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Supplemental Data

Exome Sequencing Reveals Mutations in *TRPV3* as a Cause of Olmsted Syndrome

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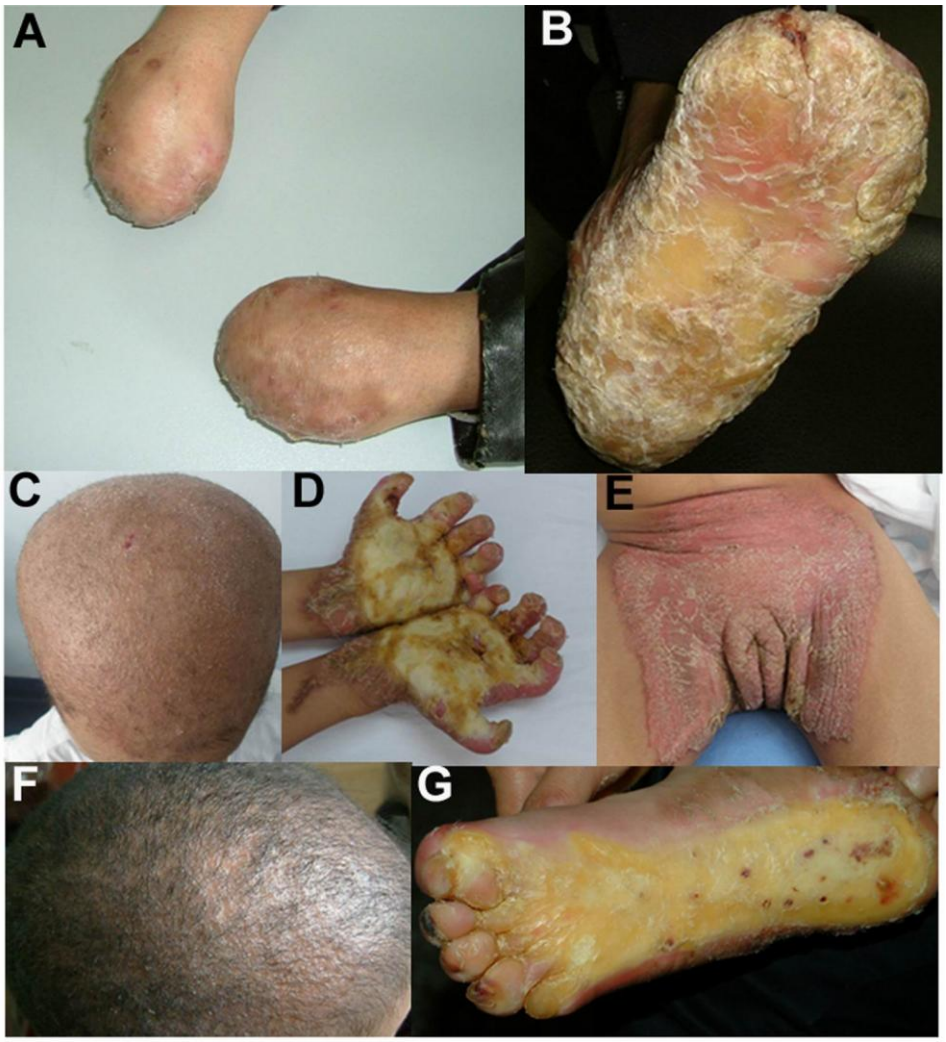

Figure S1. Clinical Manifestations of the Individuals with OS

(A, B) Spontaneous amputation of all digits in individual 3 due to palmoplantar keratoderma. (C-E) Alopecia, palmar and perineal keratosis in individual 4, note the follicular keratotic papules and the flexion deformities of digits with constricting bands. (F) Sparse, short hair, instead of total alopecia, on the scalp of individual 5, a 23-year-old male carrying p.Trp692Gly. (G) Sharply demarcated yellow keratotic plaque on the foot of individual 6.

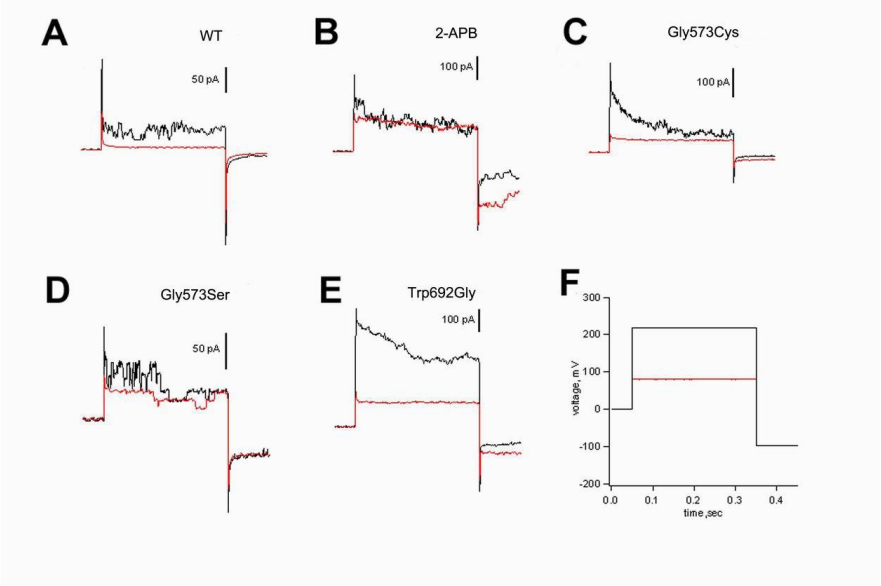

Figure S2. Fast Inactivation of Mutant Channels at a Depolarization Potential

Representative traces of channel activity in inside-out patches expressing WT TRPV3 in the absence (A) or presence (B) of 300 μM 2-APB and mutant channels under control conditions (C-E) evoked by the voltage pulse (+220 mV, black; +80 mV, red) (F).

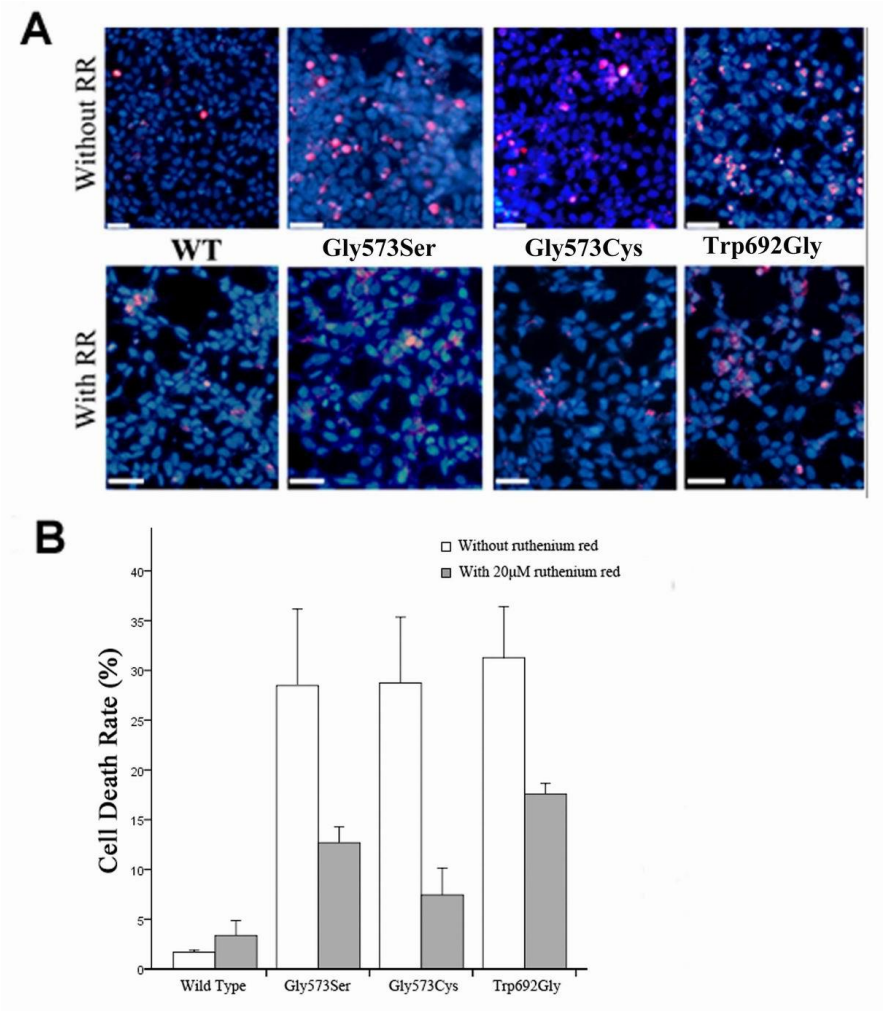

Figure S3. Cell Death Rescued by Ruthenium Red (RR) in WT and TRPV3 Mutant-Transfected HEK293 Cells

(A) Merged images of WT and TRPV3 mutant-transfected HEK293 cells stained with PI (red) and Hoechst 33342 (blue). Complete medium with or without 20 μM RR was added after 4 hours of transfection. Twenty hours later, transfected HEK293 cells were stained by PI and Hoechst 33342 for 15 minutes before assessment of morphological cell death. Cells transfected with mutant TRPV3 cultured with RR (lower panels) show fewer PI positive cells as compared to the ones without RR (upper panels). (B) Cell death rates (red nuclei / blue nuclei × 100%) in transfected HEK293 cells with (filled bars) or without RR (open bars). Data were analyzed by

one-way analysis of variance (ANOVA). Tamhane's post hoc test was used to evaluate the differences between groups treated with RR and without RR. Cell death shows a tendency to be partly rescued by RR in mutant groups, although no significant differences were obtained ($P > 0.0125$). Data are the average from three independent experiments. Error bars represent s.e.m.

Table S1. Exome Sequencing Data and the Filtration Procedure of Individual 1 and Her Parents

Individual	**OM-1 (individual 1)**	**OM-11 (father)**	**OM-12 (mother)**
Raw data yield (Mb)	3,786.00	3,775.00	2,452.00
Data mapped to target region (Mb)	1,770.09	1,575.44	1,098.73
Mean depth of target region	47.03	31.36	21.87
Coverage of target region	97.69%	98.94%	98.37%
Fraction of target covered >=10X	84.06%	82.57%	72.19%
Capture specificity	71.90%	63.06%	66.47%
Read coverage of CCDS[a] exons	197,922	200,220	199,440
Read coverage of CCDS genes	17,154	17,268	17,233
Total number of SNVs[b]	56,409	70,568	60,904
SNVs in exons	19,593	29,173	26,940

SNVs data filtration	**Filtration methods**	**SNVs number**
Step 1	De novo SNVs and not in the 1000 Genomes Project, the dbSNP131, or HapMap8 databases	239
Step 2	Step 1 data predicted damaging by SIFT software	45
Step 3	Step 2 data with Sanger sequencing validation	1 (*TRPV3*)

[a]Consensus coding sequence
[b]Single nucleotide variation

Table S2. Primers for Mutation Screening of *TRPV3*

Primer	**Sense primer (5'->3')**	**Antisense primer (5'->3')**
Exon1	ATCATTCCCATTTCCTAGTTGG	CAGACATGGCCCAGAGGA
Exon 2	GGCCCCTAAACTCCCTGAAG	ACTCGTGCCCCTCACAGT
Exon 3	GAGCTGGCCAGGGTGTGT	CTCCTCCCTCCTCCCAGACT
Exon 4	GACTTGCCCTGGGTCACGGG	TTCCTGCAGGGCCCCGGAT
Exon 5	CGGGGAAAAGGAGAGATTGA	GAAAATGGGCACCAGAAGC
Exon 6	GCAGCAACCACACCCTCT	CTACATGCTTGGGGCTCCT
Exon 7	TAATCGAGATTGCGTCTTGG	CTGTTTCCCCCTCCCTTC
Exon 8	AGAGGGCTAGGGAACCTGAG	GGTGGCAGCTGTACCTCCT
Exon 9	GCAGGTCTCCACCCATTCT	CTGGCAGCACTGGGTCTT
Exon 10	CCGCAGGCCTTTAGAAAAC	AGCTCCAAGCCCCTCCAG
Exon 11	CCTGGGTTTTGGTCCCTCTA	GAAACGCCTCCCCAGAAC
Exon 12	GAGTCTTGGTCCTGGGGAAG	TTTGTTCAAGAGGCGGACAC
Exon 13	CGTGATTCTGGTCTCTTCAGC	CCTTGGTAAACCCCTCTTCC
Exon 14	AGTGGCCCAAGTGAAGAGAC	CATGCACTTTGCCATTTTGA
Exon 15	CCTGATGAGGCTTTGAGAGG	CAATGACCACGTGCTGAACT
Exon 16	GGTGGAGTGGGCTCCCCGAC	GGGAGCCGCTGTTGGCAGTC
Exon 17	AGACAGAAGGGGAGCTGTGT	CTGCCCAAGGTTACATGGTC
Exon 18	GCGTAGCCCTAAGCCATAGA	GACTCCACCATCCCTCAAAG

Table S3. Primers for Site-Directed Mutagenesis of *TRPV3*

mutation	**Sense primer (5'->3')**	**Antisense primer (5'->3')**
G573S	CGGGGTTTCCAGTCCATGAGCATGTACAGC	TCATGGACTGGAAACCCCGCGTATAGTAGA
G573C	CGGGGTTTCCAGTCCATGTGCATGTACAGC	ACATGGACTGGAAACCCCGCGTATAGTAGA
W692G	GAGAGCGAACGCATCGGGCGCCTGCA	CGATGCGTTCGCTCTCCTTGGAGACGTTC