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Table 1 Summary of clinical information and mutations identified in Japanese patients with Krabbe disease

Patient No	Genotype	Phenotype	Age at onset	GALC activity		CSF protein (mg/dl)	MCV (m/sec)	Reference
				Lymphocytes (nmol/mg/h)	Skin fibroblasts (nmol/mg/h)			
A1**	**W115X**/P302A*	Infantile	6M	undescribed	undescribed	ND	ND	* Tatsumi et al. 1995
A2	**R204X**/12Del3Ins*	Infantile	<6M	undescribed	undescribed	ND	ND	* Tatsumi et al. 1995
A3	**R204X**/I234T	Infantile	<6M	0.08	ND	ND	ND	
A4	**L364R**/T652P	Infantile	5M	0	0.1	81	undectable	
A5	12Del3Ins/-	Infantile	6M	ND	0.27	ND	ND	
A6	T652P/T652P	Infantile	4M	0.07	0.3	244	undectable	
A7	12Del3Ins/T652P	Infantile	6M	0.1	ND	169	ND	
A8	**393delT**/-	Infantile	4M	0	ND	185	12	
A9	**S257F**/-	Infantile	6M	0.3	0.4	236	18	
A10	P302A/L618S	Late-infantile	8M	0	0.3	119	25	
A11	G270D/R515H	Late-infantile	2Y	0.03	0.08	71	50	
A12	I66M+I289V/12Del3Ins	Juvenile	5Y	0.09	0.14	95	24	
A13	I66M+I289V /W647X*	Juvenile	3Y	0.6	ND	124	low	* Fu et al. 1999
A14	I66M+I289V/**1719-1720insT**	Juvenile	3.5Y	0.09	0.23	75	low	
A15	12Del3Ins/-	Juvenile	3.5Y	0.12	0.5	84	ND	
A16	G270D/G270D	Adult	69Y	0.2	0.8	ND	ND	
A17	I66M+I289V/I66M+I289V	Adult	59Y	0.29	0.23	51	17	

Patient No	Genotype	Phenotype	Age at onset	CSF protein (mg/dl)	MCV (m/sec)	Reference
B1	12Del3Ins/12Del3Ins	Infantile	4 M	ND	ND	Tatsumi et al. 1995
B2	12Del3Ins/12Del3Ins	Infantile	3M	106	low	Tatsumi et al. 1995
B3	S52F/W410G	Infantile	<6M	ND	ND	Fu et al. 1999
B4	12Del3ins/T652P	Infantile	4M	ND	13-18	Fu et al. 1999
B5	R515H/R515H	Infantile	5M	80	low	Fu et al. 1999
B6	T262I/12Del3Ins	Infantile	1Y	42	36	Fu et al. 1999
B7	G270D/G270D	Adult	10-20Y	undescribed	undescribed	Furuya et al. 1997
B8	I66M+I289V/I66M+I289V	Adult	10-20Y	undescribed	undescribed	Furuya et al. 1997 & Kukita et al 1997-98
B9	I66M+I289V/Y354X	Adult	10-20Y	undescribed	undescribed	Furuya et al. 1997 & Kukita et al 1997-98
B10	L618S/IVS6+5G>A	Adult	10-20Y	undescribed	undescribed	Furuya et al. 1997 & Kukita et al 1997-98
B11	L618S/L618S	Adult	51Y	undescribed	undescribed	Satoh et al.1997

"A" in Patient No. column represents the subjects investigated in this study; "B" in Patient No. column represents subjects reported previously.

Bold print in Genotype column represents a novel mutation identified in this study.

"*" in the Genotype column represents previously detected mutant allele.

"**" The patient was previously reported as late-infantile type, however, it is corrected as infantile type with detailed clinical information.

"-" in the Genotype column represents that no mutation was found in the second allele in our experiment.

CSF, cerebrospinal fluid; MCV, motor nerve conduction velocity; ND, not done

Normal range of GALC activity in lymphocytes and skin fibroblasts is 2.1 ± 0.29, 4.5 ± 1.2 nmol/mg/h, respectively.

Table 2 Primer sequences used in PCR amplification for GALC gene and DHPLC oven temperatures

Exon	Forward primer (5'>3')	Reverse primer (5'>3')	Size (bp)	Predicted Tm (°C)	DHPLC oven Temperature (°C)
1	GGAGTCATGTGACCCACACA	CGCGTATCCCCGCAGCTT	242	56	55/56/57
2	GGTGTGCGTGAACAGTGTAGA	CTATGGTGAAATTCACCATCC	215	54.8	54/55/56
3	GGATGGTGAATTTCACCATAG	TCACAGTCCATATGCTGAGGT	333	54.9	54/55/56
4	GGTCCTAGGAAGTACCATTCATG	CACCAACACGATTCAGAATTTAA	190	56.4	55/58/61
5	GTTTTATTTTCAATAGCGCCAGC	CCTCATGGCATAAAATGGTTAGTC	312	57	55/57/59
6	AATGGTATCGTAACGATAATCTG	TTTCTGTGTTAGGAACCATAAGG	190	54.5	54/55/56
7	CTATTATCCAGAACGCTGATTTG	GTAATCAAATGGGGAGAAGGC	335	54.4	53/55/56
8	GAAAACCTTGGAGAAGACTCGTA	GGCTGGAAGAATAAGGAATTCC	354	53.2	54/56/58
9	CTCCAGGTTTTTAGACATTTAC	CTGCTTTGTCTCTTAGAGAAGA	251	55.7	52/55/58
10	CAGACTCAAATTGATATACAGCT	GGCATCTGTCTGTATGCTTAT	337	53.1	54/56/58
11	TTCTGTTAATCTTGGGCATTAAC	CAGGGCCTCTGTCAATTCATA	317	54.4	52/54/56
12	CATTGGTACATTCTTGCTGGTACT	GTCACCATCCACCAAGACAAA	413	54.5	53.5/54.5/56.5
13	ATTCCAAGGGCCTTGATATTG	TTTGACAGCCACTCCATCATG	413	55.7	54/56/60
14	AATATCAGCAAGGAGAGCTTCTG	GGAGGACCATTGAAAACTCTTC	339	56.7	54/56/58
15	GCATGTGCTGTGAAATGACATA	CCCACAAATAACAAGTAGGTGCT	325	55.1	55.1/56.1/57.1
16	CAGATGCCACTCAAGAACCCC	CCCCTCCTATTTTATAACAG	251	55.1	52/54/55
17	CCATACATGATCAAGAAACAGAC	GAAACAAGAATTGGCTCTGAA	301	57.9	56.9/57.9/58.9

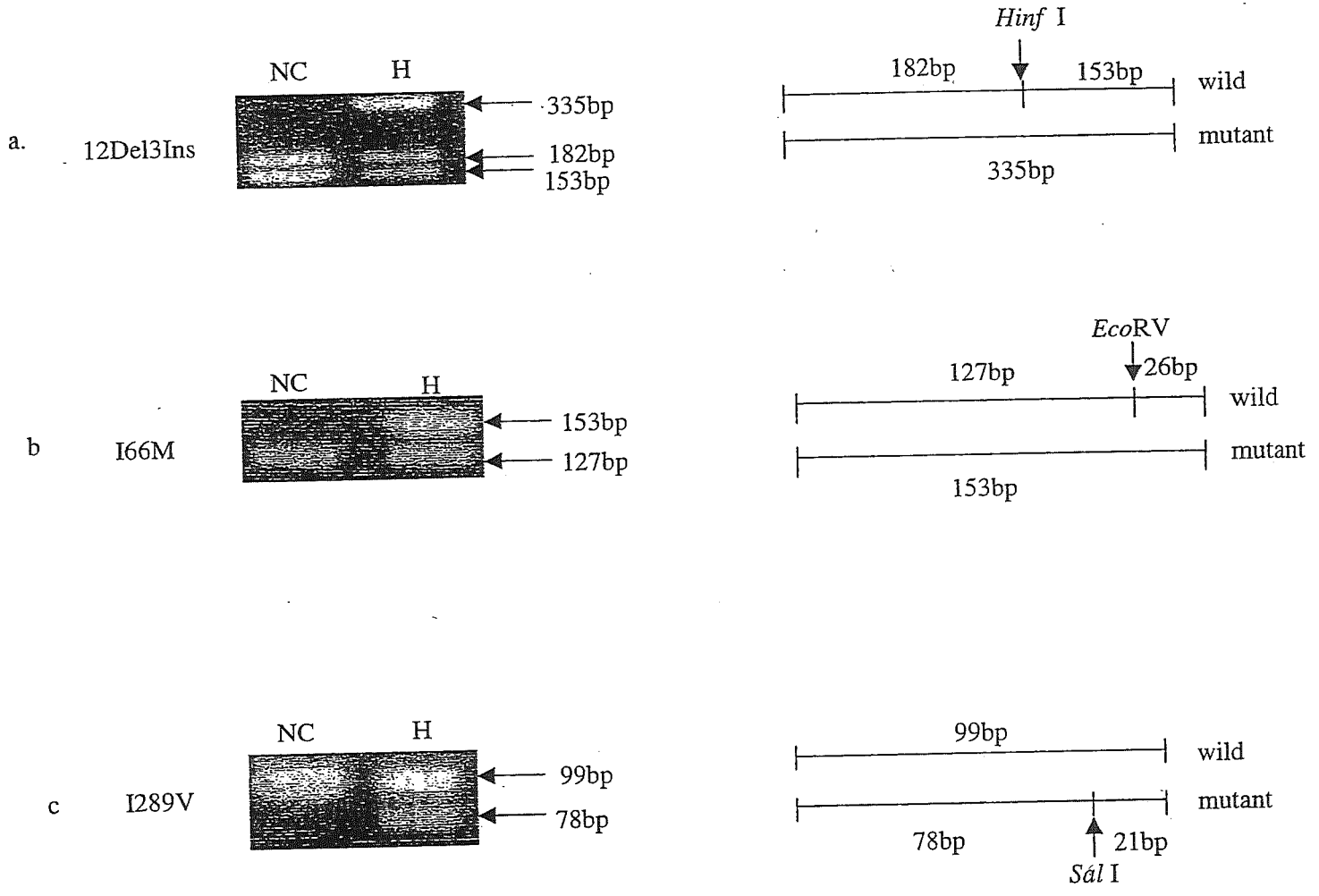
Table 3 Summary of mutations identified in 28 Japanese patients including 11 patients previously characterized

No	Exon/Intron	Nucleotide Change	Amino Acid Change	Allele Frequency	Allele Number
1	2	198A>G +865A>G	I66M+I289V	0.15	8
2	2	155C>T	S52F	0.02	1
3	4	**344G>A**	**W115X**	0.02	1
4	4	**393delT**	**L130fs; 154X**	0.02	1
5	IVS6	IVS6+5G>A	179-191 skipping	0.02	1
6	7	**610C>T**	**R204X**	0.04	2
7	7	635-646 del/ins CTC(12Del3Ins)	212-216 del (NLWES)/ins(TP)	0.22	11
8	7	701T>C	I234T	0.02	1
9	8	**770C>T**	**S257F**	0.02	1
10	8	785C>T	T262I	0.02	1
11	8	809G>A	G270D	0.1	5
12	9	904C>G	P302A	0.04	2
13	10	1062C>G	Y354X	0.02	1
14	10	**1091T>G**	**L364R**	0.02	1
15	12	1228T>G	W410G	0.02	1
16	14	1544G>A	R515H	0.06	3
17	15	**1719-1720insT**	**R574X**	0.02	1
18	16	1853T>C	L618S	0.08	4
19	17	1941G>A	W647X	0.02	1
20	17	1954A>C	T652P	0.1	5
			Total	1	52

Bold print indicates novel mutations identified in this study. "fs" indicates a frameshift starting after the respective codon.

Table 4 Correlation between genotype and phenotype in 28 Japanese subjects

Mutation	Infantile	Late-infantile	Juvenile	Adult	Total allele
12Del3Ins	9	0	2	0	11
T652P	5	0	0	0	5
R515H	2	1	0	0	3
R204X	2	0	0	0	2
P302A	1	1	0	0	2
S52F	1	0	0	0	1
W115X	1	0	0	0	1
393delT	1	0	0	0	1
I234T	1	0	0	0	1
S257F	1	0	0	0	1
T262I	1	0	0	0	1
L364R	1	0	0	0	1
W410G	1	0	0	0	1
1719-1720insT	0	0	1	0	1
W647X	0	0	1	0	1
IVS6+5G>A	0	0	0	1	1
Y354X	0	0	0	1	1
I66M+I289V	0	0	3	5	8
G270H	0	1	0	4	5
L618S	0	1	0	3	4
Total allele	27	4	7	14	52



NC: normal control

H: heterozygous