DNA EXTRACTION

Genomic DNA was purified from fresh whole blood using the Gentra Puregene Kit (Qiagen Sciences, Germantown, Md., USA) according to the manufacturer's instructions.

SNP GENOTYPING

Whole genome SNP genotyping was performed using the Affymetrix Genome Wide Human SNP Nsp/Sty 6.0 array (Affymetrix, Inc., Santa Clara,CA), according to the manufacturer's instructions.

TARGETED CAPTURE AND EXOME SEQUENCING

To capture the target regions, we used the Agilent SureSelect Human All Exon 50Mb Kit (Agilent Technologies, Santa Clara, CA) following vendor provided protocols. We performed whole-exome sequencing (paired end 100 bp reads) on the proband and his healthy brother using the Illumina HiSeq2000 platform (Illumina, Inc. San Diego, CA). We aligned each read to the reference genome (NCBI human genome assembly build 36; Ensembl core database release 50_361) [Hubbard et al., 2009] using the Burrows-Wheeler Alignment (BWA) tool [Marini et al., 2009] and identified single nucleotide variants (SNVs) and small insertion/deletions (indels) using SAM tools [Li et al., 2009]. PCR duplicates were removed using the Picard software. We also performed local realignment and base call quality recalibration using GATK [McKenna et al., 2010]. Our mean target coverage was 117X for the proband and 104X for unaffected brother. Both had 95% of the target bases with 8X coverage

IDENTIFICATION OF POTENTIALLY CAUSAL VARIANTS

We identified variants of interest using standard filtering criteria. Because the parents were consanguineous and unaffected, we prioritized functional variants (missense, nonsense, splice site variants and indels) that were homozygous or in the case of X-linked variants, hemizygous, in the proband but not in his unaffected brother. We excluded variants found in dbSNP 131, or in the Exome Variant Server and the 1000 Genome Project with a MAF > 5%. We also excluded any variant (SNVs or indels) found in our in-house controls. We also excluded variants with a GERP score of ≤ 0. Next, we analyzed the remaining variants for known association with Mendelian diseases (OMIM), mouse models (MGI), and expression pattern (Gepis tissue).

CONFIRMATION OF HOMOZYGOUS VARIANTS USING PCR AND SANGER SEQUENCING

Using Primer 3, we designed primers to amplify a 372 bp fragment surrounding the 17 bp deletion in *SCARF2*. We performed PCR using standard methods and agarose electrophoresis of the product revealed specific fragments of the predicted size. We sequenced these directly on the ABI 3730 (Applied Biosystems, Life technologies. Carlsbad, CA) using Life Technologies Big Dye Terminator V 1.1 cycle sequencing kit cat # 4336778 and analyzed the data using CodonCode Aligner 3.6.1, comparing the sequence of the proband (II-3) and unaffected brother (II-1) to the reference (GRCh37/hg19). To analyze the segregation of the c.438_454del17 (p.146_152del) deletion in the family we designed primers to amplify a 212 bp fragment surrounding the 17 bp deletion. The products of the wild type *SCARF2* exon 4 (212 bp) versus the

c.438_454del17 deletion (195 bp) were separated by electrophoresis in a NuSieve 2.5:1 agarose gel (Fig. 3). We confirmed these results by direct Sanger sequencing of the amplified products in both directions. Primer sequences are available upon request.

Figure S1

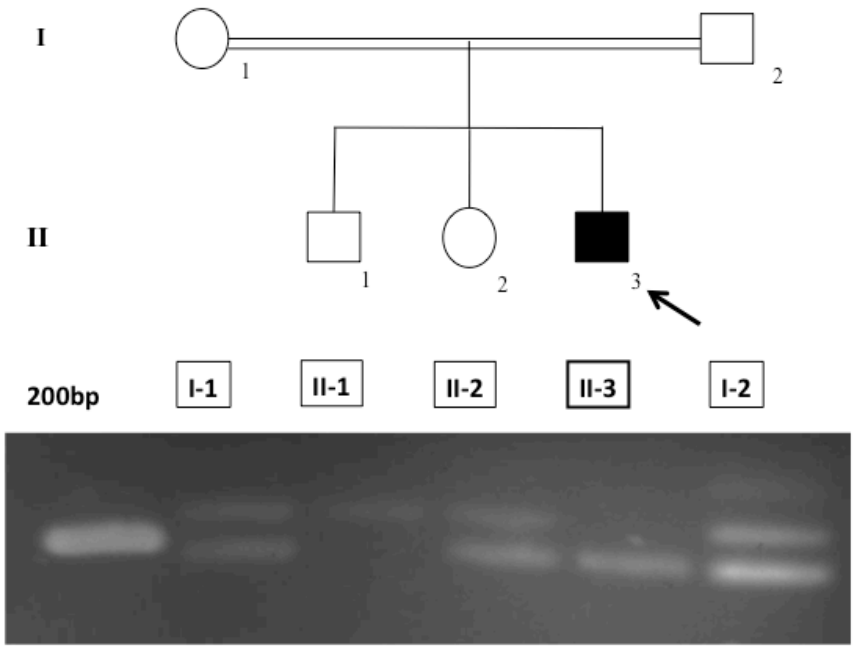

Figure S1- Gel electrophoresis of PCR products of *SCARF2* exon 4 from members of the family. The wildtype amplicon is 212 bp and the c.438_454del17 amplicon is 195bp. The numbered boxes above each lane refer to Pedigree . Affected individuals are indicated by the heavy border; unaffected individuals by the thin border.