Table 1 The effect of sub268–270 on radiological and pathological lesions of CIA

Groups	sub268–270	Irrelevant peptide	PBS
Radiological score	1.32 (0.49)*	2.63 (0.51)	2.69 (0.53)
Pathological score	1.38 (0.53)*	2.94 (0.63)	3.06 (0.65)

CIA, collagen-induced arthritis; PBS, phosphate-buffered saline.
Data were expressed as mean (SD). * $p < 0.01$

and blank control, respectively. Arthritis scores of all four paws were made by two independent observers, with a scale of 0–4 for each paw: 0 = no change, 1 = swelling and erythema of the digit, 2 = mild swelling and erythema of the limb, 3 = gross swelling and erythema of the limb, 4 = gross deformity and inability to use the limb.⁷ Radiographic films of both hind paws were taken at the 21st day of treatment and subjected to radiographic scoring by two independent radiologists according to the degree of cartilage and bone erosions: 0 = no obvious abnormality, 1 = tissue swelling and oedema, 2 = joint space narrowing, and 3 = bone erosion and osteophyte formation.⁸ After killing the rats on treatment day 21, both ankle joints of rats with CIA were detached, embedded in paraffin, stained with haematoxylin–eosin, and pathological scores were made by two independent pathologists according to the following scale: 0 = normal synovium, 1 = synovial membrane hypertrophy and inflammatory cell infiltrates, 2 = pannus formation and cartilage erosion, 3 = major erosion of cartilage and subchondral bone, and 4 = loss of joint integrity and ankylosis.⁹ These assessments were performed by two independent people who were blinded to groups of the animals. These measures might reduce the selection bias to the least level.

As shown in figure 1, the APL did not reduce the baseline arthritis ($p > 0.05$). However, from day 6 to day 21, sub268–270 effectively reduced the inflammation in CIA as compared with irrelevant peptide and blank control ($p < 0.01$). Radiological bone erosion and pathological lesions were the hallmark of rheumatoid arthritis/CIA. As shown in table 1, APL treatment significantly decreased the radiological score of CIA, implying its bone-protection potential ($p < 0.01$). APL decreased the pathological score of CIA, suggesting its role in inhibition of pathological lesions ($p < 0.01$).

In conclusion, APL sub268–270 could effectively reduce the joint inflammation and also decrease the joint injuries in CIA. These results suggest that this APL might be potentially useful in HLA-DRB1-positive patients with rheumatoid arthritis.

Authors' affiliations

Zhong-Qiang Yao, Ru Li, Zhan-Guo Li, Department of Rheumatology & Immunology, People's Hospital, Beijing University Medical School, Beijing, China

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Correspondence to: Prof Z G Li, Department of Rheumatology & Immunology, People's Hospital, Beijing University Medical School, 11 Xizhimen South Street, Beijing 100044, China; zhongqiangyao@yahoo.com

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Association of poly(ADP-ribose) polymerase 1 and a novel candidate locus, *LOC127086*, with systemic lupus erythematosus

Henk A Martens, Ilja M Nolte, Gerrit van der Steege, Martijn Schipper, Cees G M Kallenberg, Gerard J te Meerman, Marc Bijl

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Genetic predisposition probably plays an important part in the pathogenesis of systemic lupus erythematosus (SLE). Several loci have been suggested to be related to SLE, among which is the 1q41–42 region on chromosome 1.¹

This region is homologous to the *Sle1* region in an SLE mouse model.² One of the genes on this region is the poly(ADP-ribose) polymerase 1 (*PARP1*) gene, which has been associated with SLE in several studies. This gene encodes a nuclear enzyme

Figure 1 Results of the Haplotype Sharing Statistic (HSS), CROSS test, association analysis and the Transmission/Disequilibrium Test (TDT).

involved in DNA repair and apoptosis, and its activity is reduced in patients with SLE,³ thereby possibly facilitating autoimmunity and inflammation. However, conflicting results with regard to this association have been reported.^{4–6} Tsao *et al*⁴ reported preferential transmission of PARP alleles to patients with SLE, whereas Criswell *et al*⁵ and Delrieu *et al*⁶ could not confirm these results. The first two studies were performed in an American, multiethnic population, and the third used a sample of French Caucasian patients. In a comment on the negative finding of Delrieu *et al*, Tan *et al*⁷ performed additional analyses showing that *PARP1* is a candidate gene for SLE, at least in the African-American population. Another locus on this region, *LOC127086*, has not been studied before.

In this study, we analysed the involvement of the 1q41–42 region, in particular the *PARP1* gene and *LOC127086*, in a Dutch Caucasian population of 103 patients with SLE (table 1). DNA from family members was also obtained, thereby constituting 103 trios. Microsatellite markers covering this region were genotyped. Strong linkage disequilibrium was observed between markers close to *PARP1* and close to *LOC127086*. Haplotype sets of patients and controls were compared using the Haplotype Sharing Statistic (HSS) and the CROSS test. The HSS compares the length of haplotypes between patients and controls, and the

CROSS test assumes that the haplotypes spanning the disease locus differ more between patients and controls than between patients themselves. These methods have proved to be valid in other studies.^{8–10} HSS and CROSS showed significant differences between patients and controls at markers close to *LOC127086* ($p = 0.005$; fig 1). This result was confirmed by single-locus association analysis, although just not significant ($p = 0.051$; fig 1). The Transmission/Disequilibrium Test was performed on trios consisting of patients and their parents. This showed significantly lower transmission of alleles surrounding *PARP1* ($p = 0.045$; fig 1), suggesting a protective effect of these alleles.

Our study shows that *PARP1* is a candidate gene for SLE in a Dutch Caucasian population. As this gene encodes a nuclear enzyme that is involved in DNA repair and apoptosis, it is a logical candidate gene for SLE. We also found a novel candidate locus, *LOC127086*, which is a pseudogene similar to the *XRCC6* gene on chromosome 22q11–13. This gene encodes subunit p70 of the lupus Ku p70/80 autoantigen, an SLE-related gene. *LOC127086* is a pseudogene without a transcription product, hence its exact function remains unclear. However, the fact that it is a copy of an SLE-related gene is noteworthy.

Authors' affiliations

Henk A Martens*, Cees G M Kallenberg, Marc Bijl, Department of Rheumatology and Clinical Immunology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

Ilya M Nolte*, Gerrit van der Steege, Martijn Schipper, Department of Pathology and Laboratory Medicine, Section Medical Biology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

Gerard J te Meerman, Department of Medical Genetics, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

*These authors contributed equally to this work.

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Correspondence to: Mr Henk A Martens, Department of Rheumatology and Clinical Immunology, University Medical Center Groningen, University of Groningen, PO Box 30001, 9700 RB Groningen, The Netherlands; h.a.martens@int.umcg.nl

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Table 1 Basic characteristics of 103 patients with systemic lupus erythematosus

Median age (years; min–max)	43 (23–78)
Sex: female, n (%)	89 (86)
Median age of onset (years; min–max)	31 (8–73)
Median duration of disease (months; min–max)	131 (21–516)
Race, n (%)	
Caucasian	103 (100)
ACR criteria, n (%)	
Malar rash	37 (36)
Discoid rash	31 (30)
Photosensitivity	52 (50)
Oral ulcers	13 (13)
Arthritis	67 (65)
Serositis	39 (38)
Renal disorder	42 (41)
Neurological disorder	7 (7)
Haematological disorder	75 (73)
Immunological disorder	91 (88)
Anti-dsDNA	81 (79)
Anti-Sm	13 (13)
Anti-phospholipid antibodies	21 (20)
Antinuclear antibody	103 (100)

ACR, American College of Rheumatology.