

312 EZH2 MODULATES THE DNA METHYLOME AND CONTROLS LYMPHOCYTE ADHESION THROUGH JUNCTIONAL ADHESION MOLECULE-A: IMPLICATION OF ITS PATHOGENIC ROLE IN SLE

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Background and aims EZH2 is an epigenetic regulator that trimethylates lysine 27 of histone 3 (H3K27me3). We have previously suggested that increased EZH2 might be mediating a pro-inflammatory epigenetic reprogramming of naïve CD4+ T cells as an early event in lupus flares. Here we examined how overexpression of EZH2 affects the DNA methylome and function in CD4+ T cells.

Methods Naïve CD4+ T cells were isolated from lupus patients and healthy controls. EZH2 was overexpressed, and genome-wide DNA methylation changes were evaluated. Gene expression and miRNAs were assessed by qPCR while protein expression was examined by Western blotting. A cell adhesion assay was used to assess adhesion of T cells to human microvascular endothelial cells (HMVEC).

Results EZH2 expression and H3k27me3 were increased in naïve CD4+ T cells in lupus compared to healthy controls. Both miR-26a and miR-101, which regulate EZH2, were decreased. DNA methylation analysis identified 156 hypomethylated and 168 hypermethylated CpG sites in naïve CD4+ T cells transfected with EZH2. Genes involved in leukocyte adhesion and migration, such as *F11R* encoding JAM-A (junctional adhesion molecule A), and *SELPLG* encoding PSGL-1 (P-selectin glycoprotein ligand 1), were hypomethylated. Overexpression of EZH2 resulted in ~2-fold increased adhesion of CD4+ T cells to endothelial cells. Pre-incubation of EZH2-transfected CD4+ T cells with neutralising antibodies against JAM-A significantly blunted cell adhesion.

Conclusions We uncovered an important role for EZH2 in T cell adhesion. EZH2 overexpression results in hypomethylation of JAM-A, which might increase the migratory ability of T cells and contribute to aggressive T cell extravasation in lupus.

313 VERY RARE X CHROMOSOME ANEUPLOIDIES IN LUPUS AND SJOGREN'S

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Background and aims Systemic lupus erythematosus (SLE) and Sjögren's syndrome are related by clinical and serological manifestations as well as genetic risks. Both diseases are more commonly found in women compared to men at a ratio of about 10 to 1. Common X chromosome aneuploidies, 47, XXY and 47,XXX, are enriched among men and women, respectively, in either disease suggesting a dose effect on the X chromosome.

Methods We examined cohorts of Sjögren's syndrome or SLE patients with intensity plots of X chromosome single nucleotide polymorphism (SNP) alleles along with karyotype of selected subjects.

Results Among ~2500 women with SLE we found three patients with a triple mosaic consisting of 45,X/46,XX/47,XXX. Among ~2100 women with Sjögren's syndrome, one patient had 45,X/46,XX/47,XXX with a triplication of the distal p arm of the X chromosome in the 47,XXX cells. Neither the triple mosaic nor the partial triplication were found among controls. In another Sjögren's cohort, we found a mother-daughter pair with partial triplication of this same region of the X chromosome. The triple mosaic occurs in approximately 1 in 25 000 to 50 000 live female births, while partial triplications such are even rarer.

Conclusions Very rare X chromosome abnormalities are present among patients with either Sjögren's or SLE, and may inform the location of a gene(s) that mediate an X dose effect as well as critical cell types in which such effect is operative.

314 ROLE OF CYTOKINE IL-5 AND IL-25 AS BIOMARKERS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background and aims Systemic Lupus Erythematosus (SLE) is a chronic and prototypic multisystem autoimmune disease which present with extensive clinical features affecting almost every organs and tissues. At current situation, the exact cause of aetiology remains unknown, however besides genetic, environmental and other hormonal factors, faulty in the immunological system include T- and B-Cell abnormalities and the failure to clear autoantibodies which causes generation of immune complex and disparity in the level of cytokine also have been described in SLE leading to trigger inflammation and induce organ damage. There are various key cytokines been studied and identified to be therapeutic target for SLE.

Methods In the present study, we investigated on the level of IL-25, IL-35, IL-2, IL-4, IL-5, IL-6, IL-8 and IL-10 among Malaysian Malay female SLE population and the possible association to disease severity leading to lupus nephritis. In the present study, SLE group divided into two categories, one is SLE with Lupus Nephritis (SLE-LN) and one with SLE alone comparing to normal control. ELISA method were used to measure the level of cytokines.

Results From the results, we found that SLE-LN and SLE had the higher level IL-35, IL-25, IL-8 and IL-10 but lower level of IL-5, IL-2 and IL-6 compared to normal control with IL-4 have no detection. IL-5 and IL-2 significantly ($p < 0.005$) inhibited among SLE and SLE-LN while IL-25 significantly elevated in SLE and SLE-LN compared to control.

Conclusions This suggest IL-5 and IL-25 as beneficial marker for SLE disease activity.

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THE RELATIONSHIP BETWEEN IL-10, IL-17, IL-23 AND VITAMIN D LEVELS, AND DISEASE ACTIVITY OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background and aims Several cytokines such as IL-10, IL-17, IL-23, and vitamin D have been suspected in the pathogenesis of SLE. However, the association between these cytokines, vitamin D and disease activity is unknown. We aimed to determine the association between IL-10, IL-17, IL-23, vitamin D and SLEDAI score.

Methods We included 40 patients with SLE and 20 healthy controls in the study. Clinical and laboratory parameters and, SLEDAI score were evaluated. Serum IL-10, IL-17 and IL-23 were measured by nephelometry and vitamin D by HPLC. Mann-Whitney U and Kolmogorov-Smirnov test were used for statistical analysis.

Results The level of vitamin D was significantly lower ($p=0003$), and IL-23 was significantly higher ($p=0001$) in SLE patients compared to healthy controls. There was no significant difference for IL-10 and IL-17 between both group ($p>0,05$). However, a significant correlation between vitamin D and disease duration ($p=0,02$), and between IL-23 and vitamin D ($p=0019$) were found among SLE patients. Vitamin D levels were correlated with SLEDAI score and IL-23 in patients group.

Conclusions Although there are studies supporting the role of IL-10 and IL-17 in the pathogenesis of SLE in the literature, there was no significant difference between patients and healthy controls in our study. IL-23 levels were significantly higher, whereas vitamin D levels were significantly lower in SLE patients than in the control group. Also vitamin D levels were negative correlated with duration of disease and IL-23. Levels of IL-23 may be used to evaluate the disease activity, or may be a promising therapeutic approach for SLE patients.

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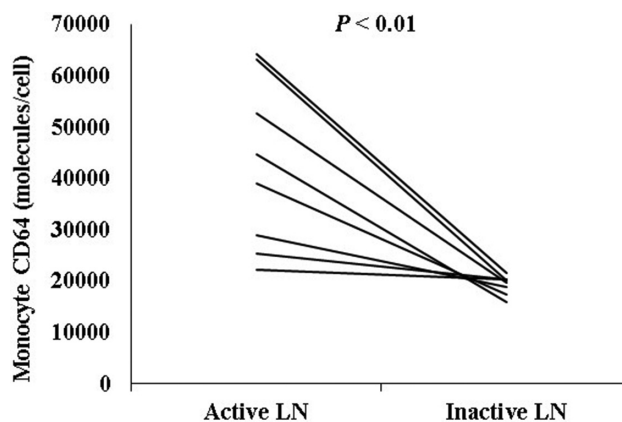
THE LEVEL OF CD64 EXPRESSION ON MONOCYTE CORRELATES WITH THE ACTIVITY OF LUPUS NEPHRITIS

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Background and aims Lupus nephritis (LN) is one of the most serious clinical manifestations of systemic lupus erythematosus (SLE). Recently, we have reported that the expression levels of CD64 on monocyte (mCD64), a high-affinity receptor for IgG (FcγRI), correlate with the disease activity of SLE (Lupus 2015;24:1076–80). However, the relation between lupus nephritis (LN) and mCD64 expression is yet to be elucidated. The aim of this study is to investigate whether or not mCD64 expression level correlates with the activity of LN.

Methods We quantitatively measured the mCD64 expression levels by flow cytometry in eight SLE patients with biopsy proven LN before and after treatment. All patients fulfilled



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the 1997 American College of Rheumatology classification criteria for SLE. The mCD64 expression levels of the individual patients were measured both at active (presence of proteinuria >0.5 g/day and/or active urinary sediment) and inactive phase (absence of proteinuria and active urinary sediment). The changes were analysed statistically (Wilcoxon signed-rank test).

Results The mean \pm SD of mCD64 expression levels before and after treatment were $42\,463 \pm 15\,466$ and $19\,190 \pm 1696$ molecules/cell, respectively ($p < 0.01$, Wilcoxon signed-rank test). The mCD64 expression levels in active LN was significantly higher than in inactive LN.

Conclusions The mCD64 expression level correlates with the activity of LN, although a larger scale study is needed to confirm the results.

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DYSREGULATION OF MIRNAS EXPRESSION LEVELS AND DISEASE ACTIVITY IN SLE PATIENTS

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Background and aims Altered expression of miRNAs have been implicated in the pathogenesis of SLE due to their role in both the adaptive and innate immunity. miRNAs control the differentiation and immunological functions of B cells, induction pathways in T cells, activation, function and maintenance of regulatory T-cells. The aim of our study was to evaluate the peripheral blood (PB) expression of miRNAs in SLE patients and to determine their correlation with the disease activity (DA).

Methods 40 SLE patients were included in the study. miR-146a and miR-155 expression levels in whole PB samples were determined by PCR (SYBR Green technology). $2^{-\Delta\Delta Ct}$ method was used for analysis. 32 healthy donors were used as controls. The DA was determined by DA index (SLEDAI) with 24 descriptors.

Results miR-146a was overexpressed in 62.5% of the patients. None of the patients showed underexpression of miR-146a. miR-155 was overexpressed in 50% and underexpressed in