Supplemental Table 1: Published CD4+ T cell epitopes within NS3-NS4a-NS4b

aa position	sequence	HLA-restriction	source	
1201-1220	LETTMRSPVFTDNSSPPVVP	DR11	line	ref. 2
1207-1226	SPVFTDNSSPPVVPQSFQVA	DRB1*1104 / *1502	PBMC	this paper
1248-1261	GYK**VLVLNPSVAA**T	**DRB1*1101,*0401,*1201, *1302,*1601**	clone	ref. 3
1241–1260	PAAYAAQGYKVLVLNPSVAA	DR11/DQ3 + DR4/10,DQ1/3	clone	ref. 2
1248-1261	GYKVLVLNPSVAATL	**DRB1*0401**	tetramer	ref. 2
1247-1262	QGYKVLVLNPSVAA	DR3 / DR11	PBMC	ref. 19
1248-1267	GYKVLVLNPSVAATLGFGAY	**DQB1*0301**	line	ref. 11
1248-1267	GYKVLVLNPSVAATLGFGAY		line	ref. 15
1281-1300	GVRTITTGSPITYSTYGKFL	DR4 / DR8	line	ref. 2
1280-1299	TGVRTITTGSPITYSTYGKF		PBMC	this paper
1291-1310	ITYSTYGKFLADGGCSGGAY	DR4 / DR10	line	ref. 2
1295-1310	TYGKFLADGGCSGGAY	DR3 / 11	PBMC	ref. 19
1289-1308	SPITYSTYGKFLADGGCAGG		PBMC	this paper
1321–1340	TDATSILGIGTVLDQAETAG	DR4 / DR8	line	ref. 2
1323-1338	ATSILGIGTVLDQAET	DR3 / DR4	PBMC	ref. 19
1325-1344	SILGIGTVLDQGETAGAKLV		PBMC	this paper
1388-1407	**GRHLIFCHSKK**KCDELATKL	**DRB1*1501/DRB5*0501**	clone	this paper
1384-1401	VIKGGRHLIFCHSKKKCD	**DRB1*1501/DRB5*0501**	clone	ref. 5
1387-1402	GGRHLIFCHSKKKC	DR1/15 + DR8/15 + DR1/15 + DR15/7	PBMC	ref. 19
1416-1425	**AYYRGLDVSV**	**DRB1*1501**	clone	this paper
1411–1430	GINAVAYYRGLDVSVIPTSG	DR4 / 10	line	ref. 2
1411-1426	GINAVAYYRGLDVSVI	DR1 / DR15	PBMC	ref. 19
1415-1430	VAYYRGLDVSVIPTSG	DR8 / DR15	PBMC	ref. 19
1450-1469	SVIDCNTCVTQTVDFSLDPT	**DRB1*1302**	clone	ref. 3
1447-1464	DFDSVIDCNTCVTQTVDF			ref. 5
1454-1471	CNTCVTQTVDFSLDPTFT			ref. 5
1521-1530	YDAGCAWYELTPAETTVRLR	DR4 / 10	line	ref. 2
1525-1534	CAWYELTPAETTVRLRAYMN		PBMC	this paper
1535-1554	TTVRL**RAYMNTPGLPV**CQDH	**DRB1*0701**	clone	this paper
1531–1550	TPAETTVRLRAYMNTPGLPV	DR4 / 8	line	ref. 2
1539-1554	LRAYMNTPGLPVCQDH	DR1 / DR15	PBMC	ref. 19
1585-1604	**YLVAYQATVCA**RAQAPPPSW	**DRB1*1501**	clone	this paper
1579-1597	SGENLPYLVAYQATVCARA	**DRB1*0401**	tetramer	ref. 2
1581–1600	ENLPYLVAYQATVCARAQAP	DR4 / 10, DR4 / 8	line	ref. 2
1601-1620	PPSWDQMWKCLIRLKPTLHG	DR4 / 8	line	ref. 2
1597-1612	AQAPPPSWDQMWKCLI	DR8 / 15	PBMC	ref. 19
1595-1614	ARAQAPPPSWDQMWKCLIRL		PBMC	this paper
1617-1636	TLHGPTPLLYRLGAVQNEIT		line	ref. 15
1617-1636	TLHGPTPLLYRLGAVQNEIT	DRB1*0407/*1104, DRB1*0801	line	ref. 11
1621–1640	PTPLLYRLGAVQNEITLTHP	DR4 / 10	line	ref. 2
1615-1644	KPTLHGPTPLLYRLGAVQNE		PBMC	this paper

1625-1654	LYRLGAVQNEITLTHPVTKY		PBMC	this paper
1655-1674	VVTS**TWVLVGGVLA**ALAAYC	DR1 / 13	clone	this paper
1671–1690	AAYCLSTGCVVIVGRVVLSG	DR11/DQ3	clone	ref. 2
1677-1696	TGCVVIVGRVVLSGKPAIIPD			ref. 15
1677-1696	TGCVVIVGRVVLSGKPAIIPD	DRB1*0407/*1104	line	ref. 11
1675-1694	LSTGCVVIVGRVVLSGKPAI		PBMC	this paper
1685-1704	RVVLS**GKPAIIPDREVLYRE**	**DRB1*0301**	clone	this paper
1686-1705	VVLSGKPAIIPDREVLYREF	**DRB1*0301**	line	ref. 9
1687-1706	VLSGKPAIIPDREVLYREFD	DRB1*1109/*0305	line	ref. 11
1687-1708	VLSGKPAIIPDREVLYREFD		line	ref. 15
1746-1765	IAPAVQTNWQKLETFWAKHM	DR16 / 3	line	ref. 9
1747-1766	APAVQTNWQKLETFWAKHMW	DRB1*0801	line	ref. 11
1745-1764	VIAPAVQTNWQKLETFWAKH		PBMC	this paper
1765-1784	MWNFISGI**QYLAGLSTLPG**N	**DRB1*1101**	clone	this paper
1767-1786	NFISGIQYLAGLSTLPGNPA	DRB1*1104	line	ref. 11
1770-1790	SGIQYLAGLSTLPGNPAIASL	**DRB1*0401**	tetramer	ref. 2
1771–1790	GIQYLAGLSTLPGNPAIASL	**DR11**, DR4 / 8	clone	ref. 2
1785-1804	PA**IASLMAFTAA**VTSPLTTS	**DRB1*0102, DRB1*0101**		this paper
1777-1796	AGLSTLPGNPAIASLMAFTA		line	ref. 15
1787-1806	IASLMAFTAAVTSPLTTSQT		line	ref. 15
1777-1796	AGLSTLPGNPAIASLMAFTA	DRB1*0801	line	ref. 11
1781–1800	LPGNPAIASLMAFTAAVTSP	DR4 / 10	line	ref. 2
1805-1824	QTL**LFNILGGWVA**AQLAAPG	**DRB1*0101, DRB1*0102**	clone	this paper
1801–1820	LTTSQTLLFNILGGWVAAQL	DR4 / 10	line	ref. 2
1807-1826	LLFNILGGWVAAQLAAPGAA		line	ref. 15
1797-1816	VTSPLTTSQTLLFNILGGWV		line	ref. 15
1807-1826	LLFNILGGWVAAQLAAPGAA		line	ref. 11
1817-1836	AAQLAAPGAATAFVGAGLAG	DRB1*0407/*1104	line	ref. 11
1875-1894	**STEDLVNLLPAILSPGALVV**	**DRB1*0101**	clone	this paper
1871–1890	GEVPSTEDLVNLLPAILSPG	DR4 / 10	line	ref. 2
1877-1896	EDLVNLLPAILSPGALVVGV	DRB1*0801	line	ref. 11
1891-1910	ALVVGVVCAAILRRHVGPGE	DR11	line	ref. 2
1907-1926	GPGEGAVQWMNRLIAFASRG	**DRB1*1104**	line	ref. 11
1909-1929	GEGAVQWMNRLIAFASRGNHV	**DRB1*1104**	line	ref. 11
1911–1930	GAVQWMNRLIAFASRGNHVS	DR11, DR4 / 10	clone	ref. 2
1905-1924	HVGPGEGAVQWMNRLIAFAS		PBMC	this paper
1977-1996	DIWDWICEVLSDFKTWLKAKL	DRB1*1109/*0305	line	ref. 11

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Supplemental Table 2: **HLA-DRB1* amplification and sequencing primers**

HLA-DRB1* amplification primers

Sense primer: DRB1-groupspecific primers (3,3 pmol/µl):

DRB1-01 GFP NEW; DRB1-04 GFP NEW; DRB1-07novel; DRB1-09 GFP NEW; DRB1-10 GFP NEW; DRB1-15 GFP NEW (DRB1*15;16); DRAA (DRB1*03; 08; 11; 12; 13; 14)

Reverse primer: DRB1-Space-91GFP (5 pmol/µl)

DRB1-01 GFP NEW; GCC ACC ATG GTG AGC AAG G**AT ATA TGC ACG TTT CTT GTG GCA GCT TAA GTT**

DRB1-04GFPNEW; GCC ACC ATG GTG AGC AAG G**AT ATA TGC ACG TTT CTT GGA GCA GGT TAA AC**

DRB1-07GFPnovel; GCC ACC ATG GTG AGC AAG G**AT ATA TTC ACG TTT CCT GTG GCA GGG**

DRB1-09 GFPNEW; GCC ACC ATG GTG AGC AAG G**AT ATC AGC ACG TTT CTT GAA GCA GGA TAA GTT**

DRB1-15GFPNEW; GCC ACC ATG GTG AGC AAG G**AT ATA TTC ACG TTT CCT GTG GCA GCC TAA GA**

DRB1-AA; GCC ACC ATG GTG AGC AAG G**CC CAC AGC ACG TTT CTT GGA GTA CT**

DRB1-rev (space); GCT GAT TAT GAT CAA GAG TCGat tat aat aaat tat aat aaGCTYACCTCGCCKCTGCA

HLA-DRB1* sequencing primers

GFP-hin; 5‘-GCC ACC ATG GTG AGC AAG G-3‘

GFP back; 5'-GCT GAT TAT GAT CAA GA GTC G-3‘

The amplification of HLA-DRB1* exon 2 was done in 50 µl PCR reaction mixes using 10 µl genomic DNA (about 300 ng) as template and Applied Biosystems (Applied Biosystems, (AB), Darmstadt, Germany) chemicals (0,25 µl (1,25 units) of Ampli Taq polymerase, 5 µl buffer I, 4 µl dNTPs (10 mM; Amersham Bioscience, Little Chalfont Buckhamshire, England), 1 µl of each groupspecific amplification primer, 1 µl of DRB1 reverse primer and 29,5 µl of water. The PCR was performed in a T3 thermocycler (Biometra; Göttingen, Germany) following the cycler profile: 10 s at 95°C; 15 x | 95°C 10 s, 60°C 10 s, 72°C 1 min|; 10 x | 95°C 10 s, 60°C 10 s, 72°C 45 s|; 25 x | 95°C 10 s, 60°C 10 s, 72°C 25 s|; 5 min 72 °C and cool down to 4°C.

Amplification control was done by loading 7 µl of the appropriate PCR sample mixed with 3 µl of an adequate loading buffer on an ethidium bromide stained 1.5% agarose gel. UV-light detection after electrophoresis revealed an amplification product of the correct size.

Removal of the amplification primers was done using the QIAquick PCR Purification Kit (Qiagen, Hilden, Germany) and eluation in 50 µl water from the columns.

The cycle sequencing reactions were performed using 5 µl purified PCR product, 1 µl sequencing primer (10 pmol/µl), 0.75 µl BigDye Terminator v3.0 Ready Reaction mix (AB), 1.25 µl PCR Buffer (AB) and 2 µl Q-solution. Sequencing was performed in both directions using the sequencing primers GFPhin and GFPback (Suppl. Table 2). The PCR follows the profile: 1 min at 96°C; 35 x |96°C 20 s, 60°C 4 min|; cool down to 4°C.

After cycle sequencing excess of dye-labeled dideoxynucleotides was removed by ethanol precipitation (30 µl blue dextran (Sigma) solution (10 ng / ml), 100 µl acetate/ethanol (stock: 1 ml 3M Na-acetate pH 4,8 solution (AB) in 50 ml of absolute ethanol (Merck, Schwalbach, Germany). The ethanol precipitation was done in an Eppendorf centrifuge 5417C in an 8-strip rotor (F45-48 PCR, Eppendorf, Wesseling-Berzdorf, Germany) for 10 min at 3500 g (rcf). The

liquid was discarded and the resulting blue-coloured DNA pellet was washed with 80% ethanol, dried, and resolved in 14 µl Hi-Di formamide (AB).

DNA sequencing was carried out using a 3100 Genetic Analyzer (AB) with a 50 cm array using standard run module conditions except 25 s injection time and 4000 s run time. The sequencing files were converted to Macintosh format and exon 2 sequences were analysed using MT Navigator PCC (AB) and SCORE software (Qiagen, Vienna, Austria).

Suppl. Table 3: Intergenotypic variability of immunodominant CD4+ T cell epitopes

gt	p22 1388 1401	p24 1415 1425	p37 1540 1550	p42 1585 1595
1b	GRHLIFCHSKKKCD..//..	VAYYRGLDVSV..//..	RAYLNTPGLPV..//..	YLVAYQATVCA
1a	----------	----------	---M-------	----------
1c	----------	--F--------	----------	----------
2a	----------	----------	---F-------	--T--------
2b	----------	----------	---F-------	--T--------
3a	----------	----------	---LS------	--T--------
4	----------	----------	K--FD------	---------S-

gt	p49 1659 1668	p52 1690 1704	p60 1773 1783	p62 1787 1796
1b	TWVLVGGVLA..//..	GKPAIIPDREVLYRE..//..	QYLAGLSTLPG..//..	IASLMAFTAS
1a	----------	----------	----------	---------A
1c	----------	----V-----------	----------	-----S---A
2a	----A-----	QRAVVA--K----EA	----------	A-M----S-A
2b	----A-----	DQVVVA--K-I--EA	----------	A-M----S-A
3a	----L-----	----LV--K----QQ	----------	V---------
4	----------	-Q--V--------QQ	----------	---------A

gt	p64 1808 1817	p71 1879 1889
1b	LFNILGGWVA..//..	LVNLLPAILS
1a	----------	----------
1c	----------	----------
2a	-L------L-	V-----G---
2b	-L--M---L-	V---------
3a	F---------	M---------
4	----------	----------

Suppl. Table 4*: Intragenotypic variability of immunodominant CD4+ T cell epitopes

No	AS	most frequent sequence variant in a given genotype (%)				
		1a (n=20)	1b (n=150)	2a (n=10)	2b (n=18)	3a (n=4)
p22	1388-1407	100	94.7	100	83.3	100
p24	1415-1425	100	95.3	77.8	94.4	100
p37	1540-1550	100	97.3	88.9	100	100
p42	1585-1595	100	96.0	66.7	100	100
p49	1659-1668	100	98.7	100	61.1	100
p52	1690-1704	50	16.6	100	22.2	100
p60	1773-1783	100	99.3	77.8	100	75.0
p62	1787-1796	100	98.6	100	100	100
p64	1808-1817	100	96.7	77.8	100	100
p71	1879-1889	94.1	89.3	88.9	88.9	75.0

* derived from the http://hcvpub.ibcp.fr