

effects on gene expression, transcription factor binding, and epigenetic characteristics. Using the correlated SNPs ( $r^2 > 0.8$ ) from the 82 SLE loci, we found only 1.5% SNPs encode mis-sense or synonymous mutations, and the majority (56%) were implicated in differential expression of cis-genes ( $9.81 \times 10^{-198} < P < 5 \times 10^{-3}$ ). Significant over-representation ( $p < 0.05$ ) of transcription factor binding sites for p53, MEF2A and E2F1. Enrichment analysis highlights the involvement of common pathways, gene ontology, protein domains, and the importance of these loci in B and T cell biology.

**Conclusions** We provide evidence of five novel SLE susceptibility loci. Integrated bioinformatics using all 82 SLE loci revealed that SLE susceptibility loci share gene regulatory features, including significant enrichment of epigenetic marks and transcription factor binding sites, suggestive of shared regulatory mechanisms of SLE etiopathogenesis.

## Plenary Session 2: Lupus nephritis: from bench to bedside

### 4 ACCELERATED LUPUS NEPHRITIS ASSOCIATED WITH INCREASED T HELPER SUBSET, SERUM TNFA AND ANTI DSDNA LEVELS IN PREGNANT PRISTANE INDUCED LUPUS MICE

<sup>1</sup>N Nurdiana\*, <sup>1</sup>U Kalsum, <sup>2</sup>E Sari Dewi, <sup>3</sup>K Handono, <sup>4</sup>H Kaliim. <sup>1</sup>Brawijaya University, Clinical Pharmacology, Malang, Indonesia; <sup>2</sup>Brawijaya University, Nursery, Malang, Indonesia; <sup>3</sup>Brawijaya University, Clinical pathology, Malang, Indonesia; <sup>4</sup>Brawijaya University, Rheumatology-Immunology Division- Internal medicine, Malang, Indonesia

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**Background and aims** To investigate the role of T helper (Th) cell subsets and TNF $\alpha$  in the pathogenesis of nephritis in pregnant SLE mice model.

**Methods** Thirty female Balb/c mice were divided into two groups: non-pregnant and pregnant lupus mice. SLE induction was done by single intraperitoneal injection of 0.5 cc pristane. After twelve weeks post injection, mice were mated. Periodically, blood pressure was monitored and urine albumin level was measured by ELISA. After 18 day, mice were euthanized, and renal biopsy was done to evaluate the development of nephritis. Placental TNF $\alpha$  and serum anti-dsDNA were measured by ELISA. Spleen Th1, Th2, and Th17 percentages were measured by flowcytometry

**Results** Th1, Th2, and Th17 percentages in were significantly higher in pregnant lupus mice compared to non pregnant group. Th1 and Th17 percentages were positively correlated with albuminuria, anti-dsDNA, systolic, and diastolic blood pressure. Incidence of lupus nephritis was higher in pregnant lupus mice with higher activity index compared to non pregnant mice. The activity index also had positive correlations with Th1 and Th2 percentages. Higher placental TNF $\alpha$  and anti-dsDNA levels were found in pregnant lupus mice. Placental TNF $\alpha$  and anti-dsDNA levels were positively correlated with albuminuria. Moreover, placental TNF $\alpha$  levels were positively correlated with systolic and diastolic blood pressure.

**Conclusions** High percentages of Th cell subsets, TNF  $\alpha$  and anti ds DNA antibody were associated with renal disorder in pregnant lupus mice which propose a new mechanism for the pregnancy complication in SLE.

### 5 IMPACT OF VASCULAR INVOLVEMENT ON OUTCOMES IN PATIENTS WITH LUPUS NEPHRITIS

<sup>1</sup>M Rathii\*, <sup>1</sup>H Prasad, <sup>2</sup>A Sharma, <sup>3</sup>R Nada, <sup>1</sup>KL Gupta. <sup>1</sup>Postgraduate Institute of Medical Education and Research, Nephrology, Chandigarh, India; <sup>2</sup>Postgraduate Institute of Medical Education and Research, Internal Medicine, Chandigarh, India; <sup>3</sup>Postgraduate Institute of Medical Education and Research, Histopathology, Chandigarh, India

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**Background and aims** The exact incidence and significance of vascular involvement (VI) in patients of lupus nephritis (LN) is not clear.

**Methods** All renal biopsy confirmed LN cases over a five years were included. The biopsy was reviewed and subjects were divided into two subgroups: Group 1 (VI present), and Group 2 (VI absent). Morphological lesions of lupus vasculopathy, vascular thrombotic microangiopathy (TMA), vasculitis, vascular immune deposits and arteriosclerosis were taken as VI. Clinical details and treatment received were noted and the outcomes were assessed at the end of six months.

**Results** A total of 241 biopsy proven LN patients (211 females, 30 males) with mean age of  $29.79 \pm 9.44$  years were included. The VI was seen in 78 patients (32.3%, Group 1). Vascular immune deposits was seen in 13 (5.3%), lupus vasculopathy in 5 (2.0%), vasculitis in 2 (0.8%), vascular TMA in 27 (11.2%) and arteriosclerosis in 55 (22.8%) patients. There was no difference between the two groups at baseline, except for a higher serum creatinine in Group 1 ( $1.87$  vs  $1.43$  mg/dL,  $p=0.004$ ). At the end of six months of treatment, Group 1 patients had higher 24 hour protein excretion ( $1.10 \pm 1.64$  vs  $0.88 \pm 2.23$  gms/day,  $p=0.001$ ) and higher serum creatinine ( $1.35 \pm 1.25$  vs  $0.92 \pm 0.56$  mg/dL,  $p=0.001$ ). 38.2% patients in Group 1 achieved complete remission as compared to 61.9% in Group 2 ( $p=0.006$ ), while, 26.3% patients in Group 1 had resistant disease as compared to 14.3% in Group 2 ( $p=0.02$ ).

**Conclusions** LN patients with VI have more severe renal presentation and poorer outcomes.

## Plenary Session 3: Challenges in drug development and clinical trial design in SLE

### 6 THE IDEAL TRIAL DESIGN: A FOCUS ON PATIENT SELECTION AND APPROPRIATE OUTCOME MEASURES

R Furie\*. USA

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Although the lupus community has not witnessed the same growth in drug approvals as in inflammatory arthritis, there have been major breakthroughs since the mid-twentieth century. The discovery in the late 1940's of cortisone revolutionised the treatment of patients not only with lupus but with all inflammatory diseases. During the 1950's, azathioprine was introduced as a chemotherapeutic agent, but it was adopted soon thereafter as a drug for patients with rheumatic diseases. The antimalarial quinacrine was first used in the early 1950's as well. The application of cyclophosphamide, the eighth cytotoxic anticancer drug approved by the FDA, to patients with