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### UNIQUE ASSOCIATION OF HLA-DRB1\*15, HLA DRB1\*03 AND EBV WITH ADULT AND PAEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS IN NORTH INDIA

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10.1136/lupus-2017-000215.306

**Background and aims** SLE is multisystem autoimmune disease, having known HLA-DRB1\*15 and DRB1\*03 risk alleles and an association with EBV in the Caucasoid population. We compared the association of HLA-DRB1 and EBV in North Indian cohort of adult and paediatric SLE

**Methods** We analysed 109 adult SLE (aSLE) and 52 paediatric SLE (pSLE) with 278 age and sex matched control adult (CA) and paediatric (CP) for HLA-DRB1 genotyping by PCR-SSP, EBV-IgM and IgG to VCAg125, VCAp19, EBNA-1, p22 and EA-D by line blot assay and EBV load by real-time PCR

**Results** The frequencies of DRB1\*15 and DRB1\*03 were higher in SLE (OR=2.57 and 1.67 respectively) compared to controls. aSLE had higher frequencies of DRB1\*03 (OR=2.33) and DRB1\*04 (OR=7.51) compared to pSLE whereas, pSLE had higher frequency of DRB1\*15 (OR=2.42) compared to aSLE. pSLE had more 3+ to 4+ positivity of EBV-IgG to VCAg125 compared to aSLE (p=0.0008). EBV-IgM to VCAp19, EBNA-1 and EA-D (25%,12.5% and 6.25% respectively) were present only in pSLE. pSLE had higher EBV load compared to aSLE (p=0.045). IgG to p22 and EA-D were associated with DRB1\*03 in aSLE (OR=3.92 and 5.28 respectively) and IgG to VCAg125, VCAp19, EBNA-1, p22 and EA-D were associated with DRB1\*15 in pSLE (OR=4.0,3.44,4.6,4.8 and 4.8 respectively)

**Conclusions** DRB1\*15 and DRB1\*03 are risk alleles in North Indian SLE. Both show strong associations with immune response to EBV proteins. pSLE has stronger association with DRB1\*15, which is associated with early infection, stronger immune response to EBV proteins and higher EB viral load, which may explain more severity of pSLE

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### THE PATHOGENIC MECHANISMS OF SYSTEMIC LUPUS ERYTHEMATOSUS ASSOCIATED GENES PNP, PLEKHF2 AND ANKRD44

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10.1136/lupus-2017-000215.307

**Background and aims** To detect the expression of three SLE-susceptible genes, PNP, PLEKHF2 and ANKRD44 in SLE PBMC and lupus nephritis kidney samples, and to investigate their function.

**Methods** We collected PBMC from 46 SLE patients and 48 healthy controls, and renal biopsy tissues from 12 lupus nephritis patients and peri carcinomatous tissues from 10 patients with kidney cancer. The mRNA expression levels of PNP, PLEKHF2 and ANKRD44 were detected by qPCR. Their expression levels with the SLE clinical features and IFN scores were analysed. ANKRD44 was tested at different time points in Raw264.7 cells during IFN stimulation. The expression of

ANKRD44 was knockdown by using siRNA in Raw264.7 cells. The change of IFIGs and the activation of IFN signalling pathway were detected by Real-time PCR and western blotting.

**Results** PNP, PLEKHF2 and ANKRD44 were found significantly decreased in SLE PBMCs compared with healthy controls. The mRNA expression of PNP and ANKRD44 were significantly decreased while the expression of PLEKHF2 was increased in kidney of lupus nephritis. The expression of PNP was negatively correlated with IFN score in SLE PBMC samples, while the expression of ANKRD44 was negatively correlated with IFN score in lupus nephritis kidney. ANKRD44, which could be down-regulated by IFN alpha, could inhibit the type I IFN signalling pathway and downregulate the expression of IFIGs.

**Conclusions** PNP and ANKRD44, expressed abnormally and associated with IFN alpha, might be used as new candidate biomarkers for SLE diagnosis; ANKRD44 could repress the IFN downstream pathway, it would be a potential drug target.

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### STUDY ON THE ROLE OF MICRORNA125A IN LUPUS DISEASE IN MICE

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10.1136/lupus-2017-000215.308

**Background and aims** To investigate whether over-expression of miRNA125a has an effect on organic injuries and its potential mechanisms by using miRNA-125a-agomir transfected MRL/lpr mice

**Methods** 5-week-old female MRL/lpr and MRL/n mice were divided into three groups : the lpr-miRNA-group, given miRNA-125a-agomir intravenously ; the lpr-PBS-group, given PBS intravenously ; MRL-control-group: receiving no treatment. Blood samples and urine were collected weekly interval from 5-week-age. At 13-week-age and 17-week-age, bronchoalveolar lavage fluid, blood sample, lung and spleen tissues were collected and analysed in half of the mice.

**Results** MiRNA-125a levels in splenocytes were significantly elevated in MRL/lpr mice.

A variety of inflammatory cell infiltration, mostly T cells, in lung tissues was statistically alleviated in lpr-miRNA group.

Flow cytometry analysis indicated that in lpr-miRNA group, the proportion of splenic plasma cells in lpr-miRNA group was significantly decreased than that in lpr-PBS group.

Cytokines analysis showed serum levels of RANTES in lpr-miRNA group were statistically reduced.

The serum level of anti-dsDNA and the high titer proportions of ANA were much lower in lpr-miRNA group than in lpr-PBS group.

**Conclusions** Intravenous injection of miRNA125a-agomir +Engreen *in vivo* transfection reagent mixture solution could transfect miRNA-125a and increase the level of miRNA-125a expression safely and effectively.

Over-expression of miRNA-125a could alleviate inflammatory cell infiltration in lung tissues in lpr mice and reduce the proportion of splenic plasma cell.

Elevation of miRNA-125a expression could inhibit the expression of RANTES in lpr mice, which in turn reduce the autoimmune inflammation to a certain extent.