Supplemental 2

SUPPLEMENTARY TABLES FOR PAPER:

Characterizing the dynamics of CD4+ T cell priming within a lymph node by Linderman et al

Below are examples of a Sensitivity Analysis that was performed for the ABM model. These data together with data not shown were compiled to make Table 2 in the main paper.

Supplementary Table 1: PRCC results used to get Tier 1 in Table 2. Only a subset (16 parameters) of the parameter listed in Table 1 are varied in this LHS design. Only significant PRCCs ($p<0.01$) are shown by day. We used N=200 and N_R=10. $^{(*)}$: $p<0.05$

TIME (days)	Cumulative primed CD4+ T cell output
2	Binding shape (0.15) Priming shape (-0.13)$^{(*)}$ Number of divisions (-0.35) Division time (-0.87) Cognate Frequency (-0.94)
4	Binding shape (0.16) Number of divisions (0.75) Division time (-0.85) Cognate Frequency (-0.94)
7	Binding shape (0.17) Number of divisions (0.87) Division time (-0.81) Cognate Frequency (-0.96)
14	Binding shape (0.18) Number of divisions (0.9) Division time (-0.8) Cognate Frequency (-0.96)

Supplementary Table 2: PRCC results used to get Tier 2 in Table 2. We list parameter description and the PRCC value in parenthesis. Only significant PRCCs ($p<0.01$) are shown by day. We varied only a subset (12) of the parameters listed in Table 1. For cognate frequency 300, we used N=300, N_R=10. For cognate frequency 3000, we used N=200, N_R=10 (see below *Sample size and replications* section in the Supplementary Material). (*): $p<0.05$

	Cumulative primed CD4+T cell output	
TIME (days)	**Cognate frequency 300**	**Cognate frequency 3000**
2	pMHC half-life (0.27) Unbinding threshold (-0.41) Priming threshold (-0.48)	
4	pMHC half-life (0.48) Unbinding threshold (-0.29) Binding threshold (-0.25) Priming threshold (-0.25)	pMHC half-life (0.14)(*)
7	pMHC half-life (0.54) Unbinding threshold (-0.2) Binding threshold (-0.32) Priming threshold (-0.2)	pMHC half-life (0.24) Binding shape (0.15) (*)
14	pMHC half-life (0.53) Unbinding threshold (-0.2) Binding threshold (-0.35) Priming threshold (-0.2)	pMHC half-life (0.25) Binding shape (0.15) (*)

Significance of Binding shape

Supplementary Table 1 describes detailed sensitivity results for the full LHS analysis (16 parameters varied simultaneously). The parameter *Binding shape* is consistently significant ($p<0.01$) over time, although the correlation with CD4+ T cell priming is not strong. Supplementary Table 2 shows detailed sensitivity results for the partial LHS where the following 5 parameters have been fixed (only 12 parameters varied simultaneously): *MDC lifespan*, *Number of divisions*, *Division time* and *Cognate Frequency, %Ab-DCs*.

The parameter *Binding shape* is now borderline significant in the Tier 2 setting ($p<0.05$) and only for cognate frequency 1:3000. A possible explanation is that for low cognate frequencies (<1:2000), *Binding shape* becomes important while *Binding threshold* and *Priming threshold*

are not relevant due to the few number of cell contacts (at low cognate frequencies the numbers of T cells drops significantly). For high cognate frequencies (>1:1000 or >1:500), *Binding threshold* and *Priming threshold* overpower *Binding shape*, due to the larger number of cell contacts.

Sample size (N) and replications (N_R)

There is no *a priori* exact rule for determining the adequate sample size for LHS-PRCC analysis. This is true for deterministic and stochastic models (such as our ABM). A way to overcome the problem for our uncertainty and sensitivity analysis is to systematically increase the sample size and/or the replications and check if the PRCCs consistently capture and rank a similar set of most important effects. If that holds between two consecutive experiments, there is no evident advantage in increasing the sample size or the replications. A measure of this type of correlation is given by the top-down coefficient of concordance (TDCC, see (1) for details).

We applied TDCC only to the partial LHS design (Tier 2, Supplementary Table 2), where we vary only 12 parameters from the list of Table 1. We compared PRCC results for N= 50, 100, 200 and 300 and for N_R= 5, 10 and 20. The strategy was to increase N first, and then N_R. We found that N_R =20 was unnecessarily large and chose N_R =10 as the optimal number of replications (data not shown). A sample size N=300 was necessary for cognate frequency 300 to get significance for some borderline significant PRCCs, while N=200 was optimal for cognate frequency 3000 (data not shown).

(1) Marino, S., I. B. Hogue, C. J. Ray, and D. E. Kirschner. 2008. A methodology for performing global uncertainty and sensitivity analysis in systems biology. *Journal of Theoretical Biology* 254:178-196.