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**Supporting Information**

**for**

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Amandine Bovay, Vincent Zoete, Garry Dolton, Anna M. Bulek, David K. Cole,  
Pierre J. Rizkallah, Anna Fuller, Konrad Beck, Olivier Michielin, Daniel E. Speiser,  
Andrew K. Sewell and Silvia A. Fuertes Marraco

**T cell receptor alpha variable 12-2 bias in the immunodominant response to  
Yellow fever virus**

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Sewell, Silvia A. Fuertes Marraco#

# Corresponding author: [silviasuncion.fuertesmarraco@unil.ch](mailto:silviasuncion.fuertesmarraco@unil.ch)

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Fig S1. High similarity between the YF5048 and MEL5 TCRs and their cognate pMHC complexes.

Fig S2. Peptide recognition signature of individual TCRs derived from TRAV12-2 positive and negative clones specific for A2/LLW.

Fig S3. Effect of the single substitution Asn4 -> Arg4 on clone YF5048.

**Table S1. Analysis of the relative frequencies of T cell clonotypes within A2/LLW-specific CD8 T cells.<sup>1</sup>**

TRAV	CDR3	TRAJ	Frequency	TRBV	CDR3	TRBJ	Frequency
12-2	CAVTDDKIIFG	30	0.11	6-8	CASSYSRTGSYEQYFG	2-7	single
12-2	CAVDSGGYQKVTFG	13	single	7-2	CASSQGLAYEQFFG	2-1	single
12-2	CAGGDDKIIFG	30	single	9	CASSVEGPGLFFG	2-2	single
12-2	CAVKDARLMFG	31	0.05	2	CASSEATGASYEQYFG	2-7	0.07
12-2	CAVGSDKIIFG	30	0.07	2	CASSEYVQYYGYTFG	1-2	single
12-2	CAVSDARLMFG	31	single	6-8	CASSEAGQAYEQYFG	2-7	single
12-2	CAAFDDKIIFG	30	0.05	9	CASSEGGQAYNEQFFG	2-1	0.07
12-2	CAASASKLIFG	4	single	9	CASSVSGSSYEQYFG	2-7	single
12-2	CAVDTNAGKSTFG	27	single	9	CASSVGTSSYEQYFG	2-7	single
12-2	CAAVNNDMRFG	43	single	9	CASSVAGGYEQYFG	2-7	single
12-2	CAVG DARLMFG	43	single	4-3	CASSPGLAGGYEQFFG	2-1	0.05
12-2	CAANNARLMFG	31	single	28	CASSPPGTGVYGYTFG	1-2	0.05
12-2	CAVNGNKL VFG	47	single	6-8	CASSYSGGAYGYTFG	1-2	single
12-2	CAVGDDKIIFG	30	0.09	27	CASSQDPGSPRTQYFG	2-5	single
12-2	CAVNSNTDKLIFG	34	single	6-8	CASSYSGGSYIEFFG	2-1	single
12-2	CAVTTSQTYKYIFG	40	single	2	CAVGDRGYEQYFG	2-7	single
12-2	CAATDDKIIFG	30	single	9	CASSTGLAYEQFFG	2-1	single
12-2	CAVNDKYKLSFG	20	single	9	CASSVGGVVYNEQFFG	2-1	single
12-2	CAGSGDKLIFG	34	single	2	CASDSGDHEQYFG	2-7	0.05
12-2	CAEEGRGNDMRFG	43	single	19	CASSIGPLGQPQHF	1-5	single
12-2	CAVSKDDKIIFG	30	single	27	CASSLNPSTDTQYFG	2-7	single
12-2	CASRDDKIIFG	30	single	19	CASSIWRRLHLRFG	1-6	single
12-2	CAVTPDKVIFG	50	single	2	CASSEYVQYYFYTFG	1-2	single
12-2	CAVTSDSWGKLQFG	24	0.04	9	CASSAGTGAYEQYFG	2-7	single
12-2	CAVVDDKLIFG	4	single	9	CASSATSGGADTQYFG	2-7	single
12-2	CAVRDDKIIFG	30	single	18	CASGPGTVSYEQYFG	2-7	single
12-2	CATSNRLAFG	7	single	29-1	CSVPFAGADTQYFG	2-7	single
12-1	CVVNADDMRFG	43	single	28	CASSSLGTGGYGYTFG	1-2	single
12-1	CGVDDKIIFG	30	single	2	CASNQGGISYGYTFG	1-2	single
12-1	CVVTGTYKYIFG	40	0.05	9	CASSVATEGYGYTFG	1-2	0.07
12-1	CVVGTDKLIFG	34	single	6-8	CASSRVGN IAGELFFG	2-2	single
13-1	CAASGTGAGSYQLTF	28	single	9	CASSPSGGGYEQYFG	2-7	single
27	CAASSLYGQNFVF	26	single				
19	CALSENNDYKLSF	20	0.05				
22	CAVVPNAGGTSYGKLT	52	single				

<sup>1</sup> TRAV, TRAJ, TRBV, TRBJ segment usage and relative frequencies are indicated for all clonotypes. Public sequences are colored in yellow.

**Table S2. Molecular interactions between TCR and pMHC in the structural model.<sup>2</sup>**

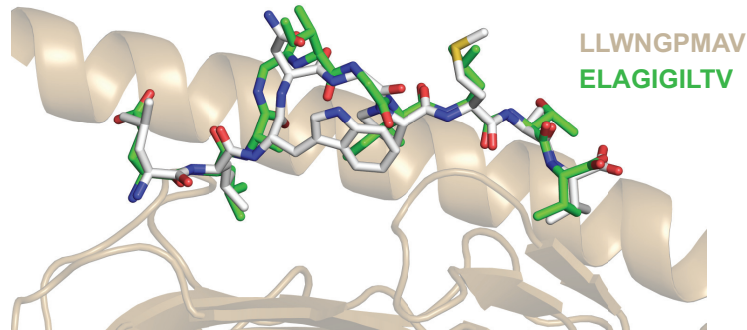
CDR loop	TCR residue	Peptide residue	MHC residue	Bond type
CDR1 $\alpha$	Arg28, N $\epsilon$		Glu166, O $\epsilon$ 1/O $\epsilon$ 2	Electrostatic
	Arg28, NH2		Glu166, O $\epsilon$ 1/O $\epsilon$ 2	Electrostatic
	Arg28, O		Trp167, N $\epsilon$ 1	Electrostatic
	Gly29, C $\alpha$		Trp167, CZ2	vdW
	Gly29, C $\alpha$	Leu1, C $\delta$ 2		vdW
	Gln31, N $\epsilon$ 2	Leu2, O		Electrostatic
	Gln31, C $\beta$	Asn4, C $\beta$ /C $\gamma$		vdW
	Gln31, C $\gamma$	Asn4, C $\gamma$		vdW
	Gln31, O $\epsilon$ 1	Asn4, N		Electrostatic
	Ser32, O $\gamma$	Asn4, N $\delta$ 2		Electrostatic
CDR2 $\alpha$	Tyr51, OH		His151, O	Electrostatic
CDR3 $\alpha$	Asn92, O $\delta$ 2	Asn4, N $\delta$ 2		Electrostatic
	Asn94, O		Arg65, NH2	Electrostatic
	Ala95, O		Arg65, N $\epsilon$	Electrostatic
	Ala95, C $\beta$		Gly62, C $\alpha$ /O	vdW
	Ala95, C $\beta$		Lys66, C $\epsilon$	vdW
CDR2 $\beta$	Asn48, O $\epsilon$ 1		Arg65, NH1	Electrostatic
	Tyr49, C $\epsilon$ 1		Arg65, C $\delta$	vdW
	Arg55, NH2		Glu19, O $\epsilon$ 1	Electrostatic
CDR3 $\beta$	Gly97, C $\alpha$		Thr73, C $\gamma$ 2	vdW
	Ser98, N	Gly5, O		Electrostatic
	Ser98, N	Pro6, O		Electrostatic
	Ser98, C $\beta$	Met7, C $\epsilon$		vdW

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<sup>2</sup> vdW: van der Waals

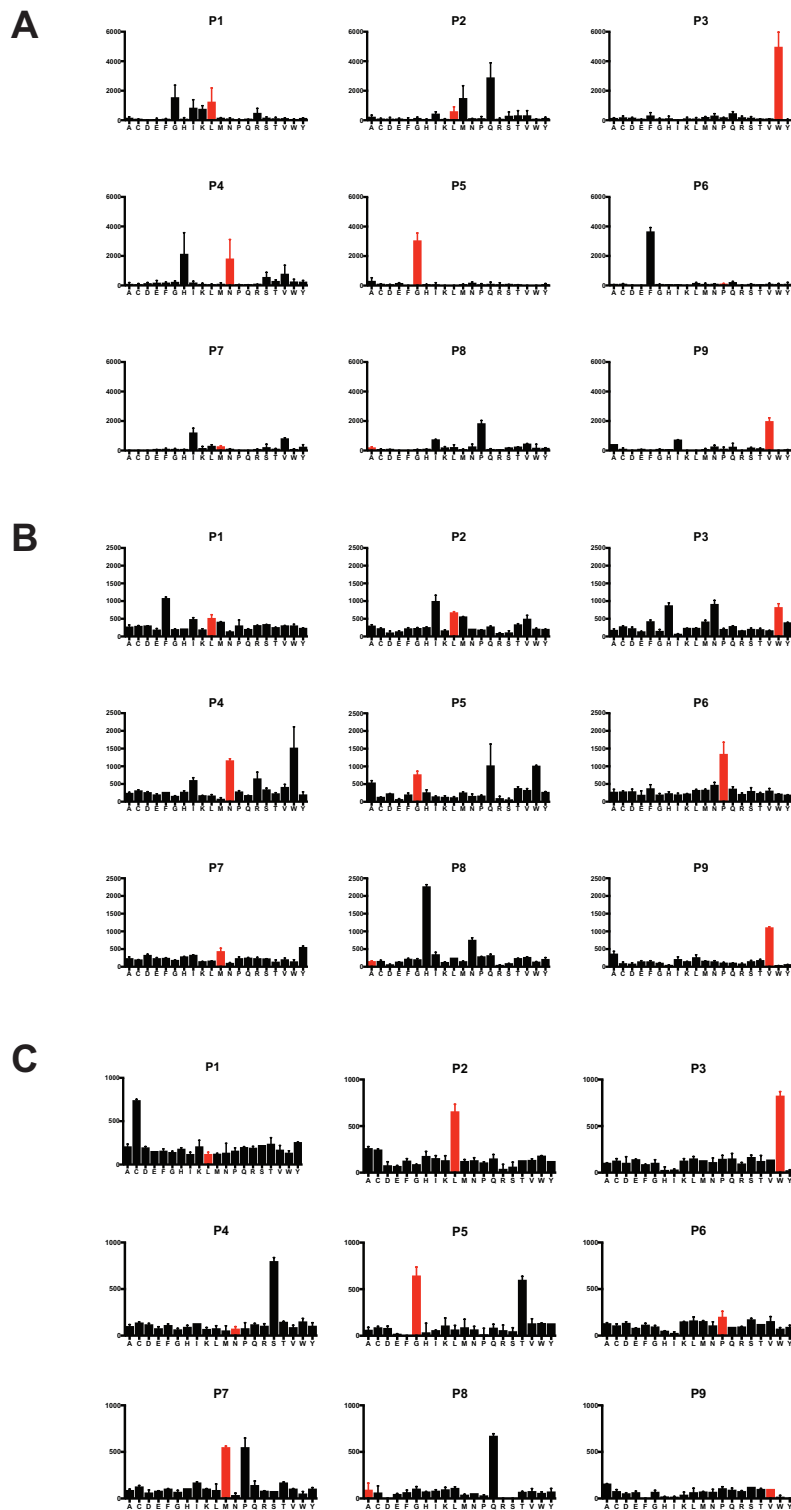
**A**

TCR alpha V domain	CDR1	CDR2	CDR3
MEL5 TRAV12-2	KEVEQNSGPL SVPEGAIASLNCTYS <b>DRGSQS</b> FFWYRQYSG KSPELIMSI <b>YSNGD</b> KEDGRFTAQLNKASQYVLLIRDSQPSPDSATYLC <b>AVNVAGKSTFG</b>		
YF5048 TRAV12-2	KEVEQNSGPLSVPEGAIASLNCTYS <b>DRGSQS</b> FFWYRQYSG KSPELIMSI <b>YSNGD</b> KEDGRFTAQLNKASQYVLLIRDSQPSPDSATYLC <b>AVNVAGKSTFG</b>		

**B**

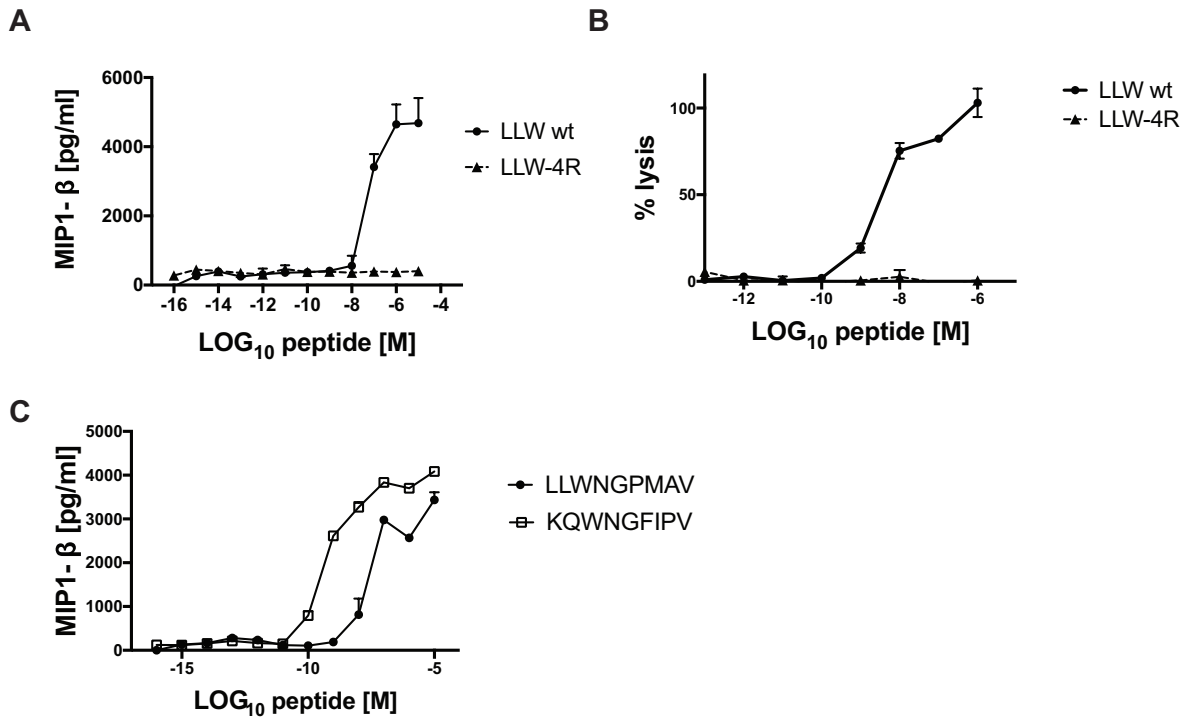
**Fig S1. High similarity between the YF5048 and MEL5 TCRs and their cognate pMHC complexes.**

(A) Alignment of the variable region of the TCR alpha chain of YF5048 and MEL5. (B) Superimposition of the peptides LLWNGPMAV in grey and ELAGIGILTV in green binding to the HLA-A2 molecule.



**Fig S2. Peptide recognition signature of individual TCRs derived from TRAV12-2 positive and negative clones specific for A2/LLW.**

Nonamer CPL scan for a TRAV12-2 positive A2/LLW-specific clone YF5031 (A), and for two TRAV12-2 negative A2/LLW-specific clones YF5001 (B) and YF5048NN1 (C) assayed by MIP-1 $\beta$  activation (mean and SD).



**Fig S3. Effect of the single substitution Asn4 -> Arg4 on clone YF5048.**

(A) Effect of the Asn4 -> Arg4 mutation on clone YF5048 assayed by MIP-1 $\beta$  activation with graded concentrations of the peptides LLWNGPMAV (LLW wt) or LLWRGPMVA (LLW-4R) (mean and SEM). (B) Killing capacity (51-chromium release assay) of clone YF5048 with titration of the LLW-wt or LLW-4R peptides (mean and SEM). (C) Effect of a strong agonist peptide on the TRAV12-2 positive clone YF5031 assayed by MIP-1 $\beta$  activation with graded concentrations of the peptides LLWNGPMAV or KQWNGFIPV (mean and SEM).