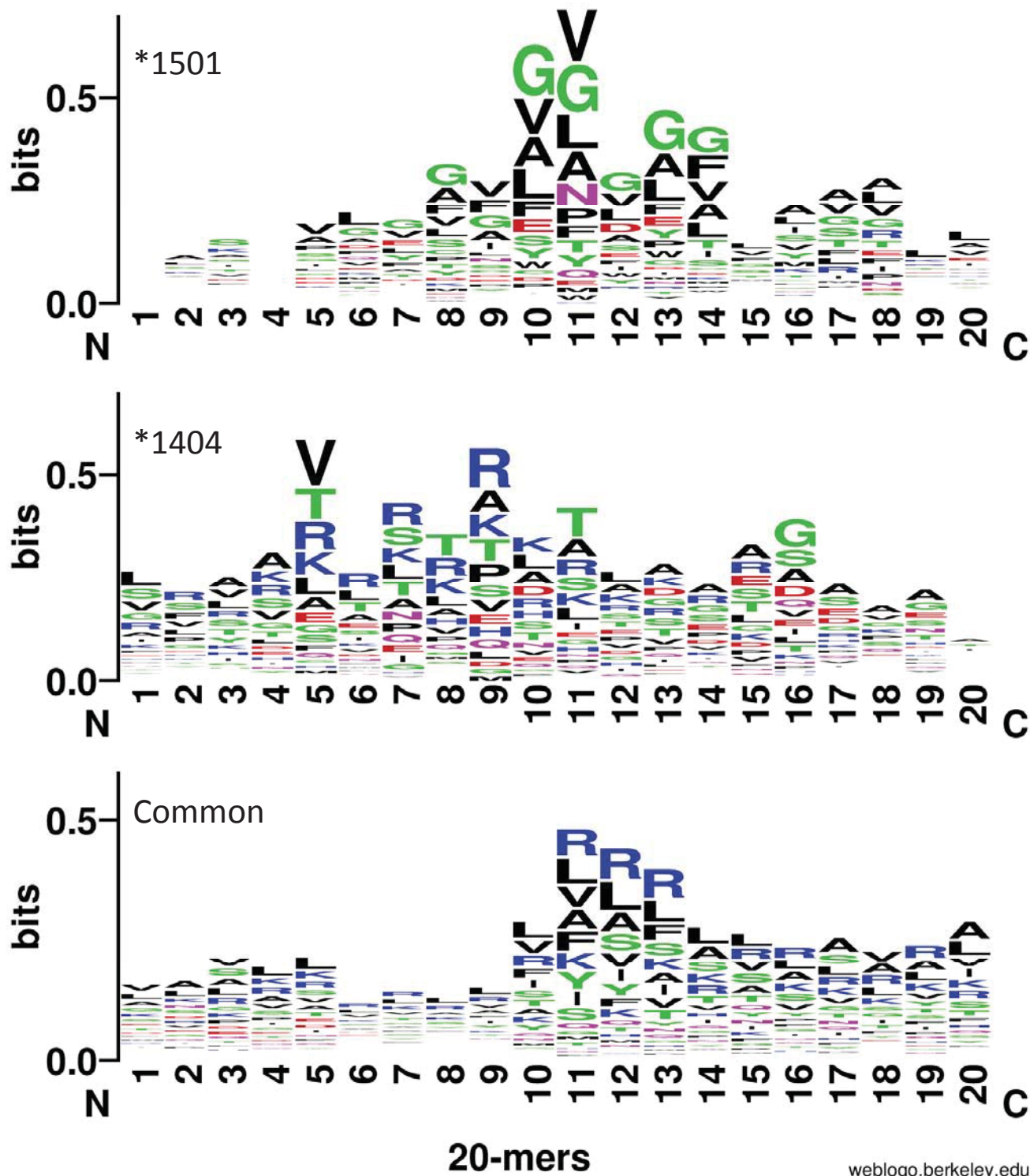
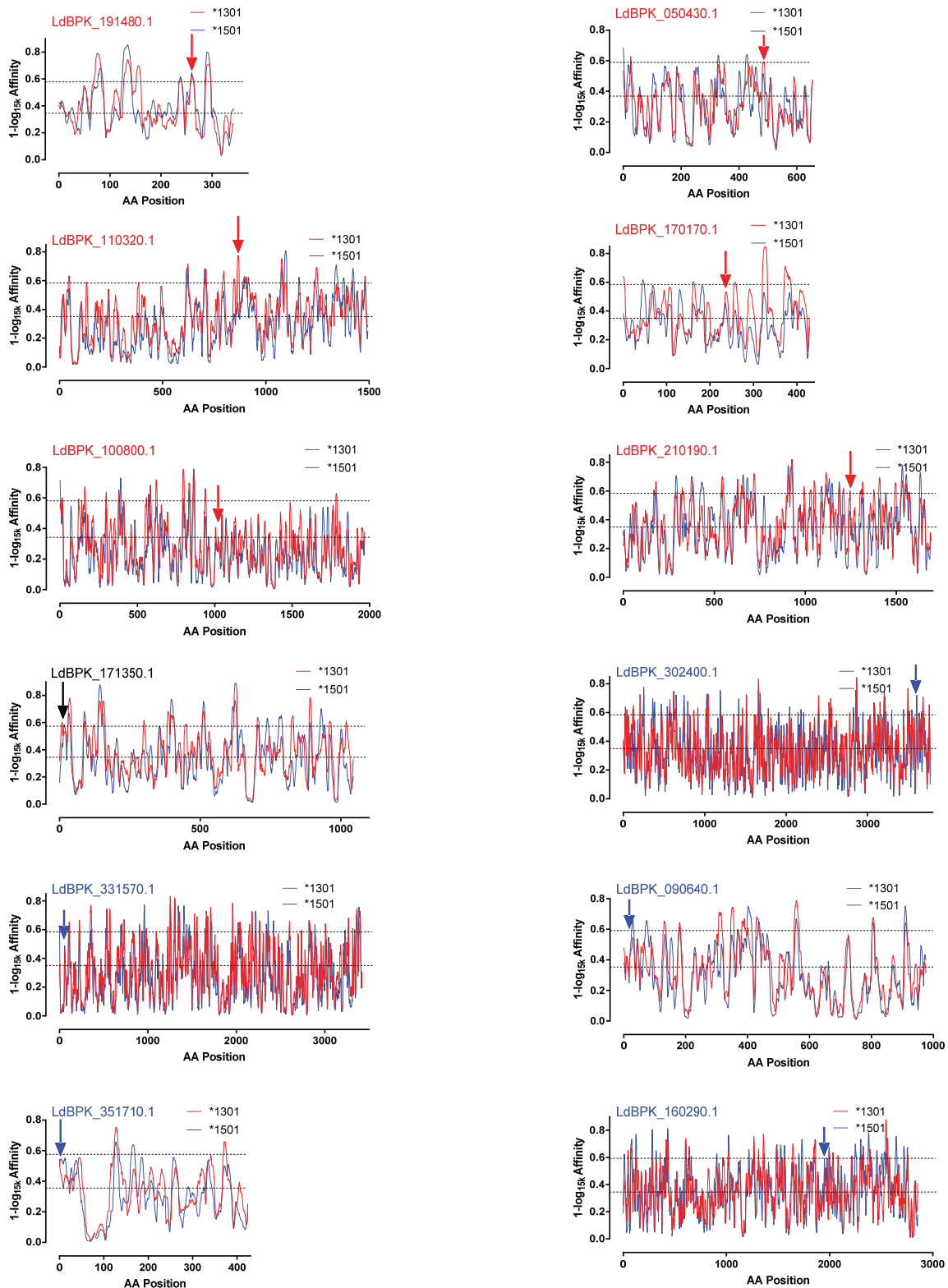


**Figure S1.** Plots showing binding affinities for epitopes across a selection of 49 Leishmania vaccine candidate proteins predicted to bind to HLA DRB1 class II molecules. Epitope binding predictions were performed in NetMHCIIpan2.1. The y-axis shows the relative binding affinity (expressed as  $1-\log_{15,000}$  of the nM binding affinity) for risk \*1404 (red) and protective \*1501 (blue) DRB1 alleles; the x-axis indicates the amino acid sequence locations for proteins, equivalent to the start position of overlapping 20mers (1-mer sliding window) in vaccine proteins as listed in Table S1. Horizontal dotted lines show cut-offs for different nM binding affinities; the upper line indicates the value above which binding achieves  $>50$  nM, the lower line indicates the value above which binding achieves  $>500$  nM.



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**Figure S2.** WebLogo plots of 20-mers at binding peaks for NetMHCIIpan v2.1 analysis.



**Figure S3.** Plots showing binding affinities across *Leishmania* proteins from which captured epitopes derive, as predicted to bind to HLA DRB1 class II molecules. Epitope binding predictions were performed in NetMHCIIpan 2.1. The y-axis shows the relative binding affinity (expressed as  $1 - \log_{15,000}$  of the nM binding affinity) for risk \*1301 (red) and protective \*1501 (blue) DRB1 alleles; the x-axis indicates the amino acid sequence locations for proteins, equivalent to the start position of overlapping 20mers (1-mer sliding window) in 12proteins as listed in Table II of the main text. Horizontal dotted lines show cut-offs for different nM binding affinities; the upper line indicates the value above which binding achieves =50 nM, the lower line indicates the value above which binding achieves =500 nM. Arrows indicated the position in the sequence of the captured epitopes, data for which was used to select 20-mer peptides to be synthesized for ex vivo stimulation assays, as outlined in Table S2. Gene names on the plots and arrows are colour -coded according to whether the epitopes were originally captured from dendritic cells homozygous for \*1301 risk (red), \*1501 protective (blue), or from both (black).

**Table S1. (A):** List of 12 20-mer peptides selected to represent epitopes with the best binding affinity for risk (DRB1\*1301) or protective (DRB1\*1501) DRB1 alleles from which peptides were captured. Affinities are based on NetMHCIIpan analysis of overlapping 20-mers across the full-length proteins identified from the epitope capture experiment. Binding affinity  $\leq 50\text{nM}$  = high;  $>50\text{nM}$  = low. Bold indicates 9-mer core for peak affinity of binding to appropriate DRB1 allele from which peptides were captured. Colour coded for cross-reference to Figures 4, 5, and S3. **(B) and (C):** Examples of selection of 9-mer core epitopes for exclusive binders to (B) DRB1\*1404 or (C) DRB1\*1501 as indicated. Exclusive binders were defined as those with  $\leq 500\text{nM}$  affinity for one DRB1 allele and  $\geq 1000\text{nM}$  for the alternative allele.

(A) Peptide name	DRB1 allele from which peptides were captured	Peptide sequence_N to C terminus	DRB1_1301 nM	DRB1_1501 nM	Affinity status relative to captured DRB1 type
P45.260_LdBPK_191480.1	DRB1*1301	LSSEAKA <b>FILSQ</b> PRRPALSF	35.3	30.3	High
P46.485_LdBPK_050430.1	DRB1*1301	GDT <b>PAIIRQ</b> PGGFTIIDADN	50.3	116.1	High
P48.865_LdBPK_110320.1	DRB1*1301	FESLEVL <b>LRANNI</b> LPFGG	8.7	252.5	High
P43.237_LdBPK_170170.1	DRB1*1301	LQDVYK <b>IGGIGT</b> VPVGRVET	87.7	249.7	Low
P47.1022_LdBPK_100800.1	DRB1*1301	FSFTNLAE <b>IGRTGELL</b> LPQ	544.2	1114	Low
P49.1382_LdBPK_210190.1	DRB1*1301	DL <b>VTASAALLQ</b> SAATHDSI	98.7	298.6	Low
P44.24_LdBPK_171350.1	DRB1*1301 and DRB1*1501	LILL <b>VGDRAK</b> DQVVNLHLM	108.4	251.9	Low for both
P53.3543_LdBPK_302400.1	DRB1*1501	MDCEAG <b>FIALTARCV</b> HSLVV	102.4	38.3	High
P50.3_LdBPK_351710.1	DRB1*1501	SNVGV <b>CSR</b> GVARLWFRVCQ	191.4	79	Low
P51.21_LdBPK_090640.1	DRB1*1501	GAGSGKT <b>QMAARIA</b> YLLQS	220	165	Low
P52.734_LdBPK_331570.1	DRB1*1501	SPP <b>RVVTAATAPV</b> GSPTAAA	34.7	1165.3	Low
P54.1934_LdBPK_160290.1	DRB1*1501	QRA <b>ALLGACTLLQ</b> QGHGMQ	483	297.9	Low

(B)		DRB1_1404					DRB1_1501				
Pos	Peptide	ID	core	Offset	1-log15k	nM	core	Offset	1-log15k	nM	
567	EVKIAAEREEL <b>LKRTKVLQ</b> SQ	PRP-2	LKRTKVLQS	10	0.399	323.5	LKRTKVLQS	10	0.213	1934	
568	VKIAAEREEL <b>LKRTKVLQ</b> SQQ	PRP-2	LKRTKVLQS	9	0.4589	181.8	LKRTKVLQS	9	0.2354	1560.3	
569	KIAAEREEL <b>LKRTKVLQ</b> SQQY	PRP-2	LKRTKVLQS	8	0.524	97.3	LKRTKVLQS	8	0.2769	1046.2	
139	GR <b>VRVLIQRK</b> SETTEGNKHK	584C_L31	VRVLIQRKS	2	0.4604	179.3	VRVLIQRKS	2	0.2488	1370.9	
140	<b>RVRVLIQRK</b> SETTEGNKHK	584C_L31	VRVLIQRKS	1	0.4179	269.8	VRVLIQRKS	1	0.2025	2140	
15	AMADRPRKL <b>TSKGKVKH</b> KRG	Lepp12	LTSKGKVKH	8	0.3812	383.9	LTSKGKVKH	8	0.2787	1028.7	
16	MADRPRKL <b>TSKGKVKH</b> KRGD	Lepp12	LTSKGKVKH	7	0.3723	418.3	LTSKGKVKH	7	0.2689	1130.2	
17	ADRPRKL <b>TSKGKVKH</b> KRGDL	Lepp12	LTSKGKVKH	6	0.3707	424.5	LTSKGKVKH	6	0.2652	1171.1	
18	DRPRKL <b>TSKGKVKH</b> KRGDLK	Lepp12	LTSKGKVKH	5	0.3773	398.4	LTSKGKVKH	5	0.2686	1132.9	
19	RPRKL <b>TSKGKVKH</b> KRGDLKM	Lepp12	LTSKGKVKH	4	0.3879	359.8	LTSKGKVKH	4	0.278	1035.7	

(C)		DRB1_1404					DRB1_1501				
Pos	Peptide	ID	core	Offset	1-log15k	nM	core	Offset	1-log15k	nM	
0	MATMEN <b>NVAFAGY</b> AYYSTGGE	L302_06	NVAFAGYAY	5	0.2789	1026.5	NVAFAGYAY	5	0.4731	158.6	
1	ATMEN <b>NVAFAGY</b> AYYSTGGEG	L302_06	NVAFAGYAY	4	0.2622	1205	NVAFAGYAY	4	0.4663	169.3	
2	TMEN <b>NVAFAGY</b> AYYSTGGEGF	L302_06	VAFAGYAY	4	0.2523	1325.4	NVAFAGYAY	3	0.4566	185.9	
3	MEN <b>NVAFAGY</b> AYYSTGGEGFI	L302_06	VAFAGYAY	3	0.2445	1429.2	NVAFAGYAY	2	0.4345	229.8	
4	<b>ENVAFAGY</b> AYYSTGGEGFIY	L302_06	VAFAGYAY	2	0.2268	1694.4	NVAFAGYAY	1	0.4012	316.8	
5	<b>NVAFAGY</b> AYYSTGGEGFIYA	L302_06	VAFAGYAY	1	0.2156	1887.6	NVAFAGYAY	0	0.3722	418.6	
142	GAVGGDQNNL <b>IGQFGVGF</b> YS	LPG3	IGQFGVGFY	10	0.1922	2362.5	IGQFGVGFY	10	0.3708	424.4	
143	AVGGDQNNL <b>IGQFGVGF</b> YSV	LPG3	IGQFGVGFY	9	0.2259	1709.6	IGQFGVGFY	9	0.4461	205.7	
144	VGGDQNNL <b>IGQFGVGF</b> YSVF	LPG3	IGQFGVGFY	8	0.2502	1353.3	IGQFGVGFY	8	0.4934	130.6	
145	GGDQNNL <b>IGQFGVGF</b> YSVFL	LPG3	IGQFGVGFY	7	0.2521	1328.5	IGQFGVGFY	7	0.4945	129.1	
146	GDQNNL <b>IGQFGVGF</b> YSVFLV	LPG3	IGQFGVGFY	6	0.2654	1168.4	IGQFGVGFY	6	0.5023	119.8	
147	DQNNL <b>IGQFGVGF</b> YSVFLVG	LPG3	LIGQFGVGF	4	0.2639	1185.8	IGQFGVGFY	5	0.5001	122.3	
148	QNNL <b>IGQFGVGF</b> YSVFLVGD	LPG3	LIGQFGVGF	3	0.2564	1274	IGQFGVGFY	4	0.4888	136.3	