will be more dependent on +2373A→G than on +2035C→G, as this latter SNP was discordant in haplotype 5.

This study confirms the association of common SNPs in the DNASE I gene with SLE, although it fails to show a correlation with low DNase I activity or production of antinuclear antibodies in patients' sera. Therefore, other mechanisms should be explored to explain the SLE susceptibility related to DNASE I variation and the low DNase I activity observed in most patients.

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High disease activity of ankylosing spondylitis in the community before the introduction of tumour necrosis factor blockers

Josef Hermann, Thomas Müller, Babak Yazdani-Biuki, Martin Aringer, Manfred Herold, Wolfgang Ebner, Petra Ofner, Winfried Graninger

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Before the introduction of tumour necrosis factor (TNF) blocking agents, the management of ankylosing spondylitis was mainly limited to physical exercise and the administration of non-steroidal anti-inflammatory drugs.^{1–3} To estimate the ankylosing spondylitis disease status in conventionally treated patients, we performed a community-based cross-sectional postal survey before TNF blocking agents became available in Austria.

Between January and April 2003, a questionnaire to assess ankylosing spondylitis disease activity, function and pain levels using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), the Bath Ankylosing Spondylitis Functional Index (BASFI) and a Visual Analogue Scale (VAS) was distributed to all 1400 members of the Austrian ankylosing spondylitis patient's association treated in the community, to patients with ankylosing spondylitis treated in tertiary rheumatology centres and to consecutive sex-matched controls with coronary artery disease, diabetes mellitus or goitre without signs of inflammatory rheumatic pain attending a general internal medicine outpatient clinic.

In all, 665 (47.6%) members of the ankylosing spondylitis patient's association (469 men and 196 women, mean (standard deviation (SD)) age 52 (12) years); 129 patients from rheumatology outpatient clinics (92 men and 37 women, mean (SD) age 40 (11) years); and 150 controls (89 men and 61 women, mean (SD) age 54 (14) years) returned an assessable questionnaire. Diagnosis of ankylosing spondylitis was confirmed in 97 of 100 randomly selected members of the ankylosing spondylitis patient's association by re-evaluating their medical records. Disease activity evaluated by the BASDAI, and the percentage of

patients with BASDAI ≥ 4 and >7 were equally high in patients in the community and in tertiary centres, but significantly lower in patients without inflammatory back pain (table 1). No correlation was found between the BASDAI and the age of patients ($r = 0.03$; $p = 0.42$). Functional impairment measured by the BASFI was significantly lower in patients treated in tertiary centres than in patients in the community and was lowest in controls (table 1). The BASFI increased significantly with age in all three groups and was highest in patients >60 years treated in tertiary centres (median (range) 7.6 (2.5–8.8)). The BASFI correlated with the BASDAI ($r = 0.67$; $p < 0.01$) and weakly with patient's age ($r = 0.23$; $p < 0.01$). The median pain score and the percentage of patients with a pain score >7 was equally high in patients treated in the community and in tertiary centres, but significantly lower in patients with non-inflammatory back pain (table 1). Pain levels correlated with the BASDAI ($r = 0.80$; $p < 0.01$) and the BASFI ($r = 0.61$; $p < 0.01$), but were independent of age ($r = -0.07$).

In summary, we have reported high disease activity, functional impairment and pain levels in 75% of conventionally treated patients with ankylosing spondylitis in the community, bearing in mind that the BASDAI may not be an appropriate measure to determine ankylosing spondylitis disease activity in a postal questionnaire. Conceivably, the population of organised patient's groups answering the questionnaire may be biased to report more severe disease than the total cohort of all patients with ankylosing spondylitis, but the disease status in our study was not different from a population of 246 patients with ankylosing spondylitis queried with a postal questionnaire between 2001 and 2003 in the UK.⁴

Table 1 Disease activity (BASDAI), functional impairment (BASFI), pain (VAS) and morning stiffness in patients with ankylosing spondylitis treated either in the community or in tertiary centres, or in controls with back pain but without inflammatory rheumatic diseases

	Community (n = 555)	Tertiary centre (n = 129)	Controls (n = 153)
BASDAI	4.8 (0–9.6)	4.4 (0.4–10)	2.7* (0.9–8.4)
BASDAI ≥ 4 , n (%)	524 (78.8)	84 (65.1)	64* (41.8)
BASDAI >7, n (%)	107 (16.1)	18 (14.0)	5* (3.3)
BASFI	4.4 (1–10)	3.7† (0–10)	1.8* (0.7–9)
BASFI >7, n (%)	122 (18.3)	21 (16.3)	11* (7.5)
Pain (VAS)	5 (1–10)	5 (0–10)	2* (0–10)
VAS >7, n (%)	177 (26.7)	37 (30.1)	14* (9.3)

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; VAS, Visual Analogue Scale. Values are median (range) unless otherwise indicated.

*p < 0.001 versus community and tertiary centre patients.

†p < 0.05 versus community patients.

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Association of tumour necrosis factor α promoter polymorphisms with ankylosing spondylitis in Taiwan

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Ankylosing spondylitis is a genetic-susceptible inflammatory spondyloarthropathy that mainly affects the sacroiliac joints. Tumour necrosis factor (TNF) α , a potent proinflammatory cytokine and immune modulator of joint destruction, is suggested to be a risk factor for the development of ankylosing spondylitis.¹ Evidence of an association between TNF α gene polymorphisms and ankylosing spondylitis showed conflicting results. Most of such studies focused on Caucasian subjects; few in the Taiwanese population were documented except for a recent study that reported the association between the interleukin 1 gene cluster and ankylosing spondylitis.²

Our study examined the distribution of TNF α promoter polymorphisms among Taiwanese patients with ankylosing spondylitis. A total of 143 patients with ankylosing spondylitis (97 men and 46 women, mean (standard deviation (SD)) age 41.7 (11.5) years), defined by the modified New York diagnostic criteria,³ were enrolled. The control population consisted of 166 unrelated and ethnic-matched healthy people (107 men and 59 women, mean (SD) age 37.7 (13.2) years). Distribution of TNF α G–238A genotypes ($p = 0.007$) and alleles ($p = 0.007$), as well as that of G–308A genotypes ($p = 0.045$) and alleles ($p = 0.018$), between patients with ankylosing spondylitis and controls were significantly different (table 1). Frequencies of high TNF α -secreting alleles –238*A and –308*A were markedly decreased in patients with ankylosing spondylitis, which suggests that TNF α –238*A and –308*A are protective alleles

for the development of ankylosing spondylitis. These observations supported previous reports which stated that frequencies of the rarer TNF α –238*A and –308*A alleles are lower in patients with ankylosing spondylitis,^{1,4} and the observation that T cell production of TNF α in patients with ankylosing spondylitis was decreased.¹

The significant difference of B27 positivity in our patients with ankylosing spondylitis (97.9%) and controls (4.2%) further indicated the important contribution of B27 to the incidence of ankylosing spondylitis. Both TNF α G–308A genotypes ($p = 0.01$) and alleles ($p = 0.012$) were significantly correlated with B60 positivity in B27+ patients (table 1). Notably, the high TNF α secreting –308*A allele was significantly decreased in B60+ patients, compared with B60– patients. It further supported the previous hypothesis that the TNF α –308*A is a protective allele for ankylosing spondylitis because B60 is an independent predisposing factor for ankylosing spondylitis.⁵

Variations in linkage disequilibrium between TNF α genotypes with HLA genes is suggested to explain the conflicting results regarding genotypic data among ethnically different populations with ankylosing spondylitis.⁶ Some studies reported that the association between TNF α and ankylosing spondylitis is secondary to B27, therefore, TNF α polymorphism is not likely to be involved in susceptibility to ankylosing spondylitis.^{7,8} This scenario does not seem suitable for the Taiwanese population because both TNF α –238*G and –308*G are the predominant