

promoted these effects through the membrane receptor GPER1 located in lipid rafts and that inhibition of lipid rafts and GPER1 suppressed SLE serum-induced skin inflammation and expression of inflammatory molecules.

**Conclusions** We conclude that oestrogen promotes the development of skin injury induced by SLE serum through the membrane receptor GPER1 and that lipid rafts play an important role in the regulatory effect of GPER1 in SLE skin inflammation.

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#### THE MAJOR ROLES OF MONOCYTES AND THEIR PRODUCT TUMOUR NECROSIS FACTOR ALPHA IN THE INDUCTION OF SKIN INFLAMMATION TRIGGERED BY INTRADERMAL LUPUS IGG

<sup>1</sup>G Xu, <sup>2</sup>L Liu, <sup>3</sup>GM Deng. <sup>1</sup>Nanjing Medical University, Key Laboratory of Antibody Techniques of Ministry of Health, Nanjing, China; <sup>2</sup>Harvard Medical School, Beth Israel Deaconess Medical Centre, Boston, USA; <sup>3</sup>Nanjing, China

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**Background and aims** Skin injury is the second most common clinical manifestation in patients with systemic lupus erythematosus (SLE), but its pathogenesis has not been thoroughly elucidated.

**Methods** Based on skin deposition of IgG in SLE, we studied the features and mechanisms of intradermal IgG-induced skin inflammation

**Results** We found that skin inflammation appeared at 3 hour and peaked at 3 d after intradermal injection of lupus IgG. This phenomenon was related to the dose of injected IgG but not to systemic disease activity. The severity of skin inflammation induced by lupus IgG was significantly decreased in mice depleted of monocytes and in mice deficient in TNF- $\alpha$  but not in mice lacking mature lymphocytes. Furthermore, lupus IgG promoted the progression of monocyte differentiation to dendritic cells (DCs) and enhanced the expression of TNF- $\alpha$ . TNF- $\alpha$  was found to stimulate the IgG-induced maturation of DCs and played a major role in the proliferation and activation of keratinocytes.

**Conclusions** The results also indicate that the deposition of IgG in skin exerts an important role in the pathogenesis of skin injury in patients with SLE; therefore, blocking the IgG/FcR signalling pathway can be a therapeutic target in skin lesions of patients with SLE.

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#### THE ROLE OF IL-1 IN SKIN INFLAMMATION INDUCED BY LUPUS SERUM IGG

X Li, X Guo, G Xu, GM Deng. Nanjing Medical University, Key Laboratory of Antibody Techniques of Ministry of Health, Nanjing, China

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**Background and aims** Systemic lupus erythematosus (SLE) is a seriously chronic autoimmune disease, which is characterised by a large number of autoantibodies and multiple organ damage. Skin lesion is one of the common clinical manifestations of lupus erythematosus, but its pathogenesis is not clear. IL-1 is a proinflammatory cytokine, the aim in this study is to investigate the role of IL-1 in the skin injury in SLE.

**Methods** We used IL-1 receptor deficient mice and other gene deficient mice to study the role of IL-1 in the lupus serum IgG-induced skin inflammation.

**Results** We found that the severity of skin lesion in IL-1 receptor deficient mice and caspase-1 deficient mice was reduced compared with that in wild type mice. IL-1 receptor deficiency suppressed the expression of Fc $\gamma$ RI (CD64) and MHC class II (CD74), and increased the level of Fc $\gamma$ RII (CD32) induced by lupus serum. IL-1 receptor deficiency also suppressed the lipid raft clustering and IFN- $\gamma$  in T cells, and reduced IgG internalisation and presentation in macrophage, and decreased expression of MCP-1 and TNF $\alpha$  in monocytes. In addition, TNF $\alpha$  could promote the proliferation of keratinocytes.

**Conclusions** Our findings indicate that IL-1 plays an important role in skin lesions of lupus erythematosus. This study suggests IL-1 is a therapeutic target in skin lesions of systemic lupus erythematosus.

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#### HEPATIC DEPOSITED IGG MEDIATED LIVER DAMAGE THROUGH KUPFFER/NATURAL KILLER CELLS AND THEIR PRODUCTS

<sup>1</sup>X Fang\*, <sup>1,2</sup>GM Deng. <sup>1</sup>Nanjing Medical University, Key Lab of Antibody Techniques of Ministry of Health, Nanjing, China; <sup>2</sup>Harvard Medical School, Beth Israel Deaconess Medical Centre, Boston, USA

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**Background and aims** Hepatic disorders are frequent in patients with systemic lupus erythematosus (SLE), yet the aetiology and pathogenesis of liver injury in SLE remains unclear. The present study primarily aimed to understand the cellular and molecular mechanisms involved in the expression of liver damage in SLE.

**Methods** We analysed clinical and serological characteristics of 404 SLE patients with liver dysfunction, and determined the pathogenesis of liver damage in SLE by using lupus-prone mice and a novel animal model of liver injury induced by lupus serum IgG.

**Results** 22.5% of SLE patients have liver dysfunction, and even 38% of them have lupus-hepatitis. There are a large amount of inflammatory cells around the portal areas of the livers, apoptotic hepatocytes and IgG deposition in the liver in lupus-prone mice. Liver injury was successfully established by intrahepatic injection of lupus serum IgG. Immune complexes (ICs) stimulated Kupffer cells (KCs) to secrete TNF- $\alpha$  involved in the development of inflammation and apoptosis in liver. IFN- $\gamma$  produced by activated natural killer cells (NKs) directly mediated liver damage and also enhanced the TNF- $\alpha$ -mediated apoptotic pathway. The depletion of KCs and NKs abolished apoptosis induced by ICs in liver, suggesting that KCs and NKs have a synergic effect on liver injury.

**Conclusions** Our findings demonstrated that liver injury was induced by hepatic IgG deposition in SLE and innate immune cells and their products exert an important role in the development of liver injury in SLE. Our results may promote to develop potential therapeutic strategies in prevention and treatment of liver injury in SLE.

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#### RHUPUS SYNDROME : A CASE REPORT AND LITERATURE REVIEW

A Fikry\*, P Faridin. Hasanuddin University, Internal Medicine, Makassar, Indonesia

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**Background and aims** Systemic lupus erythematosus (SLE) is an autoimmune and inflammatory disease with multiple clinical manifestations including arthropathy. The severity of the articular involvement or deformity to an erosive deforming arthropathy with severe functional disability. In rare cases a severe, erosive and deforming arthropathy, clinically indistinguishable from rheumatoid arthritis (RA) can be observed; this clinical entity is traditionally known as "Rhupus". It remains controversial whether Rhupus is a distinct entity, an overlap between SLE and RA or a serious articular involvement of SLE.

**Methods** Observational.

**Results** A 23 years old female presented with polyarthritis, vasculitis, and anaemia. She was having symmetrical inflammatory polyarthritis of both upper and lower limb for last 2 years and was having skin rash for last 1 year. She also gave history of recurrent oral ulcers, photosensitivity and alopecia. On Investigation, revealed anaemia, alopecia, oral ulcer, vasculitis and active synovitis of both elbows, wrists, hands, knees and ankle joints. Her report showed raised of inflammatory parameter, normochromic normocytic anaemia. Further work up showed positive result in RF and anti-IgG. Also showed positive results on some antigens ANA profile. She was started on prednisolone, Metotrexate, folic acid, hydroxychloroquine, calcium, vitamin D and Natrium Diclofenac.

**Conclusions** Rhupus Syndrome is a rare syndrome. Currently, Rhupus remains an entity not perfectly known, but the pathogenesis, the autoantibody positivity, the radiological manifestations and therapy all support the idea that it is really an overlap syndrome between SLE and RA, although its pathogenesis still remains to be fully understood.

## 215 ACTIVE ARTHRITIS IS ASSOCIATED WITH 14-3-BETA TITRE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

C Hitchon\*, D Robinson, H El-Gabalawy, A Tisseverasinghe, A Man, C Peschken. *University of Manitoba, Internal Medicine, Winnipeg, Canada*

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**Background and aims** Non-erosive arthritis is common in systemic lupus erythematosus (SLE). 14-3-3 eta, a chaperone protein that activates pro-inflammatory pathways is emerging as a novel biomarker for erosive Rheumatoid Arthritis. We investigated clinical associations of serum 14-3-3 eta in SLE focusing on arthritis.

**Methods** Sociodemographics, ACR criteria, and SLEDAI were recorded. Arthritis, assessed by the SLEDAI, was categorised as active (n=78), inactive (n=138) and never present (n=49). Serum 14-3-3 eta was measured by ELISA; titres above 0.19 ng/ml were considered positive. We report descriptive statistics and logistic regression models testing the association of 14-3-3eta with arthritis state.

**Results** SLE patients (n=265) were mainly female (92%), Caucasian (67%) with a mean (SD) age of 51.7 (14) years, and median (25%,75%) disease duration of 8 (4,10) years, number ACR criteria of 6 (5,7), and SLEDAI of 4 (2,7). 241 (81%) had active or inactive arthritis. 14-3-3 eta positivity was

similar across the three arthritis groups (active 22/78 (28%), inactive 27/138 (20%), never present 10/49 (20%) with a median (25%75%) titre of 0.6 ng/ml (0.34, 1.82). The highest quartile of 14-3-3eta associated with active arthritis (OR 3.6 (95% CI 1.33, 9.98) p=0.012) after adjusting for ethnicity and SLEDAI. There were no differences in 14-3-3 eta positivity for other lupus criteria nor correlation of 14-3-3 eta titer with number of ACR criteria or SLEDAI.

**Conclusions** 14-3-3 eta titers are highest in lupus patients with active arthritis suggesting a higher risk for more severe arthritis. Further work will explore the associations of 14-3-3 eta in lupus with erosive arthritis.

## 216 ACUTE PANCREATITIS AS AN INITIAL MANIFESTATION OF SYSTEMIC LUPUS ERYTHEMATOSUS : TWO CASE REPORTS

CG Khor\*, M Tan, PS Ong. *hospital raja permaisuri bainun, Rheumatology Unit- Internal Medicine Department, ipoh, Malaysia*

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**Background and aims** Acute pancreatitis is a rare initial presentation of systemic lupus erythematosus.

**Methods** We report two cases of Malay patients who presented with fever, abdominal pain, ascites and high level of pancreatic enzymes. They were diagnosed with acute pancreatitis associated with systemic lupus erythematosus.

**Results** First patient is a Malay male patient presented to us late. He had severe acute pancreatitis with severe hyperbilirubinemia, lupus nephritis and autoimmune haemolytic anaemia. He died despite maximal therapy was provided. The second case is a Malay lady who came to us early responded well to high dose corticosteroids and discharged well.

**Conclusions** The mortality rate of lupus-associated pancreatitis is higher than in non-lupus associated pancreatitis. Early awareness of lupus-associated pancreatitis as an initial manifestation of systemic lupus erythematosus is crucial in managing and improving outcome in lupus patients.

## 217 PRIOR SUN EXPOSURE AND SKIN-SPECIFIC AUTO-ANTIBODIES ARE ASSOCIATED WITH SKIN DISEASE IN SYSTEMIC LUPUS ERYTHEMATOSUS

<sup>1</sup>T Khosravi-Hafshejani\*, <sup>2</sup>M Ghoreishi, <sup>3</sup>A Kariminia, <sup>2</sup>S Kalia, <sup>4</sup>A Avina-Zubieta, <sup>4</sup>J Reynolds, <sup>2</sup>JP Dutz. <sup>1</sup>University of British Columbia, Undergraduate Medical Program-Faculty of Medicine, Vancouver, Canada; <sup>2</sup>University of British Columbia, Dermatology and Skin Science, Vancouver, Canada; <sup>3</sup>University of British Columbia, Pediatrics- Division of Haematology and Oncology, Vancouver, Canada; <sup>4</sup>University of British Columbia, Medicine- Division of Rheumatology, Vancouver, Canada

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**Background and aims** Almost 80% of systemic lupus erythematosus (SLE) patients manifest lupus-specific skin lesions. A pathogenic link between skin inflammation and SLE has been proposed. We hypothesised that skin-directed antibodies are present in SLE and are associated with a history of significant sun-exposure.

**Methods** Blood was collected from three patient populations; SLE with a history of lupus-specific skin lesions as cases (n=15), SLE without a history of skin lesions (n=7) and atopic dermatitis (n=6) as controls. Serum anti-dsDNA antibodies were measured by ELISA. Peripheral blood