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FIGURE LEGENDS

Fig.1 Number of amino acid substitutions per sample in the sustained viral responders (SVR) and the non-sustained viral responders (non-SVR) group.

The numbers of variations, relative to a population consensus, that were unique to either SVR or non-SVR patients are shown for the full open reading frame (ORF) (Fig.1, left) and for each HCV protein (Fig.1, right).

Fig.2a Different amino acid usages at each viral amino acid position between the sustained viral responders (SVR) and the non-sustained viral responders (non-SVR) patients.

Amino acid variation was determined between SVR and non-SVR patients by Fisher's exact probability test. The longitudinal axis shows the - logP value.

Fig.2b Sequence alignment in the core region.

Dashes indicate amino acids identical to the consensus sequence and substituted amino acids are shown by standard single letter codes.

Fig.2c Sliding window analysis.

Viral regions affecting treatment outcome are shown as red spots. There are four hot spots: at core amino acid 110, amino acids 400-403 (i.e. the hyper variable region) in Envelope2 (E2) region, amino acids 724-743 in E2 and amino acids 2258-2306 in the nonstructural (NS)5A.

Fig.2d Sequence alignment amino acids in the nonstructural (NS)5A around amino acids 2258 to 2306.

Dashes indicate amino acids identical to the consensus sequence and substituted amino acids are shown by standard single letter codes.

Fig.3 Correlation between pretreatment HCV RNA levels and the number of substitutions in the NS5A region aa 2258 to 2306.

Spearman's correlation coefficient by rank test is demonstrated.

Table

Table 1. Baseline Characteristics of All Patients (Group 1 and 2)

Characteristic	SVR (n = 58)			non-SVR (n = 20)			*P* value△
	Group 1 (n = 36)	Group 2 (n =22)	Combined (n = 58)	Group 1 (n = 7)	Group 2 (n = 13)	Combined (n = 20)	
Gender(Male/Female)	20 / 16	9 / 13	29 / 29	4 / 3	5 / 8	9 /11	0.80†
Age(yrs)	50.0 ± 12.5*	57.3 ± 10.0	52.4 ± 12.1	55.0 ± 9.7	59.8 ± 6.4	58.1 ± 7.8	0.058‡
ALT(IU/l)	86.6 ± 86.6	71.2 ± 50.4	80.5 ± 74.2	52.9 ± 29.3	88.1 ± 90.1	75.8 ± 75.5	0.81‡
Platelet($x10^4/mm^3$)	20.8 ± 6.2	19.0 ± 5.2	20.1 ± 5.8	14.7 ± 7.1	19.1 ± 4.9	17.6 ± 6.0	0.11‡
Fibrosis score(0-2 / ≥3)§	34 / 1	19 / 2	53 / 3	4 / 3	11 / 2	15 / 5	0.049†
HCV RNA(KIU/ml)	760(2-3100)**	340(54-3600)	550(12-3600)	1300 (350-30000)	1400 (180-5000)	1300 (180-30000)	0.002‖
IFN dose(≥80% / 60-80%)¶	28 / 4	21 / 1	49 / 5	4 / 3	11 / 2	15 / 5	0.12†
Ribavirin dose(≥80% / 60-80%)¶	27 / 5	17 / 5	44 / 10	4 / 3	5 / 8	9 / 11	0.003†
RVR rate (%)	87.5	54.5	74.1	33.3	46.1	42.1	0.022†
EVR rate (%)	100	100	100	66.7	100	89.4	0.07†

* : mean ± SD ** : median (range) † : Fisher's exact probability test ‡ : Student t test ‖ : Mann-Whitney's U test △: *P* values between all SVR (n = 58) vs. all non-SVR (n = 20)

Several clinical charcteristics listed below were unavailable in some patients

§ : SVR : n = 56 (35 in group1, 21 in group2), non-SVR : n = 17 (7 in group1, 10 in group2) ¶ : SVR : n = 54 (32 in group1, 22 in group2)

Table 2a. Variations in each Amino Acid Position and SVR rate

Position		Group 1 (n = 43)	*P* value	Group 2 (n = 35)	*P* value	Combined (n = 78)	*P* value
Core aa 110	T	100% (19 / 19)	0.01	92.9% (13 / 14)	0.004	97% (32 / 33)	5E - 05
	non T	70.8% (17 / 24)		42.9% (9 / 21)		57.8% (26 / 45)	
p7 aa 773	V	77.4% (24 / 31)	0.16	53.6% (15 / 28)	0.03	66.1% (39 / 59)	0.002
	non V	100% (12 /12)		100% (7 / 7)		100% (19 / 19)	
NS5A aa 2099	R	92.9% (13 / 14)	0.40	91.7% (11 / 12)	0.01	92.3% (24 / 26)	0.01
	non R	79.3% (23 / 29)		47.8% (11 / 23)		65.4% (34 / 52)	
NS5B aa 3013	L	78.9% (26 / 33)	0.17	47.8% (11 / 23)	0.01	66.1% (37 / 56)	0.008
	non L	100% (10 / 10)		91.7% (11 / 12)		95.5% (21 / 22)	

Table 2b. Number of Amino Acid Substitutions in each Region and SVR rate

Region		Group 1 (n = 43)	*P* value	Group 2 (n = 35)	*P* value	Combined (n = 78)	*P* value
E2 aa 400-403	mutation ≥2	89.3% (25 / 28)	0.22	100% (11 / 11)	0.002	92.3% (36 / 39)	0.0005
	mutation 0-1	73.3% (11 / 15)		45.8% (11 / 24)		56.4% (22 / 39)	
E2 aa 724-743	mutation ≥1	100% (28 / 28)	0.0002	72% (18 / 25)	0.12	86.8% (46 / 53)	0.0006
	no mutation	53.3% (8 / 15)		40% (4 / 10)		48% (12 / 25)	
ISDR(aa 2213-2248)	mutation ≥2	100% (15 / 15)	0.08	86.7% (13 / 15)	0.02	93.3% (28 / 30)	0.003
	mutation 0-1	75% (21 / 28)		45% (9 / 20)		62.5% (30 / 48)	
NS5A aa 2258-2306	mutation ≥5	100% (19 / 19)	0.01	84.2% (16 / 19)	0.006	92.1% (35 / 38)	0.0006
	mutation 0-4	70.8% (17 / 24)		37.5% (6 / 16)		57.5% (23 / 40)	

Table 3. Multivariate Logistic Regression Analysis

Factor	Odds (95% CI)	*P* value
Age	1.01 (0.91-1.13)	0.85
HCV RNA	1.00 (1.00-1.00)	0.09
Fibrosis score ≥3/0-2	2.37 (0.21-26.7)	0.48
RVR achievement	3.46 (0.54-22.1)	0.19
Ribavirin dose ≥ 80%	16.0 (1.66-153)	0.02
Core aa 110 T	24.7 (1.72-353)	0.02
NS5A aa 2258-2306 mutations 0-4/≥5	11.5 (1.23-108)	0.03

Table 4a. Baseline Characteristics of Patients with NS5A aa 2258-2306 mutations 0-4 or ≥5 (Group 1 and 2)

Characteristic	Mutation 0-4 (n = 40)	Mutation ≥5 (n = 38)	*P* value
Gender (Male/Female)	22 / 18	16 / 22	NS†
Age (yrs)	54.3 ± 11.4*	53.5 ± 11.5	NS‡
ALT (IU/l)	73.8 ± 70.3	85.3 ± 78.7	NS‡
Platelet ($x10^4/mm^3$)	18.0 ± 5.9	21.0 ± 5.7	0.03‡
Fibrosis score (0-2 / ≥3)§	33 / 5	33 / 2	NS†
HCV RNA (KIU/ml)	1100 (99 - 30000) **	380 (12 - 5000)	0.02‖
IFN dose (≥80% / 60-80%)¶	31 / 8	33 / 2	NS†
Ribavirin dose (≥80% / 60-80%)¶	25 / 14	28 / 7	NS†
RVR rate (%)	65.8	62.9	NS†
EVR rate (%)	94.7	100	NS†
Relapse rate (%)	35.9	7.9	0.002†
SVR rate (%)	57.5	92.1	0.0006†

*: mean ± SD, †: Fisher's exact probability test, ‡: Student t test, §: Mutation 0-4 : n = 38, mutation ≥5 : n = 35,

**: median (range), ‖: Mann-Whitney's U test, ¶: Mutation 0-4 : n = 39, mutation ≥5 : n = 35

Table 4b. Baseline Characteristics of Patients with Core 110 T or N/S (Group 1 and 2)

Characteristic	Core 110 T (n = 33)	Core 110 N/S (n = 45)	*P* value
Gender (Male/Female)	18 / 15	20 / 25	NS†
Age (yrs)	50.4 ± 13.0*	56.4 ± 9.5	0.032‡
ALT (IU/l)	64.5 ± 48.2	88.8 ± 86.2	NS‡
Platelet ($x10^4/mm^3$)	19.3 ± 4.9	19.5 ± 6.6	NS‡
Fibrosis score (0-2 / ≥3)§	30 / 1	36 / 6	NS†
HCV RNA (KIU/ml)	580 (54 - 3600) **	980 (12 - 30000)	NS‖
IFN dose (≥80% / 60-80%)¶	26 / 3	38 / 7	NS†
Ribavirin dose (≥80% / 60-80%)¶	23 / 6	30 / 15	NS†
RVR rate (%)	72.4	59.1	NS†
EVR rate (%)	100	95.5	NS†
Relapse rate (%)	3.0	38.6	9E-05†
SVR rate (%)	97.0	57.8	5E-05†

*: mean ± SD, †: Fisher's exact probability test, ‡: Student t test, §: Core 110 T : n = 31, Core 110 N/S : n = 42,

** : median (range), ‖ : Mann-Whitney's U test, ¶: Core 110 T : n = 29

Figure 1
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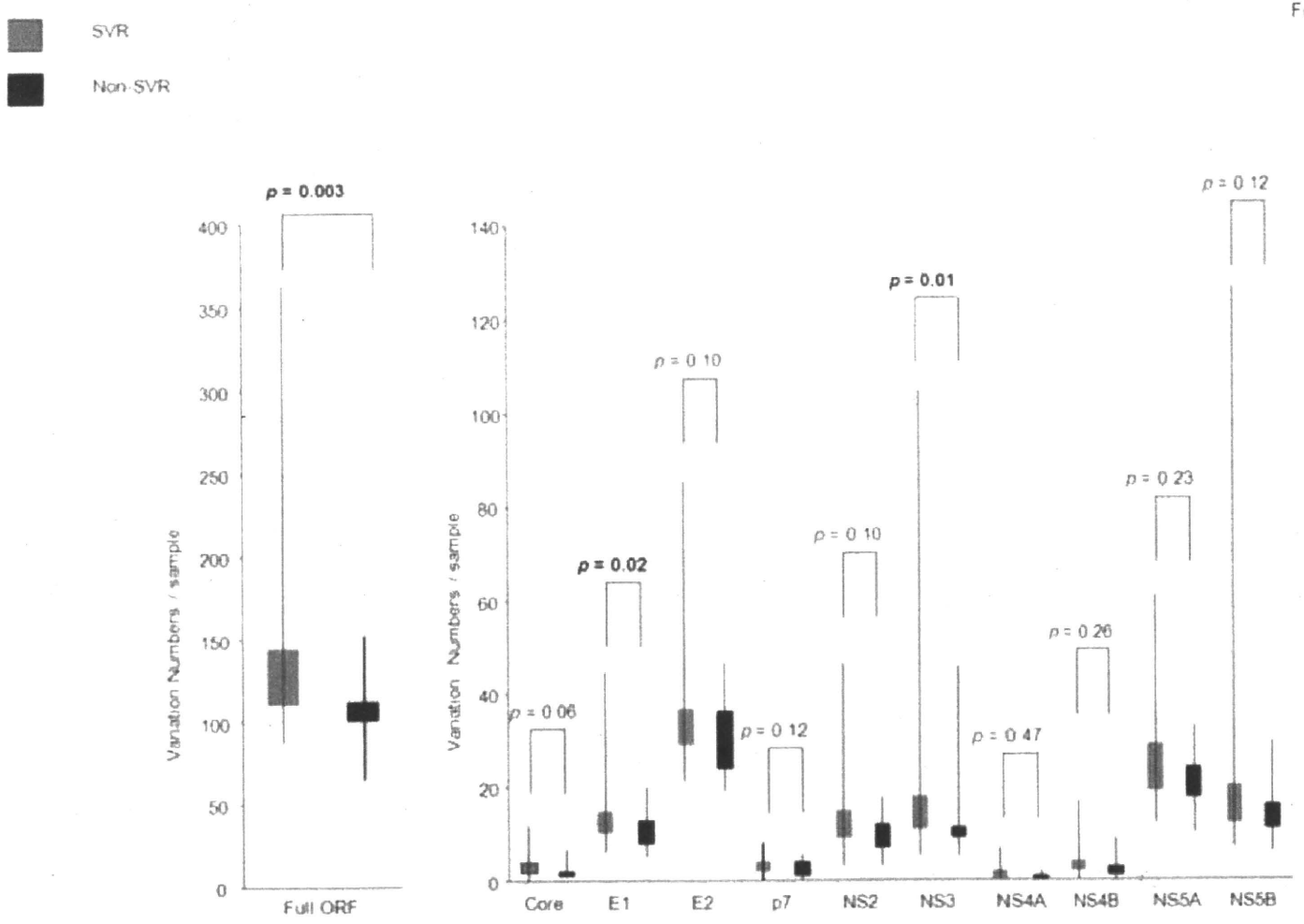

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Fig 2a

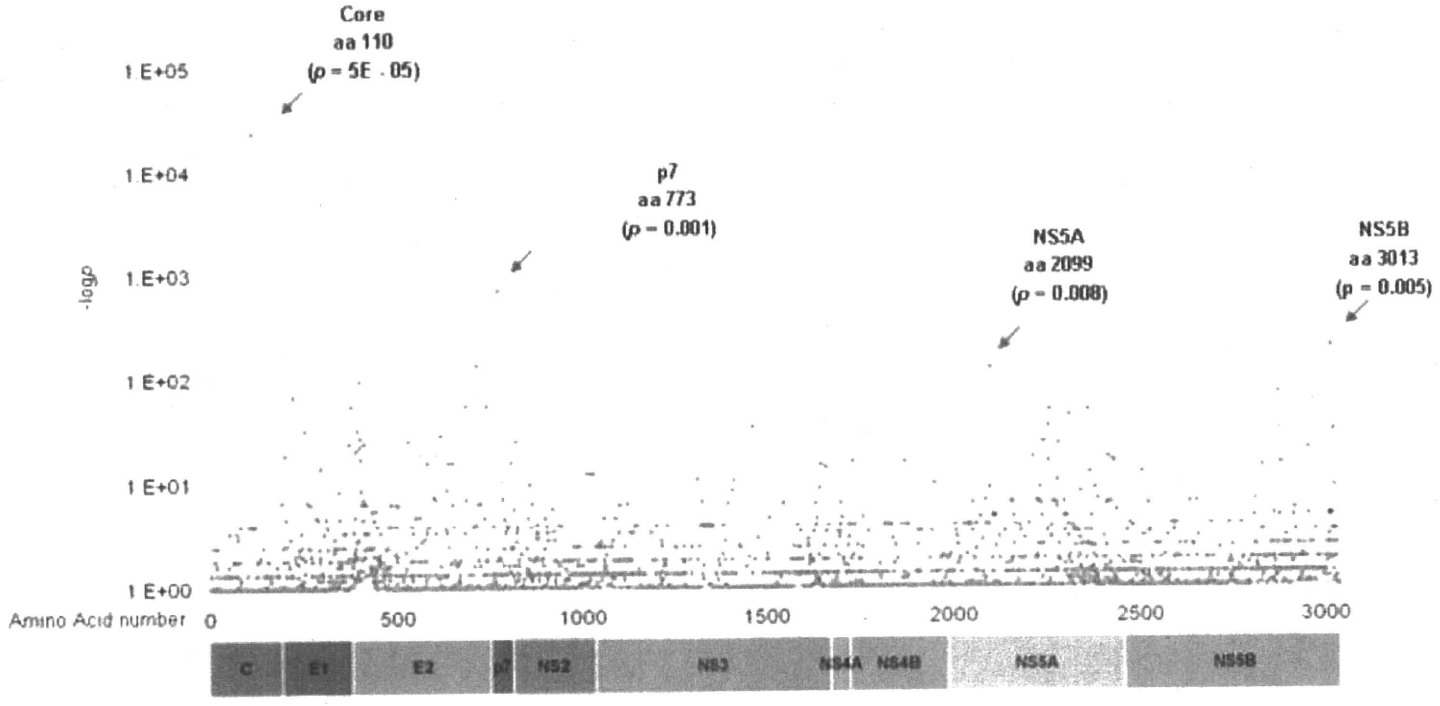

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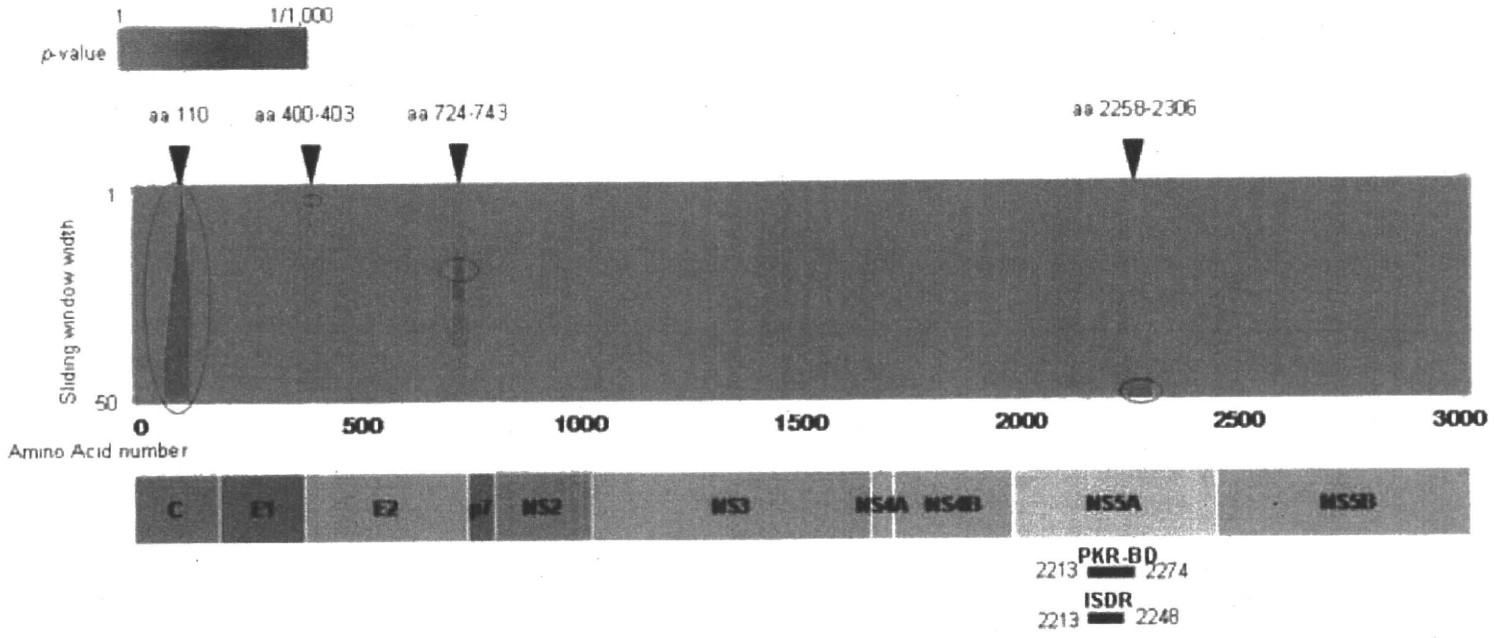
Fig 2c



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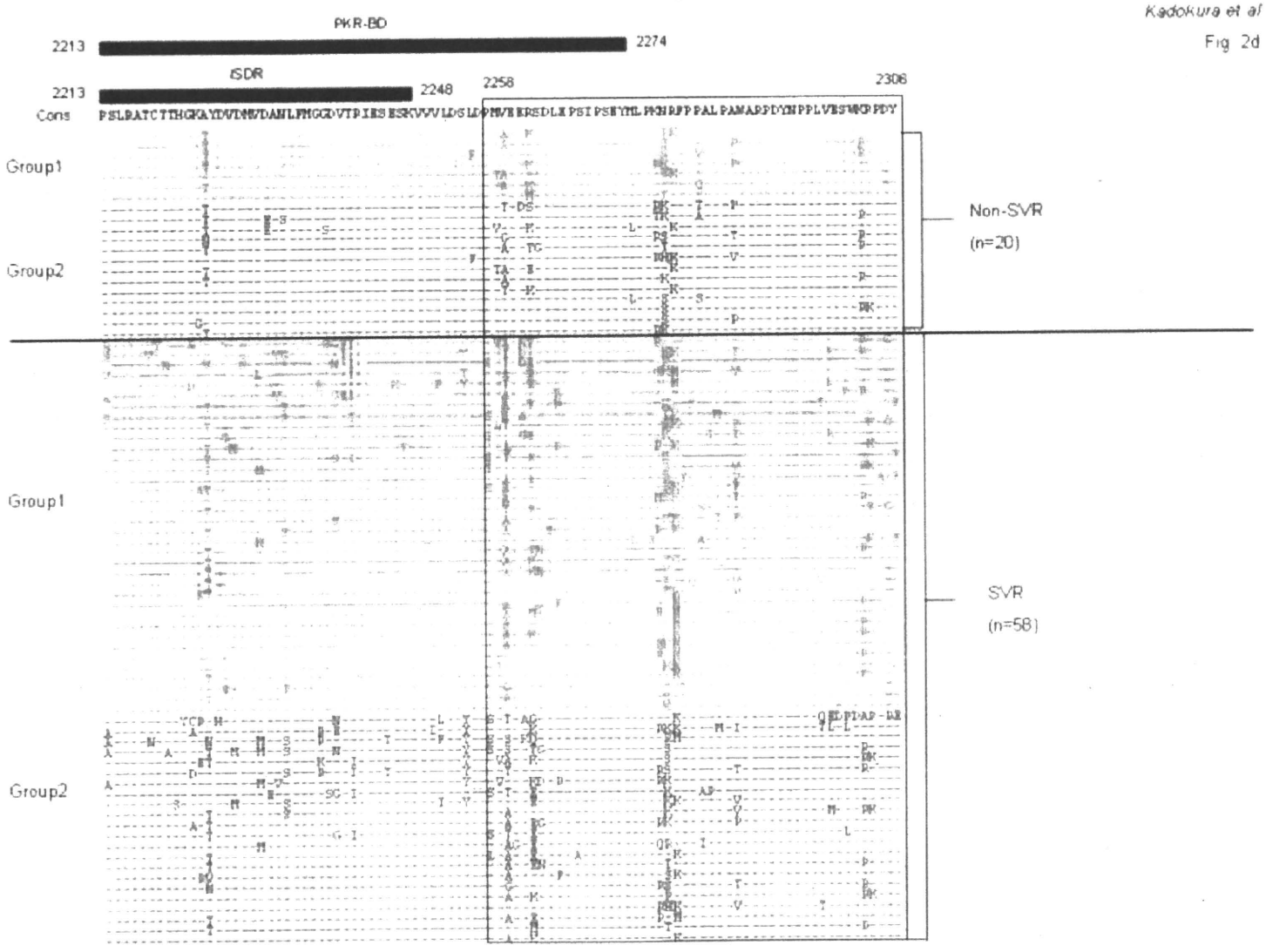

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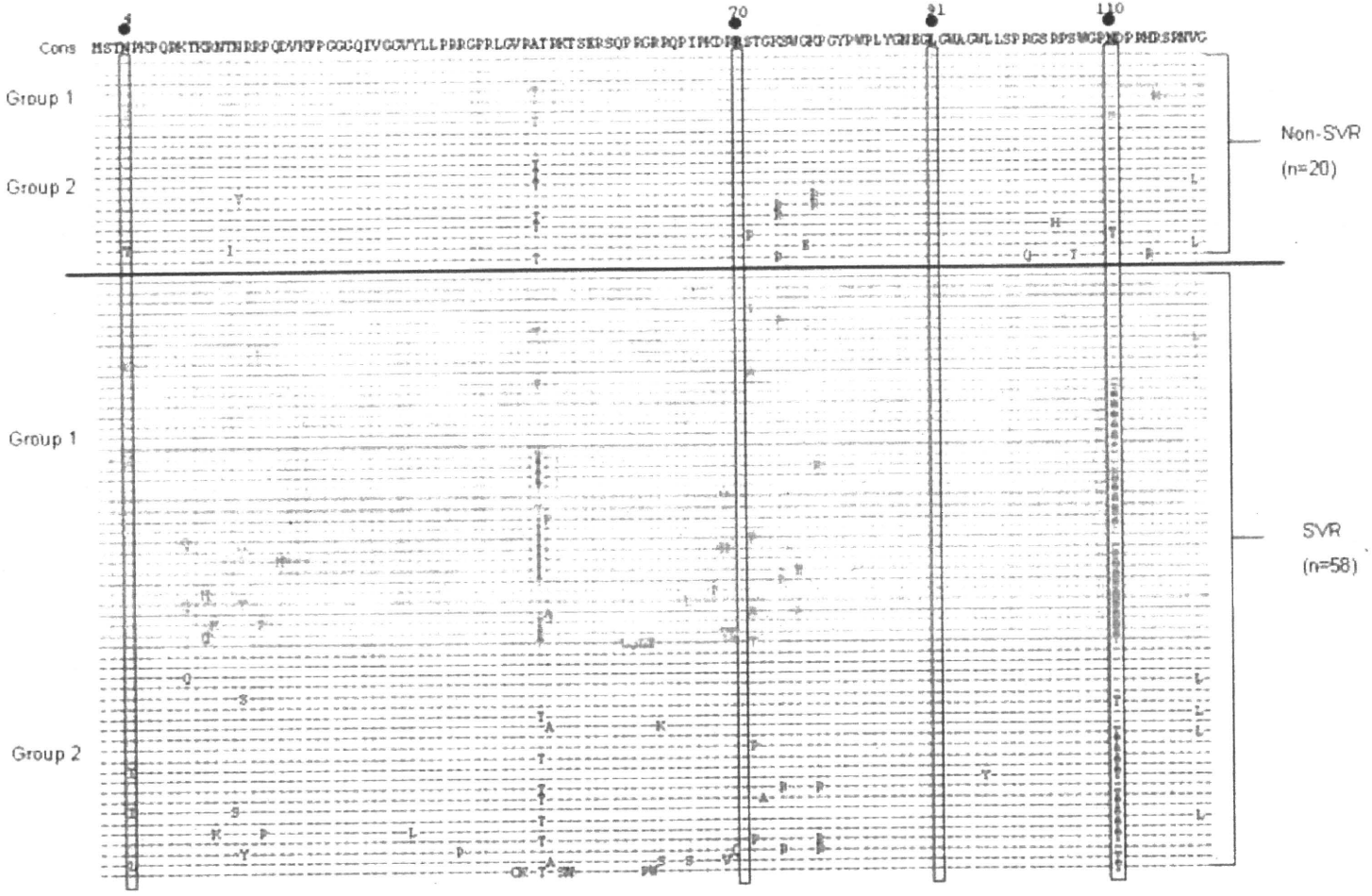

Figure 3
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