Türkiye'de hepatit virüslerinin moleküler epidemiyolojisi

Dr Hakan Abacıoğlu

XXXIV Türk Mikrobiyoloji Kongresi
Kıbrıs

Moleküler epidemiyoloji nedir?

TABLE 1. A snapshot of various definitions of molecular epidemiology

Author(s) and ref. no.	Reference	Definition
Higginson J (37)	Am J Pathol 1977;86:460–84	"the application of sophisticated techniques to the epidemiologic study of biological material" (p. 463)
Schulte PA (2)	In: Schulte PA, Perera FP, eds. San	"molecular epidemiology is the use of biologic markers or

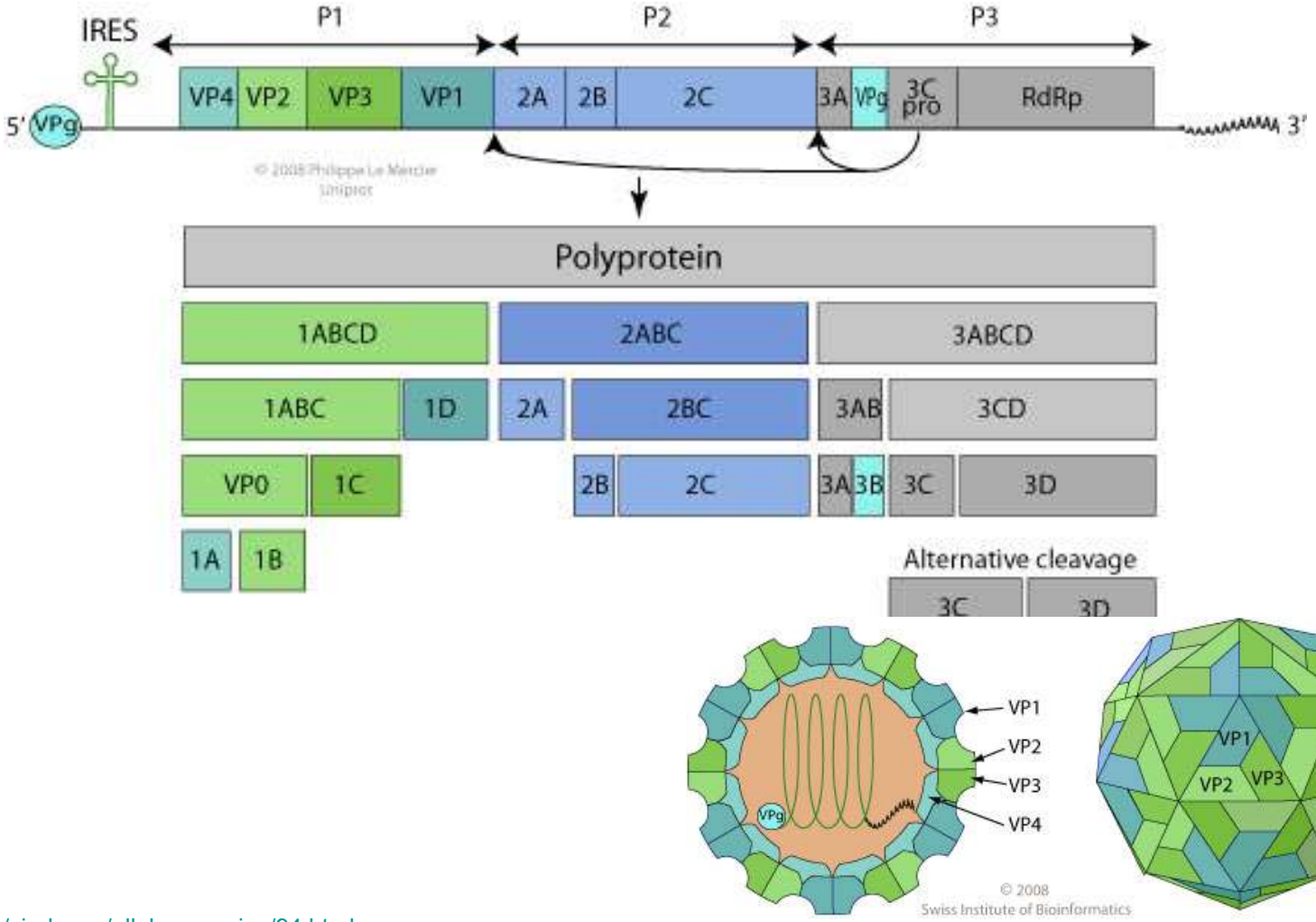
"the practical goals of molecular epidemiology are to identify the microparasites responsible for infectious diseases and determine their physical sources, their biological relationships, and their route of transmission and those of the genes responsible for their virulence, vaccine-relevant antigens and drug resistance" (p. 806)

Shpilberg O, Dorman JS, Ferrell RE, et al. (42)	J Clin Epidemiol 1997;50:633–8	"molecular epidemiology uses molecular techniques to define disease and its pre-clinical states, to quantify exposure and its early biological effect, and to identify the presence of susceptibility genes" (p. 633)
Levin BR, Lipsitch M, Bonhoeffer S (43)	Science 1999;283:806–9	"the practical goals of molecular epidemiology are to identify the microparasites responsible for infectious diseases and determine their physical sources, their biological relationships, and their route of transmission and those of the genes responsible for their virulence, vaccine-relevant antigens and drug resistance" (p. 806)

Hepatit virüslerinin moleküler epidemiyolojisi neden gerekli?

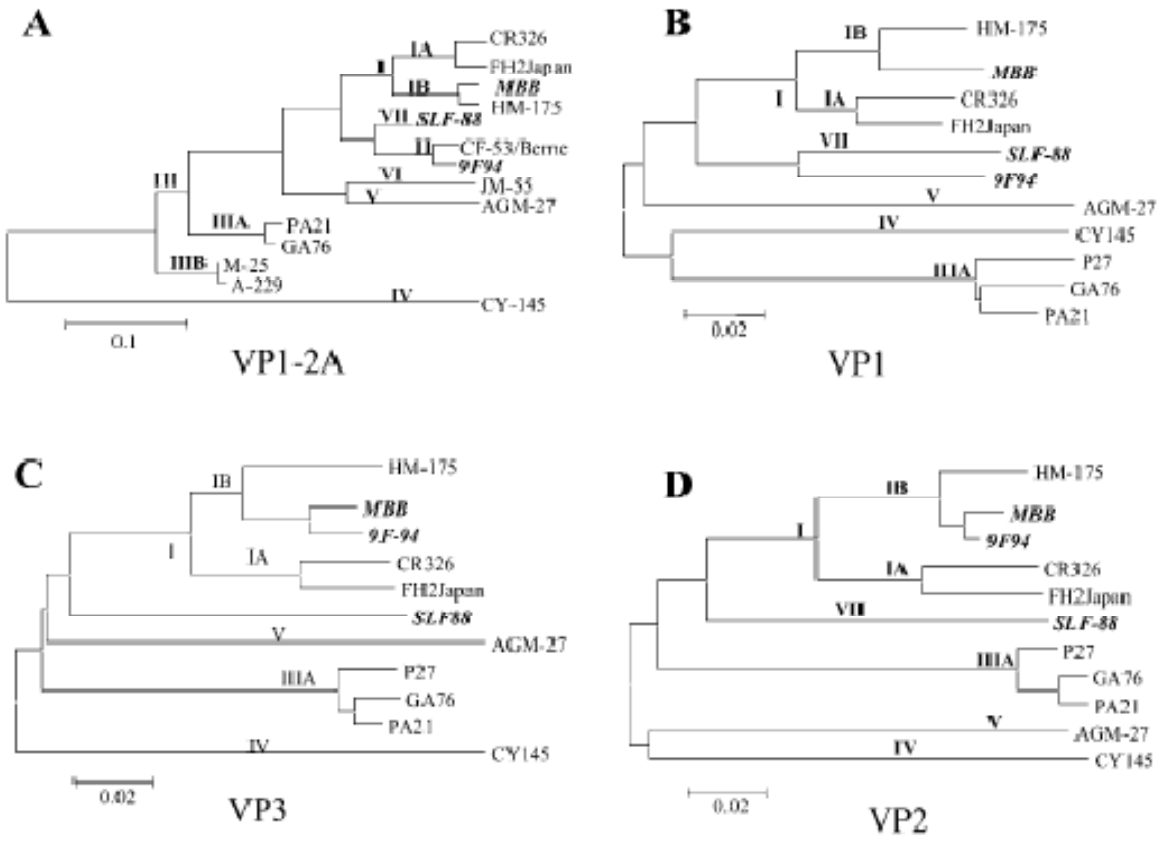
- Epidemiyolojik
  - *virus (tiplendirme)*
  - *Kaynak ve bulaş yolları*
- Tanısal
- Korunma ve Sağaltım
  - *Aşılama (kaçış mutantları)*
  - *Antiviral direnç*

Hepatit A virus



www.expasy.ch/viralzone/all_by_species/94.html

HAV genotipleri



Genotip I, II, III and VII insan olguları ile ilişkili

Journal of General Virology (2003), 84, 3191–3201

Türkiye'de HAV epidemiyolojisi

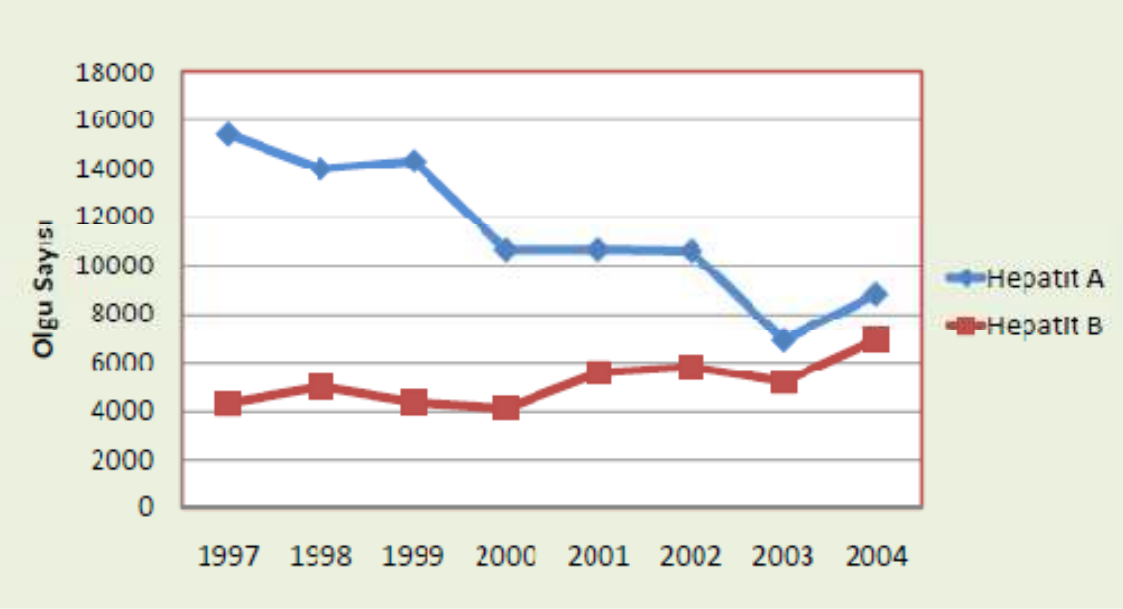


Figure 1. Seroprevalence of viral hepatitis A in various countries.

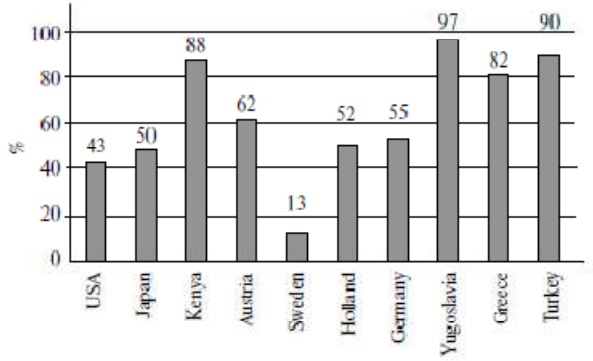
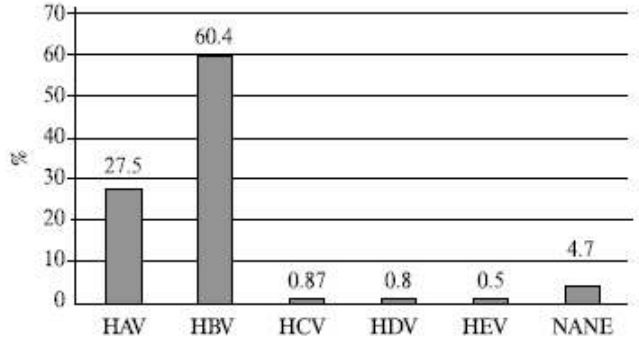


Figure 2. Etiology of acute viral hepatitis in Turkey (pooled data of 4471 cases) [26].



Genotip I (çoğu IB) infeksiyonları baskın

Roczniki Akademii Medycznej w Białymstoku · Vol. 48, 2003 · Annales Academiae Medicae Bialostocensis

Acute Hepatitis A Virus infection in Turkey

Andrea Normann,[1] Selim Badur,[2] Derya Önel,[2] Ayse Kilic,[2] Müjgan Sidal,[2] Bernard Larouzé,[3,4] Veronique Massari,[3,4] Julia Müller,[1] and Bertram Flehmig[1]*

[1]*University of Tübingen, Children's Hospital, Tübingen, Germany*
[2]*University of Istanbul, Faculty of Medicine, Istanbul, Turkey*
[3]*INSERM-U707 Epidémiologie, Systèmes d'Information, Modélisation. Paris. France*
[4]*Université Pierre & Marie Curie-Paris6, UMR-S707, Paris, France*

Journal of Medical Virology 80:785–790 (2008)

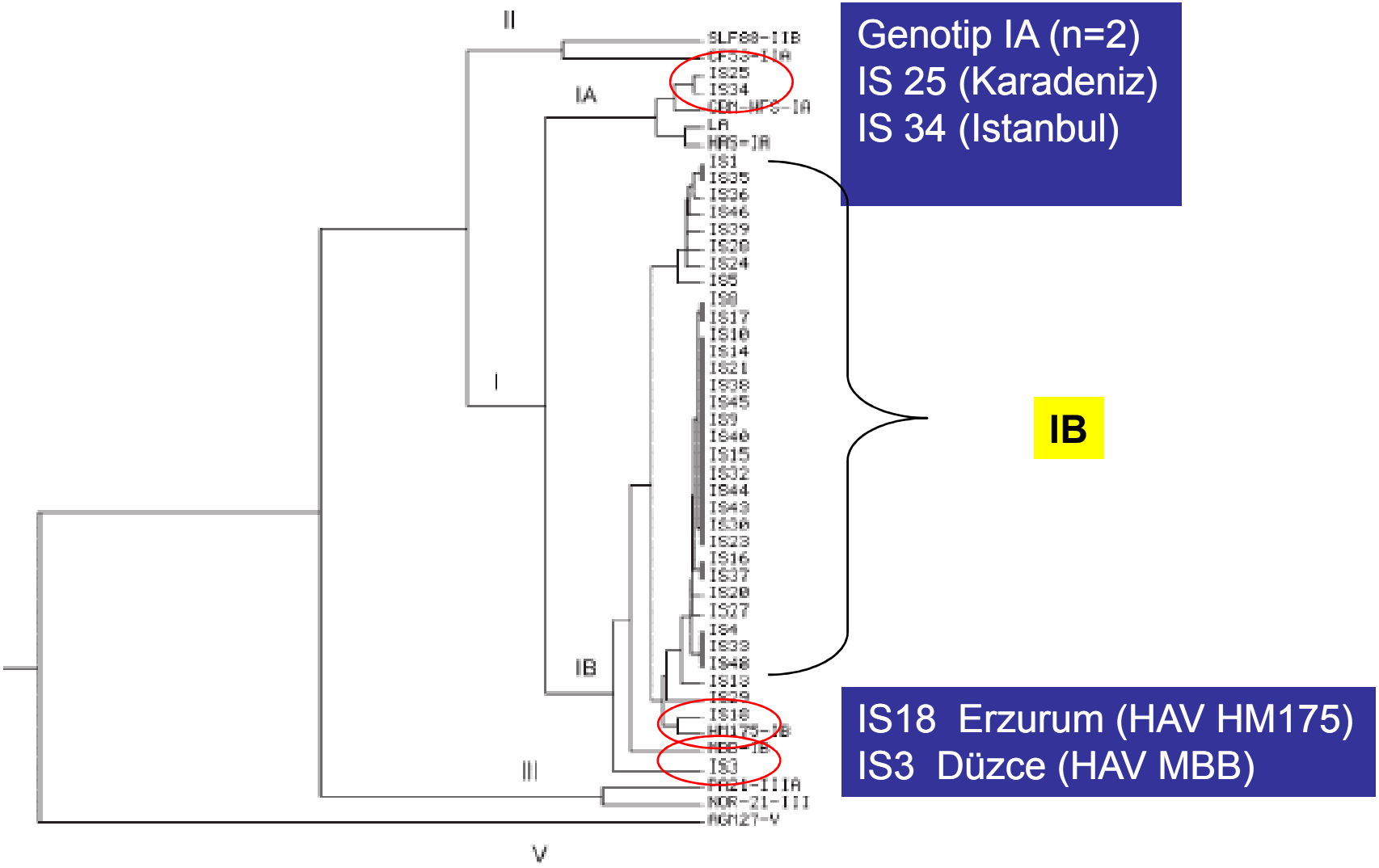
- İstanbul ve Anadolu'dan Anti-HAV IgM (+) örnekler (n=50)
- VP1-P2A bileşkesi ve 5'-NCR bölgesi çoğaltıldı ve dizilendi.

TABLE I. Characteristics of All Anti-HAV IgM Positive Patients (N = 50)

Age groups (years)	Number of patients	Mean ALT ± SD	n	Median[a]	Mean[†] AST ± SD	n	Median[b]
0–5	7	1,600 ± 1,540	6	987	1,187 ± 1,501	6	818
6–10	19	1,326 ± 936	15	1,470	884 ± 1,109	14	343
11–20	20	727 ± 734	15	238	529 ± 565	15	179
>20	4	112 ± 113	3	68	119 ± 96	3	126

[a]Kruskal–Wallis test: $\chi^2 = 7.81$; $P = 0.05$.
[b]Kruskal–Wallis test: $\chi^2 = 5.24$; $P = 0.1546$.
[†]U/L (unite/liter).

5’-NCR dizileri



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Eurosurveillance, Volume 10, Issue 48, 01 Decemb

Articles

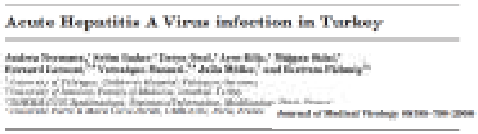
Citation style for this article: Howitz M, Mazick A, Mølbak K. Hepatitis A ou g from Turkey, October 2005. Euro Surveill. 2005;10(48):pii=2849. Available online: ht /ViewArticle.aspx?ArticleId=2849

Hepatitis A outbreak in a group of Danish tourists returning from Turkey, October 2005

Michael Howitz (how@ssi.dk), Anne Mazick and Kåre Mølbak

Table. Selected exposure factors, hepatitis A outbreak in a group of Danish tourists returning from Turkey, October, 2005

Food	Exposed			Unexposed			Relative risk	95% CI
	Cases	*Total*	*Attack rate %*	*Cases*	*Total*	*Attack rate %*		
Ice cream served in open containers	4	6	67	0	8	0	Infinite	
Dried Fruit	3	4	75	1	12	8	9	1.3-63.9
Nuts and other unpackaged snacks	3	5	60	1	11	9	6.6	0.9-48.8
Cocktails	4	8	50	0	8	0	Infinite	
Food outside the resort	4	13	31	0	3	0	Infinite	


Acute Hepatitis A Virus infection in Turkey

Sonuçlar

- 5'-NCR dizilerine yönelik RT-PCR'ın VP1-2A dizilerine göre:
  - klinik duyarlılık *(%72 ye %32)* ve
  - analitik duyarlılığı *(100 IU ye 500 IU)* daha iyi
- Tüm izolatlar genotip I (çoğu IB)
- 10 yaşın altındaki çocuklarda infeksiyon daha şiddetli

TABLE I. Characteristics of All Anti-HAV IgM Positive Patients (N = 50)

Age groups (years)	Number of patients	Mean ALT ± SD	n	Median[a]	Mean[†] AST ± SD	n	Median[b]
0–5	7	1,600 ± 1,540	6	987	1,187 ± 1,501	6	818
6–10	19	1,325 ± 936	15	1,470	884 ± 1,109	14	343
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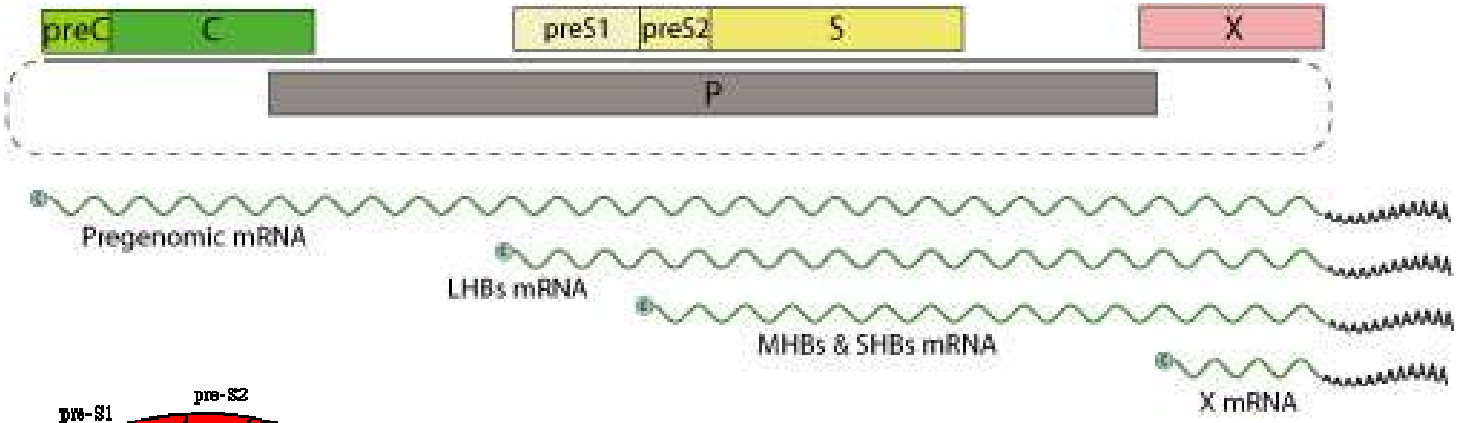
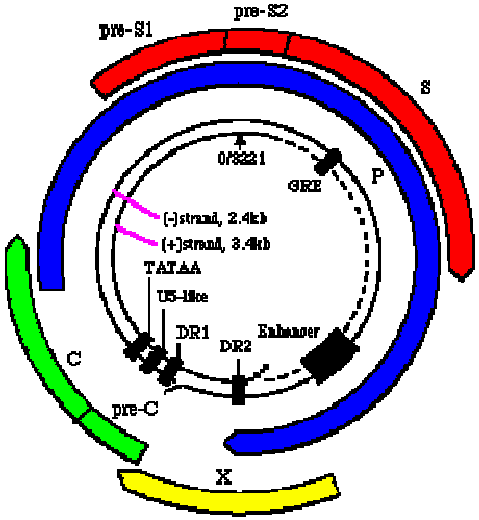
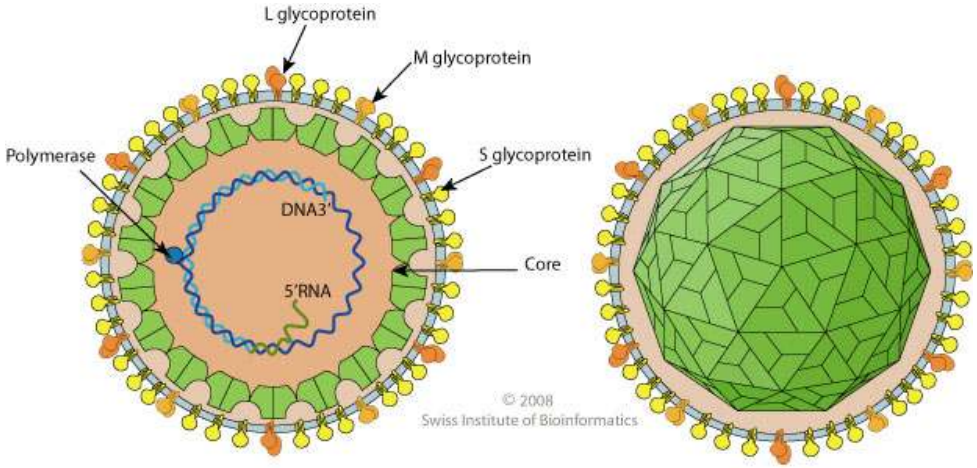
[a]Kruskal–Wallis test: $\chi^2 = 7.81$; $P = 0.05$.
[b]Kruskal–Wallis test. $\chi^2 = 5.24$, $P = 0.1546$.
[†]U/L (units/liter).

Hepatit B virus

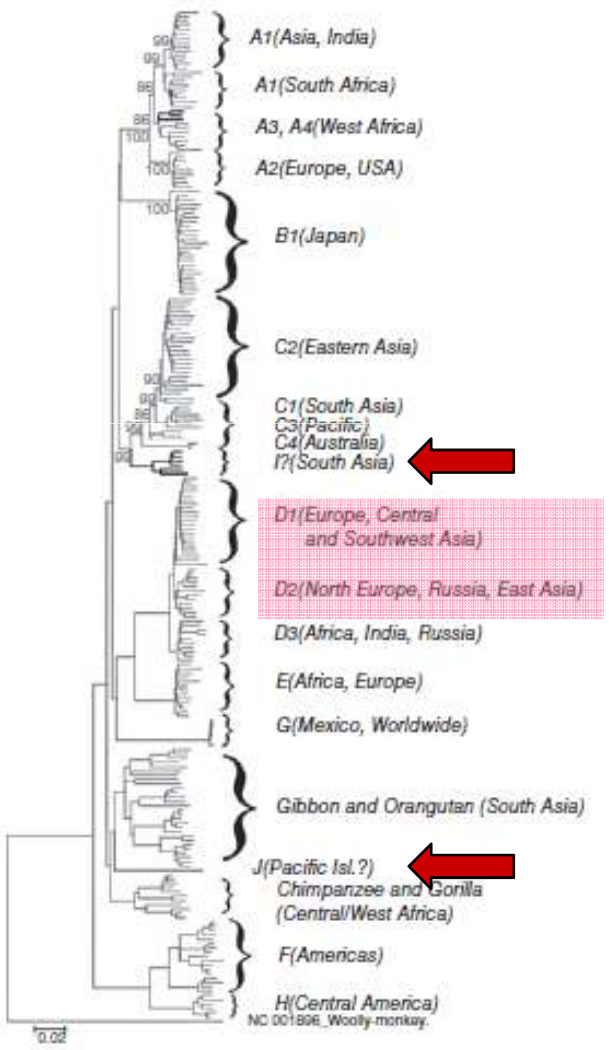






www.expasy.ch/viralzone/all_by_species/94.html

HBV genotip ve subtipleri



Genotype	Subgenotype	n	Complete genome Nucleotides diversity (complete genome)			Geography	Ref
			Clustering	Intra-subgenotype mean + SD (max)	Next closest negbour mean + SD (min)		
HBV/A							
	A1/Aa	78	yes	2.6 + 0.8 (5.5)	4.4 + 0.4 (3.3) for A4	Africa, Asia, South America	35,261,262
	A2/Ae	94	yes	1.7 + 0.9 (5.5)	4.7 + 0.7 (3.6) for A4	Europe, North America	35,261,262
	A3/Ac	8	yes	3.0 + 0.9 (4.1)	4.7 + 0.4 (3.8) for A1	Western Africa	35,21,22
	A4	3	no	2.9 + 0.9 (3.5)	3.8 + 0.2 (3.4) for A3	Western Africa	21,263
	A5	0	?	?	?	Western Africa	21
HBV/B							
	B1/Bj	38	yes	2.4 + 0.6 (4.1)	4.6 + 0.5 (3.6) for B2	Japan	264–266
	B2	173	yes	1.7 + 0.8 (4.0)	4.4 + 0.5 (2.9) for B4	China, Taiwan	150,200,264–268
	B3	5	yes	1.6 + 0.6 (2.7)	3.6 + 0.5 (2.9) for B5	Indonesia	269
	B4	21	yes	2.7 + 0.6 (4.4)	5.0 + 0.5 (4.3) for B3	Vietnam, Cambodia	269
	B5	7	yes	2.8 + 1.5 (4.5)	5.2 + 0.6 (4.0) for B2	the Philippines	166,167
	B6	27	yes	2.7 + 0.7 (4.2)	5.7 + 0.6 (4.6) for B3	Native populations in Arctic	270,271
	B7	2	no			Indonesia	161
HBV/C							
	C1/Cs	97	yes	2.4 + 0.7 (5.1)	4.4 + 0.5 (3.1) for C2	South and South East Asia	272–274
	C2/Ce	295	yes	2.5 + 0.6 (4.7)	4.9 + 0.5 (3.8) for C3	Eastern Asia (Korea, Japan) and North China	
	C3	3	yes	4.2 + 1.2 (5.2)	5.8 + 0.6 (4.6) for C1	Pacific	269
	C4	2	yes	0.9	6.6 + 0.6 (6.0) for C3	Australia	256
	C5	8	yes	2.0 + 1.0 (3.4)	6.2 + 0.5 (5.0) for C1	Philippines, Vietnam	167
HBV/D							
	D1	88	yes	2.3 + 0.8 (5.2)	3.1 + 0.6 (1.7) for D2	North Africa, Europe, Central Asia	84,269,275
	D2	53	yes	3.0 + 0.8 (5.8)	4.2 + 0.6 (2.6) for D3	North Europe, Russia, Japan (Ehime)	269,276–278
	D3	66	yes	2.9 + 1.1 (5.9)	4.1 + 0.7 (2.3) for D1	South Africa, Europe	
	D4	7	yes	2.6 + 1.2 (4.9)	4.6 + 0.6 (3.5) for D1	Australia	256
	D5	2	yes	2.4	5.2 + 0.5 (4.9) for D4	Eastern India	73
HBV/F							
	F1a	4		1.1 + 0.2 (1.4)	2.0 + 0.2 (1.6) for 1b	Central America: Costa Rica	279,280
	F1b	7		0.4 + 0.1 (0.6)	1.9 + 0.3 (1.5) for 1d	Venezuela, Argentina, Alaska	154,279,281,282
	F1d	2		2.2	2.8 + 0.3 (2.4) for 1a	Japan	279,281
	F2a	9		1.1 + 0.3 (1.4)	3.2 + 0.2 (2.8) for 2b	Brasil, Venezuella, Nicaragua	24,154
	F2b			0.5 + 0.1 (0.6)	4.1 + 0.9 (2.8) for F4		
	F3	23	yes	1.1 + 0.9 (4.2)	4.5 + 0.3 (3.9) for F2	Venezuella	
	F4	6		1.9 + 0.9 (3.7)	4.6 + 0.6 (3.8) for F3	Argentina, Bolivia	142

Türkiye'de HBV epidemiyolojisi

- Orta endemisite
  - HBsAg (+): %2-8
  - Anti-HBs (+): %30
- Aile içi bulaş var.
- Genotip D baskın
- Kronik HBV infeksiyonları
  - %70'i HBeAg negatif
  - HDV ko/super infeksiyon 5%-46%

Table 1 Prevalence of hepatitis B virus in Turkey compared with countries where vertical transmission is the main route

Group	Countries with vertical transmission	Turkey
HBsAg carrier	>10%	2–10%
Anti-HBs (+)	70%	30–50%
Pregnant HbsAg (+)	50%	4%
Pregnant HBeAg	20%	7%
Children HBsAg	20%	4%
Children anti-HBs	50%	15%
Children HCC	Frequent	Very rare
Chronic liver disease	Young adults	Middle aged adults
HBV genotype	A and E	D

Public Health (2008) 122, 1315–1317

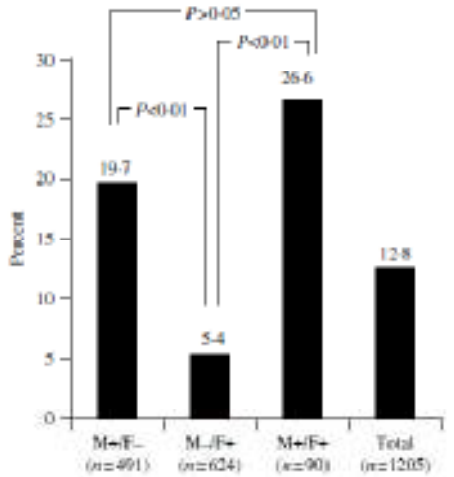


Fig. 3. HBV infection in the family and children according to HBsAg status of the parents (M, mother; F, father). ■, HBsAg(+) children (*n* = number

Epidemiol. Infect. (2007), **135**, 1338–1343.

HBV genotipleri [1]

Yayın	Olgu sayısı	Çalışma grubu	Genotipleme yöntemi	Sonuç
Bozdayı AM, et al. J Clin Virol 2001; 21: 91	67	Chronic HBV	Pre-S amp & direct seq	All genotype D (ayw)
Bozdayi AM, et al. J Viral Hepat 2003; 10: 256	31	Chronic HBV	Pre-S amp & direct seq	All genotype D (ayw)
Bozdayi AM, et al. Arch Virol 2004; 149: 2115	59	Patients from previous clinical studies (n=41) + Azerbaijan pts (n=6)+ Uzbek pts (n=12)	Pre-s and s gene amp & direct seq	All genotype D except 2 Uzbek pts who were infected w genotype A
Şentürker-Güldaş N, et al. Infection 2004; 32: 344	23	Chronic HBV	S gene amp & direct seq & REA	All genotype D (ayw2)-
Leblebicioglu H, et al. Clin Microbiol Infect 2004; 10: 537	158	Acute HBV	Pre-S amplification and REA	D2 (n=122), D1 (n=5) and D2 + del (n=2)
Yalcin K, et al. Infection 2004; 32: 24	44	Chronic HBV (n=32) & inactive HBsAg carriers (n=12)	S gene ampl & direct sequencing	All genotype D
Eroglu C et al J Virol Meth 2004; 119: 183	60	Acute (n=40) and Chronic HBV (n=20)	Detection of 33 bp deleton in pre-s region	All genotype D

HBV genotipleri [2]

Yayın	Olgu sayısı	Çalışma grubu	Genotipleme yöntemi	Sonuç
Bozdayı G, et al. J Med Virol 2005; 76: 476	11	Treatment-naive chronic HBV pts	Full genome sequencing	D1 (ayw2) (n=10) D2 (ayw3) (n=1)
Sunbul M, et al. World J Gastroenterol 2005; 11: 1976	78	Chronic HBV	Pre-s amplif & REA	D2 (n=67), D2+del (n=7), D1 (n=3), D3 (n=1)
Serin MS, et al. Diagn Microbiol Infect Dis; 2005; 53: 57-60	50	Chronic HBV	S gene amplified & sequenced	All genotype D
Özdemir FT, et al. Turk J Gastroenterol 2005; 16: 183	54	Pediatric & adult Chronic HBV	Pre-s amplification + REA	D2 (n=44), D1 (n=7) and D6 (n=3)
Aksoy A et al. Mikrobiyol Bul 2006; 40: 215	127	HBV DNA positive samples	S gene amp and REA	All genotype D
Akarsu M et al J Gastro Hepatol 2006; 21: 1783	21	Inactive HBsAg carriers	S gene amplified and sequenced	Allt type D

HBV genotipleri [3]

Yayın	Olgu sayısı	Çalışma grubu	Genotipleme yöntemi	Sonuç
Özaslan M et al. J Genet 2007; 86:195	40	Chronic HBV	S gene amplified and sequenced	Allt type D and ayw3
Ozgenc O. Hepato-gastroeneterology 2007; 54: 2319	44	Naive chronic HBV	S gene amplified and sequenced	Allt type D
Sertoz RY, et al. New Microbiol 2008; 31: 189	54	Chronic HBV	S gene amplified and sequenced OR REA	Allt type D
Sayan M et al J Viral Hepat 2009; Jun 28	88	Chronic HBV	S gene amp &direct seq	Allgenotype D
Pinarbasi B, et al. Liver Int 2009; 29: 227	13	Occult HBV in female sex workers	S gene amp &direct seq	Allgenotype D

ORIGINAL ARTICLE 10.1111/j.1469-0691.2004.00871.x

Acute hepatitis B virus infection in Turkey: epidemiology and genotype distribution

H. Leblebicioglu, C. Eroglu and members of the Hepatitis Study Group

Clin Microbiol Infect 2004; 10: 537–541

- 22 merkezden HBsAg ve Anti HBc IgM (+) örnekler (n=158)
- Pre-S bölgesi çoğaltılıp REA ile tiplendirildi
- **D2 (n=122), D1 (n=5) ve D2 + del (n=2)**

Characteristics	Patients		
	Total $n = 158$	HBeAg-positive $n = 74$	Anti-HBeAg-negative $n = 60$
Age (years)	34.2 ± 15.6	33.9 ± 15.4	32.9 ± 15.4
Female/male	59:99 (0.59)	29:45 (0.64)	19:41 (0.46)
Probable transmission route			
Unknown	78 (49.4%)	36 (48.7%)	32 (53.3%)
Blood contact	65 (41.1%)	28 (37.8%)	25 (41.7%)
Heterosexual	13 (8.2%)	9 (12.2%)	2 (33%)
Horizontal	2 (1.3%)	1 (1.3%)	1 (17%)
ALT (IU/L)	1718 ± 1089	1772.7 ± 1052.2	1651.8 ± 1113.4
AST (IU/L)	1266 ± 806	1337 ± 798.3	1171.3 ± 751.7
Total bilirubin (mg/dL)	11.3 ± 7.8	11.3 ± 7.7	10.6 ± 7.7
Died	4	2	2

There was no significant difference for all parameters between HBeAg-positive and anti-HBeAg-negative patients ($p > 0.05$).
ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Complete Genome Sequence and Phylogenetic Analysis of Hepatitis B Virus Isolated From Turkish Patients With Chronic HBV Infection

Journal of Medical Virology 76:476–481 (2005)

Gülendam Bozdayi,[1]* A. Resat Türkyilmaz,[2] Ramazan Idilman,[3] Ersin Karatayli,[2] Seyyal Rota,[1] Cihan Yurdaydin,[2,3] and A. Mithat Bozdayi[2,3]

- 11 tedavi-naif hasta [yaşları 11-54 (ort 35)]
- Tüm genom TA vektörüne klonlandı.
- Doğrudan dizileme

Pt	GenBank accession number	HBV DNA Length (nt)	Deletion (nt)	Genotype	Subtype X02496
1	AY721605	3182	No	D1	*ayw2*
2	AY721606	3182	No	D1	*ayw2*
3	AY721607	3182	No	D1	*ayw2*
4	AY721608	3182	No	D1	*ayw2*
5	AY721609	3182	No	D1	*ayw2*
6	AY721610	2999	183 (in pre-S)	D1	*ayw2*
7	AY721611	3182	No	D1	*ayw2*
8	AY721612	3182	No	D1	*ayw2*
9	AY796030	3182	No	D1	*ayw2*
10	AY796031	3182	No	D2	*ayw3*
11	AY796032	3182	No	D1	*ayw2*

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Surface gene codon number									
69 C	122 R	125 T	127 P	134 Y	160 K	195 V	pc71	Core promoter mutations nt_RNApc A(-26)T, nt_RNApc G(-24)T	Pre-core stop codon mutations nt_pcG83A, nt_pcG86A
—	—	—	—	—	—	—	T	No	No
—	—	—	—	—	—	—	T	No	No
—	—	—	—	—	—	—	T	No	No
—	—	—	—	—	—	—	T	nt_RNApc A(-26)T	No
Stop Codon	—	—	—	—	—	—	T	No	No
Stop Codon	—	—	—	—	—	—	T	No	No
Stop Codon	—	—	—	—	—	—	T	nt_RNApc A(-26)T nt_RNApc G(-24)T	No
—	—	—	—	—	—	—	T	No	No
—	—	—	—	—	—	—	T	No	nt_pcG83A
—	—	—	T	—	—	—	T	nt_RNApc A(-26)T nt_RNApc G(-24)T	No
—	—	—	—	—	—	—	T	nt_RNApc A(-26)T nt_RNApc G(-24)T	nt_pcG83A

Türkiye'deki ilk genotip A infeksiyonu

- Midilli K, et al. *The first report of genotype A of hepatitis B in Turkish population.* 12th Annual ESCV Meeting, İstanbul-Turkey, 27-30 September 2009, PVI-19
  - Aynı hastanede hematolojik malignansileri nedeniyle tedavi alan 3 hasta (nozokomiyal infeksiyon?)
  - 1 tam dizi
  - Tümü A1

Molecular epidemiology of hepatitis B, C and D viruses in Turkish patients

Arch Virol (2004) 149: 2115–2129

A. M. Bozdayı[1,2], N. Aslan[1], G. Bozdayı[3], A. R. Türkyılmaz[1], T. Sengezer[1], U. Wend[4], Ö. Erkan[1], F. Aydemir[1], S. Zakirhodjaev[1], Ş. Orucov[1], H. Bozkaya[2], W. Gerlich[4], S. Karayalçın[2], C. Yurdaydın[1,2], and Ö. Uzunalimoğlu[1]

Table 2. Patients' characteristics and methods used for genotype, type and subtype determination and the results

Virus	Patients	Number of the patients	Age (years; mean ± SD)	Sex (female/male)	Method	genotype (genotype:n:%)	subtype (subtype:n:%)
HBV	HBsAg (+) donors	83	37 ± 12	(25/58)	Multiplex PCR	–	*ayw*:82:99% ID*:1:1%
	HBsAg (+) donors	71	32 ± 16	(22/49)	ELISA	–	*ayw*:70:99% ID*:1:1%
	Chronic B hepatitis	41	37 ± 11	(9/32)	Direct Sequencing (Pre-S and S gene)	D:41:100%	*ayw2*:41:100%
	Azerbaijani HBsAg (+) patient	6	–	–	Direct Sequencing (Pre-S gene)	D:6:100%	–
	Uzbek HBsAg (+) patient	12	–	–	Direct Sequencing (Pre-S gene)	D:10:83% A:2:17%	–

Naturally Occurring MHR Variants in Turkish Patients Infected With Hepatitis B Virus

A. Arzu Sayiner,[1]* Ayla Özcan,[2] and Aylin Sengonul[1]

Journal of Medical Virology 80:405–410 (2008)

TABLE I. HBsAg Subtypes of the Study Population

		HBsAg—amino acid number				
Sample code[a]	HBsAg subtype	122	127	134	159	160
A1, A2, A4–34, A36–41 B1–3, B5–7, B9–13, B15, B16, B18–24, B26–31, B33–39	ayw2	Arg	Pro	Tyr	Gly	Lys
A35 B4, B8, B14, B25, B32, B40	ayw3	Arg	Thr	Tyr	Gly	Lys
A3	ayw4	Arg	Leu	Tyr	Gly	Lys

[a]Group A, inactive carriers; Group B, chronic hepatitis B patients.

HBsAg subtipleri

(serolojik)

ayw baskın

Table 1. Distribution of HBsAg subtypes in four provinces in Turkey

		n	Subtype			
			ayw	*adw*	*a-x*[1]*-w*	*ay-x*[1]
Total		129	113	2	5	9
Surveillance	Samsun	7	5	0	1	1
	Antalya	8	7	0	1	0
	Diyarbakir	22	20	1	0	1
	Subtotal	37	32	1	2	2
Clinical laboratory	Ankara	92	81	1	3	7
Sex	Male	83	71	1	4	7
	Female	42	38	1	1	2
	UK[2]	4	4	0	0	0
Age (years)	<10	5	5	0	0	0
	10s	6	4	1	0	1
	20s	27	24	0	1	2
	30s	38	36	0	0	2
	40s	16	14	0	1	1
	50s	12	11	0	1	0
	≥ 60	9	6	1	0	2
	UK[2]	16	13	0	2	1

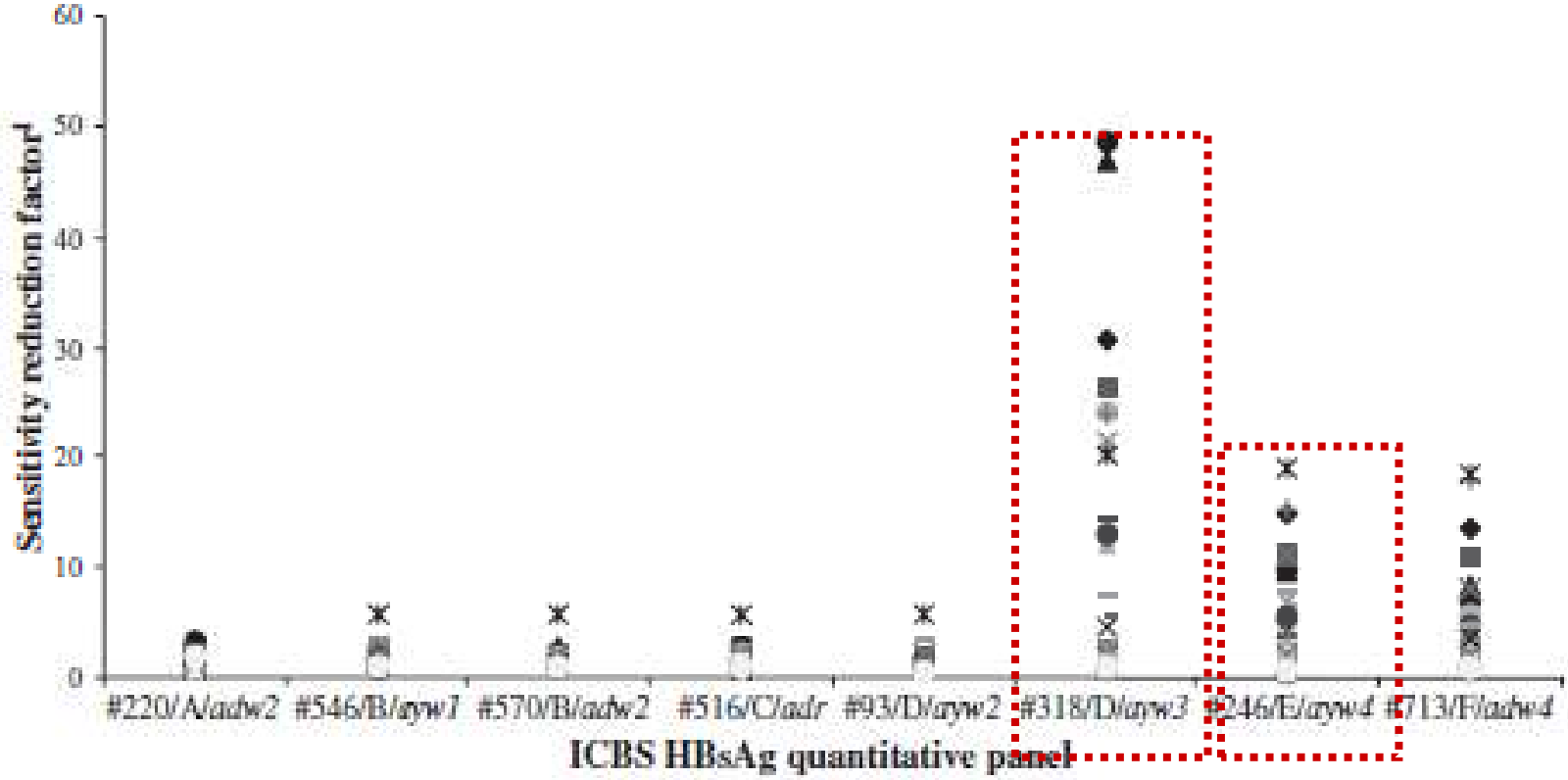
Table 1
Geographical distribution of HBV genotypes and relationship between genotype and serological subtypes

Genotype	Serological subtype	Geographical distribution
A	*adw2*, *ayw1*	NW Europe, US, Central Africa, India
B 1	*adw2*	Indonesia, China
B 2	*ayw1*	Vietnam
C	*adw2*	East Asia
	adrq+	Korea, China, Japan, Taiwan
	adrq-, *ayr*, *adr*	Polynesia, Korea, China, Japan, Australia, USA, Vietnam
D	*ayw2*, *ayw3*	Mediterranean area, Middle East
	ayw4	India, Russia, USA
E	*ayw4*	West Africa
F	*adw4q-*	Polynesia, USA (rare)
	adw2, *ayw4*	Central and South America
G		Europe, USA (rare)
H	*adw4*	Central and South America

Journal of Clinical Virology 32 (2005) 102–112

Yalcinkaya KT, et al. Jpn J Infect Dis 2005; 58: 120-122

Geno/serotiplerin HBsAg testleri üzerine etkisi



Vox Sanguinis (2010) 98, 403–414

Diagnostic Impact of the Genetic Variability of the Hepatitis B Virus Surface Antigen Gene

Journal of Medical Virology 78:S59–S65 (2006)

Bernard Weber*

Laboratoires Réunis Junglinster, Luxemburg und Institut für Medizinische Virologie, Universitätskliniken Frankfurt, Frankfurt, Germany

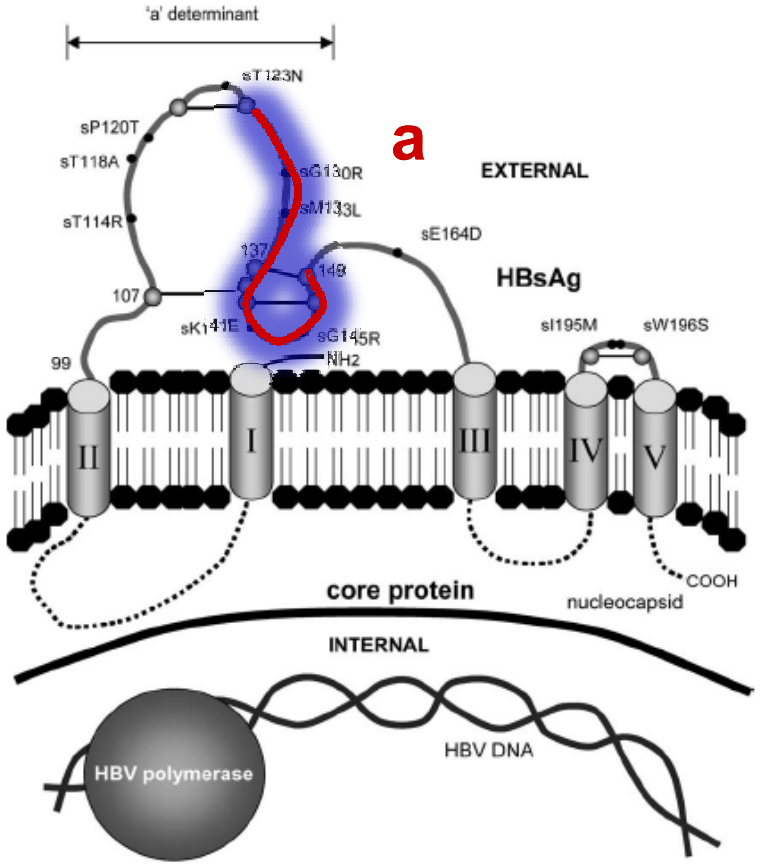
TABLE I. Results of Commercial Immunoassays With Wild Type and Mutant Recombinant HBsAg

		Results of HBsAg assays (number tested positive/total number tested)				
HBsAg mutant/configuration	Subtype	Assay A	Assay B	Assay C	Assay D	Assay E
Recombinant	ayw3	12/12	12/12	8/12	10/12	8/12
	adw2	9/9	9/9	9/9	8/9	4/9
	adw	4/4	4/4	4/4	4/4	4/4
	ady	2/2	2/2	2/2	2/2	2/2
Total recombinants		27/27	27/27	23/27	24/27	18/27
Naturally occurring mutants—diluted samples		10/10	7/10	7/10	5/8	2/10
Naturally occurring mutants—undiluted samples		4/4	4/4	4/4	4/4	3/4
Total		41/41	38/41	34/41	33/39	23/41

TABLE II. Results of Commercial Immunoassays With *adw2* Wild Type and Mutant Recombinant HBsAg Described in Table I

	HBsAg assay (index (signal/cut-off) and % signal in comparison to wild type)									
	Assay A		Assay B		Assay C		Assay D		Assay E	
HBsAg mutant/configuration	Index	%	Index	%	Index	%	Index	%	Index	%
wild-type adw2	5.1		8.6		4.0		15.0		7.8	
adw2-T126S	4.2	82	11.8	137	3.6	88	13.0	87	8.6	111
adw2-Q129H	3.7	73	11.6	135	3.2	80	12.0	92	7.2	93
adw2-M133L	4.2	82	13.3	155	3.1	76	11.0	92	7.0	90
adw2-D144A	3.3	64	8.8	102	2.3	57	5.0	45	5.4	69
adw2-G145R	3.3	65	5.6	65	2.5	61	3.0	60	0.5	6
adw2-T126S + G145R	3.1	60	4.8	56	2.3	57	2.2	15	0.5	6
adw2-P142L + G145R	3.4	67	8.4	98	2.7	66	2.7	18	0.5	6
adw2-P142S + G145R	3.6	70	6.7	78	2.9	72	3.7	25	0.5	6
adw2-D144A + G145R	2.9	57	1.7	20	1.7	41	0.7	5	0.5	6

MHR: *Major Hydrophilic Region*



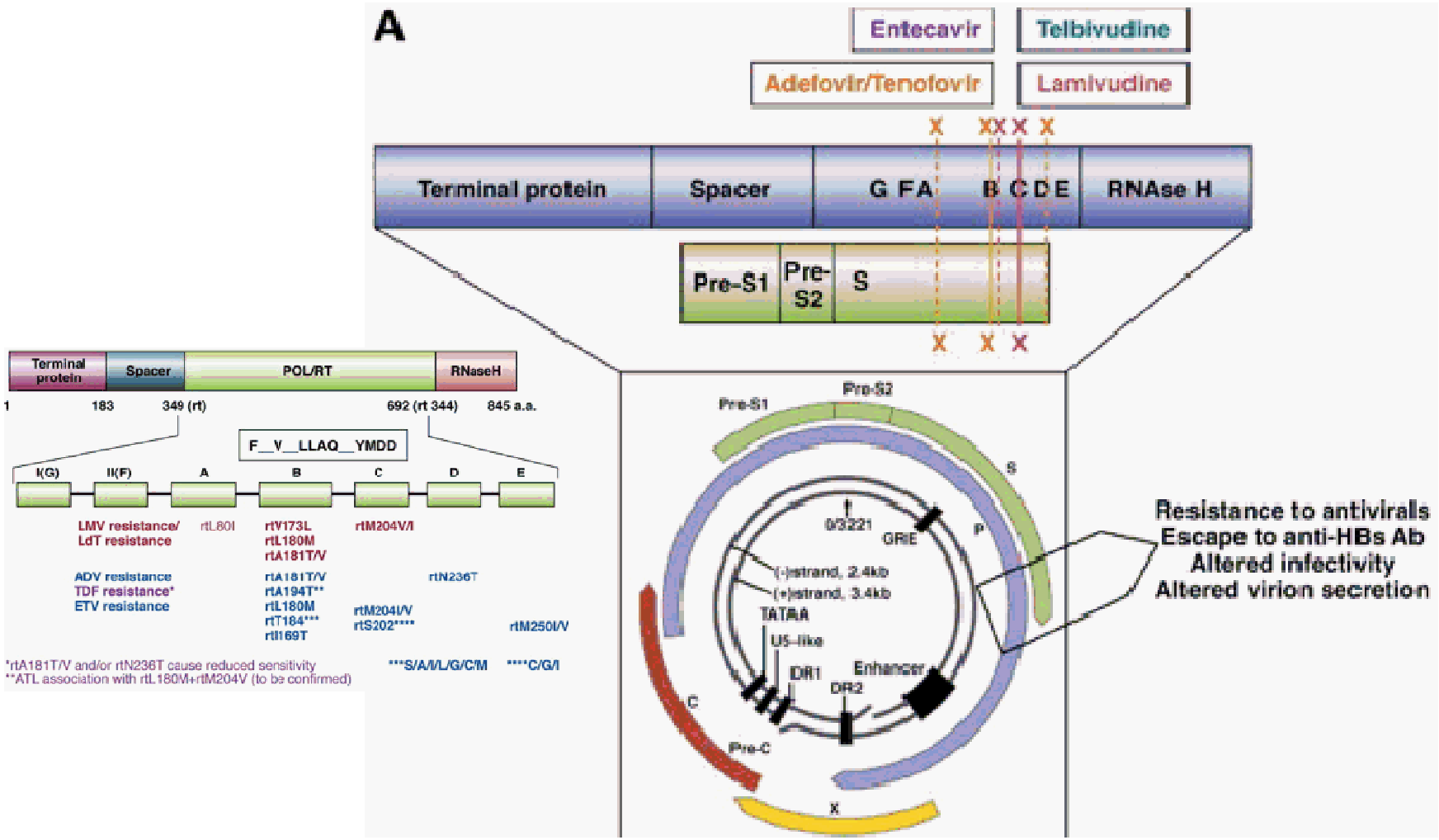
- MHR: 100-160 aa
  - HBs I: 120 öncesi
  - HBs II: 120-123
  - HBs III: 124-137
  - HBs IV: 139-147
  - HBs V: 148-169

a

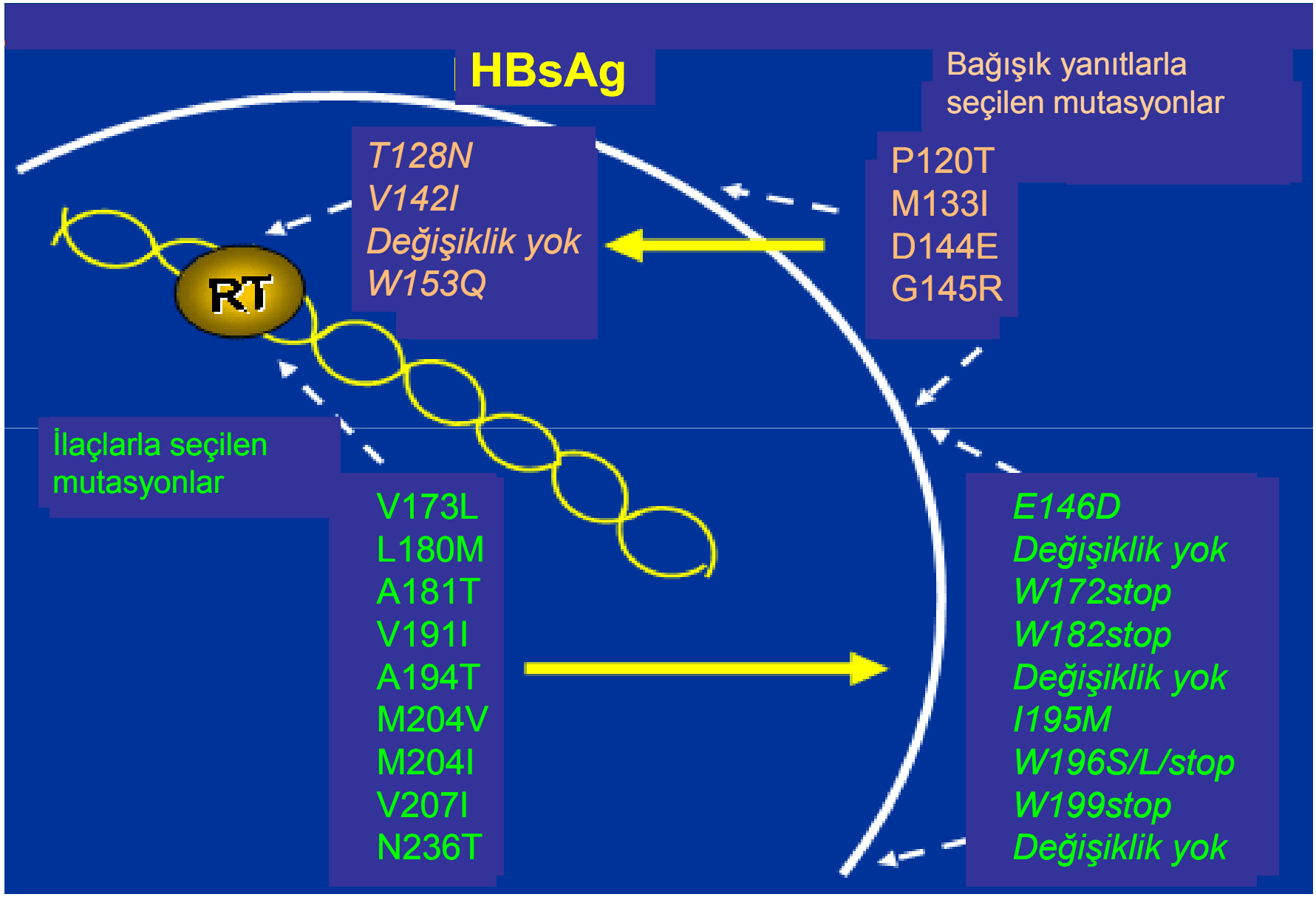
www.brown.edu
Carman WF, J Viral Hepatit 1997
Roosmalen MH et al, Intervirology 2006

Aşılama ve tedaviye bağlı kaçış mutantları

Pol ve s genleri binişiktir…



Pol ve s gen mutasyonları karşılıklı etkileşir…



Naturally Occurring MHR Variants in Turkish Patients Infected With Hepatitis B Virus

A. Arzu Sayiner,[1]* Ayla Özcan,[2] and Aylin Sengonul[1]

Journal of Medical Virology 80:405–410 (2008)

		Antigenic regions of MHR													
		HBs1					HBs2	HBs3				HBs4			
Sample code	HBsAg subtype	101	104	110	113	118	120	125[a]	127	129	136	140	142	143	144
Reference seq. AY796032	ayw2	Gln	Leu	Ile	Ser	Thr	Pro	*Thr*	*Pro*	*Gln*	*Ser*	*Thr*	*Pro*	*Ser*	*Asp*
A11	ayw2						Thr/Pro								
A16	ayw2												*Thr*		
A35	ayw3					Ala									
A38	ayw2	Arg													
A40	ayw2									*His*					
B1	ayw2	Arg													
B3	ayw2						Thr								
B4	ayw3					Ala									
B6	ayw2					Lys									
B9	ayw2	His													
B13	ayw2	Lys									*Ala*				
B14	ayw3							*Met*							
B17	ayw2					Ala			*Ala*						
B18	ayw2													*Leu*	
B20	ayw2			Leu											
B22	ayw2		Trp												
B25	ayw3					Ala									
B31	ayw2			Leu											
B32	ayw3	His			Thr			*Met*							
B35	ayw2														*Glu*
B38	ayw2											*Ile*			
B40	ayw3					Ala									
Number of substitutions at the position (total: 26)		5	1	2	1	6	2	2	1	1	1	1	1	1	1

Monitoring of hepatitis B virus surface antigen escape mutations and concomitantly nucleos(t)ide analog resistance mutations in Turkish patients with chronic hepatitis B

International Journal of Infectious Diseases 14S (2010) e136-e141

M. Sayan[a,*], Ö. Şentürk[b], S.Ç. Akhan[c], S. Hülagü[b], M.B. Çekmen[d]

Characteristics of HBsAg escape mutation-positive subjects and concomitant nucleos(t)ide analog resistance mutations

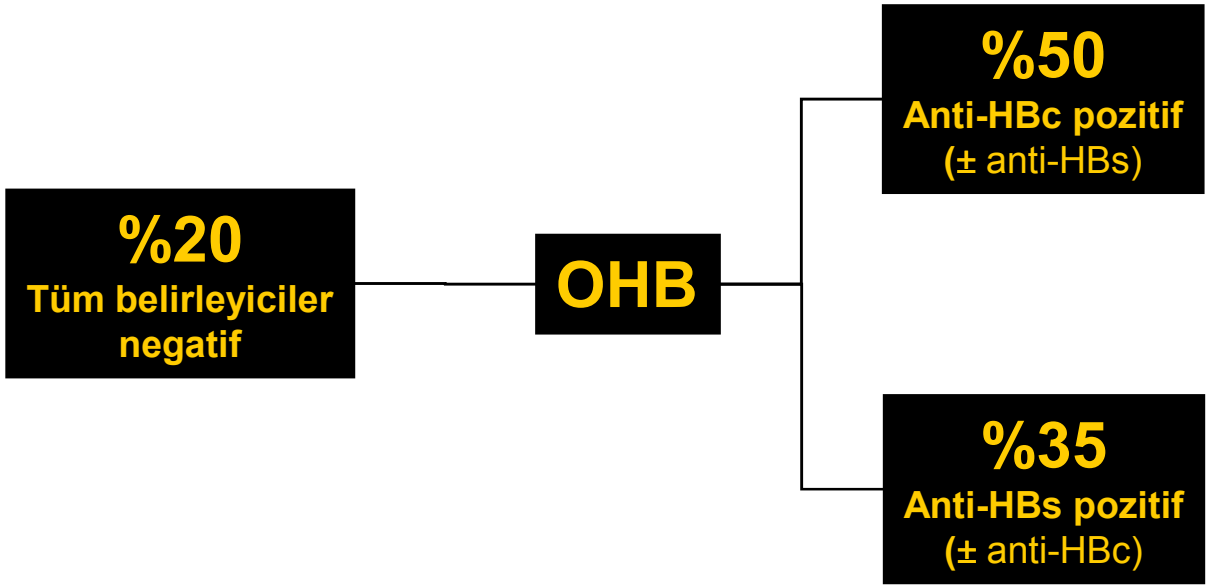
Patient	Gender, age (years)	Treatment status	Typical HBsAg escape mutation	Nucleos(t)ide analog resistance mutation	Compensatory mutation	Drug resistance
1	Male, 52	Treatment-naive	sL109I	rtA181V[a]	-	LAM, ADV
2	Female, 36	Treatment-naive	sI110V	-	-	-
3	Female, 64	Treatment-naive	sI110V	-	-	-
4	Female, 54	Treatment-naive	sI110V		rtA194V, rtQ215H	-
5	Female, 44	Treatment-naive	sS117INST	-	-	
6	Female, 25	Treatment-naive	sP12(			LAM, LdT
7	Male, 76	Treatment-naive	sP12			ADV
8	Female, 52	Treatment-naive	sP12			-
9	Female, 36	Treatment-naive	sP12			-
10	Male, 55	Treatment-naive	sP12			ADV
11	Male, 48					-
12	Female,					-
13	Female,					LAM, LdT
14	Male, 56					ADV
15	Male, 26					TDF
16	Male, 55					LAM, ADV
17	Male, 53	LAM, 6 months	sL109I	rtA181V	-	LAM, ADV
18	Male, 35	LAM, 18 months	sP120T	rtL180M + rtM204I[b]	-	LAM, LdT
19	Female, 38	ETV, 3 months	sP127I[b]	rtM204I[b]	-	LAM, LdT
20	Male, 32	LAM, 36 months	sS132A + sY134N	rtL180M + rtS202C + rtM204V	rtV214P	ETV
21	Male, 44	ADV, 48 months ADV + LAM, 12 months	sY134N + sG145R	rtI233V	rtN236S	ADV
22	Female, 32	LAM, 36 months ADV, 24 months	sG130R + sG145X	rtA181V	-	LAM, ADV
23	Female, 41	ADV, 12 months	sC137G	rtL180M + rtM204I, rtI233S	rtL180V	LAM, LdT, ADV
24	Male, 53	LAM, 24 months	sD144E	rtL180M + rtM204V	rtL80F	LAM
25	Male, 14	LAM, 24 months	sD144E	rtQ215S	rtQ215P	ADV
26	Male, 42	ADV, 48 months ADV + LAM, 12 months	sG145R	rtN236T[c]	-	ADV
27	Male, 76	LAM, 1 month	sG145R	-	-	-

mutasyonlar

	HBsAg	NUC direnç
142 NUC tedavisi alan	12/142 (%8.5)	11/142 (%7.7)
185 tedavi naif	15/185 (%8.1)	7/185 (%3.3)

Okült Hepatit B (OHB)

- Yalancı OHB: *HBsAg mutantlarına bağlı yalancı negatiflik*
- Gerçek OHB
  - *OHB'li olgularda ortanca HBV DNA değeri ~5-10 IU/mL (~ 32-62 kopya/mL).*
  - *Olguların %95'de 200 kopya/mL (~30-40 IU/mL) altında.*



ELSEVIER

Journal of Hepatology 38 (2003) 506–510

www.elsevier.com/locate/jhep

Occult HBV infection and YMDD variants in hemodialysis patients with chronic HCV infection

Fatih Besisik[1,*], Çetin Karaca[1], Filiz Akyüz[1], Sibel Horosanlı[2], Derya Önel[2], Selim Badur[2], Mehmet Şükrü Sever[3], Ahmet Danalıoğlu[1], Kadir Demir[1], Sabahattin Kaymakoğlu[1], Yılmaz Çakaloğlu[1], Atilla Ökten[1]

12/33= %36.4

Table 2
Patients' clinical features and results

	Occult HBV infection positive (n = 12)	Occult HBV infection negative (n = 21)	Total group (n = 33)	*P*
Age (mean (range), years)	33 ± 9.0 (20–53)	39.1 ± 10.6 (22–60)	36.9 ± 10.4	> 0.05
Gender (female:male)	3:9	8:13	11:22	
ALT (mean (range), IU/l)	116.8 ± 85.9 (56–312)	145.6 ± 146.6 (60–594)	137.0 ± 125.2	> 0.05
Dialysis period (mean (range), years)	5.1 ± 3.5 (1–15)	4.6 ± 2.8 (2–11)	4.8 ± 3.1	> 0.05
Isolated antiHBs seropositivity	4 (33.3%)	10 (83.3%)	14 (42.4%)	
Isolated antiHBc IgG seropositivity	0	1 (4.7%)	1 (3%)	
AntiHBs and antiHBcIgG(+)	5 (41.6%)	7 (33.3%)	12 (36.3%)	
AntiHBs and antiHBcIgG(−)	3 (25%)	3 (14.2%)	6 (18.2%)	
HBV DNA(PCR), *n* (%)	12 (100%)	0 (0%)	12 (36.4%)	

***Conclusions*: Occult HBV infection is frequent in hemodialysis patients with chronic HCV infection. YMDD variants are common in this setting.**

Aşı kaçış mutantları

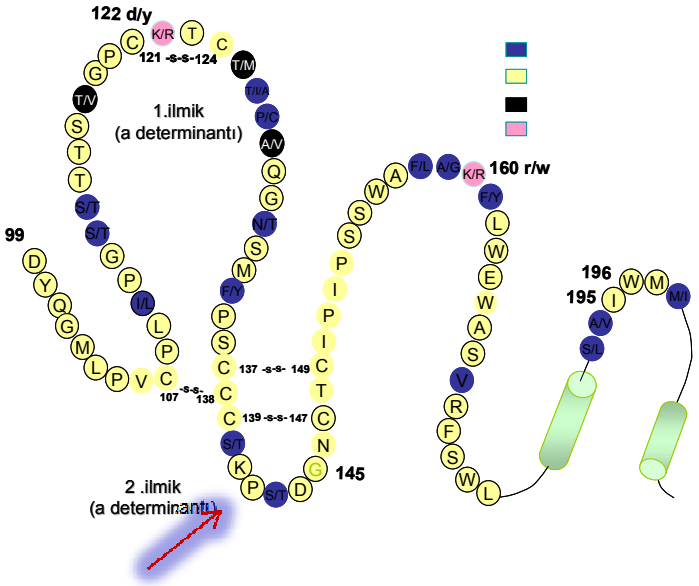
Yenidoğan döneminde 3 kez aşılanmış 3,5 yaşında ALL'li hasta

The first identified hepatitis B virus vaccine escape mutation in Turkey

Journal of Clinical Virology 35 (2006) 201–202

Tufan Kutlu [a]
Lebriz Yüksel Soycan [b]
Ersin Karaaylı [c]
Ahmet Reşat Türkyılmaz [c]
Cihan Yurdaydın [c,d]
A. Mithat Bozdayı [c,d,*]

kit, Invitrogen, USA). Ten clones were sequenced by using cycle sequencing on an automatic analyzer (ABI, USA). The sequence of eight clones yielded the most common vaccine escape mutation pattern, glycine to arginine change at codon 145 (G145A). One clone displayed a sequence change at codon 142 from proline to serine (P142S). There was a dual amino acid change in just 1 clone; P142S + threonine to stop codon at codon 143 (T143stop codon). The last pattern seems to be a novel vaccine escape mutation pattern.



Aşı kaçış mutantları

aa 101 aa 130

AY721605 CAAGGTATGTTGCCCGTTTGTCCTCTAATTCCAGGATCTTCGACCACCAGCACGGGACCATGCAGAACCTGCACGACTCCTGCTCAAGGA

Q G M L P V C P L I P G S S T T S T G P C R T C T T P A Q G

HBVFA ..C.....A.....A..T....A..G.....A.....

H G M L P V C P L I P G S S T T N R G Q C R T C T T P A Q G

S143L ("*a*" determinant)

AY721605 ACCTCTATGTATCCCTCCTGTTGCTGTACCAAACCTTCGGACGGAAATTGCACCTGTATTCCCATCCCATCATCCTGGGCTTTCGGAAAA

Table 2

HBV HBsAg results of the serum sample by different commercial assays

Assay name	Axsyme, Abbott	Architect, Abbott	Liaison, DiaSorin	Vitros, Ortho
AY Assay format (capture antibody/detection antibody)	monoclonal/polyclonal	monoclonal/polyclonal	Three monoclonals/ polyclonal	monoclonal/monoclonal
Result	Positive (S/CO: 119)*	Positive (>250 IU/mL)	Positive (S/CO: >225)*	Negative

HBV * S/CO: sample signal/cutoff.

F L W E W A S A R F S W L S L L V P F V Q W F V G L S P T V

aa 161 aa 190

the detection of HBsAg (Cooreman et al., 2001). HBsAg 'a' determinant (amino acids 124–147) is located within the major hydrophilic region (MHR, amino acids 99–169) of the S protein (Carman, 1997). Mutations within 'a' determinant

A new hepatitis B virus vaccine escape mutation in a renal transplant recipient

A. Arzu Sayiner[a,*], Harun Agca[b], Aylin Sengonul[a], Ali Celik[c], Mesut Akarsu[d]

Journal of Clinical Virology 38 (2007) 157–160

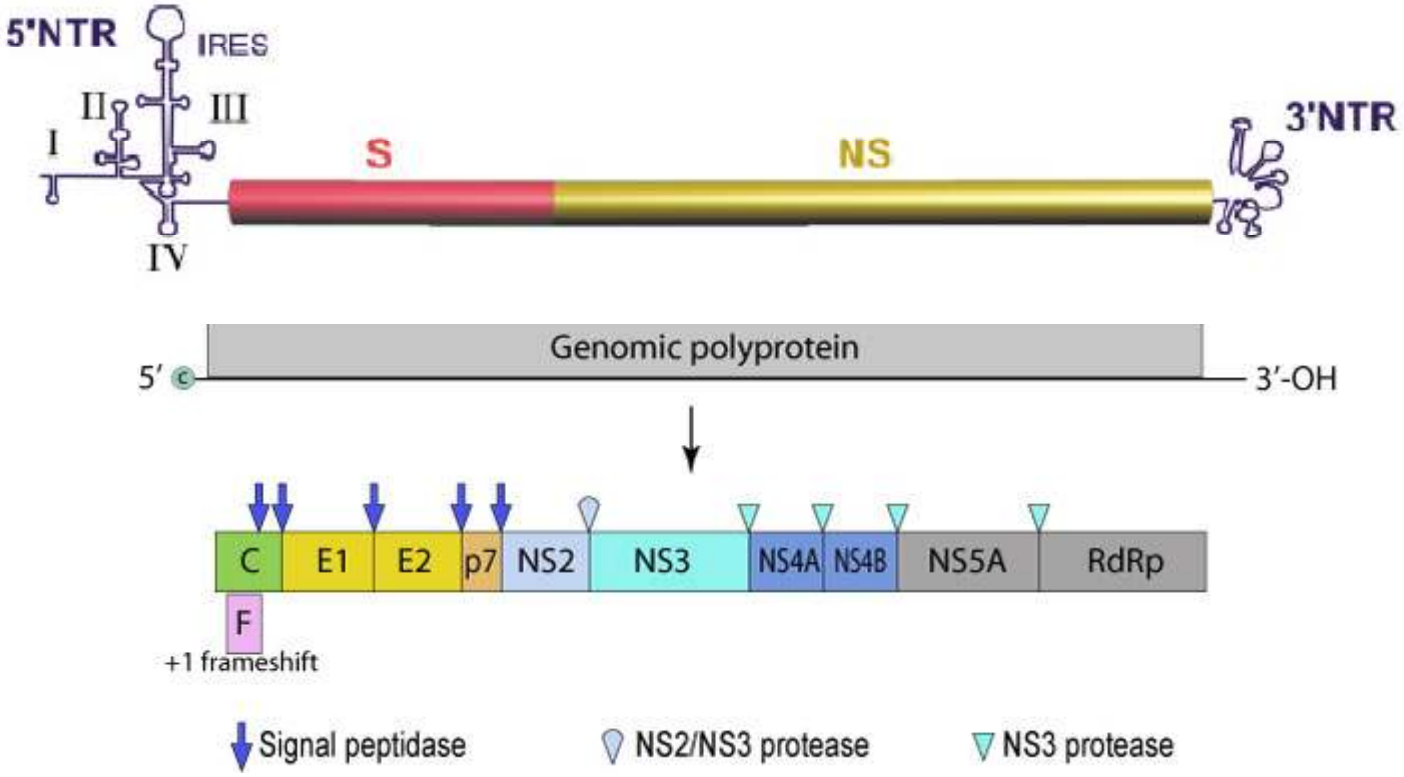
HBV: *sonuçlar*

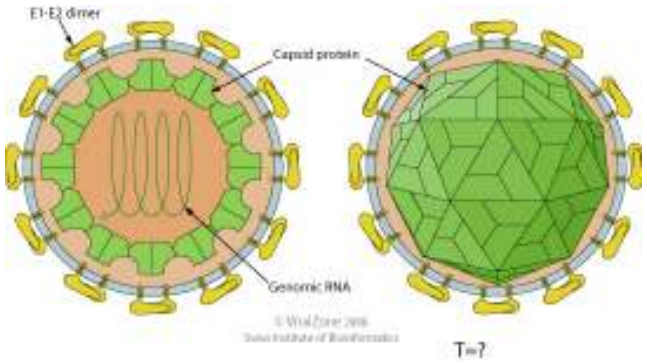
- Genotype D baskın(*D1 ağırlıklı) ancak diğer genotipler de* (A1 ve B) var.
- HBsAg subtip ayw baskın
  - *ayw2 baskın ancak ayw3 ve çok ender olarak ayw4*

HBV: *sonuçlar [2]*

- “Precore” ve “core promoter” mutasyonları sık
- Tedavi-naif hastalarda MHR varyantları var.
- Gerçek OHB: *immunosüpresif hastalarda akla gelmeli.*
- Aşı kaçış mutantları var.

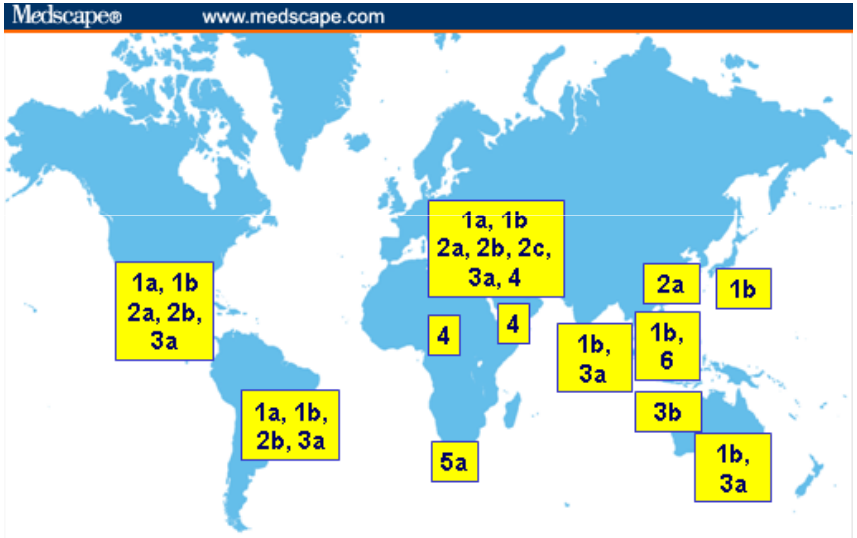
Hepatit C virus

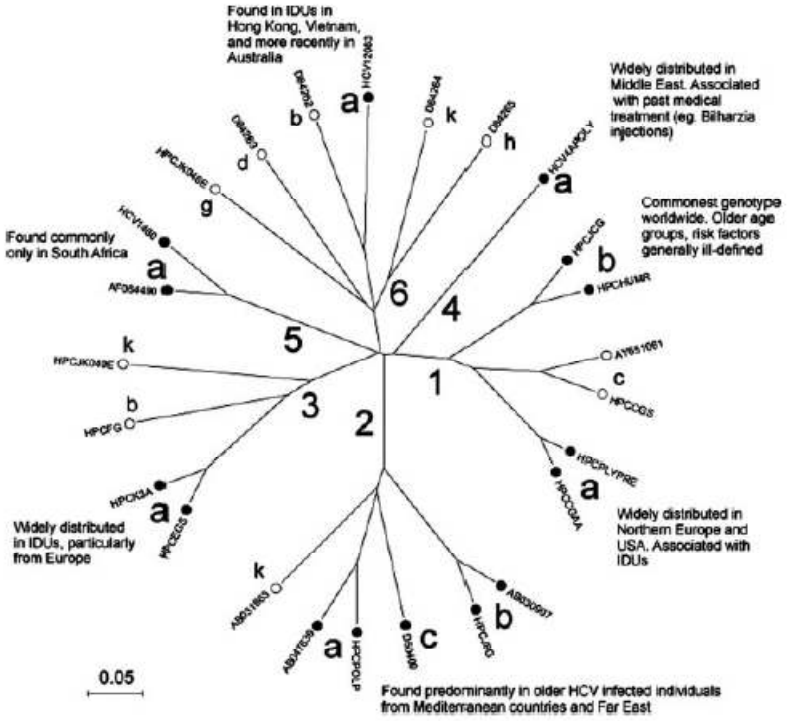




www.expasy.ch/viralzone/all_by_species/94.html

HCV genotipler





Türkiye: *HCV infeksiyonlarının temel özellikleri*

- Prevalans ~ % 1,8
  - Yaşlı populasyonda daha yüksek
- Sağlık hizmetleri ile ilişikili

TABLE 1. HEPATITIS C RISK FACTORS IN OUR GROUPS

	Patient with hepatitis C n (%)	*Control group* n (%)	p *value*
Number (M/F)	151 (76/75)	151 (76/75)	>0.05
Mean age (year)	42.9 ± 13.3	41.8 ± 14.6	>0.05
History of surgery	104 (68.9)	55 (36.4)	≤0.001
Frequent dental therapy	33 (21.9)	21 (13.9)	<0.05
Dental extraction	117 (77.5)	88 (58.3)	<0.001
Blood transfusion	32 (21.2)	3 (2)	<0.001
Multi-partner sex	19 (12.6)	0	<0.05
Circumcision (only men)	18 (23.7)	9 (11.8)	NS
Tattooing	2 (1.3)	0	NS
Acupuncture therapy	1 (0.7)	0	NS
Sharing toothbrush	4 (2.6)	1 (0.7)	NS
Sharing razor blade (only men)	3 (3.9)	1 (1.3)	NS
IV drug abuse	2 (1.3)	1 (0.7)	NS
Healthcare worker	8 (5.3)	7 (4.6)	NS

Note. NS: Nonsignificant

Digestive Diseases and Sciences, Vol. 50, No. 12 (December 2005)

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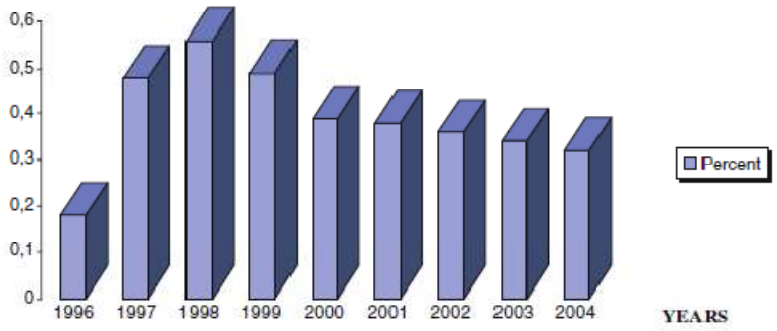


Figure 3. Trends of anti-HCV in blood donors.

RISK FACTORS FOR HEPATITIS C VIRUS IN TURKEY

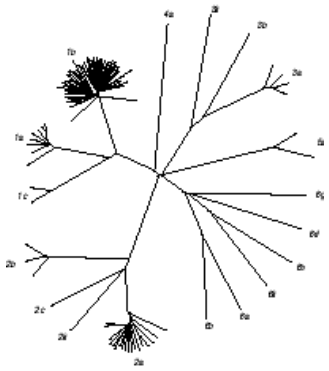
TABLE 1. EVALUATION OF THE PROBABLE RISK FACTORS INVOLVED IN HCV TRANSMISSION IN THE WHOLE GROUP

Risk factor	N	%
Surgical operation	305	98.1
History of transfusion	123	39.7
Dental procedure	86	27.5
Abortion	66	21.2
Hemodialysis	31	10
Intravenous drug abuse	10	3.1
Long-term hospitalization	10	3.1
Other*	28	8.1

*Suspected sexual contact, manicure/pedicure, common circumcision ritual, tattoo, percutaneous needle puncture.

Digestive Diseases and Sciences, Vol. 51, No. 2 (February 2006), pp. 365–369 (© 2006)

Tükiye'de HCV genotipleri (1994-2001)



		1a	1b	2	3	4	M	UT
Dusheiko et al			1					
Viazov et al			17		1			
Abacıoğlu et al		17	67	3		2		
Akkız et al		1	63					
Sönmez et al			41				3	15
Bozdayı et al		9	57	4	1	1		
Okamoto et al		2	32		3			
Bozdayı et al		2	18					
Türkoğlu et al		14	166	9	10	6	12	22
Özacar et al		17	138	4	1	2	8	
Erensoy et al		15	30					
Gökahmetoğlu et al		2	93					
TOTAL	(n=909)	79	723	20	16	11	23	37
	(%)	8,7	79,5	2,2	1,8	1,2	2,5	4,1

Türkiye'de HCV genotipleri (2001 sonrası)

Arch Virol (2004) 149: 2115–2129
DOI 10.1007/s00705-004-0363-2

Archives of Virology

Molecular epidemiology of hepatitis B, C and D viruses in Turkish patients

A. M. Bozdayı[1,*], N. Adan[1], G. Bozdayı[1], A. R. Türkyılmaz[1], T. Sungurtekin[1], U. Wand[2], O. Erkan[1], F. Aydemir[1], S. Zekiklioğlu[1], S. Ormeci[1], H. Berkoya[1], W. Gerlich[3], S. Karayalçın[2], C. Turdaydın[1,2], and O. Uzunalimoğlu[1]

Table 2. Patients' characteristics and methods used for genotype, type and subtype determination and the results

Virus	Patients	Number of the patients	Age (years; mean ± SD)	Sex (female/male)	Method	genotype (genotype:n:%)	subtype (subtype:n:%)	
HBV	HBsAg (+) donors	83	37 ± 12	(25/58)	Multiplex PCR	–	*ayw*:82:99% ID*:1:1%	
	HBsAg (+)	71	32 ± 16	(22/49)	ELISA	–	*ayw*:70:99%	
HCV	Chronic C hepatitis	365	42 ± 18	(125/240)	PCR-RFLP***	1a:43:11% 1b:306:84% 2:10:3% 3:3:1% 4:3:1%		–
	Hemodialysis patients**	36	47 ± 19	(18/18)	PCR-RFLP***	1a:8:22% 1b:28:78%		–

hepatitis

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	Hemodialysis patients**	36	47 ± 19	(18/18)	PCR-RFLP***	1a:8:22% 1b:28:78%	–

*ID: Indeterminate, **HCV RNA positive patients, ***PCR-RFLP patterns were confirmed by direct sequencing in reasonable number of the patients. Pre-S region (nt 2883 to 43) and S region (nt 284 to 760)

Türkiye'de HCV genotipleri (2001 sonrası)

Brief report

Investigation of the gen among Turkish populati countries

Table 1. Risk factors analysis of all anti-hepatitis C virus antibody positive cases

Risk factors	Group I [*n* (%)]	Group II [*n* (%)]	OR (95% CI)	*P* value
Intravenous drug abuse	56 (80.0)	3 (4.1)	19.7 (6.5–60.2)	0.000
Dental therapy	16 (22.9)	39 (52.7)	0.4 (0.3–0.7)	0.000
Surgical operation	19 (27.1)	30 (40.5)	0.6 (0.3–1.1)	0.090
Blood transfuson	8 (11.4)	19 (25.7)	0.4 (0.2–0.9)	0.029
Tattoos	28 (40.0)	8 (10.8)	3.7 (1.8–7.6)	0.000
Having spent time in prison	50 (71.4)	5 (6.8)	10.6 (4.5–25.0)	0.000
Multiple sexual partners	55 (78.6)	14 (18.9)	4.2 (2.6–6.8)	0.000
Unknown	5 (7.1)	9 (12.2)	0.6 (0.2–1.8)	0.310

Group I: Turkish patients who have lived in European countries for long periods (5–30 years); Group II: Turkish patients living in Turkey. The total numbers in Group I and Group II are 70 and 74, respectively. OR: odds ratio; CI: confidence interval.

Türkiye'de HCV genotipleri (2001 sonrası)

Distribution of hepatitis C virus genotypes in patients with chronic hepatitis C infection in Western Turkey

Imre Altuglu*, Ilknur Soyler, Tijen Ozacar, Selda Erensoy

International Journal of Infectious Diseases (2008) 12, 239–244

Table 2 Patients with uncommon hepatitis C genotypes: age, risk factors, and possible modes of transmission

Patient	Genotype	Age	Risk factors, possible modes of transmission	Origin of the patient
1	2	21	Thalassemia major, blood transfusions	Turkish
2	2	58	Dental surgery	Turkish
3	2	60	NA	NA
4	3	55	Suspected sexual contact, multiple number of surgeries	Turkish; lived and worked in Germany
5	3	26	Hemodialysis	Turkish
6	3	24	Piercing	Turkish
7	3	64	NA	NA
8	3	24	NA	NA
9	4	51	Blood transfusion	Turkish; transfusion was given in Saudi Arabia
10	4	45	Multiple surgeries, use of non-disposable sharps	Turkish; worked and lived in Iraq, Russia, and Ireland

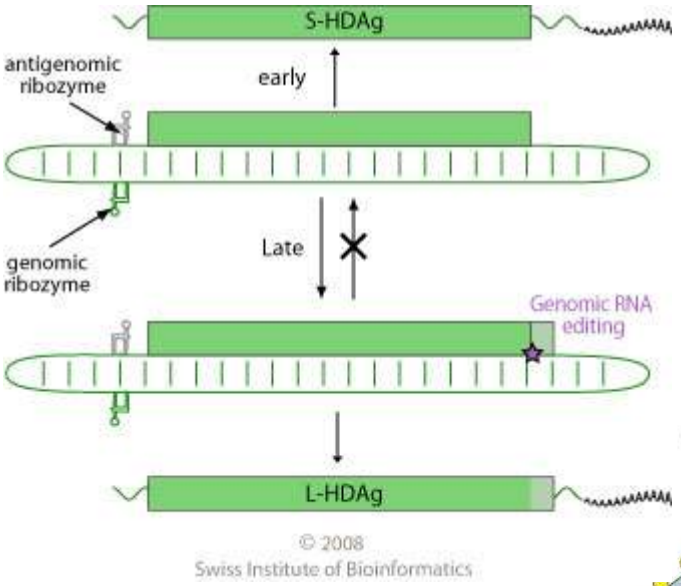
HCV, hepatitis C virus; NA, not available.

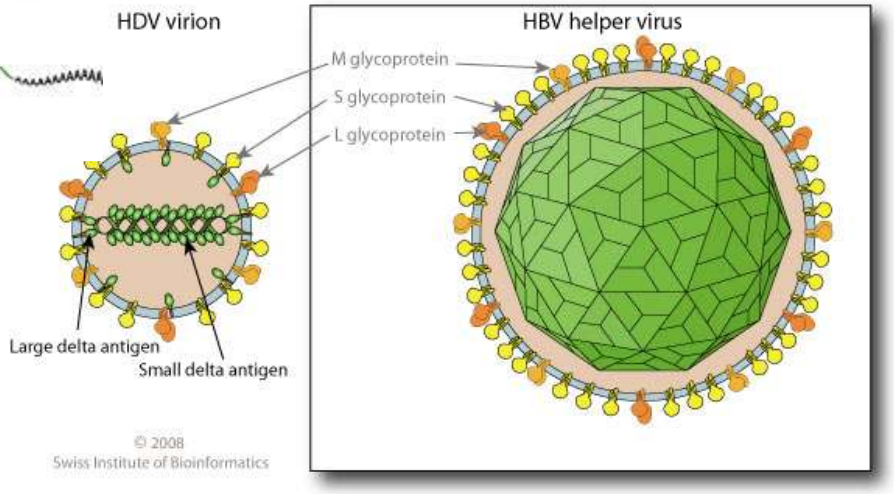
HCV epidemiyolojisi: *sonuçlar*

- Genotip 1 baskın, ancak tip 2, 3 ve 4 infeksiyonlarına da rastlanıyor.
- 2001 öncesi ve sonrasında genotip dağılımında belirgin bir değişim yok.
- Risk gruplarında yerni çalışmalar gereksinim var.
- Suriye'de olduğu gibi Ülkemizde de tip 5 infeksiyonu var mı?

Epidemiol. Infect. (2009), **137**, 79–84.

Hepatit D virus





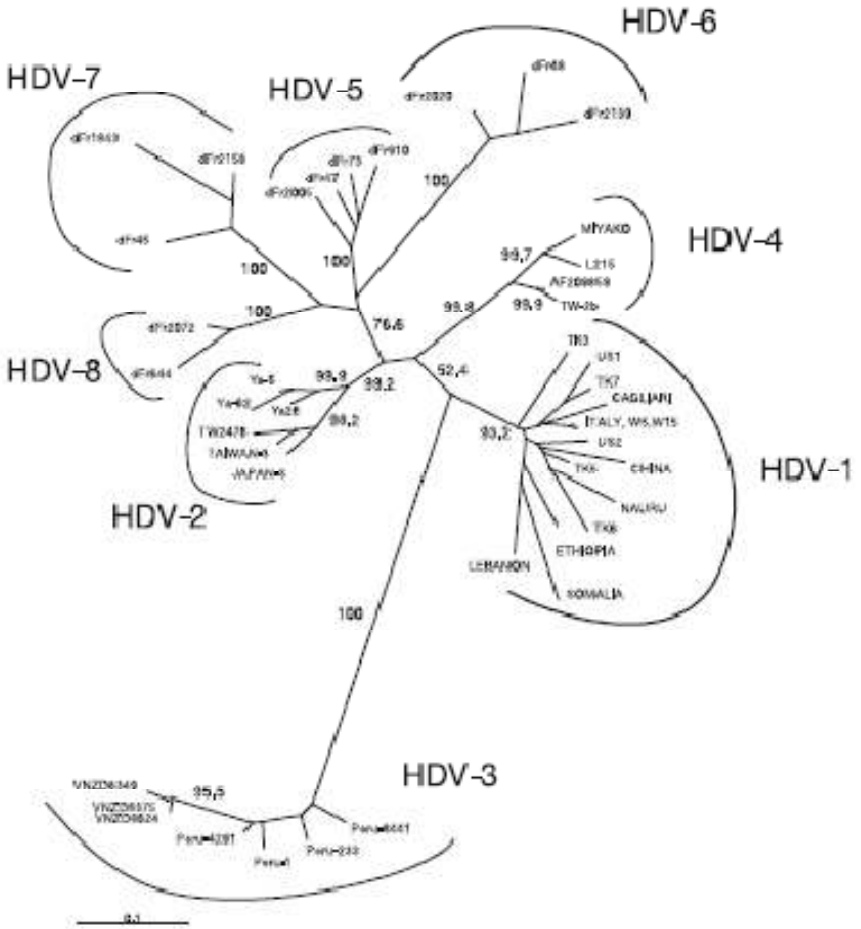
www.expasy.ch/viralzone/all_by_species/94.html

HDV genotipleri

CTMI (2006) 307:151–171

Hepatitis Delta Virus Genetic Variability: From Genotypes I, II, III to Eight Major Clades?

P. Dény (✉)



Türkiye: *HDV infeksiyonlarının temel özellikleri*

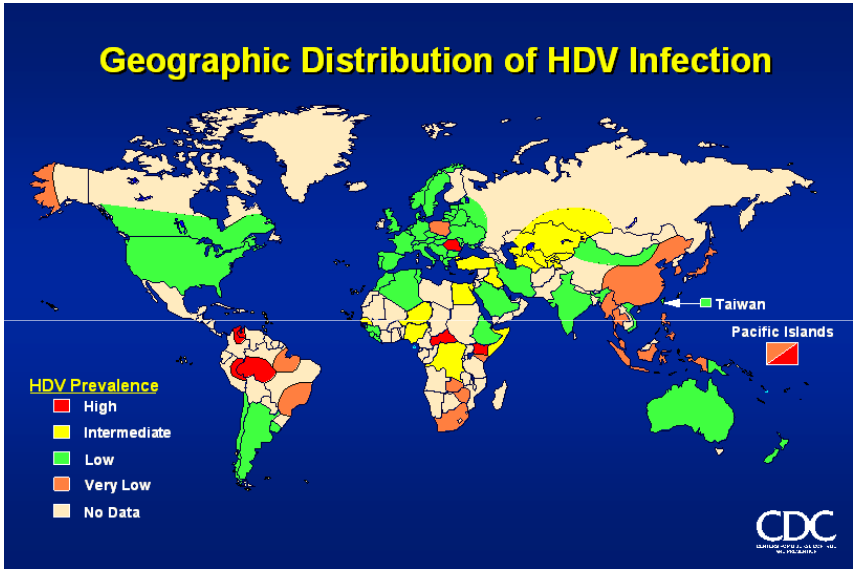


Table 4. Change in delta hepatitis prevalence among patients with chronic hepatitis B in different regions of Turkey

	Disease group	< 1995 *n* (%)	> 1995 *n* (%)	*P* value
Central Turkey	CHB	106/365 (29.0%)	20/166 (12.1%)	< 0.001
Southeast Turkey	CHB	58/154 (37.7%)	78/288 (27.1%)	< 0.001
Western Turkey	LC	70/183 (38.3%)	113/564 (20.0%)	< 0.001
Southeast Turkey	LC	73/110 (66.4%)	83/179 (46.4%)	< 0.001

CHB, chronic hepatitis B; LC, liver cirrhosis.

Liver International ISSN 1478-3223
Liver International (2008)

CLINICAL STUDIES

Seropositivity for delta hepatitis in patients with chronic hepatitis B and liver cirrhosis in Turkey: a meta-analysis

Halil Değertekin[1], Kendal Yalçın[2], Mustafa Yakut[2] and Cihan Yurdaydin[3]

Arch Virol (2004) 149: 2115–2129
DOI 10.1007/s00705-004-0363-2

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Molecular epidemiology of hepatitis B, C and D viruses in Turkish patients

A. M. Bozdayı[1,2], N. Aslan[1], G. Bozdayı[3], A. R. Türkyılmaz[1], T. Sengezer[1], U. Wend[4], Ö. Erkan[1], F. Aydemir[1], S. Zakirhodjaev[1], Ş. Orucov[1], H. Bozkaya[2], W. Gerlich[4], S. Karayalçın[2], C. Yurdaydın[1,2], and Ö. Uzunalimoğlu[1]

- HDV-RNA + hastalar
  (Güneydoğu'dan delta superinfeksiyonu olan HBsAg + hastalar)
  - n= 59
  - 39 yaş (18-67)
- Genotipleme
  - REA (n=59)
  - HDAg dizileri (904-1210) (n:13)
- Tümü genotip I
- Grup içi ortalama nükleotid değişkenliği
  - 2.5% (0%-3.9%)

- HDV-RNA + hastalar (İzmir & İstanbul'dan HBsAg + hastalar)
  - n= 60
  - 42 yaş (17-70)
- Genotipleme
  - REA (n=60)
  - HDAg dizileri (950-1232) (n:26)
- Tümü genotip I
- Grup içi ortalama nükleotid değişkenliği
  - 5.4%

T.C.
DOKUZ EYLÜL ÜNİVERSİTESİ
TIP FAKÜLTESİ
MİKROBİYOLOJİ VE KLİNİK MİKROBİYOLOJİ
ANABİLİM DALI

HEPATİT DELTA VİRUS RNA'SININ SAPTANMASI VE GENOTİPLENMESİ

Dr. SİBEL ÖZSU CAYMAZ

UZMANLIK TEZİ

İZMİR 2004

International Journal of Infectious Diseases (2007) 11, 35–41

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http://intl.elsevierhealth.com/journals/ijid

Hepatitis delta virus (HDV) genotypes in patients with chronic hepatitis: molecular epidemiology of HDV in Turkey

Imre Altuğlu*, Tijen Özacar, Ruchan Yazan Sertoz, Selda Erensoy

- HDV-RNA + KDH'li hastalar
  - n=26
  - 44.2 yaş (23-70)
- Genotipleme
  - HDAg dizileri (923-1262)
- Tümü genotip I
- Grup içi ortalama nükleotid değişkenliği
  - 10.2% (3%-16%)

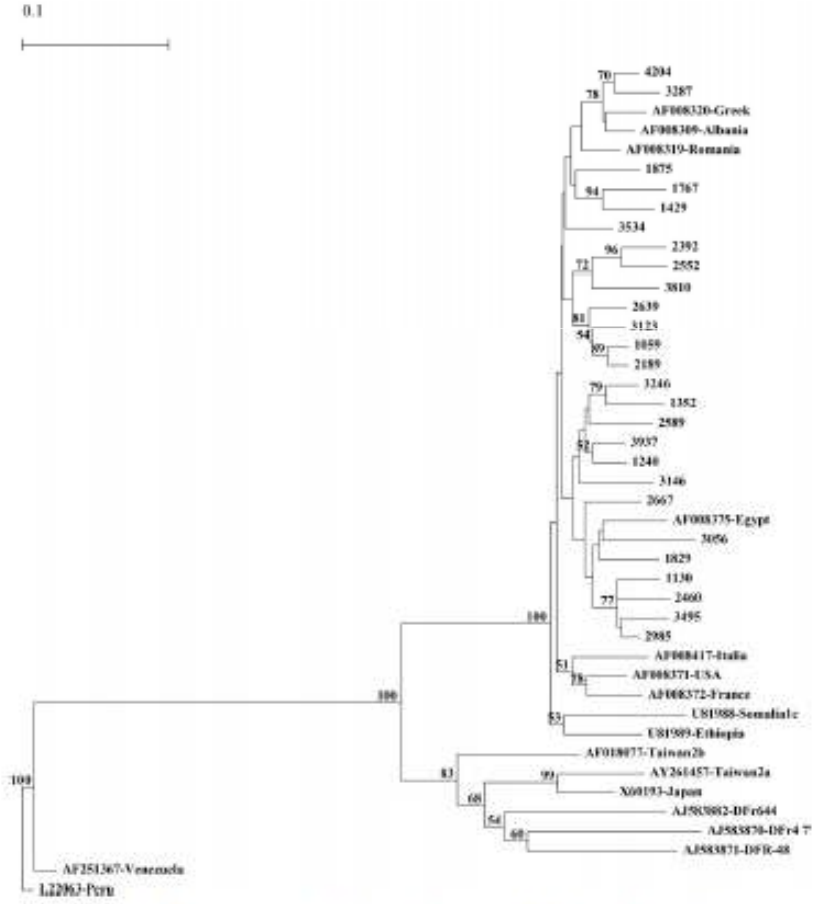

Figure 1 Phylogenetic tree of 26 sequences with 17 references by TREECON version 1.3b.[30]

DIVERSITE GENETIQUE DU VIRUS DE L'HEPATITE DELTA DANS L'EST DE LA TURQUIE

S. Oymak (1), F. Le Gal (2), D. Onel (1), P. Deny (2), S. Badür (1), E. Gault (2)
(1) Laboratoire de Virologie et d'Immunologie, Université d 'Istanbul, Faculté de Médecine d'Istanbul, Istanbul, Turquie
(2) Service de Bactériologie-Virologie-Hygiène, Centre National de Référence de l'Hépatite Delta,
Hôpital Avicenne, AP-HP, UPRES 3406, Université Paris 13, Bobigny, France

- 10 hasta
- Genotipleme
  - HDAg dizileri (923-1262)
  - *Tüm genom dizisi (n=4)*
- Tümü genotip I
- Grup içi ortalama nükleotid değişkenliği
  - 3.7%-12.7%

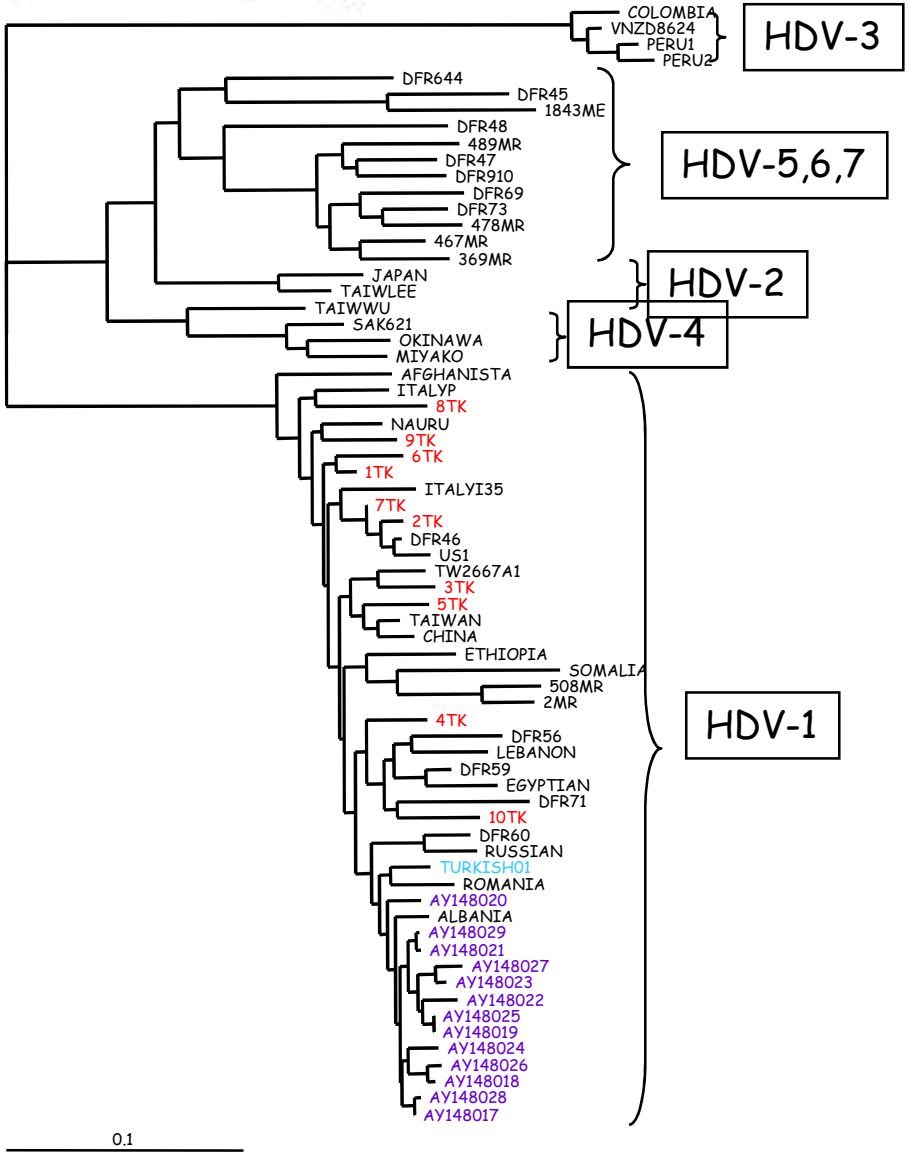

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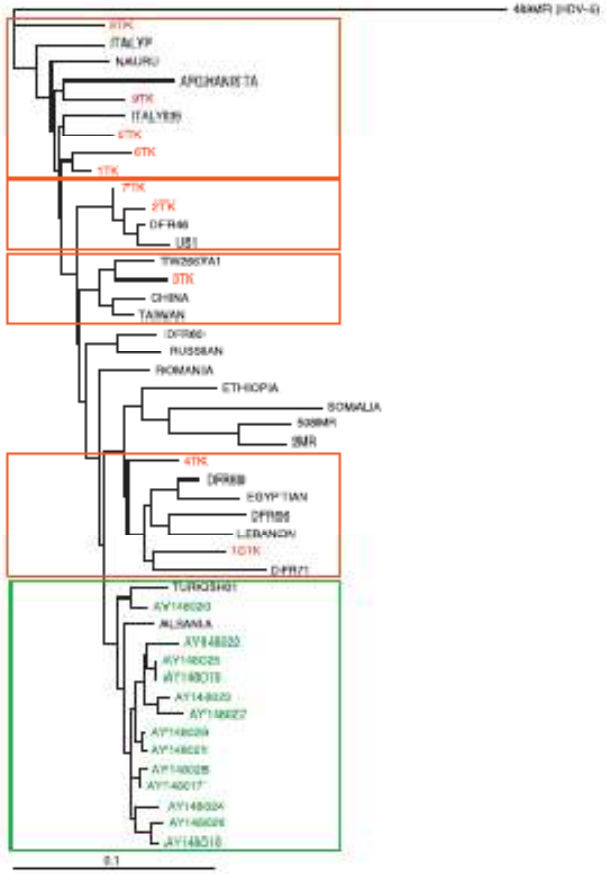
Fig.2: Analyse phylogénétique de la région R0
en rouge: notre étude, en vert: étude Bozdayi et al



N°	Origine	CV HDV*	CV HBV*	génotype HBV
1TK	Van	3.78	2.84	D
2TK	Erzurum	6.00	4.76	D
3TK	Hakkari	5.38	<2.00	NA**
4TK	Hakkari	6.90	<2.00	D
5TK	Hakkari	7.76	<2.00	NA
6TK	Mardin	5.15	3.85	D
7TK	Sivas	4.96	<2.00	NA
8TK	Kars	3.2	<2.00	B
9TK	Kars	5.94	>5.30	D
10TK	Istanbul	6.79	>5.30	D

*$\log_{10}$ copies/ml
*NA: non amplifiable

Asya, Orta Doğu ve Avrupa kökenleri ile kümelenme

HDV: *sonuç*

- Genotip I şu ana kadar saptanan tek tip
- İzolatlar arasındaki değişkenlik %16 ya kadar çıkabiliyor.
- HDV kökenleri Asya, Orta Doğu ve Avrupa kökenleri ile kümeleniyor.

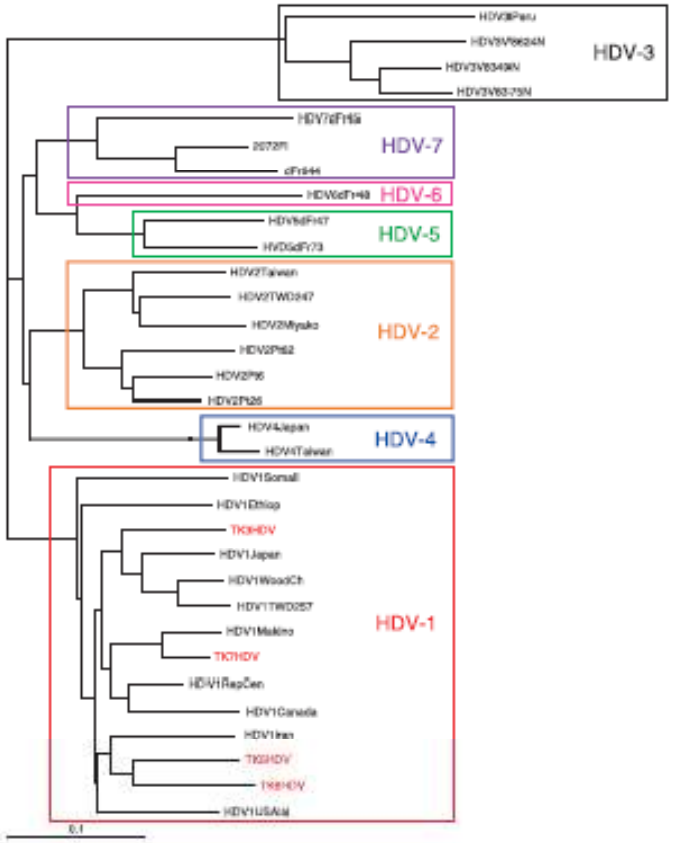


Fig.5: Analyse phylogénétique du génome complet de 4 isolats HDV turcs (en rouge)