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Tumour necrosis factor receptor 2 (TNFRSF1B) association study in Sjögren's syndrome

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Primary Sjögren's syndrome (pSS) is a complex disease involving both genetic and environmental factors. Among the genetic susceptibility factors, *HLA-DRB1* has been extensively studied as a strong candidate gene and the association of *HLA-DRB1*0301* (DR3) with pSS has been frequently reported among Caucasians.[1 2] As the Tumour Necrosis Factor α (*TNFα*) gene is located within the *HLA* region, its contribution to disease susceptibility has also been studied. We have previously reported a significant association of *TNF-308A* allele with pSS, in strong linkage disequilibrium with *HLA-DRB1*03*.[3] This association was restricted to patients with anti-SSB antibodies. TNF exerts its action through two cell surface receptors, TNF receptors 1 and 2 (TNFR1 and TNFR2, 55 and 75 kDa respectively). Due to the functional interaction between TNF and TNFR2, we considered this receptor (also named TNFRSF1B) as another interesting candidate gene for the genetic susceptibility to pSS. *TNFR2 T676G* polymorphism replacing a methionine by an arginine (TNFR2 196 M/R) is functional as the cytotoxic activity induced by TNFR2 196R (*TNFR2 696 G* allele) is increased.[4] Moreover, *TNFR2 T676G* polymorphism has been previously associated with the genetic susceptibility to other autoimmune diseases: familial, but not sporadic, rheumatoid arthritis (RA)[5] and systemic lupus erythematosus (SLE).[6]

We carried out a case–control association study of *TNFR2 T676G* polymorphism among 119 unrelated patients with pSS according to European–American consensus group (46 patients without autoantibodies (Ab), 33 patients with anti-SSA Ab only, 40 patients with anti-SSA and anti-SSB Ab) and 95 healthy controls. Both patients and controls were of Caucasian origin. *TNFR2 T676G* polymorphism was genotyped by polymerase chain reaction–restriction fragment length polymorphism analysis (*Nla* III).

No significant differences in allele and genotype frequencies of *TNFR2 T676G* polymorphism were detected between patients with pSS and controls (Table 1). *TNFR2 T676G* polymorphism was not involved in the genetic predisposition to a specific pattern of autoantibody secretion ($p = 0.61$). No association was found with extraglandular involvement ($p = 0.34$). Interestingly, there was a trend in favour of an association with joint involvement (arthritis and arthralgia) ($p = 0.06$). An epistatic effect between *TNF -308A/G* and *TNFR2 T676G* polymorphisms was then looked for, but not evidenced, among 55 pSS patients.

Table 1 Allelic and genotypic frequencies of *TNFR2 T676G* polymorphism in 119 patients with pSS and 95 controls

TNFR2 T676G **Allele frequencies**	**pSS n = 238**	**Controls n = 190**	**p**	**Odds ratio (95% CI) pSS versus controls**
676T (%)	191 (80.3)	149 (78.4)	NS	1.12 (0.7 to 1.79)
676G (%)	47 (19.7)	41 (21.6)		
Genotype frequencies	**n = 119**	**n = 95**		
TT	72 (60.5)	56 (58.9)	NS	0.85 (0.62 to 1.15)
TG	47 (39.5)	37 (38.9)	NS	1.17 (0.86 to 1.60)
GG	0	2 (2.2)		

pSS, primary Sjögren's syndrome; CI, confidence interval; NS, not significant.

This study failed to demonstrate an association of *TNFR2 T676G* polymorphism with pSS. These results, together with the lack of efficacy of infliximab in pSS[7] rather suggest a poor involvement of the TNF/TNF receptor system in the susceptibility to pSS.

To date, among rheumatic diseases, *TNFR2 T676G* polymorphism association with lupus led to conflicting results.[4 6 8 9] A recent case–control study performed in an Asian population of patients also failed to demonstrate any association of *TNFR2 T676G* polymorphism with SLE.[10] However, this study also provided a metaanalysis of seven case–control studies in eight different ethnic populations. Stratification by ethnicity revealed a significant association among Asians while the effect of *TNFR2 T676G* polymorphism on SLE was not significant in two case-control studies involving Caucasians (OR = 0.99, 95%CI = 0.68 to 1.45; p = 0.96). Thus, as observed among Caucasian SLE patients, our study provides evidence suggesting that *TNFR2 T676G* polymorphism is not involved in the genetic predisposition to pSS in French Caucasian patients.

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International survey on the diagnosis and management of gout

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The pathogenesis of urate crystal deposition is reasonably well understood, and with appropriate urate-lowering therapy (ULT) and lifestyle advice, the objective of management is cure. Nonetheless, many patients with gout continue to experience frequent and recurrent episodes of gout and progression of their disease. This is because the condition is often misdiagnosed, or diagnosed late, and treatment is frequently suboptimal.[1 2] These concerns led to the development of evidence-based recommendations relating to the diagnosis and management of gout by a task force from the European League Against Rheumatism (EULAR). The EULAR recommendations were developed using a combination of research-based evidence and expert consensus, and provide a valuable resource for physicians.[1 2]

The current diagnosis and management of gout was investigated in a survey conducted among delegates attending EULAR 2006. Delegates visiting the commercial stands were invited to complete a written questionnaire of 12 questions designed to evaluate awareness of the impact of gout, the goals of treatment, and patterns of clinical practice. A total of 741 respondents (6.7% of attendees), predominantly rheumatologists from Europe, completed the questionnaire.

The results indicate a good level of understanding concerning gout and its management, but also highlight some marked variations in clinical practice.

Respondents reported using both the measurement of serum uric acid (sUA) (97%) and the examination of synovial fluid (91%) to confirm suspected gout. Only 15% said they would prescribe ULT when the diagnosis of gout was made, most reported that they would usually wait for the next gout attack (24%) or for at least two further attacks (32%) to occur before initiating treatment. Whereas 29% said they would initiate ULT during an attack, the remainder confirmed they would wait until after an attack, and most (60%) would then begin therapy