

Table S1: Performance of PepBridge on peptide immunogenicity (IMM) and MHC-peptide binding prediction under different R'_P alignment settings during training.

setting	MP_independent AUC	MP_independent AUPR	MP_external AUC	MP_external AUPR	IMM AUC	IMM AUPR
no_align	0.97	0.94	0.94	0.95	0.80	0.76
align1	0.97	0.94	0.94	0.94	0.81	0.77
align1_In	0.97	0.94	0.94	0.94	0.81	0.78
align2	0.97	0.94	0.93	0.94	0.80	0.77
align2_In	0.97	0.94	0.94	0.95	0.81	0.77
align3	0.97	0.95	0.93	0.94	0.80	0.77
align3_In	0.97	0.94	0.94	0.95	0.81	0.77

align1, align2 and align3: alignment on the last 1, 2 or all 3 layers of R'_P in R_{MP} and R_{PT} , respectively; In: layer normalization before alignment; independent: independent test dataset; external: external test dataset.

Table S2: Performance of PepBridge on MHC-peptide residue contact and distance prediction under different R'_P alignment settings during training.

setting	MP_contact AUC	MP_contact AUPR	MP_distance MSE	MP_distance MAPE	MP_distance Pearson	MP_distance Spearman
no_align	0.97	0.82	1.69	0.14	0.97	0.96
align1	0.97	0.80	1.66	0.14	0.97	0.96
align1_In	0.97	0.83	1.61	0.13	0.97	0.96
align2	0.96	0.78	2.17	0.16	0.97	0.96
align2_In	0.97	0.81	1.69	0.14	0.97	0.96
align3	0.97	0.83	1.57	0.13	0.97	0.96
align3_In	0.97	0.82	1.63	0.13	0.97	0.96

align1, align2 and align3: alignment on the last 1, 2 or all 3 layers of R'_P in R_{MP} and R_{PT} , respectively; In: layer normalization before alignment.

Table S3: Performance of PepBridge on MHC-peptide-TCR binding prediction under different R'_P alignment settings during training.

setting	MPT_independent	MPT_independent	MPT_benchmark	MPT_benchmark
	AUC	AUPR	AUC	AUPR
no_align	0.88	0.69	0.98	0.98
align1	0.89	0.71	0.98	0.97
align1_In	0.89	0.72	0.98	0.96
align2	0.89	0.71	0.98	0.97
align2_In	0.89	0.71	0.98	0.97
align3	0.89	0.72	0.97	0.96
align3_In	0.89	0.72	0.98	0.97

align1, align2 and align3: alignment on the last 1, 2 or all 3 layers of R'_P in R_{MP} and R_{PT} , respectively; In: layer normalization before alignment.

Table S4: Performance of PepBridge on peptide-TCR residue contact and distance prediction of post-2022 test dataset under different R'_P alignment settings during training.

setting	PT_contact	PT_contact	PT_distance	PT_distance	PT_distance	PT_distance
	AUC	AUPR	MSE	MAPE	Pearson	Spearman
no_align	0.93	0.48	7.27	0.22	0.92	0.92
align1	0.94	0.50	6.64	0.20	0.93	0.93
align1_In	0.94	0.52	6.81	0.20	0.93	0.92
align2	0.94	0.48	7.08	0.20	0.92	0.92
align2_In	0.94	0.49	6.60	0.20	0.93	0.93
align3	0.94	0.52	6.31	0.20	0.93	0.93
align3_In	0.94	0.48	6.88	0.21	0.93	0.92

align1, align2 and align3: alignment on the last 1, 2 or all 3 layers of R'_P in R_{MP} and R_{PT} , respectively; In: layer normalization before alignment.

Table S5: Performance of PepBridge on MHC-peptide and peptide-TCR binding prediction under different R'_P alignment settings without structural conformation task.

setting	MP_independent AUC	MP_independent AUPR	MP_external AUC	MP_external AUPR	PT_random AUC	PT_random AUPR	PT_hybrid AUC	PT_hybrid AUPR	PT_benchmark AUC	PT_benchmark AUPR
no_align	0.97	0.94	0.93	0.94	0.74	0.62	0.77	0.68	0.65	0.69
align1	0.97	0.93	0.94	0.94	0.75	0.64	0.79	0.70	0.65	0.69
align1_In	0.97	0.94	0.93	0.94	0.76	0.65	0.78	0.70	0.69	0.73
align2	0.97	0.93	0.92	0.93	0.75	0.63	0.77	0.68	0.64	0.68
align2_In	0.97	0.94	0.94	0.94	0.76	0.65	0.77	0.69	0.65	0.69
align3	0.97	0.94	0.93	0.94	0.76	0.65	0.78	0.70	0.68	0.71
align3_In	0.97	0.94	0.93	0.94	0.77	0.66	0.78	0.70	0.67	0.71

align1, align2 and align3: alignment on the last 1, 2 or all 3 layers of R'_P in R_{MP} and R_{PT} , respectively; In: layer normalization before alignment; independent: independent test dataset; external: external test dataset; random, hybrid and benchmark: prediction on the random_mismatch, hybrid_strategy and third-party benchmark test dataset, respectively.

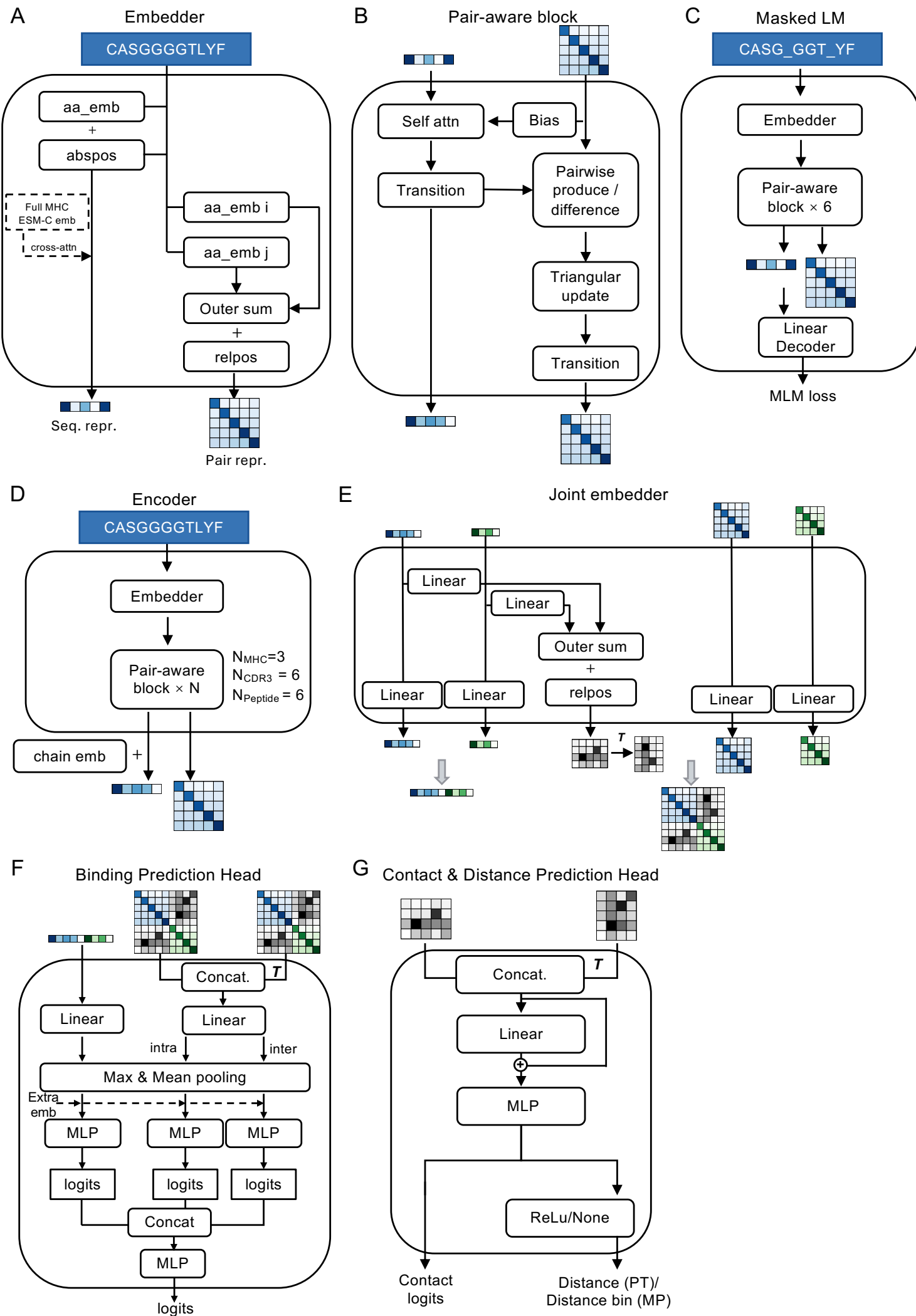
Figure S1

Figure S2

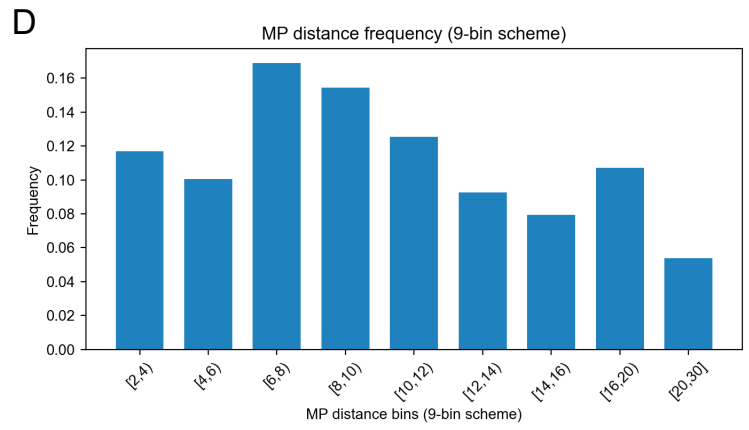
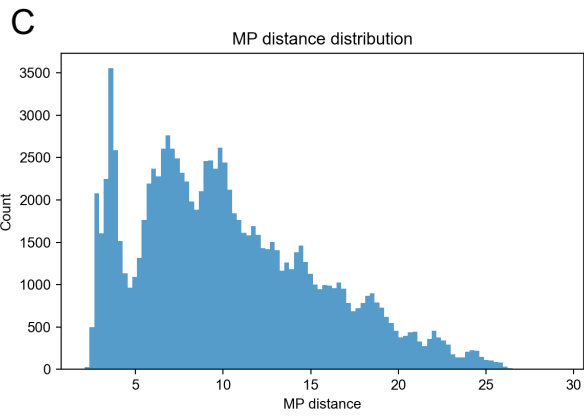
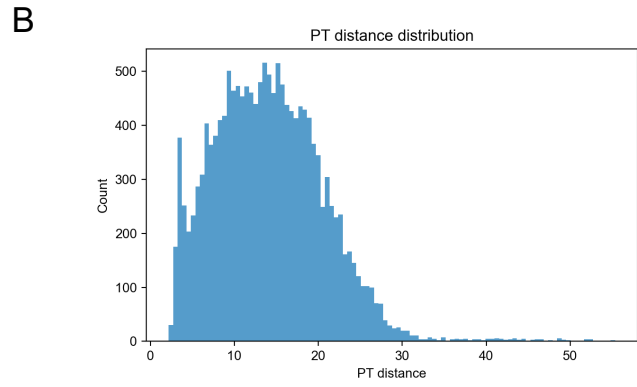
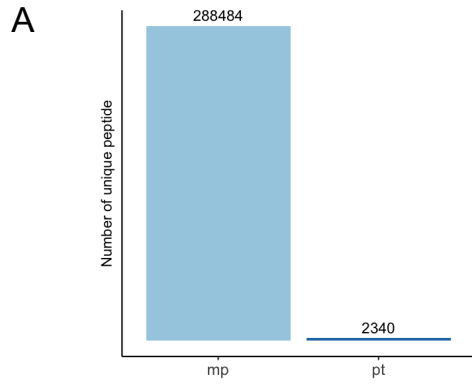


Figure S3

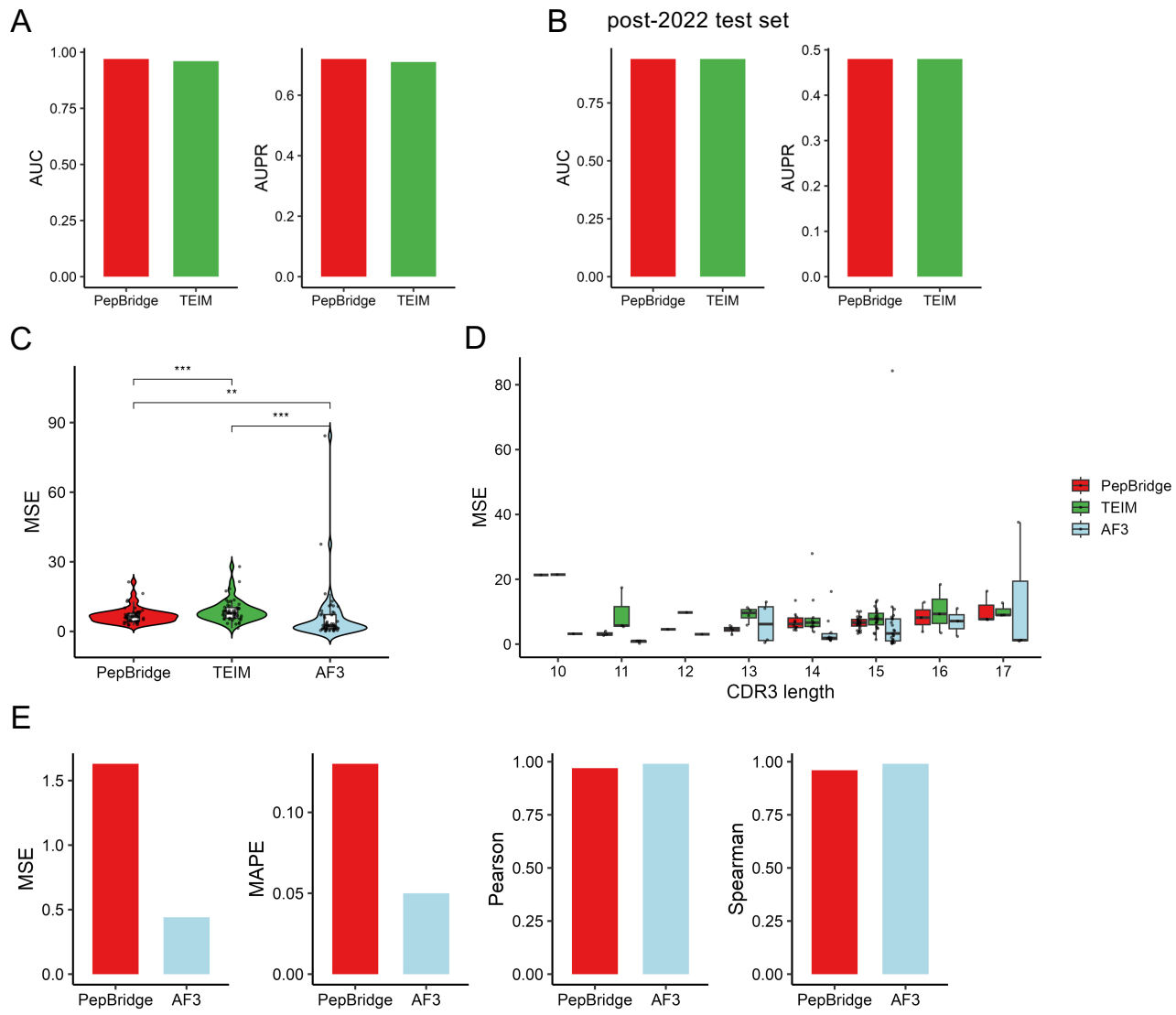
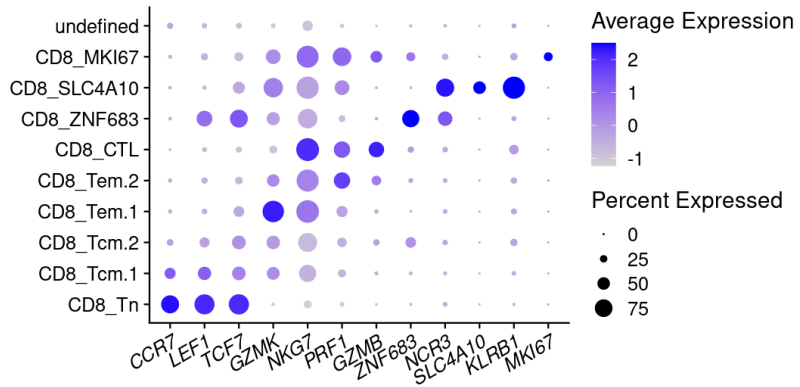
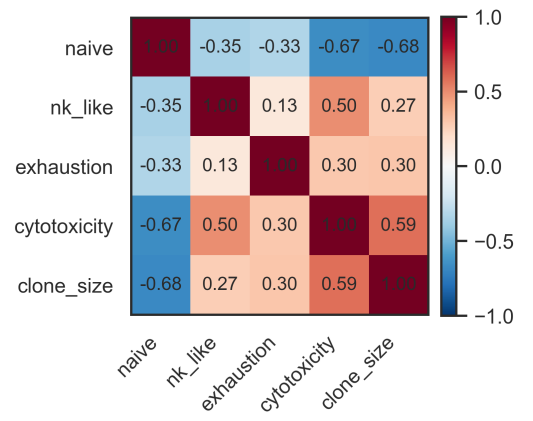


Figure S4

A



B



Supplementary tables:

Table S1: Performance of PepBridge on peptide immunogenicity (IMM) and MHC-peptide binding prediction under different R'_P alignment settings during training.

Table S2: Performance of PepBridge on MHC-peptide residue contact and distance prediction under different R'_P alignment settings during training.

Table S3: Performance of PepBridge on MHC-peptide-TCR binding prediction under different R'_P alignment settings during training.

Table S4: Performance of PepBridge on peptide-TCR residue contact and distance prediction of post-2022 test dataset under different R'_P alignment settings during training.

Table S5: Performance of PepBridge on MHC-peptide and peptide-TCR binding prediction under different R'_P alignment settings without structural conformation task.

Supplementary figure legends:

Figure S1: Detailed architecture of the subunits of PepBridge.

A-G: Diagram illustration of amino acid sequence Embedder (A), Pair-aware block (B), Masked protein language model (C), amino acid sequence Encoder (D), amino acid sequence Joint embedder (E), Binding Prediction Head (F) and Contact & Distance Prediction Head (G), respectively. aa: amino acid; emb: embedding; abspos: absolute position; attn: attention; relpos: relative position; Seq.: sequence; repr.: representation; Concat: Concatenate; MLP: Multi-Layer Perceptron.

Figure S2: Statistics of data distribution.

A: Bar chart for comparing the number of unique MHC-peptide and peptide-TCR data pairs. mp: MHC-peptide; pt: peptide-TCR. B: Histogram of peptide-TCR residue distance. C: Histogram of MHC-peptide residue distance. D: Bar chart of binned MHC-peptide distance frequency.

Figure S3: Additional performance comparison between PepBridge and other existing tools.

A: Bar charts for comparing AUC (left) and AUPR (right) between PepBridge and TEIM on MHC-peptide contact map prediction. B: Same as A, but for the post-2022 test dataset. C: Violin plots showing the MSE distribution on the post-2022 test dataset for PepBridge, TEIM, and AF3. Each dot represents one test sample. Statistical significance was assessed using paired Wilcoxon signed-rank tests (** $P < 0.01$, *** $P < 0.001$). D: Box plots showing MSE on the post-2022 test dataset stratified by CDR3 β length for PepBridge, TEIM, and AF3. E: From left to right, bar charts for comparing MSE, MAPE, Pearson's correlation and Spearman's correlation values between PepBridge and AlphaFold3 on MHC-peptide residue distance prediction.

Figure S4: Additional characterization of the CD8+ T cells in 10x_200k dataset.

A: Dot plot of marker genes for the defined T cell clusters in the 10x_200k dataset. B: Heatmap visualization of pair-wise Spearman's correlations between distinct T cell functional scores and TCR clone size for T cells in the 10x_200k dataset.