SLEDAI at active and remission phases were 4.25 vs 0.45 and 8.32 vs 1.25, respectively. Fever, rash, and arthritis were the most common features and kidney was the most common involved organ at active phase. The mean serum complement factor H and I levels at active phase were significantly lower than that at remission phase. The mean serum CD46 level at active phase was higher significantly compared with that at remission phase. The serum C5a and C5b-9 at active and remission phases were no significant difference. Five patients had sequelae including 1 intracranial haemorrhage and 4 chronic kidney disease.

Conclusions Serum complement factor H, I and CD46, but not C5a and C5b-9 were associated with disease activity of SLE.

280 THE ROLE OF PI3K, MTOR IN THE EXPRESSION OF INTERFERON -ALPHA INDUCED PROTEIN IFIT4 IN LUPUS

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Background and aims The role of Phosphoinositide 3-kinase (PI3K), mammalian target of rapamycin (mTOR) and dexamethasone in IFN-α-induced-human interferon-induced protein with tetratricopeptide repeats 4 (IFIT4) expression was investigated.

Methods HT1080 cells were pre-treated with specific inhibitors of PI3K/mTOR, PKC or JNK transduction factors, then further incubated with IFN-α for different times. The mRNA and protein expression of IFIT4 or other indicated signal transduction factors were detected by qRT-PCR or western-blot.

Results LY294002, a dual mTOR and PI3K inhibitor, but not wortmannin, blocked IFIT4 promoter activation, mRNA and protein, as well as phosphorylation of STAT1, JNK, PKC8 induced by IFN-α. Interestingly, rapamycin, mTOR inhibitor, had the same effects as LY294002, counteracting the IFN-α-dependent upregulation of IFIT4 and phosphorylation of STAT1, JNK, PKC8. Rottlerin or Sp600125, specific inhibitor of PKC8, JNK, inhibited IFN-induced IFIT4 expression, but not the phosphorylation of AKT and mTOR. Interestingly, in vivo, bolus intravenous injection of methylprednisolone rapidly decreased the IFIT4 expression. In vitro, dexamethasone could prohibit IFN-α-induced IFIT4 transcription and the phosphorylation of STAT1, JNK, PKC-8.

Conclusions IFN-α activate the PI3K and mTOR pathways, which converge to regulate PKC8, JNK, STAT1-dependent transcription of IFIT4 in a mTOR dependent and AKT independent manner. The induction of IFIT4 transcription by IFN-α depends upon sequential activation of mTOR, PKC8, JNK and STAT1. Steroid might play the role in treatment for systemic lupus erythematosus (SLE) partially by the reason of decreasing IFN alpha induced protein IFIT4 expression via sequential inhibition of the phosphorylation of PI3K, mTOR, PKC8, JNK, STAT1.
SLE RISK HAPLOTYPES ARE ASSOCIATED WITH DEVELOPMENT OF SEROLOGIC AUTOIMMUNITY IN HEALTHY INDIVIDUALS

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Background and aims ANA are one of the earliest features of lupus, preceding the onset of clinical symptoms. The genetic risk factors that underlie the development of serological autoimmunity are unknown. A genome-wide association study was undertaken to understand the genetics of ANA development.

Methods Serum and DNA were collected from 2633 healthy individuals with no personal history of autoimmunity. Sera from 724 individuals (ANA-, ANA+, and SLE) were assayed by protein microarray quantifying IgM and IgG responses to 96 human autoantigens. A nested cohort of subjects consisting of all the ANA+ Caucasian individuals and matched ANA-controls were genotyped.

Results In healthy individuals, 16.2% had moderate and 8.0% had high levels of IgG antinuclear antibodies. ANA+ healthy individuals had a high prevalence of antibodies to non-nuclear and cytoplasmic antigens, while subjects with SLE predictably produced antibodies to a variety of nuclear antigens. A quantitative genetic association test with ANA identified genomic loci associated with high ANA phenotype. HLA was second strongest signal (p=6.2x10^-5). The frequencies of SLE risk haplotypes at several loci were significantly increased in the ANA high positive group compared to ANA negative subjects. However, SLE risk haplotypes at other loci were only high in the SLE group, suggesting their main role in a transition to clinical disease.

Conclusions The genetic risk for the development of ANA includes many of the previously documented SLE risk haplotypes. However, other genetic associations are specific for SLE, suggesting distinct risk factors for ANA and for lupus.