Online Supplement 1.

Details of the genotyping analyses

The assays spotted on the OpenArray genotyping plate for *NLRP3* SNPs (rs35829419 and rs10925027), *CARD8* SNPs (rs2043211, rs1062808 and rs2288877), *TNF* SNPs (rs1799724 and rs1800629), *TGFB1* SNPs (rs1800469 and rs2241718), *GC* SNPs (rs7041 and rs4588), *MMP12* SNP (rs652438), and *TIMP2* SNP (rs2277698) were C__25648615_10, C__30713882_10, C__11708080_1_, C___3218826_10, C__15879993_10, C__11918223_10, C___7514879_10, C___8708473_10, C___7818377_1_, C___3133594_30, C___8278879_10, C____785907_10, and C__15885241_10, respectively. Plate format of 16 SNPs and 144 samples per array was used. The allele calling analysis was performed by using OpenArray™ SNP Genotyping Analysis software (BioTrove Inc).

The *TGFB1* rs1800470 SNP was genotyped by using an allelic discrimination assay on the ABI 7500 Real-Time PCR system (Applied Biosystems, Foster City, CA, USA) with TaqMan® probes.[1] The primers and probes used in the assay were as follows: forward primer: 5´-GCG CTC TCG GCA GTG C-3´; reverse primer: 5´-CCA GGC GTC AGC ACC AGT A-3´; VIC-probe: 5´-AGC AGC GGC AGC A-3´; and FAM-probe: 5´-CAG CAG CAG CAG C-3´. The primer and probe concentrations in the PCR reaction were 1200 nM and 200 nM, respectively, and the cycling conditions were 50 °C for 2 minutes, 95 °C for 10 minutes, 40 cycles of 95 °C for 15 seconds, and 62 °C for 1 minute. Sequence Detection Software 1.4 (Applied Biosystems) was used for the allele calling analysis.

The *MMP1* rs1799750 SNP was analysed with a pyrosequencing-method based on an assay from PyroMark Assay Database (Qiagen). The concentrations of the forward (5´-biotin-CCC TTA TGG ATT CCT GTT TTC-3´) and reverse (5´-CCC ATT CTT CTT ACC CTC TTG-3´) primers in PCR reactions were 500 nM, and the cycling conditions were 95 °C for 5 minutes, 35 cycles of 95 °C for 30 seconds, 54 °C for 30 seconds, and 72 °C for 30 seconds followed by a final extension of 72 °C for 5 minutes. The pyrosequencing run was performed with PSQ™96MA (Qiagen) by using Pyromark Gold Q96 Reagents (Qiagen) according to manufacturer's recommendations. Briefly, 40 µl of the PCR product was mixed with 37 µl of Binding buffer and 3 µl of Streptavidin Sepharose High Performance beads (GE Healthcare, Uppsala, Sweden). PCR products bound to the beads were collected and denatured to single-stranded by treatment with 70% Ethanol (Aa), Denaturation Buffer, Washing Buffer, and mQ water in Pyrosequencing Washing Station. The sequencing primer 5´-GTA GTT AAA TAA TTA GAA AG-3´ was attatched to the template by incubating for 2 minutes in 80°C in annealing buffer. The Pyrosequencing run was conducted in the dispensation order of CAGCTACTAGCA. The pyrograms were generated and analyzed with PSQ 96 SNP Software 1.1.

The *MMP9* rs3918242 SNP was genotyped by using a PCR-RFLP-based method essentially according to Joos *et al.*[2] Briefly, the concentrations of the forward (5´-TTC GTG ACG CAA AGC AGA-3´) and reverse (5´-AGC AGC CTC CCT CAC TCC T-3´) primers were 670 nM, and the cycling conditions were 95 °C for 4 minutes, 34 cycles of 95 °C for 30 seconds, 58 °C for 30 seconds, and 72 °C for 45 seconds followed by a final extension of 72 °C for 5 minutes. After digestion with *Sph*I in 37 °C

for 3 hours the PCR product was electrophoresed on a 2% agarose gel containing EtBr and visualized under UV-light.

The pyrosequencing re-analysis of *TNF* rs1799724 SNP was performed with PSQ™96MA (Qiagen) by using Pyromark Gold Q96 Reagents (Qiagen) as described above for the analysis of the *MMP1* SNP rs1799750. The primers and probes for the pyrosequencing protocol designed by using PyroMark Assay Design 1.0 -tool (Qiagen) were as follows: forward primer: 5´-GGT AGG AGA ATG TCC AGG GCT ATG-3´, biotinylated reverse primer: 5´-biotin-ACT CCC TGG GGC CCT CTA-3´ and sequencing primer: 5´-TCG AGT ATG GGG ACC-3´. The primer concentrations in PCR reactions were 200 nM, and the cycling conditions were: 95 °C for 5 minutes, 39 cycles of 95 °C for 15 seconds, 56 °C for 30 seconds, and 72 °C for 15 seconds followed by a final extension of 72 °C for 5 minutes. The pyrosequencing run was performed as described with *MMP1* rs1799750 SNP.

References

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3. Ozen S, Alikasifoglu M, Bakkaloglu A, Duzova A, Jarosova K, Nemcova D, Besbas N, Vencovsky J, Tuncbilek E. Tumour necrosis factor alpha G-->A -238 and G-->A -308 polymorphisms in juvenile idiopathic arthritis. *Rheumatology* 2002, **41**(2):223-227.