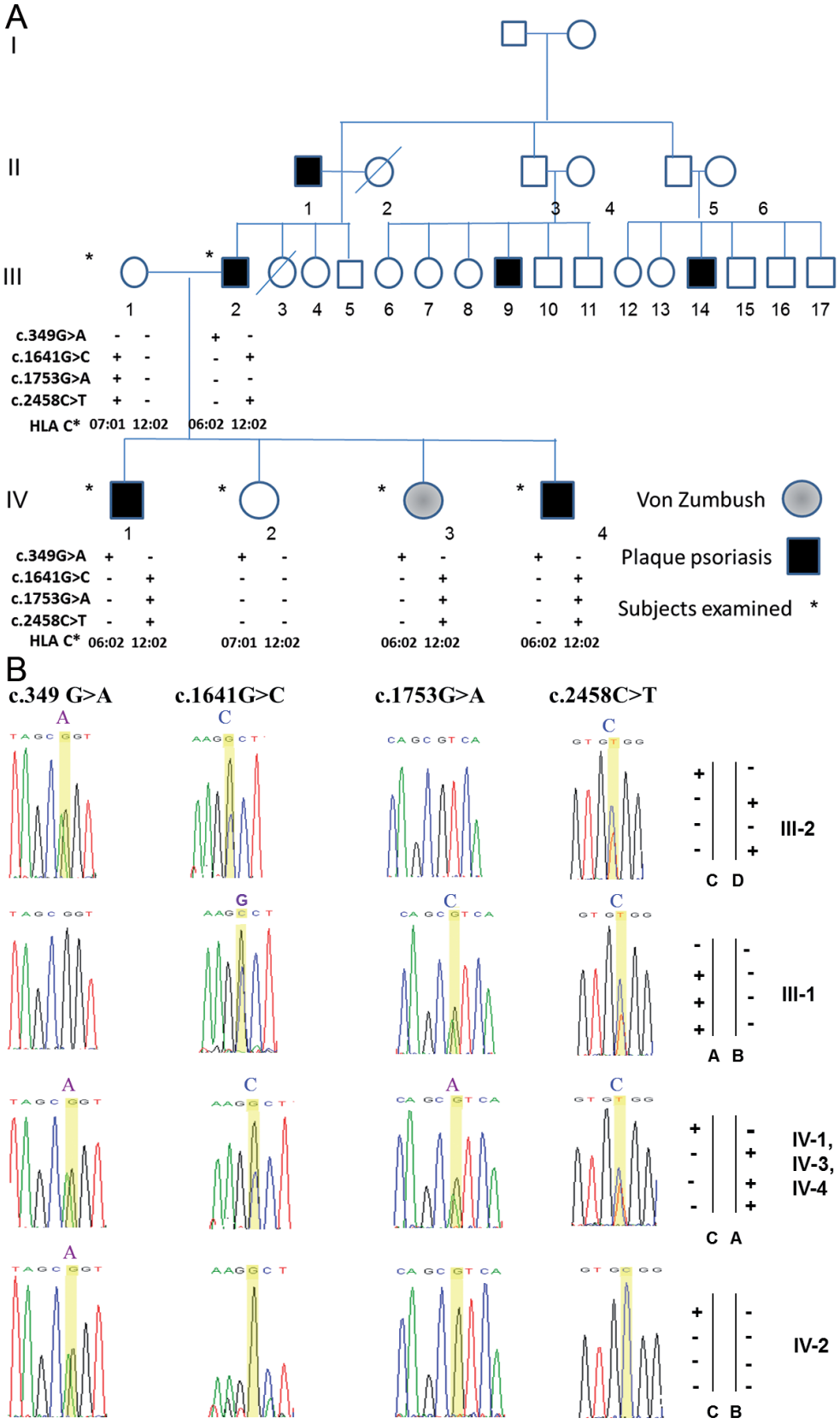

Fig. S1. (A) Family pedigree and haplotypes. *Black squares* and *grey circles* represent affected individuals. (*) Examined family members. (B) Sequence chromatogram from genomic DNA of examined family members.

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.).

Table SI. *Primers used to screen family members for c.349G>A [p.Gly117Ser] mutation and the coding region polymorphisms (c.1641G>C [p.Arg547Ser], c.1753G>A [Val585Ile] and c.2458C>T [p.Arg820Trp] of the* CARD14 *gene*

Primer pair number	Mutation/polymorphism	Primer sequence (5'→3')	
		Forward	Reverse
1	c.349G>A (p.Gly117 Ser)	cccttggtagctgggttct	Gtagggcaaatcggcaagta
2	c.1641G>C (p.Arg547 Ser)	tgaagaaggggctgaggtta	Tgttgcctcccattggtatt
3	c.1753G>A (p.Val585Ile)	ggggaggagaattccagaac	Gtctgggggaggtgaagtct
4	c.2458C>T (p.Arg820Trp)	gtgagcaaagcagacccagt	Gaggaaggagggaggaagg

Table SII. *Clinical features of the examined family members*

Patient code	Age, years	Age at disease onset (months/ years)	Clinical presentation of psoriasis		Current therapy	Past treatment	CARD 14 c.349G>A [p.Gly117Ser] mutation	Other CARD 14 polymorphisms (heterozygous state)	HLA-C Type
			Skin	Joints					
III-1	44	–	No	No	None	None	No	c.1641G>C c.1753G>A c.2458C>T	07:01 12:02
III-2	47	Childhood	Mild plaque-type	No	None	None	Yes	c.1641G>C c.2458C>T	06:02 12:02
IV-1	16	5 months	Severe plaque-type	No	Etanercept+MTX	Acitretin MTX (as a single agent)	Yes	c.1641G>C c.1753G>A c.2458C>T	06:02 12:02
IV-2	14	–	No	No	None	None	Yes	None	07:01 12:02
IV-3	11	8 years	Generalized pustular type with flares following infections	No	Adalimumab+MTX	Cyclosporin A Acitretin MTX (as a single agent) Dapsone Infliximab Etanercept	Yes	c.1641G>C c.1753G>A c.2458C>T	06:02 12:02
IV-4	5	Previously undiagnosed	Mild plaque-type	No	None	None	Yes	c.1641G>C c.1753G>A c.2458C>T	06:02 12:02