Appendix S1.

METHODS

Subjects

We ascertained a non-consanguineous Jewish family of Yemenite-Ashkenazi origin, including both parents and their 4 children. Informed consent was obtained from all family members or their legal guardians, according to a protocol approved and reviewed by the National Committee for Genetic Studies, Israel Ministry of Health, and the Rabin Medical Center.

Candidate gene sequencing

Genomic DNA was isolated from peripheral blood according to standard methods.

Candidate gene sequencing of the exons, exon intron junctions, 5' UTRs and 3' UTRs of the *IL36RN, IL1RN* and *CARD14* genes was initially performed in 1 affected family member (IV-1 – Fig. 1) (Gene by Gene Ltd, Houston, TX, USA).

Other family members were subsequently screened for the *CARD14* c.349G>A [p.Gly117Ser] mutation and the 3 coding region polymorphisms, found in IV-1, including (c.1641G>C [p.Arg547Ser], c.1753G>A [Val585Ile] and c.2458C>T [p.Arg820Trp]). For that purpose genomic DNA was amplified by polymerase chain reaction (PCR) with primer sets designed from the genomic sequences available from the University of California-Santa Cruz (UCSC) Genome Browser, using the Primer 3 program (Table SI[1]). The PCR products were separated by 2% agarose gel electrophoresis, subjected to extraction with illustra GFX PCR DNA and Gel Band Purification Kit (GE Healthcare Europe GmbH, Freiburg, Germany) and sequenced with BigDye Terminators (Applied Biosystems, Foster City, CA,US) on an ABI PRISM 3100 sequencer. Sequence chromatograms were analysed using SeqScape software version 1.1 (Applied Biosystems).

HLA type I genotyping.

DNA-based low-medium resolution analysis for HLA-C alleles was performed by means of PCR amplification with sequence-specific primers (SSP) methodology (Micro SSP generic HLA DNA typing tray, catalogue SSP2LB, One Lambda Inc., Mannheim, Germany). Interpretation of results was performed with the assistance of HLA software (One Lambda Inc.).