Table 1. Multiple Regression Analyses for the First and Second Definitions of Protection

<table>
<thead>
<tr>
<th>Definition of protection, covariate</th>
<th>Adjusted RR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>First definition*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibody titers</td>
<td>0.35 (0.20–0.59)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CD4 cell responses</td>
<td>0.87 (0.79–0.97)</td>
<td>.011</td>
</tr>
<tr>
<td>Second definitionb</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibody titers</td>
<td>0.09 (0.03–0.29)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CD4 cell responses</td>
<td>0.89 (0.74–1.10)</td>
<td>.202</td>
</tr>
</tbody>
</table>

**NOTE.** CI, confidence interval; RR, relative risk.

* Full protection from infection after malaria challenge.

b Full protection plus delayed time to infection.

References


Potential conflicts of interest: none reported.

To do this, we used the coordinates from the scatterplot to deduce the values of the antibody titers and CD4 cell responses by individual. In the plot, individuals were classified as either fully protected, partially protected (i.e., a delay in the appearance of parasites in the blood occurred), or not protected. For our analysis, we used 2 definitions of protection: the first definition included only fully protected individuals, and the second definition included both fully protected and partially protected individuals. We reasoned that time-to-event models did not match the biology of the situation and that logistic models to calculate odds ratios as the measure of effect were not appropriate given the high frequency of the outcome. Therefore, we used a modified Poisson regression model [2] with a robust error variance to determine the relative risk of infection after malaria challenge as a function of log-transformed antibody titers and CD4 cell responses, using Stata software (version 9, StataCorp). We investigated the possible interaction between CD4 cell responses and antibody titers by comparing the fit of models with and without interaction terms.
Antibody titers and CD4 cell responses were both independently associated with protection from malaria challenge (Table 1). Increasing antibody titer was associated with reductions in the relative risk of infection after malaria challenge, corresponding to an efficacy of 65% (95% confidence interval [CI], 41%–80%) for each 10-fold increase in antibody titer for the first definition of protection and an efficacy of 91% (95% CI, 71%–97%) for the second definition. Increasing CD4 cell responses were associated with more modest reductions in risk—corresponding to efficacies of 13% (95% CI, 3%–21%) and 11% (95% CI, −10 to 26%) for each 10-fold increase in cellular responses—that were of marginal statistical significance.

There was no significant difference between the model with and the model without an interaction term (likelihood ratio χ² test, 2.09 [P = .15] and 0.34 [P = .56] for the first and second definitions of protection, respectively). Terms for the interaction between antibody titers and CD4 cell counts gave relative risk estimates of 0.46 (95% CI, 0.16–1.35) and 1.54 (95% CI, 0.36–6.5) for the first and second definitions of protection, respectively. These relative risks suggest nonsignificant tendencies toward synergistic and antagonistic interactions, respectively; assessments of interactions are limited by a modest sample size.

Overall, these findings suggest that antibody titers are strongly associated with vaccine efficacy and that CD4 cell responses are less strongly associated with protection. Despite the lack of evidence for interactions in these data, there is evidence for synergy between antibody and cellular responses in mouse challenge models [3], and interactions between antibody and cellular responses in humans should be examined further with larger sample sizes from field studies.

**References**

