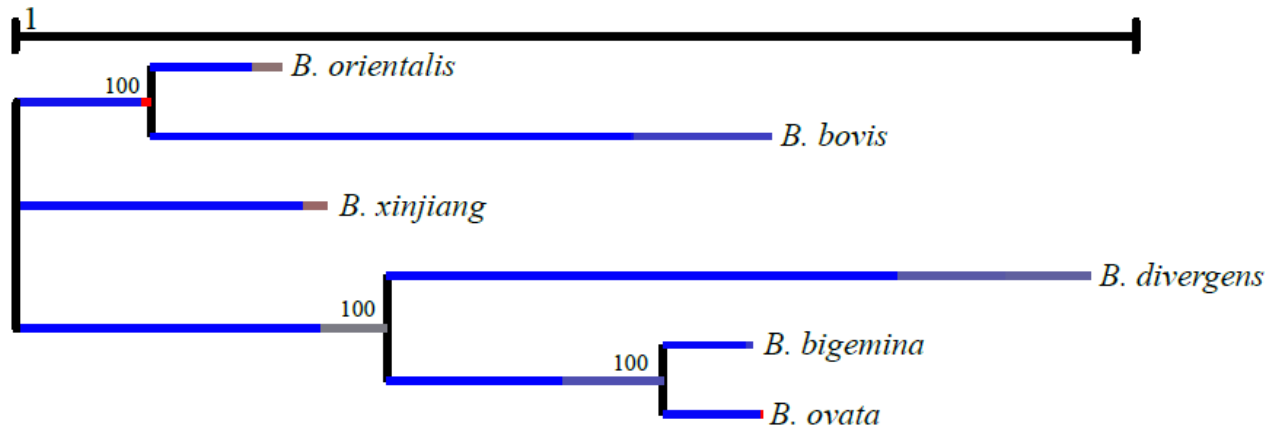




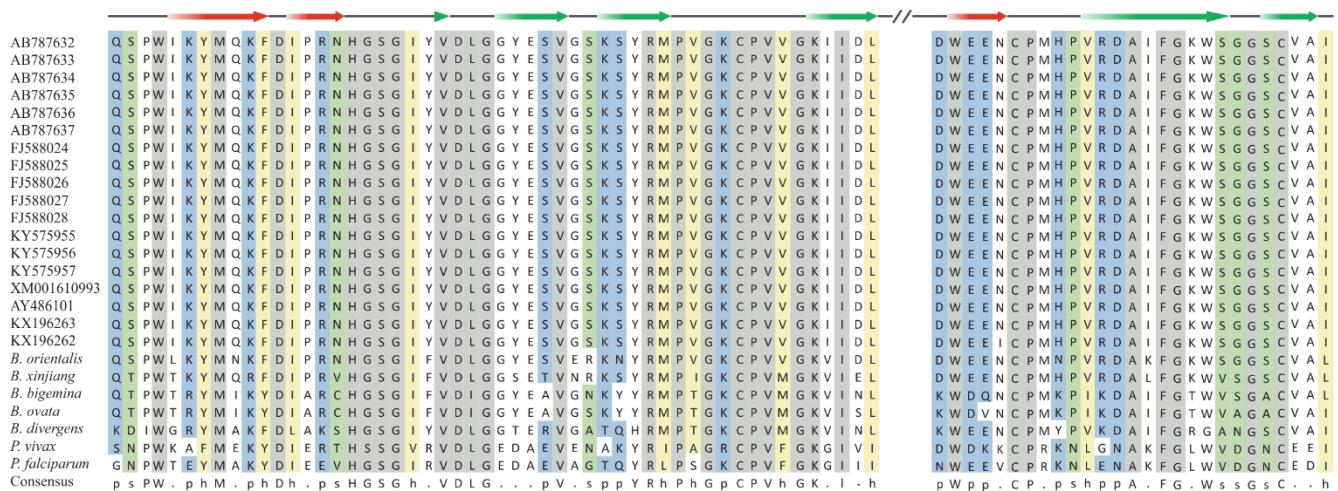
1. Supplementary files

Supplementary Figure 1. Lineages under episodic positive selection identified by the branch site REL method.



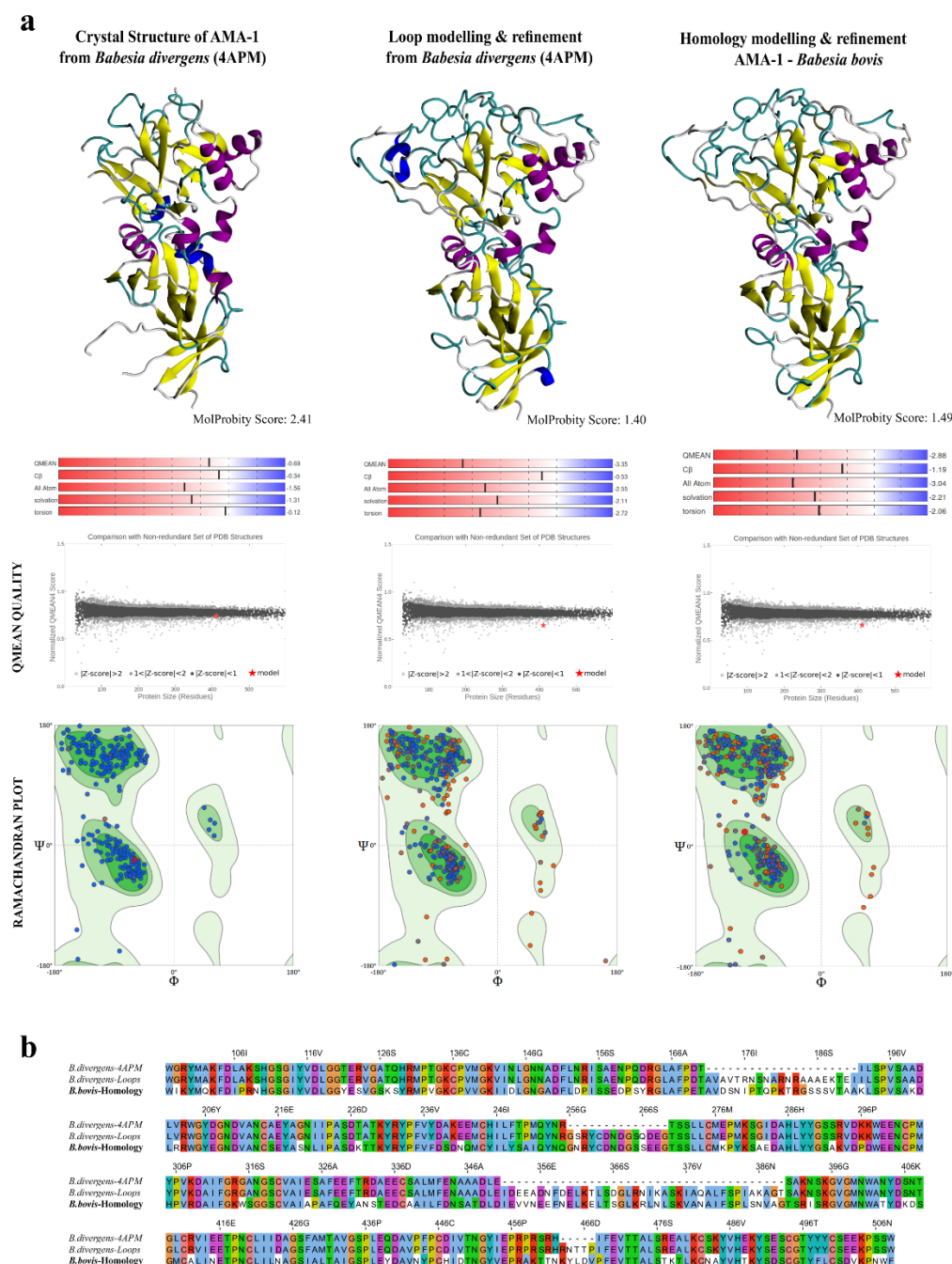
Phylogeny was inferred by using the MEGA X sequence alignment tool, along with the maximum likelihood method, using the K2P+G (5) evolutionary model and was scaled on the expected amount of substitutions/nucleotides. Each colour's hue indicates selection strength, primary red being $\omega > 5$, primary blue $\omega = 0$ and grey $\omega = 1$.

Supplementary Figure 2. Sequence and secondary structure conservation of two AMA-1 regions derived from Babesia and Plasmodium species.



B. bovis sequences are designated by their accession numbers. Red arrows above the alignment represent α -helices and green ones β -sheets/turns; polar (p), small (s) and hydrophobic (h) residues are indicated on the consensus sequence.

Supplementary Figure 3. *B. bovis* AMA-1 ectoplasmic domain structure refinement.



(a) Babesia AMA-1 modelling structures and quality parameters. MolProbity structure validation score (combined protein quality score reflecting the crystallographic resolution at which such quality would be expected, a lower score being better). QMEAN4 is a scoring function calculated by comparison with reference structures and ranges from -4 to 4; the smaller the value, the worse a model's quality. Normalised QMEAN4, comparing the models studied here with reported crystallographic structures. Note how the homology model was close to acceptable structural parameters. The models had good



Ramachandran map profiles, with few outliers. (b). AMA-1 sequence alignment regarding the structures studied here.

Supplementary Table 1. *B. bovis* AMA-1-DI-DII HABP T-cell epitopes.

Start position	Allele	Peptide (15 mer)	Core (P1-P9)	Rank-EL	<i>B. bovis</i> AMA-1 HABP
111	BoLA-DRB3_010_02	GSGIYVDLGGYESVG	YVDLGGYES	1.22	42437 / 42438
111	BoLA-DRB3_020_02	GSGIYVDLGGYESVG	YVDLGGYES	1.26	42437 / 42438
111	BoLA-DRB3_060_01	GSGIYVDLGGYESVG	YVDLGGYES	1.50	42437 / 42438
111	BoLA-DRB3_031_01	GSGIYVDLGGYESVG	IYVDLGGYE	1.65	42437 / 42438
111	BoLA-DRB3_031_03	GSGIYVDLGGYESVG	IYVDLGGYE	1.65	42437 / 42438
111	BoLA-DRB3_015_06	GSGIYVDLGGYESVG	IYVDLGGYE	1.66	42437 / 42438
111	BoLA-DRB3_043_03	GSGIYVDLGGYESVG	YVDLGGYES	1.68	42437 / 42438
111	BoLA-DRB3_033_01	GSGIYVDLGGYESVG	IYVDLGGYE	1.70	42437 / 42438
111	BoLA-DRB3_043_01	GSGIYVDLGGYESVG	IYVDLGGYE	1.79	42437 / 42438
111	BoLA-DRB3_066_01	GSGIYVDLGGYESVG	YVDLGGYES	1.79	42437 / 42438
111	BoLA-DRB3_027_04	GSGIYVDLGGYESVG	YVDLGGYES	1.85	42437 / 42438
111	BoLA-DRB3_007_02	GSGIYVDLGGYESVG	YVDLGGYES	1.88	42437 / 42438
111	BoLA-DRB3_027_06	GSGIYVDLGGYESVG	IYVDLGGYE	1.90	42437 / 42438
111	BoLA-DRB3_005_04	GSGIYVDLGGYESVG	IYVDLGGYE	1.93	42437 / 42438
111	BoLA-DRB3_043_02	GSGIYVDLGGYESVG	IYVDLGGYE	1.96	42437 / 42438
111	BoLA-DRB3_014_01_01	GSGIYVDLGGYESVG	IYVDLGGYE	1.97	42437 / 42438
111	BoLA-DRB3_014_01_02	GSGIYVDLGGYESVG	IYVDLGGYE	1.97	42437 / 42438
116	BoLA-DRB3_028_01	VDLGGYESVGSKSYR	YESVGSKSY	0.75	42437 / 42438
116	BoLA-DRB3_028_02	VDLGGYESVGSKSYR	YESVGSKSY	0.75	42437 / 42438
116	BoLA-DRB3_011_01	VDLGGYESVGSKSYR	YESVGSKSY	1.24	42437 / 42438
116	BoLA-DRB3_028_03	VDLGGYESVGSKSYR	YESVGSKSY	1.25	42437 / 42438
116	BoLA-DRB3_031_04	VDLGGYESVGSKSYR	YESVGSKSY	1.27	42437 / 42438
116	BoLA-DRB3_075_03	VDLGGYESVGSKSYR	YESVGSKSY	1.28	42437 / 42438
116	BoLA-DRB3_022_03	VDLGGYESVGSKSYR	YESVGSKSY	1.36	42437 / 42438
116	BoLA-DRB3_075_02	VDLGGYESVGSKSYR	YESVGSKSY	1.37	42437 / 42438
116	BoLA-DRB3_010_02	VDLGGYESVGSKSYR	YESVGSKSY	1.40	42437 / 42438
116	BoLA-DRB3_066_01	VDLGGYESVGSKSYR	YESVGSKSY	1.41	42437 / 42438
116	BoLA-DRB3_060_01	VDLGGYESVGSKSYR	YESVGSKSY	1.47	42437 / 42438
116	BoLA-DRB3_022_01	VDLGGYESVGSKSYR	YESVGSKSY	1.51	42437 / 42438
116	BoLA-DRB3_022_02	VDLGGYESVGSKSYR	YESVGSKSY	1.51	42437 / 42438
116	BoLA-DRB3_022_04	VDLGGYESVGSKSYR	YESVGSKSY	1.51	42437 / 42438
116	BoLA-DRB3_022_05	VDLGGYESVGSKSYR	YESVGSKSY	1.51	42437 / 42438
116	BoLA-DRB3_026_01	VDLGGYESVGSKSYR	YESVGSKSY	1.56	42437 / 42438
116	BoLA-DRB3_007_02	VDLGGYESVGSKSYR	YESVGSKSY	1.57	42437 / 42438
116	BoLA-DRB3_006_01	VDLGGYESVGSKSYR	YESVGSKSY	1.63	42437 / 42438



116	BoLA-DRB3_074_01	VDLGGYESVGSKSYR	YESVGSKSY	1.63	42437 / 42438
116	BoLA-DRB3_007_01	VDLGGYESVGSKSYR	YESVGSKSY	1.66	42437 / 42438
116	BoLA-DRB3_043_01	VDLGGYESVGSKSYR	YESVGSKSY	1.75	42437 / 42438
116	BoLA-DRB3_075_01	VDLGGYESVGSKSYR	YESVGSKSY	1.76	42437 / 42438
116	BoLA-DRB3_031_01	VDLGGYESVGSKSYR	YESVGSKSY	1.86	42437 / 42438
116	BoLA-DRB3_031_03	VDLGGYESVGSKSYR	YESVGSKSY	1.86	42437 / 42438
116	BoLA-DRB3_010_01	VDLGGYESVGSKSYR	YESVGSKSY	1.99	42437 / 42438
118	BoLA-DRB3_028_01	LGGYESVGSKSYRMP	YESVGSKSY	1.24	42437 / 42438
118	BoLA-DRB3_028_02	LGGYESVGSKSYRMP	YESVGSKSY	1.24	42437 / 42438
118	BoLA-DRB3_043_01	LGGYESVGSKSYRMP	YESVGSKSY	1.73	42437 / 42438
118	BoLA-DRB3_066_01	LGGYESVGSKSYRMP	YESVGSKSY	1.91	42437 / 42438
118	BoLA-DRB3_043_02	LGGYESVGSKSYRMP	YESVGSKSY	1.94	42437 / 42438
317	BoLA-DRB3_022_03	GGSCVAIAPAFQEYA	VAIAPAFQE	1.43	42443
317	BoLA-DRB3_028_03	GGSCVAIAPAFQEYA	VAIAPAFQE	1.50	42443
317	BoLA-DRB3_011_01	GGSCVAIAPAFQEYA	VAIAPAFQE	1.62	42443
317	BoLA-DRB3_014_01_01	GGSCVAIAPAFQEYA	VAIAPAFQE	1.72	42443
317	BoLA-DRB3_014_01_02	GGSCVAIAPAFQEYA	VAIAPAFQE	1.72	42443
317	BoLA-DRB3_020_01_01	GGSCVAIAPAFQEYA	VAIAPAFQE	1.84	42443
317	BoLA-DRB3_020_01_02	GGSCVAIAPAFQEYA	VAIAPAFQE	1.84	42443
317	BoLA-DRB3_020_09	GGSCVAIAPAFQEYA	VAIAPAFQE	1.84	42443
317	BoLA-DRB3_020_10	GGSCVAIAPAFQEYA	VAIAPAFQE	1.84	42443
317	BoLA-DRB3_033_01	GGSCVAIAPAFQEYA	VAIAPAFQE	1.86	42443
317	BoLA-DRB3_007_02	GGSCVAIAPAFQEYA	VAIAPAFQE	1.87	42443
317	BoLA-DRB3_077_01	GGSCVAIAPAFQEYA	VAIAPAFQE	1.98	42443

Peptides having $\leq 2\%$ rank in a frame of 15 aa for a panel of 135 BoLA-DR molecules.