Title	CD5+ and CD5- plaque-forming cells (PFC) against poly-l-lysine (PLL) treated sheep erythrocytes in systemic lupus erythematosus (SLE): a longitudinal study
Author(s)	Tong, KK; Lau, WCS; Jones, B; Wong, RWS
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CD5+ AND CD5- PLAQUE-FORMING CELLS (PFC) AGAINST POLY-L-LYSINE (PLL) TREATED SHEEP ERYTHROCYTES IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): A LONGITUDINAL STUDY KK Tong, CS Lau, B Jones*, RWS Wong. University Departments of Medicine and Pathology, Queen Mary Hospital, Hong Kong, China.

CD5+ B cells produce low affinity, multi-specific 'natural' antibodies (Ab) against both self and foreign antigens which may be important in protection against autoimmunity, while CD5- B cells produce high affinity, mono-specific Ab which are responsible for pathological damage if directed against self. In SLE, we wondered whether fluctuations in disease activity might be accompanied by changes in activity of CD5+ and CD5- auto-Ab secreting B cells.

39 patients with SLE were studied. 30 were either newly diagnosed to have the disease or had a recent disease relapse and were serially followed up. Clinical features, drug history and disease activity (SLEDAI) were recorded. A haemolytic plaque assay using sheep red cells pretreated with PLL for conjugation with dsDNA was used to evaluate the number of CD5+ and CD5- anti-DNA-secreting PFC/10^6 (spontaneous and after stimulation with PWM and SAC I) at each visit. Results were compared with controls. CD5- IgG and IgM production were significantly increased in patients with active disease (SLEDAI $\geq$8) when compared with patients with inactive disease (SLEDAI$\leq$4) and controls (IgG: active disease 96.9 $\pm$ 52.5 vs inactive disease 34.2 $\pm$ 12.0 vs controls 0 anti-PLL PFC/10^6 B cells, p=0.01; IgM: active disease148.3 $\pm$ 60.7 vs inactive disease 29.38 $\pm$ 9.0 vs controls 1.5 $\pm$ 1.5 anti-PLL PFC/10^6 B cells, p<0.01). There were no significant changes in CD5+ B cell activity with disease activity. There was a significant relative increase in CD5- expansion in proportion to CD5+ B cells in patients with active disease. Fluctuation in disease activity during serial follow up was accompanied by changes in CD5- but not CD5+ B cell activity. Treatment with >30 mg prednisone/day or equiv caused no significant changes in CD5+ or CD5- activity at 1 month.

In conclusion, CD5- B cells are the main producers of pathological Ab in SLE. CD5+ B cells are neither pathological towards or protective against SLE.

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The effects of cyclophosphamide on T cell physiology in a mouse model of autoimmune diabetes

Wu A., Schulman S. and Lo D. The Scripps Research Institute, La Jolla, California

Cyclophosphamide treatment induces or accelerates autoimmune diabetes in genetically susceptible mice but the mechanism by which this occurs is unknown. To test the hypothesis that the drug's effects involve changes in CD4 T cell physiology, we studied double transgenic mice expressing influenza hemagglutinin (HA) on pancreatic islet beta cells and an HA specific T cell receptor (TCR) on CD4 T cells. Such mice are protected from autoimmune insulitis and diabetes when backcrossed to the resistant BALB/c strain. On a susceptible B10.D2 strain, double transgenic mice made heterozygous at the MHC ("d/b mice") by breeding to the MHC congenic strain C57BL/6 are protected from diabetes but not insulitis. Cyclophosphamide treatment induced diabetes in 100% of young d/b transgenic mice, but not in BALB/c backcrossed mice. Immunohistochemical analysis showed increased islet infiltrates induced by cyclophosphamide, with altered organization of lymphocyte compartments. After cyclophosphamide treatment, most spleen CD4 T cells from BALB/c backcrossed mice have an activated phenotype, but cells from d/b mice showed a shift toward a naive phenotype. Using a competitive reverse transcriptase-polymerase chain reaction (RT-PCR) assay, Cyclophosphamide was shown to induce higher interferon γ/Interleukin 4 (IFNγ/IL-4) ratios among splenic T cells, suggesting a strong shift towards Thl cytokines, perhaps through direct effects on patterns of gene expression in CD4 T cells.