explained by different environmental exposures, and warrant further epidemiological studies.

ACKNOWLEDGEMENTS

We thank staff at the Department of Rheumatology, Norfolk and Norwich University Hospital, Norwich, Norfolk, UK, for assistance in data collection.

Authors' affiliations

J H M Lee, T Attygalle, K Gaffney, D G I Scott, Department of Rheumatology, Norfolk and Norwich University Hospital, Norwich, Norfolk, UK

Competing interests: None.

Correspondence to: Dr J H M Lee, Norfolk and Norwich University Hospital, Colney Lane, Norwich, Norfolk NR4 7UY, UK; jsaxx999@doctors.org.uk

Accepted 15 July 2006

REFERENCES

- 1 Stone JH, Hoffman GS. Wegener's granulomatosis and lymphomatoid granulomatosis. In: Hecberg MC, Silman AJ, Smolen JS, Weinblatt ME, Weisman MH, eds. *Rheumatology*. 3rd edn. New York: Mosby, 2003.
- 2 Nuyts GD, van Vlem E, de Vos A, Dalemans RA, Rorive G. Wegener's granulomatosis is associated to exposure to silicon compounds: a case-control study [correction appears in *Nephrol Dial Transplant* 1995;10:2168. *Nephrol Dial Transplant* 1995;10:1162-5.
- 3 Pai P, Bone JM, Bell GM. Hydrocarbon exposure and glomerulonephritis due to systemic vasculitis. *Nephrol Dial Transplant* 1998;13:1321-3.
- 4 Duna GF, Cotch MF, Galperin C, Hoffman DB, Hoffman GS. Wegener's granulomatosis: role of environmental exposures. *Clin Exp Rheumatol* 1998;16:669-74.
- 5 Lane SE, Watts RA, Bentham G, Innes NJ, Scott DGI. Are environmental factors important in primary systemic vasculitis? *Arthritis Rheum* 2003;48:814-23.
- 6 Carruthers DM, Watts RA, Symmons DP, Scott DGI. Wegener's granulomatosis—increased incidence or increased recognition? *Br J Rheumatol* 1996;35:142-5.
- 7 Jayne D. Update on the European Vasculitis Study Group trials. *Curr Opin Rheumatol* 2001;13:48-55.
- 8 Savage J, Davies D, Falk RJ, Jennette JC, Wiik A. Anti-neutrophil cytoplasmic antibodies and associated diseases: a review of the clinical and laboratory features. *Kidney Int* 2000;57:846-62.

MATN3 (matrilin-3) sequence variation (pT303M) is a risk factor for osteoarthritis of the CMC1 joint of the hand, but not for knee osteoarthritis

O Pullig, A Tagariello, A Schweizer, B Swoboda, P Schaller, A Winterpacht

Osteoarthritis has a multifactorial aetiology with a strong genetic component.^{1,2} Recently, Stefansson *et al*³ identified a missense mutation (pT303M) in the *MATN3* (matrilin-3) gene (designated as single-nucleotide polymorphism (SNP)5) in a large cohort of patients from Iceland, which cosegregates with hand osteoarthritis in several families and shows a frequency of approximately 2% in the Icelandic population (relative risk 2.1). Min *et al*⁴ were not able to repeat this result in two Dutch cohorts of patients with hand osteoarthritis, but reported association of this SNP with spinal disc degeneration in one of their populations (odds ratio 2.9). In contrast, they found that the A allele of SNP6 (nomenclature as in Stefansson *et al*³), a silent base exchange in *MATN3*, is associated with hand osteoarthritis in one of their cohorts (odds ratio = 2.0). Here, we carried out a case-control study of the two polymorphisms for putative association with hand osteoarthritis and knee osteoarthritis in two small cohorts of German patients.

We investigated a sample group of 50 consecutive Caucasian patients (mean age 59.2 years, 84% women) with radiographic and symptomatic hand osteoarthritis of the first carpometacarpal joint (CMC1; late-stage arthritis, EATON stage II-IV), 176 consecutive Caucasian patients (mean age 69.8 years, 79% women) with radiographic and symptomatic knee osteoarthritis (late-stage primary osteoarthritis with complete collapse of the femorotibial joint space) and 356 unrelated Caucasian controls (mean age 38.8 years, 41% women, healthy blood donors recruited in Germany). Patients with CMC1 and knee osteoarthritis were not handled separately. Genotyping of SNP5 and SNP6 in the *MATN3* gene was performed by polymerase chain reaction amplification and subsequent cycle sequencing as described previously.⁵

Ann Rheum Dis 2007;66:279-280. doi: 10.1136/ard.2006.058263

We analysed the frequency of SNP5 in patients with hand osteoarthritis and in 356 controls and observed a difference in allele frequency ($\chi^2 = 10.84$, $p = 0.001$). The rare T allele of SNP5 was present in 10% of the patients with hand osteoarthritis and in 2.5% of controls (table 1, $\chi^2 = 7.35$, $p = 0.007$). The p value remained significant even after Bonferroni correction for multiple testing. Thus, carriers of the T allele had an increased risk for developing hand osteoarthritis, with an odds ratio of 4.28 (95% CI, 1.18 to 14.8). Interestingly, three of these five patients presented with more scaphotrapezotrapezoidal (STT) joint involvement, a characteristic already described.⁷ Thus, we could replicate the results for hand osteoarthritis reported by Stefansson *et al*.³ Our data support the importance of SNP5 for this specific form of osteoarthritis, but not for knee osteoarthritis (table 1). In contrast with the recent report by Min *et al*,⁴ we did not find association of SNP6 with hand osteoarthritis (or knee osteoarthritis; table 1).

The partly contradictory data between the different studies may possibly be due to differences in common diagnostic criteria,⁷ or in allele frequencies in the control group.⁴ In this respect, it has to be emphasised that our control cohort was randomly selected and is thus not age/sex matched or specifically evaluated for any signs of osteoarthritis. Nevertheless, the fact that the group of patients with knee osteoarthritis (n = 176) exhibit genotype and allele distributions very similar to that of the control cohort (table 1) strongly supports the present association data.

Although the exact role of *MATN3* and *MATN3* variations in osteoarthritis is still not clear,^{8,9} the present data support the importance of variations in the *MATN3* gene region for the aetiology of specific forms of osteoarthritis.

Table 1 Genotype and allele frequencies of SNP5 and SNP6 in patients with osteoarthritis and in controls

	Hand osteoarthritis				Knee osteoarthritis		
	Controls	Patients	p Value (χ^2)	p Value (exact)	Patients	p Value (χ^2)	p Value (exact)
N	356	50			176		
SNP5							
Genotype							
C C	347 (97.5)	45 (90)	0.007*	0.019*	172 (97.7)	0.857*	1*
C T	9 (2.5)	4 (8)			4 (2.3)		
T T	0	1 (2)			0		
Allele							
C	703 (98.7)	94 (94)	0.001	0.005	348 (98.9)	0.858	1
T	9 (1.3)	6 (6)			4 (1.1)		
SNP6							
Genotype							
A A	16 (4.5)	1 (2)	0.156†	0.167†	9 (5.1)	0.820†	0.851†
A G	128 (36)	14 (28)			64 (36.4)		
G G	212 (59.5)	35 (70)			103 (58.5)		
Allele							
A	160 (22.5)	16 (16)	0.141	0.155	82 (23.3)	0.763	0.756
G	552 (77.5)	84 (84)			270 (76.7)		

SNP, single-nucleotide polymorphism

Genotypes and allele frequencies % were compared using the χ^2 and Fisher's exact test on a 2×2 contingency table. A value of $p < 0.05$ was considered as significant. The value for SNP5 (in bold) remained significant even after correction for multiple testing. Both SNPs were in Hardy-Weinberg equilibrium in controls as calculated by the program Haploview.⁶

*TT + CT v CC in genotype analysis.

†AA + AG v GG in genotype analysis.

ACKNOWLEDGEMENTS

We are grateful to our patients for their participation in this study.

Authors' affiliations

O Pullig*, **B Swoboda**, Division of Orthopaedic Rheumatology, Department of Orthopaedic Surgery, Friedrich-Alexander University Erlangen-Nuremberg, Erlangen, Germany

A Tagariello*, **A Schweizer**, **A Winterpacht**, Institute of Human Genetics, Friedrich-Alexander University Erlangen-Nuremberg, Erlangen, Germany

P Schaller, Department of Hand and Plastic Surgery, Kliniken Dr Erler GmbH, Nuremberg, Germany

*Joint first authors.

This work was supported by a grant from the Bundesministerium für Bildung und Forschung (BMBF) to AW, and from the Deutsche Forschungsgemeinschaft (DFG) to OP and BS.

Competing interests: None.

Correspondence to: Dr Prof A Winterpacht, Institute of Human Genetics, Friedrich-Alexander-University Erlangen-Nuremberg, Schwabachanlage 10, Erlangen 91054, Germany; winterp@humgenet.uni-erlangen.de

Accepted 1 September 2006

REFERENCES

- 1 **Spector TD**, MacGregor AJ. Risk factors for osteoarthritis: genetics. *Osteoarthritis Cartilage* 2004;**12**:S39–44.
- 2 **Peach CA**, Carr AJ, Loughlin J. Recent advances in the genetic investigation of osteoarthritis. *Trends Mol Med* 2005;**11**:186–91.
- 3 **Stefansson SE**, Jonsson H, Ingvarsson T, Manolescu I, Jonsson HH, Olafsdottir G, et al. Genomewide scan for hand osteoarthritis: a novel mutation in matrilin-3. *Am J Hum Genet* 2003;**72**:1448–59.
- 4 **Min JL**, Meulenbelt I, Riyazi N, Kloppenburg M, Houwing-Duistermaat JJ, Seymour AB, et al. 2006. Association of matrilin-3 polymorphisms with spinal disc degeneration and with osteoarthritis of the CMC1 joint of the hand. *Ann Rheum Dis* 2006;**65**:1060–6.
- 5 **Zenker M**, Rauch A, Winterpacht A, Tagariello A, Kraus C, Rupprecht T, et al. A dual phenotype of periventricular nodular heterotopia and frontometaphyseal dysplasia in one patient caused by a single FLNA mutation leading to two functionally different aberrant transcripts. *Am J Hum Genet* 2004;**74**:731–7.
- 6 **Barrett JC**, Fry B, Maller J, Daly MJ. Haploview: analysis and visualization of LD and haplotype maps. *Bioinformatics* 2005;**21**:263–5.
- 7 **Eliasson GJ**, Verbruggen G, Stefansson SE, Ingvarsson T, Jonsson H. Hand radiology characteristics of patients carrying the T(303)M mutation in the gene for matrilin-3. *Scand J Rheumatol* 2006;**35**:138–42.
- 8 **Pullig O**, Weseloh G, Klatt AR, Wagener R, Swoboda B. Matrilin-3 in human articular cartilage: increased expression in osteoarthritis. *Osteoarthritis Cartilage* 2002;**10**:253–63.
- 9 **Otten C**, Wagener R, Paulsson M, Zaucke F. Matrilin-3 mutations that cause chondrodysplasias interfere with protein trafficking while a mutation associated with hand osteoarthritis does not. *J Med Genet* 2005;**42**:774–9.

FORTHCOMING EVENTS

12th International Congress on aPL

18–20 April 2007, Firenze, Italy

Tel: +39 02 28172 300

Fax: +39 02 70057965

Email: pregnancyrheumaticdiseases2007.edraspa.it

Web: <http://www.edraspa.it>

5th International Conference: Sex Hormones, Pregnancy and Rheumatic Disease

20–21 April 2007, Firenze, Italy

The main aim of the Conference is to report most recent achievements on pregnancy in autoimmune rheumatic diseases, with particular final emphasis on the problems related to the pharmacological treatments.

Tel: +39 02 28172 300

Fax: +39 02 70057965

Email: pregnancyrheumaticdiseases2007.edraspa.it

Web: <http://www.edraspa.it>

Future EULAR congresses

13–16 June 2007; EULAR 2007; Barcelona, Spain
11–14 June 2008; EULAR 2008; Paris, France

VI Meeting of the European Forum on Antiphospholipid Antibodies

12–13 October 2007, Ljubljana, Slovenia

Informal meeting of the clinicians, scientists that are active in the field of antiphospholipid antibodies and antiphospholipid syndrome
Vodnikova 62, 1000 Ljubljana, Slovenia

Tel: +386 1 5225533

Fax: +386 1 5225598

Email: info.apl2007@revma.net

Web: <http://www.revma.net>