中文題目：干擾素調控因子7在台灣全身性紅斑狼瘡患者的可能角色

英文題目： The Potential Role of Interferon-regulatory Factor 7 Among Taiwanese Patients with Systemic Lupus Erythematosus

作　　者：林理信[1] 凌斌[2] 劉明煇[3]

服務單位：奇美醫療財團法人佳里奇美醫院內科[1] 成功大學醫學院微免所[2] 成功大學醫學院附設醫院內科[3]

**Background:** Type I interferons (IFN), especially IFN-α, have been proposed to underlie the pathogenesis of systemic lupus erythematosus (SLE). Members of the IFN regulatory factor (IRF) family, which regulate IFN expression, have been implicated as risk factors for SLE. Our aims were to investigate the expression of IRF7 and its correlation with disease activity and to explore the association in Taiwanese patients between 2 genetic single-nucleotide polymorphisms (SNP) of IRF7 and SLE.

**Materials and Methods:** IRF7 messenger RNA (mRNA) levels were measured in peripheral blood mononuclear cells by real-time reverse transcription polymerase chain reaction in 51 adult patients with SLE and 65 age-matched and sex-matched controls. Their serum IFN-α levels were determined by ELISA and the clinical manifestations were recorded at the same time. Two IRF7 SNP, rs1061501 and rs1061502, were examined by genotyping across 92 patients with SLE and 92 age and sex-matched healthy control subjects.

**Results:** Compared with controls, the expression of IRF7 mRNA was significantly increased in patients with SLE and was positively correlated with both the serum level of IFN-α and lupus disease activity (Figures 1-3). The distribution of SNP rs1061501 by genotype (CC, CT, and TT) and by allele (C, T) was significantly different between the SLE and the control group ($p = 0.028$ for genotype and $p = 0.009$ for allele). There were no significant differences for SNP rs1061502 (Table 1).

**Conclusion:** The results suggest that dysregulation of IRF7 might mediate an excessive production of IFN-α, which then exerts a crucial effect on the pathogenesis of human SLE. The IRF7 SNP rs1061501 TT genotype and T allele are enriched in Taiwanese patients with SLE and thus would seem to be associated with an increased risk of developing SLE.

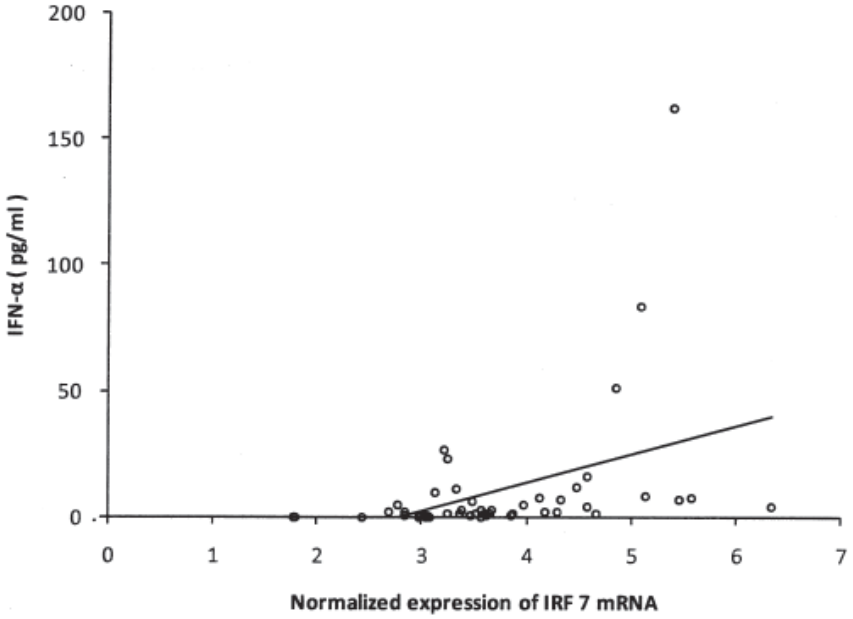


**Figure 1:** The expression levels of interferon (IFN) regulatory factor (IRF7) messenger RNA (mRNA) in peripheral blood mononuclear cells were significantly correlated with serum IFN-α levels in patients with systemic lupus erythematosus ($p < 0.001$).

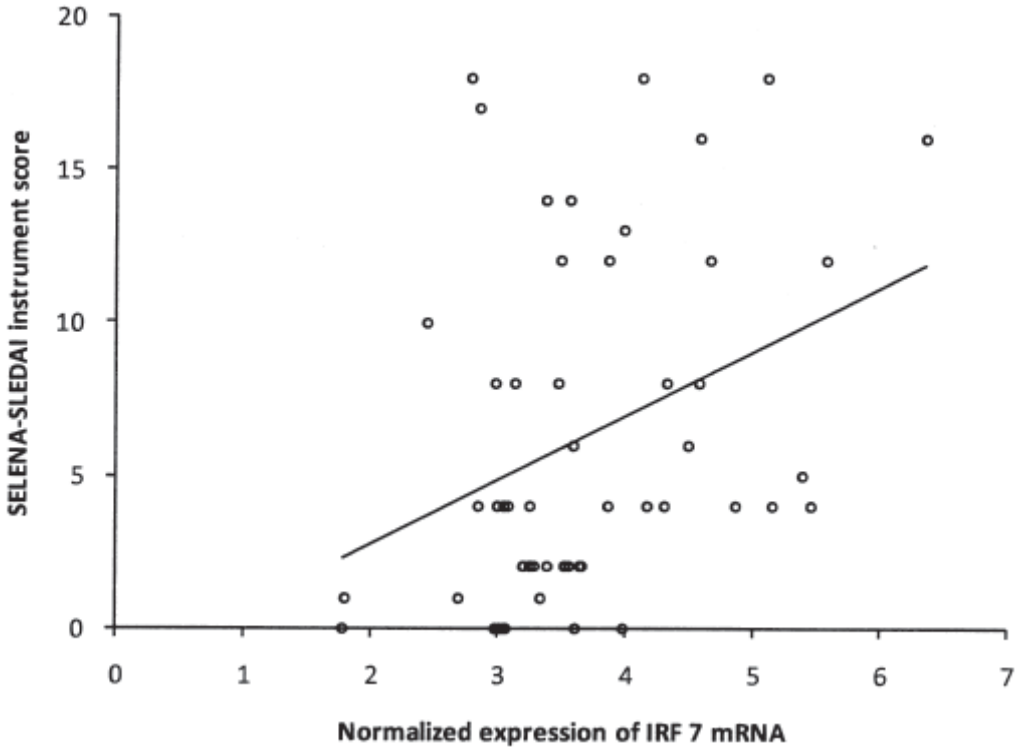


**Figure 2:** The expression levels of interferon regulatory factor (IRF7) messenger RNA (mRNA) in peripheral blood mononuclear cells were positively correlated with the Safety of Estrogens in Lupus Erythematosus: National Assessment - Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) instrument scores of patients with SLE ($p = 0.01$).

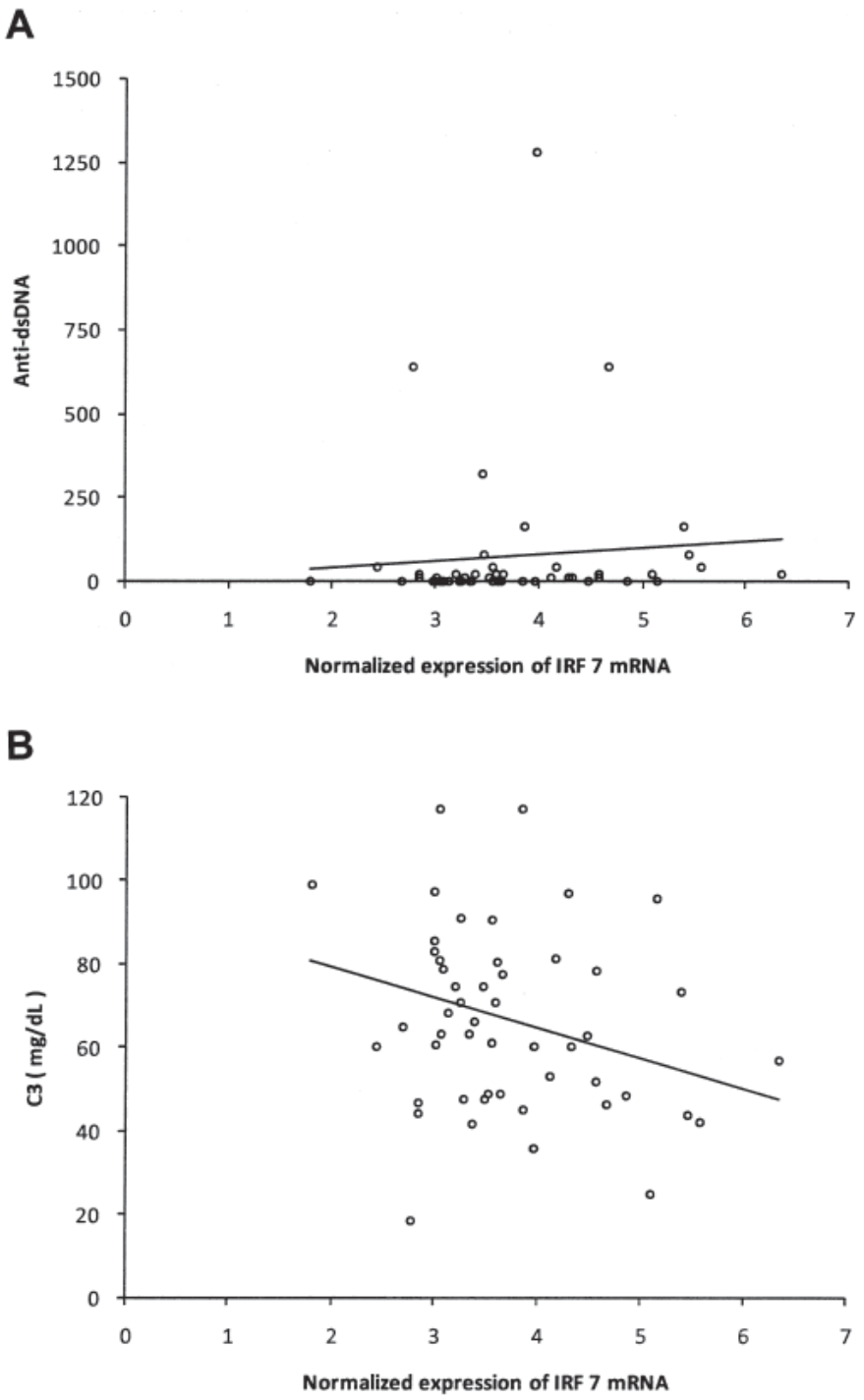


**Figure 3A:** The expression levels of interferon regulatory factor (IRF7) messenger RNA (mRNA) in peripheral blood mononuclear cells were positively correlated with anti-dsDNA titers ($p = 0.017$) in patients with systemic lupus erythematosus (SLE).

**Figure 3B:** The levels were negatively correlated with serum C3 level ($p = 0.032$) in patients with SLE.

**Table 1:** Frequency of the IRF7 rs10611501 and rs10611502 SNPs compared between SLE patients and healthy controls

| SNP[†] **rs1061501** | SLE (n = 92) | Control (n = 92) | *p* value[‡] |
|---|---|---|---|
| Genotype | | | |
| CC | 7 (7.6) | 12 (13.0) | 0.028[*] |
| CT | 30 (32.6) | 43 (46.7) | |
| TT | 55 (59.8) | 37 (40.2) | |
| Allele[§] | | | |
| C | 44 (23.9) | 67 (36.4) | 0.009[*] |
| T | 140 (76.1) | 117 (63.6) | |
| SNP[†] **rs1061502** | SLE (n = 92) | Control (n = 92) | *p* value[‡] |
| Genotype | | | |
| CC | 0 (0) | 0 (0) | 0.720 |
| CT | 3 (3.3) | 5 (5.4) | |
| TT | 89 (96.7) | 87 (94.6) | |
| Allele[§] | | | |
| C | 3 (1.6%) | 5 (2.7%) | 0.724 |
| T | 181 (98.4%) | 179 (97.3%) | |

Data are shown as n (%). Percentages may not sum to 100% because of rounding up or down.

SNP, single-nucleotide polymorphism

SLE, systemic lupus erythematosus.

[†]The SNP rs1061501 and rs1061502 genotypes were assessed for Hardy-Weinberg equilibrium (*p* value of both = 1.000).

[‡]The *p* values were calculated by Fisher's exact test between groups.

[§]Each SNP has two alleles and hence the sum of both groups is 92 x 2 = 184 rather than 92.

*$p < 0.05$.