

**Table 1. Cholesterol absorption and plasma lipid and lipoprotein concentrations in a family segregating a defective NPC1L1 allele (R693C)**

Subject	Genotype	Age (years)	Sex	Campesterol: Lathosterol	Cholesterol Absorption Index	TC (mg/dl)	TG (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dl)
DHS09-3	+/+	37	F	1.0	2.7	143	120	44	82
DHS09-4	+/+	13	F	3.4	7.2	182	66	54	119
DHS09-5	+/+	7	M	2.7	4.6	127	38	44	78
DHS09-6	+/+	7	F	2.4	9.0	139	41	50	84
DHS09-8	+/+	19	F	1.9	3.8	151	68	60	81
DHS09-10	+/+	11	F	2.9	3.8	188	66	52	127
DHS09-12	+/+	58	F	1.8	4.1	191	82	50	129
DHS09-14	+/+	33	F	3.2	5.6	196	45	71	119
DHS09-15	+/+	15	F	2.2	5.5	174	37	67	102
DHS09-22	+/+	50	F	2.4	4.4	200	75	66	123
DHS09-23	+/+	28	F	1.5	4.0	171	146	58	90
DHS09-24	+/+	14	F	2.1	4.1	159	72	84	65
DHS09-25	+/+	8	M	2.3	7.2	180	80	70	98
DHS09-30	+/+	30	M	1.8	3.9	220	190	70	115
Mean		24		2.3	5.0	173	80	60	101
SD		16		0.7	1.7	26	44	12	21
DHS09-1	+/-	62	M	0.4	1.0	223	355	38	120
DHS09-2	+/-	31	M	1.3	4.5	148	69	49	89
DHS09-7	+/-	42	F	0.8	3.0	208	258	40	125
DHS09-9	+/-	18	F	3.5	2.5	152	70	62	80
DHS09-11	+/-	9	F	1.7	4.2	191	84	52	127
DHS09-13	+/-	77	F	0.5	2.8	361	666	56	171
DHS09-16	+/-	66	F	2.8	5.1	254	111	87	153
DHS09-17	+/-	24	M	1.0	2.8	191	80	49	130
DHS09-18	+/-	57	F	0.7	3.7	212	121	69	126
DHS09-19	+/-	24	F	1.3	5.6	121	56	49	64
DHS09-20	+/-	22	M	1.8	5.4	152	162	58	66
DHS09-21	+/-	22	M	1.3	3.5	196	47	53	137
DHS09-26	+/-	42	F	1.2	3.2	162	88	65	84
DHS09-27	+/-	62	M	1.6	2.7	158	94	45	99
DHS09-28	+/-	26	F	1.8	4.1	139	39	53	81
DHS09-29	+/-	30	F	2.1	3.8	153	39	76	72
Mean		38		1.5	3.6	189	146	56	108
SD		20		0.8	1.2	58	162	13	33

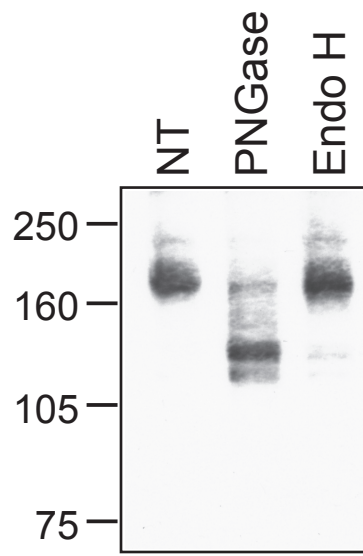
Genotype, + = 693R, - = 693C. Cholesterol absorption index = (deuterated cholesterol/total cholesterol)\*1000. TC = total cholesterol, TG = triglyceride, HDL-C = high density lipoprotein cholesterol, LDL-C = low density lipoprotein cholesterol

**Table 2. Cholesterol absorption and plasma lipid and lipoprotein concentrations in a family segregating a defective NPC1L1 allele (I647N)**

Subject	Genotype	Age (years)	Sex	Campesterol: Lathosterol	Cholesterol Absorption Index	TC (mg/dl)	TG (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dl)
DHS14-4	+/+	49	F	1.5	3.9	164	59	42	110
DHS14-5	+/+	76	F	1.1	3.6	138	75	54	68
DHS14-8	+/+	23	F	1.7	2.8	200	67	47	139
DHS14-9	+/+	17	F	1.2	4.5	199	45	46	144
DHS14-10	+/+	13	F	4.2	8.3	191	35	57	126
DHS14-11	+/+	37	F	1.1	3.0	169	45	48	112
DHS14-12	+/+	18	F	1.6	3.7	181	95	47	115
DHS14-13	+/+	26	F	1.0	2.6	138	76	39	84
DHS14-15	+/+	6	F	1.8	8.1	151	47	57	84
DHS14-17	+/+	31	F	1.2	4.9	121	40	47	66
DHS14-18	+/+	53	M	1.1	3.2	131	43	51	72
DHS14-19	+/+	50	M	1.5	5.8	113	65	50	50
DHS14-20	+/+	56	M	1.5	3.3	108	67	62	33
DHS14-22	+/+	15	M	1.4	2.4	113	27	38	69
DHS14-23	+/+	42	F	2.7	3.7	176	110	62	92
DHS14-26	+/+	27	M	1.3	4.1	176	68	45	117
DHS14-27	+/+	13	F	1.3	6.1	122	55	37	74
DHS14-28	+/+	12	M	2.2	5.5	168	55	44	112
DHS14-29	+/+	31	F	2.2	9.6	157	44	43	105
DHS14-30	+/+	48	F	1.5	5.1	183	63	52	118
DHS14-31	+/+	34	M	1.5	3.5	182	157	58	93
DHS14-32	+/+	10	F	1.2	3.0	137	71	47	75
DHS14-33	+/+	15	M	1.9	3.4	130	41	48	73
DHS14-35	+/+	16	M	3.1	3.4	141	24	45	91
DHS14-37	+/+	11	F	1.9	4.1	139	29	36	97
DHS14-38	+/+	11	M	2.0	7.7	137	108	40	75
Mean		28		1.7	4.6	153	62	48	92
SD		18		0.7	1.9	28	30	7	27
DHS14-2	+/-	66	F	0.9	2.1	177	57	63	102
DHS14-3	+/-	72	F	0.7		ND	ND	ND	ND
DHS14-6	+/-	69	M	1.0	2.5	130	141	36	65
DHS14-7	+/-	27	F	1.1	4.3	131	55	39	80
DHS14-14	+/-	23	F	1.1	3.7	171	66	46	111
DHS14-16	+/-	44	M	0.8	3.2	147	98	47	81
DHS14-24	+/-	42	M	1.4	3.3	165	32	64	94
DHS14-25	+/-	29	M	1.2	4.1	163	44	47	107
DHS14-34	+/-	55	M	1.4	3.8	173	159	49	92
DHS14-36	+/-	14	F	0.6	3.4	180	78	42	123
Mean		44		1.0	3.4	160	81	48	95
SD		21		0.3	0.7	19	44	10	18
DHS14-1	-/-	58	F	0.7	1.4	197	236	59	90
DHS14-21	-/-	61	F	0.6	1.6	166	44	75	81

Genotype, + = 647I, - = 647N. Cholesterol absorption index = (deuterated cholesterol/total cholesterol)\*1000. TC = total cholesterol, TG = triglyceride, HDL-C = high density lipoprotein cholesterol, LDL-C = low density lipoprotein cholesterol

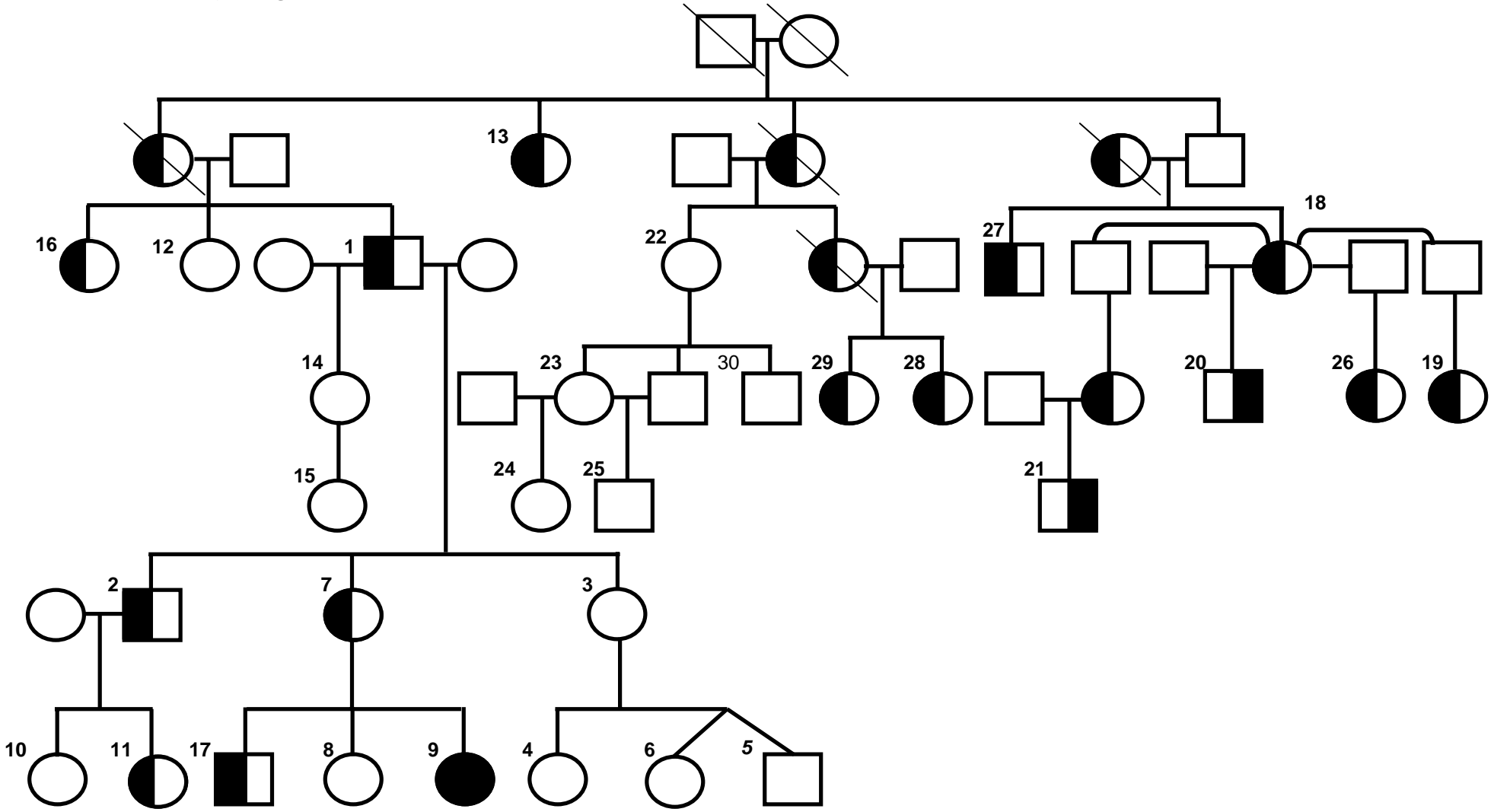
Supplementary Figure 1



**Supplementary Figure 1.**

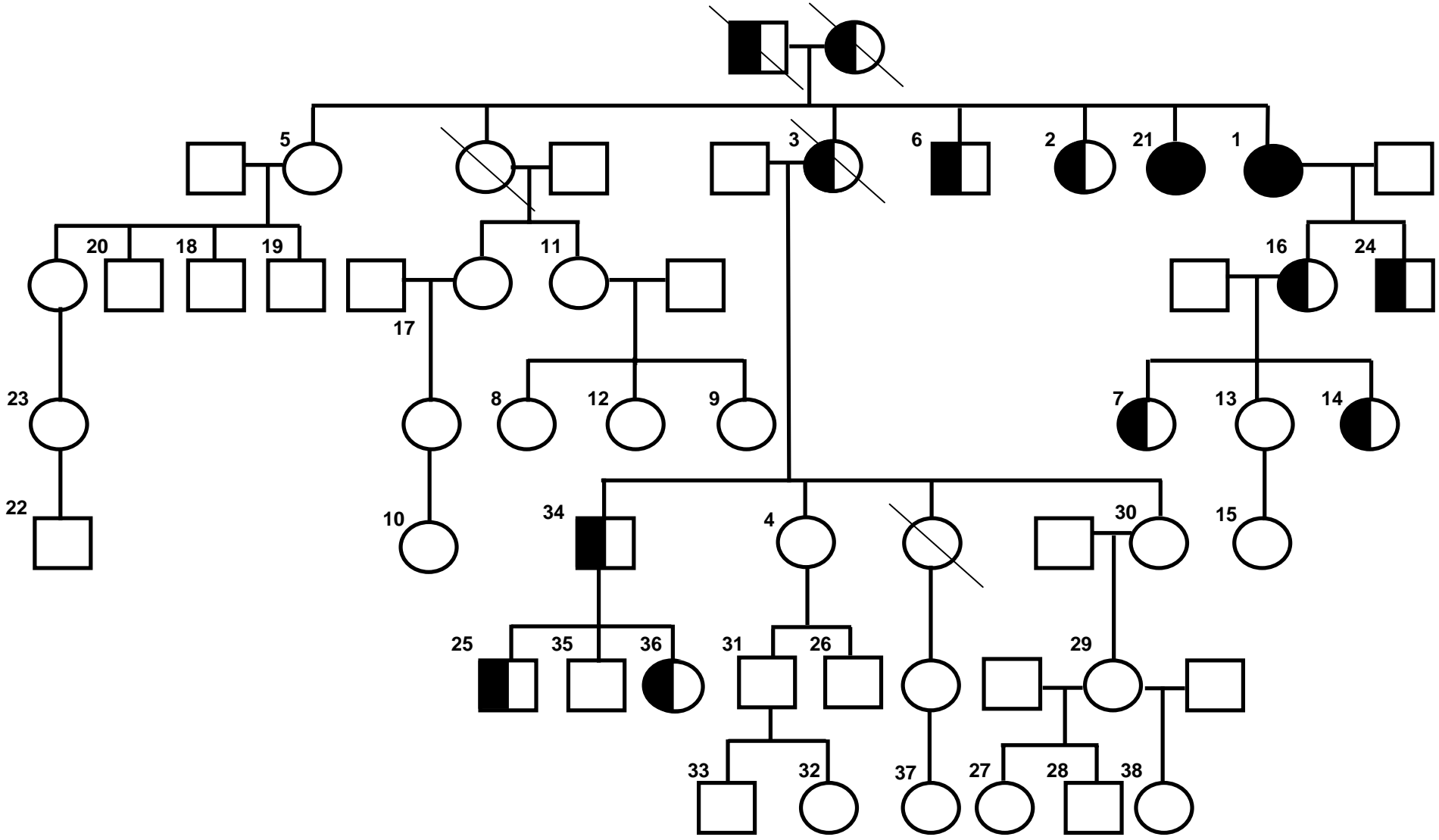
Glycosylation of NPC1L1. CHO-K1 cells were transiently transfected with an expression construct encoding NPC1L1. Cell membranes were prepared as described in the Methods, heated in 0.5% SDS, 1 mM -mercaptoethanol (95 °C, 5 min), and incubated in the presence or absence of 10 units of N-glycosidase F (PNGase F, Calbiochem) in 60 mM Tris, pH 8.6, and 1% (w/v) Triton X-100. Samples were diluted with protein sample buffer, heated to 95 °C for 5 min, and subjected to SDS-PAGE and immunoblot analysis using a rabbit anti-NPC1L1 antiserum.

Supplementary Figure 2



Supplementary Figure 2. Pedigree of family DHS-9. Numbers on the pedigree correspond to the subject identities in Supplementary Table 2.

Supplementary Figure 3





Supplementary Figure 3. Pedigree of family DHS-14. Numbers on the pedigree correspond to the subject identities in Supplementary Table 2.