complement and other innate protective systems against infectious and autoimmunity diseases.
Methods Components of the patient serum complement (CPSC) were registered by immunochemical methods in microplates (variants of functional analyses of isotypes C4A and C4B, and C1-inhibitor upon supramolecular assembling on well bottom) and on the blot (preliminary isoelectrophoresis of sera in the plate of polyacrylamide gel). Rabbit and goat polyclonal antibodies against purified CPSC were used. Activity of antibodies-peroxidase conjugates bound to CPSC was detected in the presence of TMB (microplate) or chemiluminescent substrate in a real time [*BioChemi System* (UVP)].
Results 1.Sera of patients having autoimmune diseases were characterised on the blot by appearance of aggregated C4B and C4A within pI 4,0–4,7 compared to less acidic free isotypes. Functional status of isotypes was confirmed in microplate. Absolute amounts of isotypes and their subisotypes as well as ratio of isotypes characterised prognostic-diagnostic patient groups of diseases (SLE, antiphospholipid syndrome, rheumatoid arthritis). Appearance and relative intensities of the system of aggregated isotypes and subisotypes of C4 indicated the presence of disease, its initiation, reached phase of disease and disease character. 2.Similar localization on the blot for the complex C4B and C1-inhibitor of patients was registered.
Conclusions Results indicate possible cofunctioining C4B and C1-inhibitor in protection complement network upon development of autoimmune diseases. New mechanisms of cascade protection involving new combinations of CPSC may be revealed. Results open new practical possibilities in diagnostics of early, progressive and chronic autoimmune diseases.

343 COMPLEMENT LECTIN SYSTEM COFUNCTIONS TO OTHER PROTECTIVE PRO-TEIN SYSTEMS INVOLVING RELATIONSHIPS BETWEEN LECTINS AND GLYCOCONJUGATES AGAINST AUTOIMMUNE AND INFECTIOUS DISEASES

M Lakhtin, V Lakhtin*, S Andina, S Afanasiev, V Aleshkin. *G.N. Gabrichevsky research Institute for Epidemiology and Microbiology, Medical Biotechnology, Moscow, Russia*

10.1136/lupus-2017-000215.343

Background and aims Innate protection recognising systems of human organism are important and perspective in respect of investigation autoimmune and infectious diseases. The aim was to evaluate lectin system (LS) of complement and its importance for innate interactome against infectious and autoimmune diseases.
Methods Patient complement components (PCC) of sera were estimated by immunochemical methods in microplates (hybrid plate for C4A and C4B functionality testing) and on the blot (for PCC separated by isoelectrophoresis). Peroxidase activity was detected using TMB or chemiluminescent substrate (for blot, *BioChemi System*, UVP).
Results Additional glycoconjugates(GC)-binding PCC were registered.

C1-inh revealed affinity to heparin. Patient (SLE, antiphospholipid syndrome, rheumatoid artritis) subisotypes of C4B (up to 5) and C4A (up to 7) were observed as aggregated forms together with GC.

Conclusions 1. Extended complement LS includes MBL, Factor H, C1-inh, CR1, CR2, CR3, C3, C4B, others. 2. Complement serve as a universal communicator among protective systems involving their LS—GC communications. 3. Complement (as mostly advanced innate protection system) possesses structure-function principles prognostic for any innate recognition systems. 4. There is superLS network in organism. Probiotic LS is important cofunctioning part of it. 5. The data support idea that any protection protein system partially functions involving LS—GC recognition (also for antibodies recognised by Fc-receptors as LS). 6. New prognostic-diagnostic possibilities in investigation of autoimmune and infectious diseases are opened using interactome LS—GC network.

Innate immunity

344 LINKING MACROPHAGE MIGRATION INHIBITORY FACTOR AND NLRP3 IN THE PATHOGENESIS OF IL-1 DEPENDENT INFLAMMATORY DISORDERS

[1]T Lang*, [1]J Lee, [1]A Pinar, [1]H Fan, [2]A Mansell, [1]E Morand, [1]J Harris. *[1]Monash University, School of Clinical Sciences at Monash Health, Clayton, Australia; [2]Hudson Institute of Medical Research, Centre for Innate Immunity and Infectious Diseases, Clayton, Australia*

10.1136/lupus-2017-000215.344

Background and Aims Macrophage migration inhibitory factor (MIF) is a mediator of innate immunity and is implicated in the pathogenesis of numerous autoinflammatory disorders. Clinical studies have shown correlations between elevated levels of IL-1β and MIF in serum with disease outcomes of patients with autoimmune disorders. To date, it is unclear whether MIF specifically regulates the expression and secretion of IL-1 family cytokines. Therefore, we aim to characterise mechanisms by which MIF may modulate the secretion of IL-1 family cytokines.
Methods The biological activity of MIF in murine bone marrow derived macrophages (BMDM) was inhibited using a small molecule inhibitor, COR123625. Concurrently, BMDM derived from $Mif^{-/-}$ mice were employed to evaluate the effects of MIF depletion on regulation of IL-1 family cytokines. mRNA expression was analysed by qRTPCR. Protein expression and secretion of IL-1α, IL-1β and IL-18 was assessed by western blot and ELISA.
Results We show that depletion of MIF in macrophages significantly reduced IL-1 cytokine release specifically in response to NLRP3 stimuli, but has no effect on the secretion of TNF-α and IL-6. Moreover, diminished IL-1 responses were independent of production of pro-IL-1β. Instead, MIF depletion specifically inhibits NLRP3-mediated IL-1 responses as levels were unaffected following activation of AIM2 or NLRC4 inflammasomes.
Conclusions Our findings reveal a novel role for MIF in the modulation of IL-1-dependent inflammatory responses, linking MIF directly to NLRP3 inflammasome activation. This study for the first time implicates a specific role for MIF in the release of IL-1 family cytokines and highlights the potential of targeting MIF in IL-1-dependent pathologies.

345 DELETION OF THE BAFF RECEPTOR TACI FULLY PROTECTS AGAINST SLE WITHOUT REDUCTION OF B CELL NUMBERS AND FUNCTION

[1]F Mackay*. [1]*University of Melbourne, School of Biomedical Sciences, University of Melbourne, Australia*

10.1136/lupus-2017-000215.345

Background and aims B cell-activating factor of the TNF family (BAFF) is an essential B cell survival factor. However, high levels of BAFF promote systemic lupus erythematosus (SLE) in mice and humans. Belimumab (anti-human BAFF) limits B cell survival and is approved for use in patients with SLE. Surprisingly, the efficacy of rituximab in SLE remains controversial, despite depleting B cells more potently than belimumab. This raises the question of whether B cell depletion is really the mechanism of action of belimumab. In BAFF transgenic (BAFF-Tg) mice , SLE development is T cell-independent but relies on innate activation of B cells in cooperation with the BAFF receptor TACI. Therefore, in this study we tested whether TACI, a BAFF receptor dispensable for B cell survival may have a role in the pathogenesis of SLE.
Methods To test the role of TACI in driving BAFF-mediated autoimmunity, we reconstituted BAFF Tg mice with a TACI-deficient bone marrow and also crossed BAFF Tg mice onto $TACI^{-/-}$ mice.
Results We show that loss of TACI on B cells protected against BAFF-mediated autoimmune manifestations while preserving B cells, suggesting that loss of BAFF signalling through TACI, rather than loss of B cells, may underpin the effect of belimumab in the clinic. Moreover, a multimeric form of BAFF, is very effective at activating TACI, suggesting that this abnormal form of BAFF may also be a pathogenic factor in SLE.
Conclusions B cell-sparing blockade of TACI may offer a more specific and safer therapeutic alternative to broad B cell depletion in SLE.

346 THE CONTRIBUTION OF INTERFERON LAMBDA TO SLE

[1]C Macri*, [1]ES Pang,[1]J Pooley, [2]K Radford, [1]M O'Keeffe. [1]*Monash University, Biochemistry and Molecular Biology, Clayton, Australia*; [2]*Mater Research-UQ, TRI, Brisbane, Australia*

10.1136/lupus-2017-000215.346

Background and aims Interferon lambda (IFN-λ) is a novel type of interferon produced by dendritic cells (DC). Despite its binding to a different receptor, IFN-λ shares functional similarities with type I IFN (IFN-I) by upregulating the expression of IFN-stimulated genes. The role of IFN-λ in DC biology and in autoimmunity remains unknown.

- to identify the DC subsets producing IFN-λ.
- to investigate the role of IFN-λ in DC functions.
- to investigate the role of IFN-λ in SLE.

Methods

- Mouse and human DC subsets were stimulated *ex vivo* and the IFN-λ expression was measured.
- The maturation and the capacity of DC to cross-prime T cells was compared in WT and $IFN\text{-}\lambda R^{-/-}$ mice. T cell cross-priming by human DCs was measured *ex vivo* in the presence of exogenous IFN-λ.
- Serum levels of IFN-λ was measured in lupus-prone mice and in SLE patients. The phenotype of the blood DC subsets from SLE patients was also characterised.

Results

- Mouse plasmacytoid DC (pDC) and $CD8^+$ DC highly secrete IFN-λ. In humans, the $CD141^+$ DC are the major IFN-λ producers.
- IFN-λ enhances the capacities of mouse and human DCs to maturate and to cross-prime T cells.
- High serum levels of IFN-λ were detected in lupus-prone mice and in some SLE patients. SLE patients display increased activation of the IFN-producing DC subsets: the pDCs (producing IFN-I) and the $CD141^+$ DCs (producing IFN-λ).

Conclusions IFN-λ is produced by some DC subsets and enhances their functions. Furthermore, IFN-λ is expressed during SLE, suggesting a potential role of the cytokine in the aetiology of SLE.

347 IMPACT OF CD200-FC ON DENDRITIC CELLS IN LUPUS-PRONE NZB/WF1 MICE

W Mo*, Y Yin, X Zhang. *Beijing peking union medical college hospital, rheumatology, Beijing, China*

10.1136/lupus-2017-000215.347

Background and aims Abnormal expression of CD200/CD200R1 may contribute to the immunologic abnormalities in patients with systemic lupus erythematosus (SLE). This study aimed to assess the function of CD200/CD200R1 and impact of CD200-Fc on dendritic cells in lupus-prone NZB/WF1 mice.
Methods Female NZB/WF1 mice were treated with CD200-Fc or control for 4 weeks. Plasma samples were collected to measure autoantibody levels. The expression levels of CD200/CD200R1 in peripheral blood mononuclear cells (PBMCs) and splenocytes were examined.
Results The percentage of CD200/CD200R1-positive cells in splenocytes from NZB/WF1 mice was lower than that of C57BL/6 mice ($p<0.05$). The plasma level of anti-dsDNA was significantly higher in NZB/WF1 mice than C57BL/6 mice ($p<0.001$). However, the anti-dsDNA levels decreased ($p=0.047$) after CD200-Fc treatment. Finally, CD200-Fc reduced the levels of IL-6 ($p=0.017$) and IL-10 ($p=0.03$) in the dendritic cell culture supernatant.
Conclusions The immunosuppressive CD200/CD200R1 signalling pathway might be involved in the immunopathology of NZB/WF1 mice; the present results merit further exploration of agents that can modulate the CD200/CD200FR1 pathway as a therapy for human lupus

348 DECTIN-1 ON MONOCYTIC CELLS MEDIATES ABERRANT INNATE AND ADAPTIVE IMMUNE RESPONSES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

[1]MY Mok*, [2]KY Lam, [2]D Luk, [2]Y Lo. [1]*City University of Hong Kong, Department of Biomedical Sciences, Hong Kong, Hong Kong S.A.R*; [2]*University of Hong Kong, Department of Medicine, Hong Kong, Hong Kong S.A.R*

10.1136/lupus-2017-000215.348