SUPPLEMENTAL MATERIALS

METHODS

Patients provided written informed consent and were investigated under National Institute of Allergy and Infectious Diseases and National Cancer Institute Institutional Review Board-approved research protocols. Written informed consent was obtained before DNA isolation from blood of all family members.

Whole-exome sequencing

Genomic DNA samples for whole-exome sequencing were prepared from peripheral blood by using the PureGene DNA extraction kit (QIAGEN). Exome sequence libraries were prepared with a SeqCap EZ Human Exome Library v3.0 kit (Roche NimbleGen, Madison, WI). Paired-end sequencing was performed on the Illumina HiSeq2000 (NIAID Genomics Core Facility, Rocky Mount, MT). BWA software was used to align the sequence reads to the Human Reference Genome Build hg19. The GATK Unified Genotyper was used to identify single nucleotide variants and insertions/deletions. ANNOVAR was used for annotation.

Sanger sequencing

Pre-transplant DNA of the region of interest in *CECR1* was amplified with the primers 5′-AGCAGCAGAGACAATGCCCAAGGCCGTAGAG-3′ and 5′-ACGTGCCAGGCCACGCACATGGTACTACTG-3′. Resulting PCR products were treated with ExoSAP-IT (USB/Affymetrix) and sequenced using the primer 5’-CAGAGCTCGTTGATGGCTGGGAAGGAGTTGACT-3’ and Big Dye Terminators v3.1 (Applied Biosystems) chemistry. The reactions were purified with DTR spin plates (EDGE Biosystems) and run on an ABI 3730 XL Genetic Analyzer (Applied Biosystems,

Foster City, Calif). Sequencing data were analyzed using Sequencher (GeneCodes Corporation).

Flow cytometry

PBMCs were isolated from heparinized blood of patients and control subjects using lymphocyte separation medium (MP Biomedicals, Solon, Ohio) and frozen in 10% dimethyl sulfoxide (Sigma). Thawed cells were stained with antibodies (from eBioscience (San Diego, CA), unless stated otherwise) against CD3 (SK7), CD19 (HIB19), CD56 (MEM188), CD14 (61D3). All data were acquired on BD FACSCanto II and analyzed with FlowJo (Tree Star, Ashland, OR).

Measurements of ADA2 activity in plasma

ADA2 activity in plasma was measured at Duke University by using the HPLC method described by Zhou et al. [reference 3] and Van Eyk et al [reference 7].

Chimerisms

The Department of Laboratory Medicine at the National Institutes of Health Clinical Center is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88) and performed donor chimerism assays. Donor chimerism was measured using predetermined differences in Short Tandem Repeats (STRs) to quantitate the proportion of donor nucleated cells in samples obtained from transplant recipients. The assay can consistently measure donor chimerism ranging form 5-95% with a standard deviation of +/-5%.

Transplant regimen

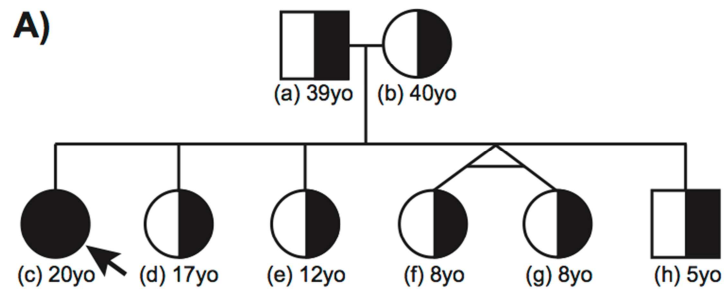
The patient was conditioned with fludarabine 24 mg/m^2/day on days -6 to -2, cyclophosphamide 14.5 mg/kg on days -6 and -5, busulfan 3.2 mg/kg/day on days -4 and

-3, and 200 cGy total body irradiation (TBI) on day -1. On day 0 she received 1.24 x 10^8 total nucleated cells (TNC)/kg and 0.48 x 10^6 CD34+ cells/kg from her donor. Because of low donor bone marrow cell dose, the donor was remobilized with filgrastim for 4 days along with a single dose of plerixafor 20 mg/kg subcutaneously 15 hours prior to apheresis. The patient received 5.7 x 10^6 of mobilized CD34+ peripheral blood stem cells/kg on day +3. Post-transplant immunosuppression consisted of cyclophosphamide 50 mg/kg recipient body weight on days +3 and +4, followed by tacrolimus starting at day +5 until day +180, and mycophenolate mofetil on day +5 until day +35.

FIG S1. Familial inheritance of *CECR1* mutation**, A,** Pedigree with carriers designated by half-filled boxes and solid circle for the homozygous proband (arrow). Ages at the time of transplant are shown; lower case letters correspond to Table 1 designations. **B,** Diagram of the *CECR1* gene (NG_033943.1) isoform a (NM_001282225). The arrow indicates the location of the C>G mutation in exon 5 of the *CECR1* gene causing the substitution of a stop codon (X) for serine (S). Wide bars indicate coding sequence, narrow bars untranslated cDNA, thin line indicates intron.

Supplemental Figure 1

A)



B)