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Supplemental Data

Mutations in *POFUT1*, Encoding

Protein O-fucosyltransferase 1, Cause

Generalized Dowling-Degos Disease

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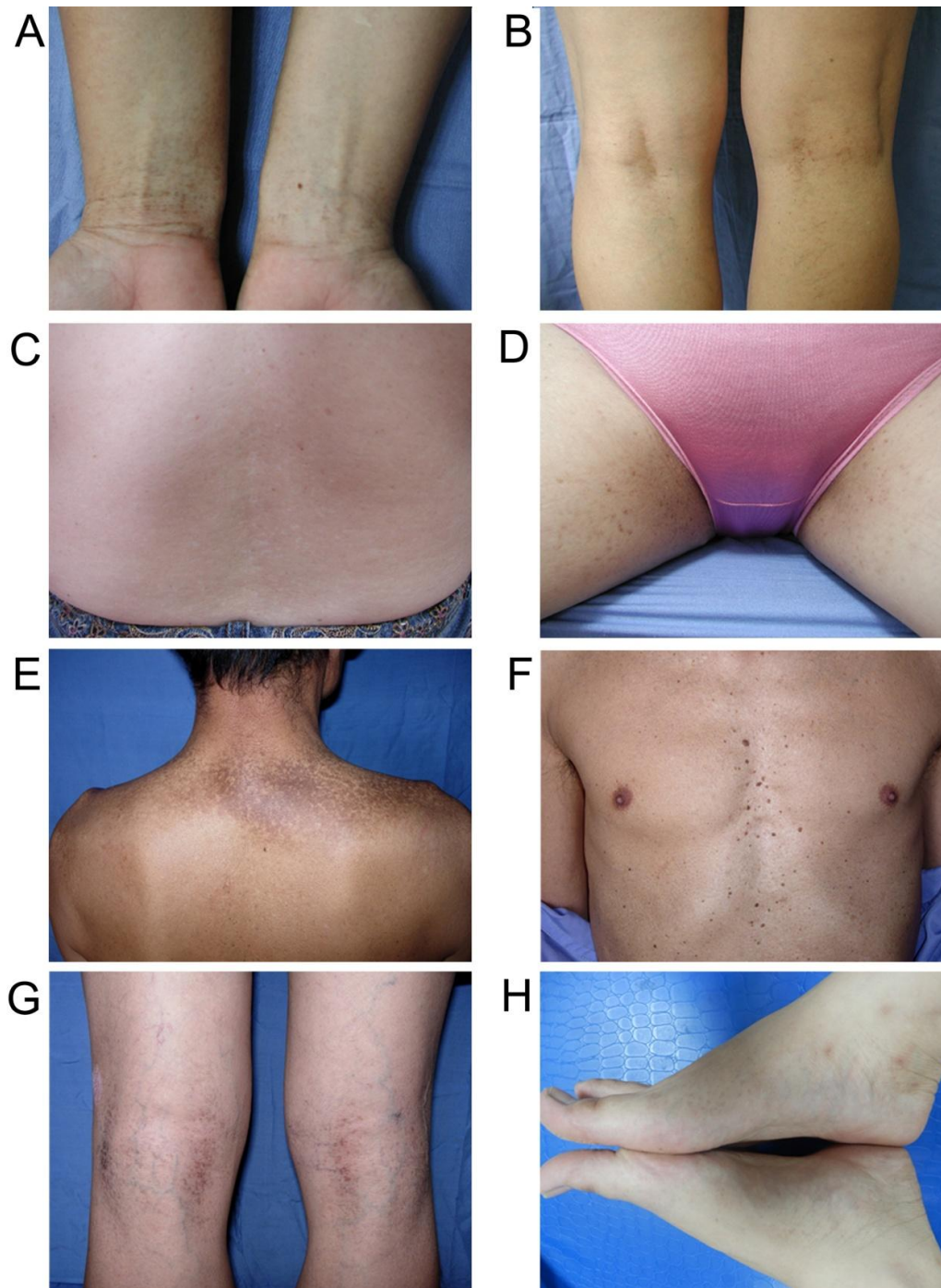


Figure S1. Clinical Findings of Patients with Generalized DDD in Family 1

(A–D) Clinical photographs of the patient (III:10). Reticulate on the wrists (A) and hyperpigmentation on the popliteal region (B), hyperpigmentation and hypopigmentation on the back (C) and spots of hyperpigmentation on the groin (D).

(E–G) Clinical photographs of the patient (III:4) in family 1. Reticulate hyperpigmentation and hypopigmentation on the neck and back (E), spots of hypopigmentation and hyperkeratotic dark brown papules on the chest and abdomen (F) and hyperpigmentation on the popliteal region (G).

(H) Spots of hyperpigmentation on the feet of the patient (IV:4).

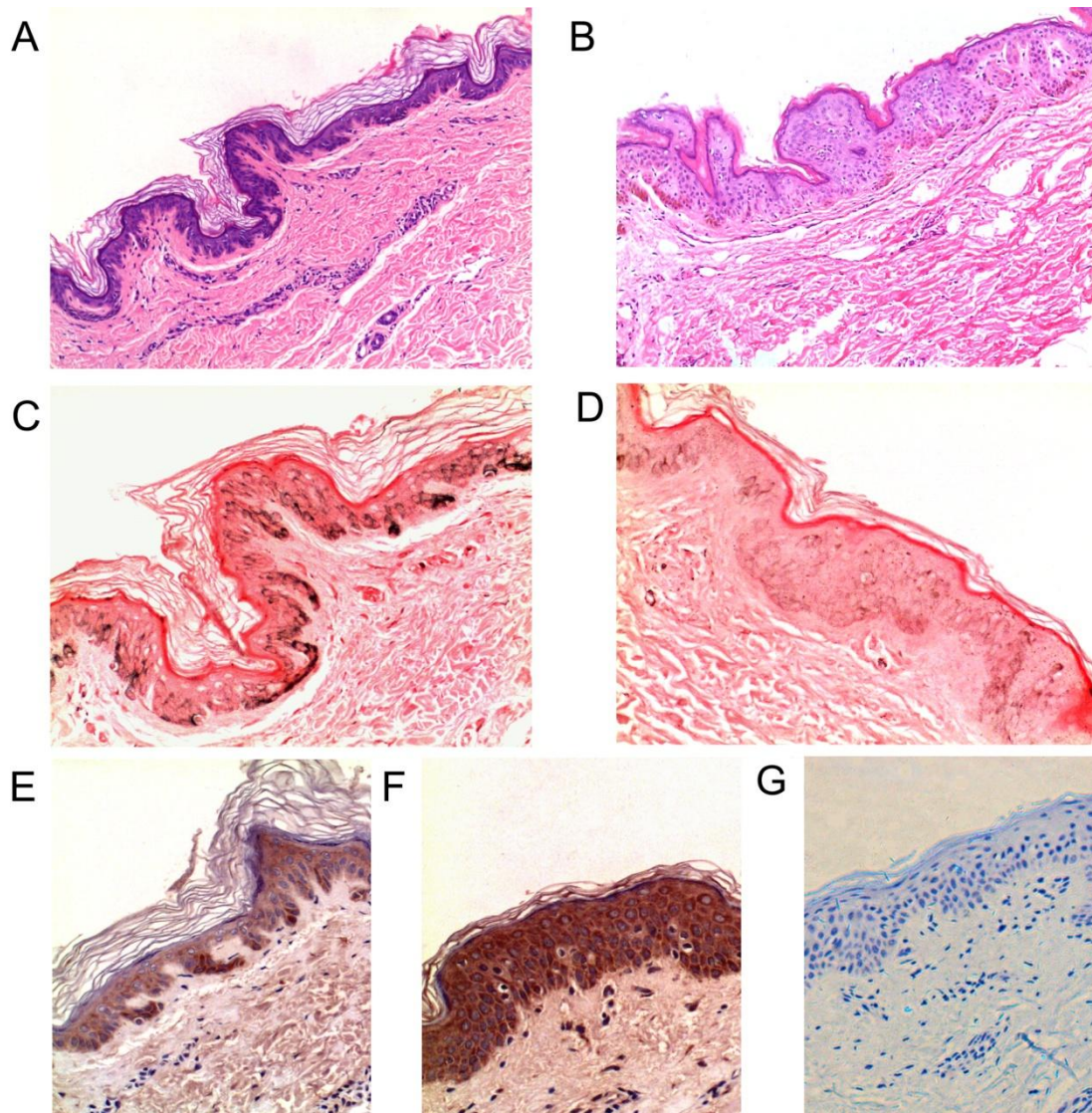


Figure S2. Light Microscopy, Fontana-Masson Staining, and Immunohistochemistry of Sections from Individuals with DDD and Control Skin

(A and B) Hematoxylin and eosin staining of sections from patient III:11 (100×) in family 1(A) and patient II:3 (200×) in family 2 (B) with DDD demonstrates papillary epidermal downgrowth with abnormal basal pigment granule distribution.

(C and D) Fontana-Masson staining (200×) shows uneven distribution of melanin in epidermis. A region of stratum basale was full of melanin particles, which were even distributed in the whole layers of epidermis(C). Another region of epidermis, however, rarely showed any positive staining (D).

(E–G) Immunohistochemical staining (200×) shows that the protein expression of POFUT1 was obviously decreased in patient (E) compared with that in control (F). Negative control (G).

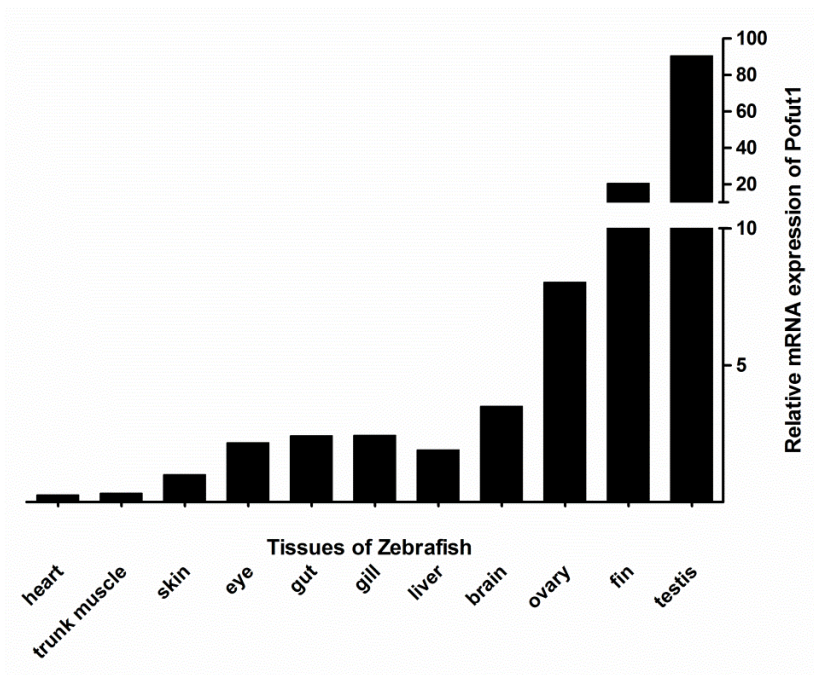


Figure S3. RNA-Expression Level of *pofut1* Was Determined by Quantitative RT-PCR in Zebrafish

Pofut1 expression level was higher in the testis than in other tissues or organs in adult zebrafish.

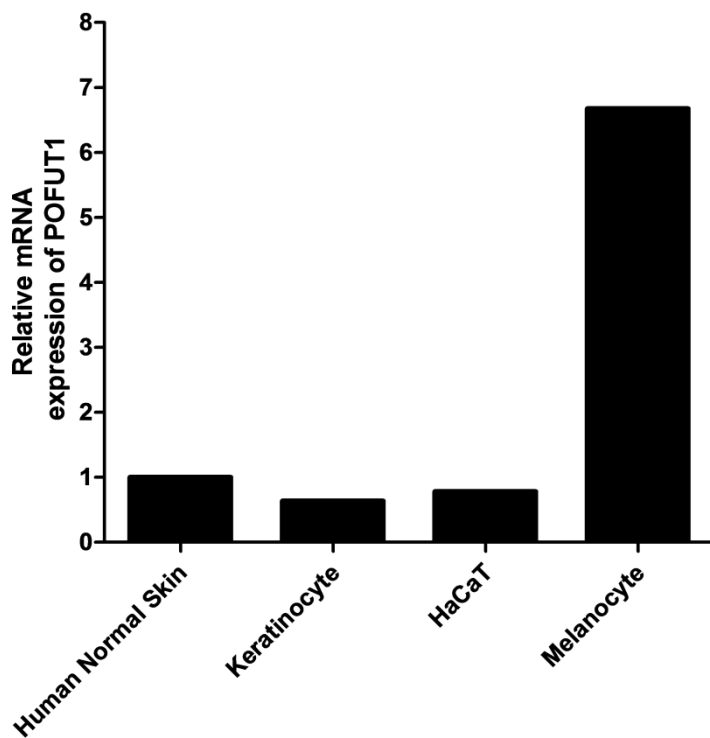


Figure S4. RNA-Expression Level of *POFUT1* Was Determined by Quantitative RT-PCR in Human Cells

POFUT1 expression in melanocyte cell is much higher than in other cell lines and in normal skin.

Table S1. PCR Primers for *POFUT1*

	Forward Primers (5'-3')	Reverse Primers (5'-3')	Annealing Temperature (°C)	Amplicon Size (bp)
Exon-1	CTTCCCTCCCCGACTGTGC	GCGCATCTGAGGAGTGGCTT	60.8	247
Exon-2	CTTGGTATCCCTGACTTTCTAC	GGACTTGAGGGTTAAGTGTAAG	55	307
Exon-3	ACGGGACCTCTGCTCCTCCTT	TGCTTTTCCCCACATTTTGC	55	303
Exon-4	ATCCAGAATTGAAGCCACG	CTAAACCCAGAAACGCTACC	53	342
Exon-5	CTGACTTCCCTCATTCATCTCC	ACAGGCCAGGGCCATGCTC	60.8	288
Exon-6	CACCTTACCAGGTCTTGCTTCT	TTCTACTGCACTCCCCTT	53	348
Exon-7	AGCTCAGGGAATAAGGTTGG	CTCCAGGATCAGAGGGTCTG	55	310

Table S2. Primer Pairs for qRT-PCR for Zebrafish

	Forward Primers (5'-3')	Reverse Primers (5'-3')	Amplicon Size(bp)
<i>gapdh</i>	ACCAACTGCCTGGCTCCTT	CCATCCCTCCACAGCTTCC	137
<i>pofut1</i>	AATGCTGAACCGAACTCTCG	GTCCACTCCAATATGGTCCCAG	298
<i>notch1</i>	CCTCGTGAACACCTACAAATGCT	CACAACCGTAACCACCGACAC	161
<i>notch2</i>	CCGTTGCCGTCTCGTTAT	CACTGAGGGCGGCTCTTATC	240
<i>hey1</i>	GGAGGGACCGGATAAATAACAGT	CCAGAGCGTGAGCATCAAAGT	174
<i>mitf</i>	TACAGTGATGACATTCTTGGGTTT	CAGGGCTCTGACTTCTGCTTCTA	285
<i>tyr</i>	ACGACGGATACTTCATGGTGC	CCGATGCGATTATTCCTGCTA	222
<i>krt5</i>	TCCGCACCCAGGAGAAAGA	GTTGGATCGGGTAGTGGTCTGT	146

Table S3. Primer Pairs for qRT-PCR for HaCaT Cells

	Forward Primers (5'-3')	Reverse Primers (5'-3')	Amplicon Size(bp)
<i>GAPDH</i>	TGAAGGTCGGAGTCAACGGA	CCTGGAAGATGGTGATGGGAT	255
<i>POFUT1</i>	CTAAACCGTACCTTGGCTGTCC	GCCTCTGGCTCCATTGTTCT	364
<i>NOTCH1</i>	ACATCAACGAGTGTGCCAGTG	GCAGTCAGGCGTGTGTTCT	128
<i>NOTCH2</i>	GTGAATCCCTGACTCCAGAACG	TCTCGGCGAAGAGTGAAACC	157
<i>HES1</i>	GAGGCGGCTAAGGTGTTTGG	GCTGTTGCTGGTGTAGACGG	126
<i>KRT5</i>	AACCTGGACCTGGATAGCATCA	ACATTGTCAATCTCGGCTCTCAG	215

Table S4. Result of Linkage Analysis on Chromosome 20

Chr. No.	Physical Position (Mb)	Genetic Position (cM)	SNP	Analysis Model	HLOD	Alpha
20	24230229	54.04	rs1293713	Dominant	-2.7207	1
20	26257255	54.85	rs2211139	Dominant	2.5839	1
20	29310062	55.23	rs1474945	Dominant	2.7502	1
20	29428674	55.25	rs709045	Dominant	2.7572	1
20	30313908	55.51	rs2377473	Dominant	2.8389	1
20	31946046	57.05	rs736264	Dominant	3.1557	1
20	32624885	57.1	rs764597	Dominant	3.1636	1
20	33229276	57.14	rs1415774	Dominant	3.1712	1
20	34136337	57.18	rs2746097	Dominant	3.1774	1
20	34994883	57.9	rs6130139	Dominant	2.911	1
20	35106469	57.98	rs3897903	Dominant	2.8918	1
20	35379653	58.19	rs7272911	Dominant	2.8337	1
20	35933726	59.47	rs717599	Dominant	2.6841	1
20	38023441	61.19	rs729429	Dominant	2.5048	1
20	38219457	61.27	rs1406966	Dominant	2.4973	1
20	40018906	63.74	rs6029893	Dominant	2.2189	1
20	41555865	66.55	rs765147	Dominant	1.5592	1
20	42622691	68.83	rs244123	Dominant	-3.0951	1
20	42846611	69.33	rs1080026	Dominant	-6.724	1