SUPPLEMENTARY INFORMATION

Supplementary Table 1. Antigen presentation-relevant polymorphisms associated with TB susceptibility.

Gene	Allele	Odds ratio	References
HLA class II	DR2 (serotype)	1.8-2.7	64, 65, 67
	DRB1*1501 (DR2 subtype)	2.7–7.9	42, 50, 58, 61
	DQB1*0503	N/A[1]	66
IFN-γ	+874A	1.6-3.8	32, 35, 52
TAP	TAP2*0201	2.4-4.3	17, 48

[1]This polymorphism was not detected in the control population.

A more complete list of polymorphisms associated with TB susceptibility can be found elsewhere (3, 15, 22). Odds ratios represent a measure of the relative risk associated with each allele.

APC Model Equations

Equations 1-16 constitute the APC model and are identical to the equations presented in Chang *et al.* (8).

$$dG/dt = [-k_{\text{on-IFN-}\gamma}\, G\, R_G + k_{\text{off-IFN-}\gamma}\, C_G]\, [n_{\text{cells}} / (N_A\, v_{\text{medium}})] - k_{\text{deg-IFN-}\gamma}\, G \quad [1]$$

$$dR_G/dt = -k_{\text{on-IFN-}\gamma}\, G\, R_G + k_{\text{off-IFN-}\gamma}\, C_G + k_{\text{recyc}}\, C_G \quad [2]$$

$$dC_G/dt = k_{\text{on-IFN-}\gamma}\, G\, R_G - k_{\text{off-IFN-}\gamma}\, C_G - k_{\text{recyc}}\, C_G \quad [3]$$

$$dC_{2m}/dt = k_{\text{txn-C2}}\, (1 + \alpha_{C2}\, C_G) - k_{\text{deg-C2m}}\, C_{2m} \quad [4]$$

$$dC_2/dt = k_{\text{tsl-C2}}\, C_{2m} - k_{\text{deg-C2}}\, C_2 \quad [5]$$

$$dM_m/dt = k_{\text{txn-M}}\, C_2 - k_{\text{deg-Mm}}\, M_m \quad [6]$$

$$dA^*/dt = -(k_{\text{pino}}\, n_{\text{cells}} / v_{\text{medium}})\, A^* - k_{\text{deg-A}^*}\, A^* \quad [7]$$

$$dA/dt = (k_{\text{pino}} / v_{\text{MIIC}})\, A^* - k_{\text{deg-A}}\, A - k_{\text{lys}}\, A \quad [8]$$

$$dE/dt = k_{\text{deg-A}}\, A + (-k_{\text{on-MHC}}\, M\, E + k_{\text{off-MHC}}\, M_E)\, [1 / (N_A\, v_{\text{MIIC}})] - k_{\text{lys}}\, E \quad [9]$$

$$dS/dt = k_{\text{source}} + [k_{\text{deg-MHC}}\, (M_S + M_S^*) - k_{\text{on-MHC}}\, M\, S + k_{\text{off-MHC}}\, M_S]\, [1 / (N_A\, v_{\text{MIIC}})] - k_{\text{lys}}\, S \quad [10]$$

$$dM/dt = k_{\text{tsl-M}}\, (1 + \alpha_M\, C_G)\, M_m - k_{\text{on-MHC}}\, M\, S + k_{\text{off-MHC}}\, M_S - k_{\text{on-MHC}}\, M\, E + k_{\text{off-MHC}}\, M_E - k_{\text{out}}\, M + k_{\text{in}}\, M^* - k_{\text{deg-MHC}}\, M \quad [11]$$

$$dM^*/dt = k_{\text{out}}\, M - k_{\text{in}}\, M^* - k_{\text{deg-MHC}}\, M^* \quad [12]$$

$$dM_S/dt = k_{\text{on-MHC}}\, M\, S - k_{\text{off-MHC}}\, M_S - k_{\text{out}}\, M_S + k_{\text{in}}\, M_S^* - k_{\text{deg-MHC}}\, M_S \quad [13]$$

$$dM_S^*/dt = k_{\text{out}}\, M_S - k_{\text{in}}\, M_S^* - k_{\text{deg-MHC}}\, M_S^* \quad [14]$$

$$dM_E/dt = k_{\text{on-MHC}}\, M\, E - k_{\text{off-MHC}}\, M_E - k_{\text{out}}\, M_E + k_{\text{in}}\, M_E^* - k_{\text{deg-MHC}}\, M_E \quad [15]$$

$$dM_E^*/dt = k_{\text{out}}\, M_E - k_{\text{in}}\, M_E^* - k_{\text{deg-MHC}}\, M_E^* \quad [16]$$

Descriptions of the terms in each equation are provided in Chang *et al.* (8). Variables and parameters are defined, and values provided, in Supplementary Tables 2 and 3.

TCR Internalization Model Equations

Equations 17-27 constitute the T cell model and are approximated from the PDEs of Coombs *et al.* (10) that pertain to the contact zone.

$$dM_E^C/dt = \underset{\text{pMHC-TCR association}}{-k_{on\text{-}B}\,(T^C + T_{activ}{}^C)\,M_E^C} + \underset{\text{pMHC-TCR dissociation}}{k_{off\text{-}B}\,(B_0 + B_1 + B_2 + B_3 + B_4 + B_5 + B_N)} + \underset{\text{internalization}}{\lambda_B\,B_N} - \underset{\text{degradation}}{k_{deg\text{-}MHC,C}\,M_E^C} \quad [17]$$

$$dT^C/dt = \underset{\text{activation}}{-k_{on\text{-}B}\,T^C\,M_E^C} + \underset{\text{deactivation}}{k_{off\text{-}B}\,(B_0 + B_1 + B_2 + B_3 + B_4 + B_5 + B_N)} \quad [18]$$

$$dB_0/dt = \underset{\text{activation}}{k_{on\text{-}B}\,T^C\,M_E^C} - \underset{\text{deactivation}}{k_p\,B_0} - \underset{\text{deactivation}}{k_{off\text{-}B}\,B_0} \quad [19]$$

$$dB_1/dt = \underset{\text{activation}}{k_p\,B_0} - \underset{\text{deactivation}}{k_p\,B_1} - \underset{\text{deactivation}}{k_{off\text{-}B}\,B_1} \quad [20]$$

$$dB_2/dt = \underset{\text{activation}}{k_p\,B_1} - \underset{\text{deactivation}}{k_p\,B_2} - \underset{\text{deactivation}}{k_{off\text{-}B}\,B_2} \quad [21]$$

$$dB_3/dt = \underset{\text{activation}}{k_p\,B_2} - \underset{\text{deactivation}}{k_p\,B_3} - \underset{\text{deactivation}}{k_{off\text{-}B}\,B_3} \quad [22]$$

$$dB_4/dt = \underset{\text{activation}}{k_p\,B_3} - \underset{\text{deactivation}}{k_p\,B_4} - \underset{\text{deactivation}}{k_{off\text{-}B}\,B_4} \quad [23]$$

$$dB_5/dt = \underset{\text{activation}}{k_p\,B_4} - \underset{\text{deactivation}}{k_p\,B_5} - \underset{\text{deactivation}}{k_{off\text{-}B}\,B_5} \quad [24]$$

$$dB_N/dt = \underset{\text{association}}{k_{on\text{-}B}\,T_{activ}{}^C\,M_E^C} + \underset{\text{activation}}{k_p\,B_5} - \underset{\text{deactivation}}{k_{off\text{-}B}\,B_N} \quad [25]$$

$$dT_{activ}{}^C/dt = \underset{\text{association}}{-k_{on\text{-}B}\,T_{activ}{}^C\,M_E^C} + \underset{\text{dissocation}}{k_{off\text{-}B}\,B_N} - \underset{\text{internalization}}{\lambda_T\,T_{activ}{}^C} \quad [26]$$

$$dT_{int}/dt = \underset{\text{internalization (free)}}{\lambda_T\,(T_{activ} + T_{activ}{}^T)} + \underset{\text{internalization (bound)}}{\lambda_B\,B_N} \quad [27]$$

Briefly, Equations 17-19 describe the processes by which free pMHC complexes on the APC surface and free TCRs on the T cell surface bind and form pMHC-TCR tri-molecular complexes. Equations 20-25 describe the progressive activation of pMHC-TCR tri-molecular complexes that occurs during kinetic proofreading. Finally, Equations 26 and 27 describe the association and dissociation of fully activated TCRs to and from pMHC complexes and the internalization of activated TCR in free or bound forms. In this model, only the contact zone of Coombs et al. (10) was represented, and therefore terms representing diffusion between the contact zone and other zones in the Coombs model

were excluded. Variables and parameters are defined, and parameter values provided, in Supplementary Tables 4 and 5. The model recapitulated major features of the model of Coombs *et al.* (10) and Gonzalez *et al.* (18) such as the existence of an optimal pMHC-TCR half-life for TCR internalization (data not shown).

Cytokine Production Model Equations

Equations 28-31 describe the cytokine production portion of the T cell model.

$$dF_{activ}/dt = \underset{\text{activation}}{k_{resp}\,(T_{activ} + B_N)\,F} - \underset{\text{de-activation}}{k_{decay}\,F_{activ}} \quad [28]$$

$$F = 1 - F_{activ} \quad [29]$$

$$dG_m/dt = \underset{\text{transcription}}{k_{txn\text{-}IFN\text{-}\gamma}\,F_{activ}} - \underset{\text{degradation}}{k_{deg\text{-}Gm}\,G_m} \quad [30]$$

$$dG_2/dt = \underset{\text{translation}}{k_{tsl\text{-}IFN\text{-}\gamma}\,G_m\,[n_{cells} / (N_A\,v_{medium})]} - \underset{\text{degradation}}{k_{deg\text{-}IFN\text{-}\gamma}\,G_2} \quad [31]$$

Briefly, Equation 28 represents the first-order activation and deactivation of a transcription factor for cytokines produced by the T cell, e.g., NF-κB, in units of fraction total transcription factor. Equation 29 represents the pool of un-activated transcription factor. Equation 30 represents the first-order synthesis (i.e., transcription) and degradation of cytokine mRNA and in particular the absolute dependence of the synthesis of cytokine mRNA on the presence of activated transcription factor. Equation 31 represents the first-order synthesis (i.e., translation) and degradation of cytokine protein. Like cytokine mRNA, cytokine protein in the model is dependent on the presence of its activator, cytokine mRNA. Variables and parameters are defined, and parameter values provided, in Supplementary Tables 4 and 5.

Supplementary Table 2. Initial values in the APC model

Variable	Description	Initial value[(1)]
G	IFN-γ concentration in medium	Varies by experiment
R_G	Free IFN-γ receptors per cell	1×10^3
C_G	IFN-γ/IFN-γ receptor complexes per cell	0
C_{2m}	CIITA mRNA as fraction of basal level	1
C_2	CIITA protein as fraction of basal level	1
M_m	MHC[(2)] mRNA per cell	1×10^5
A^*	Antigen concentration in medium	Varies by experiment
A	Antigen concentration within MIIC	0
E	Peptide concentration within MIIC	0
S	Self peptide concentration within MIIC	4×10^{-4} M[(3)]
M	Free intracellular MHC per cell	$p_{in}\ (1 - p_{bound})\ M_{tot} \approx 6.7 \times 10^3$
M^*	Free surface MHC per cell	$[(1 - p_{in}) / p_{in}]\ M_0 \approx 1.3 \times 10^4$
M_S	Intracellular self-MHC complexes per cell	$[p_{bound} / (1 - p_{bound})]\ M_0 \approx 2.7 \times 10^4$
M_S^*	Surface self-MHC complexes per cell	$[(1 - p_{in}) / p_{in}]\ M_{S,0} \approx 5.3 \times 10^4$
M_E	Intracellular peptide-MHC complexes per cell	0
M_E^*	Surface peptide-MHC complexes per cell	0

[(1)]When used in the definition of another parameter or variable, the subscript 0 refers to the initial value of a particular variable such that, e.g., M_0 refers to the initial value of M. Units are numbers of molecules per cell (APC or T cell) unless otherwise indicated.
[(2)]MHC in this and following entries refers to MHC class II.

[(3)]This value was estimated from $[k_{deg\text{-}Mm}\ (M_{S,0} + M_{S,0^*}) + k_{off\text{-}MHC}\ M_{S,0}] / k_{on\text{-}MHC}\ M_0$ (8).

Supplementary Table 3. Parameters in the APC model

Parameter	Description	Value[(1)]
$k_{\text{on-IFN-}\gamma}$	IFN-γ / IFN-γR association rate constant	3×10^{9} M^{-1} h^{-1}
$k_{\text{off-IFN-}\gamma}$	IFN-γ / IFN-γR dissociation rate constant	7×10^{-1} h^{-1}
n_{cells}	Number of APC in medium	Varies by experiment
v_{medium}	Volume of culture medium	Varies by experiment
$k_{\text{deg-IFN-}\gamma}$	IFN-γ degradation rate constant	1×10^{-2} h^{-1}
k_{recyc}	IFN-γ receptor recycling rate constant	1×10^{1} h^{-1}
$k_{\text{txn-C2}}$	CIITA transcription rate constant	$k_{\text{deg-C2m}}\, C_{\text{2m,0}} = 2 \times 10^{-1}$ h^{-1}
α_{C2}	IFN-γ-dependent CIITA scaling factor	1×10^{-1}
$k_{\text{deg-C2m}}$	CIITA mRNA degradation rate constant	2×10^{-1} h^{-1}
$k_{\text{tsl-C2}}$	CIITA mRNA translation rate constant	$k_{\text{deg-C2m}}\, C_2 / C_{\text{2m,0}} = 1.4 \times 10^{0}$ h^{-1}
$k_{\text{deg-C2}}$	CIITA degradation rate constant	1.4×10^{0} h^{-1}
$k_{\text{txn-M}}$	MHC transcription rate constant	$k_{\text{deg-Mm}}\, M_{\text{m,0}} \approx 4 \times 10^{3}$ h^{-1}
$k_{\text{deg-Mm}}$	MHC mRNA degradation rate constant	4×10^{-2} h^{-1}
k_{pino}	Pinocytosis rate	1×10^{-13} L h^{-1}
$k_{\text{deg-A*}}$	Antigen degradation rate constant in medium	1×10^{-2} h^{-1}
v_{MIIC}	Volume of MIIC compartment	4×10^{-16} L
$k_{\text{deg-A}}$	Antigen processing rate constant	4×10^{0} h^{-1}
k_{lys}	Lysosomal degradation rate constant	6×10^{0} h^{-1}
k_{source}	Self peptide synthesis rate constant	$k_{\text{lys}}\, S_0 \approx 2.4 \times 10^{-3}$ M^{-1} h^{-1}
$k_{\text{deg-MHC}}$	MHC degradation rate constant	2×10^{-2} h^{-1}

$k_{\text{on-MHC}}$	Peptide-MHC association rate constant	7.2×10^{8} M^{-1} h^{-1}
$k_{\text{off-MHC}}$	Peptide-MHC dissociation rate constant	7.2×10^{4} h^{-1}
$k_{\text{tsl-M}}$	MHC mRNA translation rate constant	$k_{\text{deg-MHC}}$ $(M_0 + M^*_0 + M_{S,0} + M_S{}^*_0) \approx 2 \times 10^{-2}$ h^{-1}
α_M	IFN-γ-dependent MHC scaling factor	1×10^{-1}
k_{out}	MIIC-to-surface trafficking rate constant	4×10^{0} h^{-1}
k_{in}	Surface-to-MIIC trafficking rate constant	$[p_{\text{in}}/(1-p_{\text{in}})]$ $k_{\text{out}} - k_{\text{deg-MHC}} \approx 2 \times 10^{0}$ h^{-1}
p_{in}	Proportion of MHC intracellular at time 0	1/3
p_{bound}	Proportion of MHC bound to self at time 0	4/5
M_{tot}	Total number of MHC per cell	1×10^{5}

(1)When used in the definition of another parameter or variable, the subscript 0 refers to the initial value of a particular variable such that, e.g., M_0 refers to the initial value of M.

Supplementary Table 4. Initial values in the T cell model

Variable	Description[(1)]	Initial value
M_E^C	Peptide-MHC complexes within contact zone	0
T^C	Free TCR within contact zone, inactive	$(\sigma_C/\sigma_{tot\text{-}Tcell})\ T_{tot} \approx 4.2 \times 10^3$
B_0	Peptide-MHC-TCR complex, inactive	0
B_1	Peptide-MHC-TCR complex, state 1	0
B_2	Peptide-MHC-TCR complex, state 2	0
B_3	Peptide-MHC-TCR complex, state 3	0
B_4	Peptide-MHC-TCR complex, state 4	0
B_5	Peptide-MHC-TCR complex, state 5	0
B_N	Peptide-MHC-TCR complex, activated	0
T_{activ}^C	Free TCR within contact zone, activated	0
T_{int}	Internalized TCR	0
F	Inactive NF-κB as fraction of total NF-κB	1
F_{activ}	Activated NF-κB as fraction of total NF-κB	0
G_m	IFN-γ mRNA	0
G_2	IFN-γ secreted	0

[(1)]Units are numbers of molecules per cell (APC or T cell) unless otherwise indicated.

Supplementary Table 5. Parameters in the T cell model

Parameter	Description	Value[(1)]
σ_C	Surface area of APC-T cell contact zone	7×10^{-11} m^2
$\sigma_{tot\text{-}APC}$	Total surface area of APC	5×10^{-10} m^2
$k_{on\text{-}B}$	pMHC-TCR association rate constant	3.6×10^{-2} h^{-1} molecule^{-1}
$k_{off\text{-}B}$	pMHC-TCR dissociation rate constant	3.6×10^{1} h^{-1}
$\sigma_{tot\text{-}Tcell}$	Total surface area of T cell	5×10^{-10} m^2
μ	TCR deactivation rate constant	0 h^{-1}
k_p	TCR activation rate constant	9×10^{2} h^{-1}
λ_T	Free TCR internalization rate constant	1.08×10^{1} s^{-1}
λ_B	Bound TCR internalization rate constant	1.08×10^{0} s^{-1}
k_{resp}	NF-κB activation rate constant	5×10^{-3} h^{-1} molecule^{-1}
k_{decay}	NF-κB deactivation rate constant	1×10^{-1} h^{-1}
$k_{txn\text{-}IFN\text{-}\gamma}$	IFN-γ transcription rate constant	$k_{deg\text{-}Gm}\, G_{m,0} \approx 1 \times 10^{2}$ h^{-1}
$k_{deg\text{-}Gm}$	IFN-γ mRNA degradation rate constant	1×10^{-2} h^{-1}
$k_{tsl\text{-}IFN\text{-}\gamma}$	IFN-γ translation rate constant	6×10^{1}
T_{tot}	Total number of TCR per cell	3×10^{4}

[(1)]When used in the definition of another parameter or variable, the subscript 0 refers to the initial value of a particular variable such that, e.g., M_0 refers to the initial value of M.

The values of most parameters are identical to the parameters in Coombs et al. (10), including surface areas of the APC and T cells, surface area of the contact zone, TCR activation and de-activation rate constants, and TCR internalization rate constants. Association and dissociation rate constants for the pMHC-TCR complex were estimated from values measured *in vitro* (reviewed in ref. 12). The NF-κB activation rate constant was estimated by summing constituent rate constants d4, d5, d6, r4, r5, and r6 from Hoffmann *et al.* (23). The NF-κB de-activation rate constant was estimated by fitting the

time course of activated NF-κB in the model to an experimentally observed peak in NF-κB levels occurring approximately 1 h after activation (23). The IFN-γ transcription rate constant and mRNA degradation rate constant were estimated by fitting the time course of cytokine IFN-γ mRNA to match an experimentally observed peak in expression approximately 20 hours after exposure to APC (33). The IFN-γ translation rate constant was estimated by fitting the time course of cytokine IFN-γ to match an experimentally observed peak in protein levels detected by ELISA approximately 96 hours after exposure to APC (33).

Supplementary Table 6. PRCC values for all 16 parameters that were varied during sensitivity analysis

Biological process / factor	No IFN-γ initially present			IFN-γ initially present		
	pMHC[1]	TCR[2]	IFN-γ[3]	pMHC[1]	TCR[2]	IFN-γ[3]
IFN-γ dose[4]	N/A	N/A	N/A	0.64	0.14	0.15
MHC expression[5]	0.41	0.19	0.15	0.29	(0.07)	(0.05)
pMHC affinity[6]	-0.80	-0.44	-0.40	-0.65	-0.29	-0.28
Ag dose	0.97	0.70	0.68	0.97	0.71	0.72
Ag processing[7]	0.66	0.17	0.16	0.62	0.21	0.24
pMHC export to surface	0.53	(0.06)	(0.08)	0.16	(0.05)	(0.06)
pMHC deg. within contact	N/A	-0.26	-0.20	N/A	-0.25	-0.20
TCR expression	N/A	0.55	0.42	N/A	0.55	0.34
pMHC-TCR affinity[8]	N/A	-0.58	-0.60	N/A	-0.56	-0.60
pMHC-TCR activation[9]	N/A	0.51	0.49	N/A	0.46	0.46
Act'd, freeTCR internal.[10]	N/A	(-0.10)	-0.15	N/A	(0.07)	(0.01)
Act'd, bound TCR internal.[11]	N/A	(0.08)	-0.24	N/A	(0.07)	-0.23
IFN-γ signaling[12]	N/A	N/A	0.56	N/A	N/A	0.66
Trans. factor deactivation	N/A	N/A	(-0.04)	N/A	N/A	(-0.07)
IFN-γ mRNA synthesis	N/A	N/A	0.56	N/A	N/A	0.66
IFN-γ mRNA degradation	N/A	N/A	(0.03)	N/A	N/A	(0.03)

Parameters corresponding to processes in which genetic polymorphisms have been observed are indicated in bold. Non-significant PRCC values (α=0.05, Bonferroni-adjusted) are shown in parentheses. N/A is indicated for parameters representing processes that occur later in the antigen presentation pathway than the indicated output and therefore do not affect output value.

[1]Number of pMHC on the APC surface 4 h after Ag exposure
[2]Number of TCR internalized by the T cell 5 h after APC-T cell contact
[3]Amount of IFN-γ produced by the T cell 24 h after APC-T cell contact
[4]Amount of IFN-γ to which APCs are exposed 24 h prior to Ag exposure
[5]Number of MHC molecules initially expressed on the APC
[6]As pMHC K_D when peptide-MHC dissociation rate constant was varied
[7]Rate constant for antigen processing
[8]As pMHC-TCR K_D when pMHC-TCR dissociation rate constant was varied
[9]Rate constant for progressive activation of pMHC-TCR complexes
[10]Rate constant for internalization of bound, activated TCR
[11]Rate constant for internalization of free, activated TCR
[12]Rate constant for TCR-induced IFN-γ transcription

Parameters for Figures and Tables

Parameter values and initial conditions used in solving Equations 1-31 of the model were as provided in Supplementary Tables 2-5 with the following exceptions:

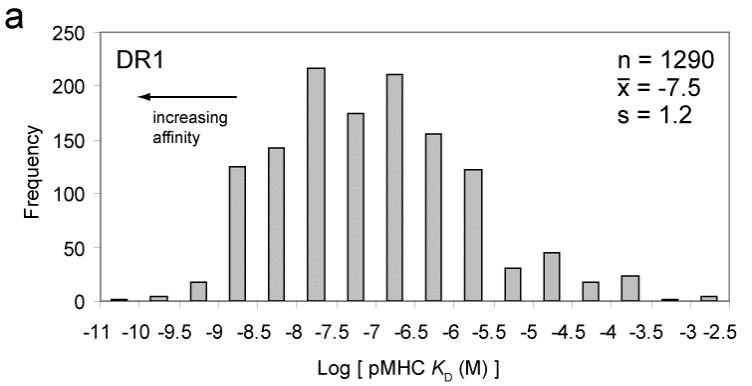
For Fig. 2: (a)-(c) $n_{cells}=1 \cdot 10^6$, $v_{medium}=1 \cdot 10^{-3}$ L, $G_0=0$, $A_0=1 \cdot 10^{-5}$ M, $k_{off\text{-}MHC}=2 \cdot 10^{-3}$ s^{-1}, $k_{on\text{-}TCR}=1 \cdot 10^{-6}$ $molecule^{-1}s^{-1}$. (d) $n_{cells}=8 \cdot 10^6$, $v_{medium}=1 \cdot 10^{-3}$ L. (e) $k_{on\text{-}TCR}=1 \cdot 10^{-6}$ $molecule^{-1}s^{-1}$. (f) $n_{cells}=2 \cdot 10^4$, $r_{vol}=2 \cdot 10^{-4}$ L.

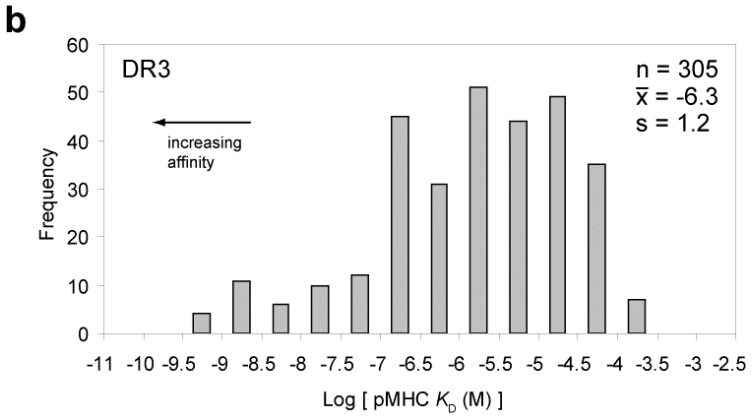
For Table 1: $n_{cells}=1 \cdot 10^6$, $v_{medium}=1 \cdot 10^{-3}$ L, $k_{off\text{-}MHC}=2 \cdot 10^{-3}$ s^{-1}, $k_{on\text{-}TCR}=1 \cdot 10^{-5}$ $molecule^{-1}s^{-1}$.

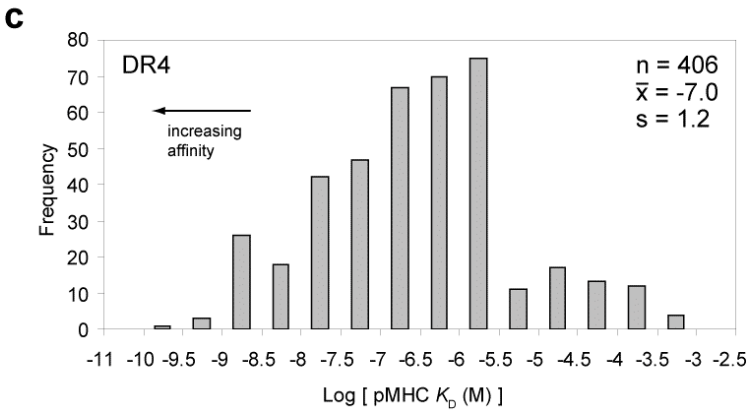
For Fig. 3: $n_{cells}=1 \cdot 10^6$, $v_{medium}=1 \cdot 10^{-3}$ L, $G_0=0$, $A_0=1 \cdot 10^{-5}$ M, $k_{off\text{-}MHC}=2 \cdot 10^{-3}$ s^{-1}, $k_{on\text{-}TCR}=1 \cdot 10^{-6}$ $molecule^{-1}s^{-1}$.

For Fig. 4: $n_{cells}=1 \cdot 10^6$, $v_{medium}=1 \cdot 10^{-3}$ L, $G_0=0$, $A_0=1 \cdot 10^{-5}$ M, $k_{off\text{-}MHC}=2 \cdot 10^{-3}$ s^{-1}, $k_{on\text{-}TCR}=1 \cdot 10^{-6}$ $molecule^{-1}s^{-1}$.

For Supplementary Table 6: $n_{cells}=1 \cdot 10^6$, $v_{medium}=1 \cdot 10^{-3}$ L, $k_{off\text{-}MHC}=2 \cdot 10^{-3}$ s^{-1}, $k_{on\text{-}TCR}=1 \cdot 10^{-5}$ $molecule^{-1}s^{-1}$.


a
DR1
n = 1290
x̄ = -7.5
s = 1.2
increasing affinity
Frequency
250
200
150
100
50
0
-11 -10 -9.5 -9 -8.5 -8 -7.5 -7 -6.5 -6 -5.5 -5 -4.5 -4 -3.5 -3 -2.5
Log [pMHC K_D (M)]


b
DR3
n = 305
x̄ = -6.3
s = 1.2
increasing affinity
Frequency
60
50
40
30
20
10
0
-11 -10 -9.5 -9 -8.5 -8 -7.5 -7 -6.5 -6 -5.5 -5 -4.5 -4 -3.5 -3 -2.5
Log [pMHC K_D (M)]


c
DR4
n = 406
x̄ = -7.0
s = 1.2
increasing affinity
Frequency
80
70
60
50
40
30
20
10
0
-11 -10 -9.5 -9 -8.5 -8 -7.5 -7 -6.5 -6 -5.5 -5 -4.5 -4 -3.5 -3 -2.5
Log [pMHC K_D (M)]

Supplementary Figure 1. Experimentally quantified effects of MHC polymorphisms on peptide-binding affinities. IC_{50} data for peptides binding MHC alleles HLA-DR1, -DR3, and -DR4 were collected from the Immune Epitope Database (46) and plotted. n = number of peptides, $\bar{x}$ =mean value, s = standard deviation. Graph for HLA-DR2 shown in main text.

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