIIB on monocytes in BD. Furthermore, the abnormal expression was correlated with disease activity. These findings suggested that FcγRs ratio imbalance might play a role in the pathogenic role of BD.

REFERENCES


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