diseases. Our current study developed a new nanoparticle (NP) containing PDMAEMA-PLGA copolymer for target-oriented delivery to DCs in situ.

Methods The in vitro tolerogenic effects of PDMAEMA-PLGA NPs and dexamethasone-incorporated PDMAEMA-PLGA NPs (Dex-NPs) were tested in conventional DCs generated from murine bone marrow (BM-cDCs) using FLT3L and GM-CSF in comparison with pure dexamethasone. The uptake of PDMAEMA-PLGA NPs by DCs was investigated in vivo and the in vivo therapeutic efficacy of Dex-NPs was observed in Fcgr2b-/- lupus-prone mice.

Results PDMAEMA-PLGA NPs provided sustained drug release profiles and exhibited immunosuppressive activity in BM-cDCs. PDMAEMA-PLGA NPs strengthened the dexamethasone capability to convert wild-type and Fcgr2b-/- BM-cDCs from immunogenic to tolerogenic state, and BM-cDCs treated with Dex-NPs efficiently mediated Treg expansion in vitro. PDMAEMA-PLGA NPs were actively captured by DCs in vivo probably in a particle size-dependent manner. Furthermore, Dex-NPs potentially ameliorated lupus activity in Fcgr2b-/- mice by reducing renal inflammation, anti-double-strand DNA antibodies, serum IL-6, serum creatinine, and proteinuria. Dex-NP therapy markedly enhanced Foxp3+ Treg expansion in an antigen-specific manner in Fcgr2b-/- mice.

Conclusions These findings substantiate the superior efficacy of our Dex-NPs and provide further support for clinical development as a potential therapy for SLE. Furthermore, Dex-NPs may be a versatile platform for DC-targeted therapy to induce antigen-specific immune tolerance to unwanted immune responses that occur in autoimmune diseases.

LP-087 LILRA3 PLAYS A PROTECTIVE ROLE IN MAS-LIKE DISEASE

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10.1136/lupus-2023-KCR.192

Background Macrophage activation syndrome (MAS) is a rare and life-threatening disease, characterized by inappropriate activation of lymphocytes and histiocytes, leading to a cytokine storm, haemophagocytosis and multi-organ damage. Our previous studies demonstrated that the leukocyte immunoglobulin-like receptors A3 (LILRA3) plays a pathogenic role in multiple autoimmune diseases, such as rheumatoid arthritis, systemic lupus erythematosus and antiphospholipid syndrome. However, the role of LILRA3 in MAS has not been investigated. This study was undertaken to examine the in vivo role of LILRA3 in MAS model.

Methods To functionally study the role of LILRA3 in MAS pathogenesis, we generated a novel LILRA3 knock-in (LILRA3-KI) mouse. Human LILRA3 gene (Gene ID: 11026) was inserted into Rosa26 allele in C57BL/6 (B6) mice based on Cas9/sgRNA system. The MAS-like disease model was induced by repeated intraperitoneal injection of CpG-ODNs in either B6 wild-type (B6-WT) or LILRA3-KI mice. Mice were assessed for the development of splenomegaly, hematological indices, immune cellular response, cytokine expression, and spleen pathology.

Results Compared with untreated B6-WT control mice, both B6-WT and LILRA3-KI treated mice displayed decreased haemocytes; inappropriate activation of lymphocytes; increased organ damage; and elevated levels of cytokines. Notably, compared with CpG-ODN treated B6-WT mice, the treated LILRA3-KI mice displayed a less pronounced MAS-like phenotypes and immune responses, including an increase of erythrocytes, hemoglobin, and platelets; an expansion of CD4+ and CD8+ T cells; decreased spleen enlargement; less disorganized spleen architecture and inflammatory cell infiltration; and reduced serum levels of cytokines (IL-6, IL-10, IL-12p70, IL-18 and IFN-γ).

Conclusions Our data indicate that LILRA3 plays a protective role in MAS-like disease probably through suppressing the inappropriate activation of both CD4+ and CD8+ T cells, and subsequently leading to decreased production of cytokines, less haemophagocytosis and reduced spleen impairment.

LP-088 IL-21 REGULATING AGE-ASSOCIATED B CELLS (ABCS) DRIVE AUTOIMMUNE DISEASE PHENOTYPE IN AGED MICE

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10.1136/lupus-2023-KCR.193

Background Age-associated B cells (ABCs) are a particular population of B cells that CD11c and T-bet double positive, rarely observed in healthy young individuals. These atypical B cells are from an extrafollicular (EF) response, unlike T cell-dependent germinal center (GC) response that produces long-lived, high-affinity antibody-secreting B cells. Since ABCs not going through GC response, somatic hypermutation or class-switching poorly happens, and they secrete pathogenic autoantibodies. ABCs expansion and chronic autoimmune disease correlation are well-established, especially in systemic lupus erythematosus (SLE). Some individuals with active SLE display abnormal expansion of ABCs regardless of age, but how ABCs impact the disease remains unclear. Not just aged or autoimmune disease individuals, the infectious condition could increase the ABCs differentiation. In such case, IL-21 drives extrafollicular CD11c+ B cells. It means IL-21, which plays a multifunctional role in B cell differentiation, could influence the expansion of ABCs also in aged and autoimmune diseases. Therefore, we experimented to confirm whether ABCs can express autoimmune disease phenotypes and whether IL-21 is related with ABCs.

Methods We inspected the ABCs expansion in Aged (> 60 weeks) and Young (6 weeks) mice without autoimmune disease and collected the spleen and lymph nodes. The organ samples are used in comparing ABCs-inducing inflammatory phenotypes between two groups. Furthermore, measured the titer of autoantibodies from serum.

Results The extrafollicular (CD23-CD21-) ABCs (CD11c+ T-bet+) are dramatically increased in aged mice, and some inflammatory reactions are observed.

Conclusions We confirmed the inflammatory phenotype by ABCs in aged mice without autoimmune diseases. These results represent that ABCs could affect the autoimmune disease phenotype. Recently we revealed the transcription factor 'Mef2d' could regulate the cytokine IL-21. To figure out the mechanism of ABCs expansion in aged and autoimmunity, we