Conclusions: Our results suggest that ADAMTS14 play a relevant role in susceptibility to OA, in particular to knee OA in women.

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ASSOCIATION OF THE ASPARTIC ACID-REPEAT POLYMORPHISM IN THE ASPORIN GENE WITH AGE AT ONSET OF KNEE OSTEOARTHRITIS IN HAN CHINESE POPULATION

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Purpose: Recent genetic studies for osteoarthritis (OA) have been focused on *ASPN*, the gene encoding asporin, where aspartic acid (D)-repeat polymorphisms are associated with OA in several ethnic groups. The purpose of the present study is to further examine the association of the D-repeat polymorphism in a Han Chinese population.
Methods: The D-repeat polymorphism was genotyped in 354 knee OA patients (257 women and 97 men) who suffered from primary symptomatic knee OA with radiographic confirmation, and the association of the repeat with various clinical parameters was examined.
Results: The age at onset (years) in patients with the D14 allele (mean: 51.9, SD: 8.5) was younger than that those without the D14 allele (mean: 54.9, SD: 10.9) (P=0.023). Survival analysis showed D14 was significantly associated with age at onset of OA (P=0.004 in the dominant model) (Fig. 1 at the foot). The average age at onset of patients with the D13/D13 genotype (mean: 56.1, SD: 11.1) was older than those without the D13/D13 genotype (mean: 53.0, SD: 9.9) (P=0.013).
Conclusions: Our study further highlighted the significance of asporin in OA.

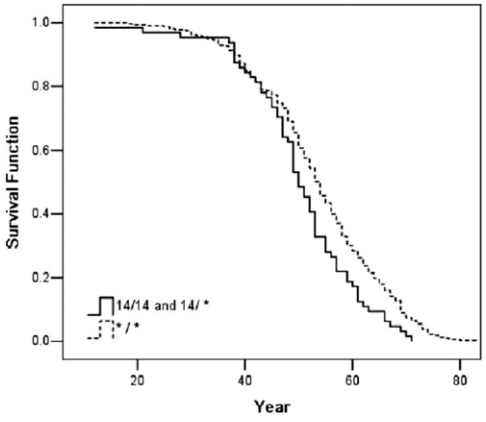

Figure 1

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LACK OF ASSOCIATION OF SINGLE-NUCLEOTIDE POLYMORPHISM IN *LRCH1* WITH KNEE OSTEOARTHRITIS SUSCEPTIBILITY

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Purpose: A genetic association of knee osteoarthritis (OA) and a C/T transition SNP (rs912428) located in intron 1 of the *LRCH1* gene has recently been reported in European Caucasians; however, the results are contestable. Our objective is to evaluate the association in different knee OA populations.
Methods: Three case-control association studies were conducted in Han Chinese, Japanese and Greek Caucasian populations. The *LRCH1* SNP was genotyped in patients who had primary symptomatic knee OA with radiographic confirmation and in matched controls, and the association was examined. We performed meta-analysis for the studies together with results of two previous papers using the DerSimonian-Laird procedure.
Results: A total of 1145 OA patients and 1266 controls were genotyped. No significant difference was detected in genotype or allele frequencies between knee OA and control groups in the three populations (all $P > 0.05$) (Table 1). The association was also negative even after stratification by sex and K/L scores. Meta-analysis also supported the negative result for association between LRCH1 and knee OA. The strong heterogeneity between original and replication studies was detected in Caucasian populations (Table 2, see p. C164).
Conclusions: The *LRCH1* SNP is not a risk factor for knee OA etiology in East Asians and is most unlikely so in European Caucasian populations.

Abstract 294 – Table 1. Association of the C/T polymorphism of LRCH1 gene in patitents with knee osteoarthritis in three populations

Groups compared	CC vs Others			TT vs Others			All Genotypes	C allele vs T allele		
	OR	*P* value	95% CI	OR	*P* value	95% CI	*P* value	OR	*P* value	95% CI
Chinese study										
All patients (n=315) vs All controls (n=485)	0.99	0.97	0.69–1.48	1.16	0.85	0.25–5.20	0.98	1.00	1.00	0.70–1.43
Female patients (n=151) vs Female controls (n=289)	1.33	0.66	0.71–1.79	1.55	0.60	0.22–11.7	0.82	1.13	0.56	0.74–1.74
Male patients (n=67) vs Male controls (n=165)	0.74	0.83	0.36–1.51	0.77	0.48	0.07–8.55	0.70	0.75	0.40	0.39–1.46
Japanese sample										
All patients (n=218) vs All controls (n=454)	1.07	0.67	0.79–1.43	1.29	0.78	0.22–7.70	0.89	1.07	0.65	0.81–1.41
Female patients (n=151) vs Female controls (n=289)	1.01	0.97	0.68–1.48	–	0.23	–	0.49	1.04	0.83	0.72–1.50
Male patients (n=67) vs Male controls (n=165)	1.18	0.56	0.68–2.06	–	0.39 –	0.53	1.12	0.68	0.66–1.90	
Greek sample										
All patients (n=107) vs All controls (n=161)	0.79	0.38	0.47–1.33	1.52	0.55	0.37–6.23	0.48	0.88	0.57	0.56–1.37
Female patients (n=151) vs Female controls (n=289)	0.91	0.75	0.51–1.63	4.06	0.19	O.41–39.8	0.36	1.01	0.96	0.61–1.68
Male patients (n=67) vs Male controls (n=165)	0.33	0.09	0.08–1.26	0.73	0.79	0.07–7.44	0.42	2.41	0.12	0.13–1.30

CC, CT, TT genotypes were grouped together; and a 2*3 contingency-table analysis was performed.

Abstract 294 – Table 2. Summary of association and heterogeneity of the C/T polymorphism of LRCH1 gene in patitents with knee osteoarthritis in the three populations

Groups	CC vs Others				TT vs Others				C allele vs T allele			
	Summary			Heterogeneity	Summary			Heterogeneity	Summary			Heterogeneity
	OR	*P* value	95% CI	*P* value	OR	*P* value	95% CI	*P* value	OR	*P* value	95% CI	*P* value
All studies	1.43	0.06	0.98–2.08	0.91	1.16	0.24	0.91–1.48	0,002	1.16	0.14	0.95–1.40	0.01
Replication studies	1.34	0.91	0.89–2.03	0.91	1.1	0.003	0.84–1.44	0.003	1.11	0.33	0.90–1.37	0.02
European studies	1.46	0.06	0.98–2.17	0.75	1.21	0.28	0.85–1.71	0.0005	1.20	0.17	0.93–1.57	0.004
Asian studies	1.21	0.75	0.38–3.83	0.93	1.04	0.75	0.82–1.31	0.77	1.04	0.17	0.93–1.57	0.79

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GENETIC LINKAGE ANALYSIS AND META ANALYSIS OF STIMULATED CYTOKINE LEVELS IN DUTCH FAMILY BASED STUDIES

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Purpose: In our studies, consisting of affected sibpairs with OA at multiple joint sites and a random population based cohort of twin families, we focus on identification of loci involved in the inflammatory response.
Methods: A 10 cM genome scan comprising 400 microsatellite markers taken from the Human Linkage Set v2.5 MD10 (Applied Biosystems) was finished in a generalised OA sibpair study (GARP) and in the twin sample (Zaterdag samples) using an ABI3700 (Applied Biosystems). The GARP study consists of 382 probands (aged 40-70 years) and their siblings of Dutch ancestry with predominantly symptomatic familial OA at multiple joint sites of the hand or in two or more of the following joints sites (hand, spine, knee or hip). The Zaterdag sample consists of 139 families comprising 309 subjects which were included in a twin study with no further inclusion criteria.
LPS stimulated cytokine profiles of sibling pairs were available for TNF-alpha, IL-1 beta, IL1 receptor antagonist and IL-10 in both studies.
Results: By use of Merlin-regress and a grid based analysis of the data both studies was performed for the phenotypes indicated. A meta analysis was performed using the output from the initial analysis. Based on LOD scores in the individual studies as well as LOD scores obtained by use of the meta analysis a selection of 5 peaks was made for follow up. These 5 peaks were finemapped by additional microsattalite markers upon which analyses were repeated for the regions finemapped. 2 peaks appeared to be robust upon finemapping, resulting in a maximum LOD score in the unaffected study group of 4,52 for IL-10 in a region in which other cytokines also showed evidence for linkage and a linkage peak resulting from the meta analysis of both studies on chromosome 4 with a LOD score of 1,5.
TagSNPs and possible functional variants for the genetic regions under linkage will be selected by use of online genetic databases, to further elucidate the genetic regions or genes which cause the linkage signals.
Conclusions: In our OA sibling pair study and a random sample of twin based families, a major locus involved in the inflammatory response was identified on chromosome 14 and chromosome 4. Tag SNPs in the genetic regions under linkage are currently being selected for further analysis of the linkage signal to possibly identify new genes involved in the regulation of inflammation.

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COL2A1 GENE POLYMORPHISMS AND SUSCEPTIBILITY TO POLYARTICULAR HAND OSTEOARTHRITIS IN FINNISH WOMEN

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Purpose: Both environmental and genetic factors have been shown to play a role in the etiology of osteoarthritis (OA). COL2A1 is a major structural component in joint cartilage and polymorphisms within this gene have previously been associated with OA. Our aim was to study the possible association of COL2A1 polymorphisms and their haplotypes with hand osteoarthritis.
Methods: Radiographs of both hands of 543 Finnish women aged 45-63 years were examined and classified for the presence of OA using reference images. Hand OA was defined by the presence of radiographic findings of grade 2 or more in at least three joints. The genotyping of two polymorphisms in COL2A1-gene (located in exon 5B and intron 33) was accomplished using PCR-based methods. The haplotypes were statistically reconstructed from population genotype data using the PHASE program. The common alleles of the polymorphisms were labelled as 1 and the rare alleles as 2. Data regarding anthropometric measures and other risk factors were collected by questionnaire. Logistic regression analysis was used to evaluate the association between the genotypes/haplotypes and hand OA.
Results: Allowing for age and occupation, the carriage of at least one A-allele in intron 33 was associated with hand OA (OR = 1.58, 95% CI 1.05-2.36, p=0.028). Four of the nine possible haplotypes were identified. The 1-1 haplotype was the most common (63.5%) followed by the 1-2 haplotype (18.9%). Compared with women without hand OA, the frequency of the 1-1 haplotype was lower (58% vs. 66%, p=0.01), whereas that of the haplotype 2-1 was higher among women with hand OA (3% vs. 1%, p=0.002). Allowing for age and occupation the carriers of the 2-1 haplotype had higher risk of hand OA (OR= 3.21, 95% CI 1.08-9.55, p=0.036) as compared with the non-carriers.
Conclusions: Our results suggest that the studied COL2A1 gene polymorphisms may play a role in the etiology of polyarticular hand OA.