Figures and figure supplements

Identification of highly-protective combinations of Plasmodium vivax recombinant proteins for vaccine development

Camila Tenorio França et al
Figure 1. Breadth of IgG antibodies to 38 P. vivax proteins in Papua New Guinean children aged 1–3 years. For each protein, antibody levels were stratified into tertiles and scored as 0, 1 or 2 for the low, medium, and high tertiles, respectively. Scores were then added up to reflect the breadth of antibodies per child. (a) Antibody breadth by age group. Age is shown as median (interquartile range). (b) Antibody breadth by lifetime exposure group. For each child, exposure was defined as the total number of P. vivax blood-stage clones acquired per time-at-risk (molFOB), and lifetime exposure as a product of age and molFOB. P values are from negative binomial regression and were deemed significant if <0.05.

DOI: https://doi.org/10.7554/eLife.28673.003
Figure 2. Association between cumulative IgG levels to 38 P. vivax proteins and exposure to P. vivax infections in Papua New Guinean children aged 1–3 years. (a) Association with age. (b) Association with lifetime exposure. For each child, exposure was defined as the total number of P. vivax blood-stage clones acquired per time-at-risk (molFOB), and lifetime exposure as a product of age and molFOB. n = 225. P values < 0.05 were deemed significant.

DOI: https://doi.org/10.7554/eLife.28673.004
Figure 3. Association between high IgG levels to 38 P. vivax proteins and protection against clinical malaria (density >500/μL) in Papua New Guinean children aged 1–3 years old. Data are plotted as incidence rate ratios and 95% confidence intervals adjusted for exposure (molFOB), age, season, and village of residency. Incidence rate ratios are for high versus low tertiles of responders, 95% confidence intervals and P values are from GEE models. P values < 0.05 were deemed significant.

DOI: https://doi.org/10.7554/eLife.28673.006
Figure 4. Correlations between IgG to 38 P. vivax proteins in Papua New Guinean children aged 1–3 years. Correlation coefficients between antibody levels to every pair of antigens were calculated using Spearman’s rank correlation tests.

DOI: https://doi.org/10.7554/eLife.28673.009
Figure 5. Association between antibodies to combinations of *P. vivax* proteins and malaria risk in Papua New Guinean children aged 1–3 years. (a) Potential protective efficacy (PPE) for combinations of antigens with the maximum number of antigens indicated on the x-axis. Dashed lines represent potential protective efficacy (PPE) for combinations of antigens with the maximum number of antigens indicated on the x-axis. (b) Sum of residuals. (c) Frequency of antigen inclusion. (d) Potential protective efficacy (single antigen). (e) Immunogenicity (single antigen).

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the range of PPE for all possible combinations. Solid lines represent the range of PPE from 1000 implementations of the simulated annealing algorithm. (b) Sum of residuals (as a measure of model goodness of fit). (c) The heatmap shows the frequency of including an antigen (x-axis) in a multi-component vaccine with a fixed number of antigens (y-axis). (d) Predicted PPE of a single antigen. (e) Immunogenicity of each antigen represented as seroprevalence with a cut-off as 10% of the antibody levels of fully-immune PNG adults.

DOI: https://doi.org/10.7554/eLife.28673.010
Figure 6. Estimated dose-response curves for the associations between antibody responses specific to *P. vivax* antigens and protection from clinical malaria. Solid black lines depict exposure-adjusted dose-response curves, and the grey shaded regions depict the 95% credible intervals. Histograms show the observed distribution of antibody levels (relative to the PNG immune pool) colored per tertiles (low = blue; medium = green; high = red), and the darkly-colored portions of the histograms show the proportion of individuals with that antibody level who had a *P. vivax* episode (>500 parasites/µL). (a–c) Examples of antigens that need low antibody levels to provide 50% of protection. (d–f) Examples of antigens that need medium antibody levels to provide 50% of protection. (g–i) Examples of antigens that need high antibody levels to provide 50% of protection.

DOI: https://doi.org/10.7554/eLife.28673.011
Figure 6—figure supplement 1. Estimated dose-response curves for the associations between antibody levels to *P. vivax* antigens and protection from clinical malaria. Solid black lines depict exposure-adjusted dose-response curves, and the grey shaded regions depict the 95% credible intervals.

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Figure 6—figure supplement 1 continued

Histograms show the observed distribution of antibody levels (arbitrary antibody units relative to standard curves made of immune pooled serum), and the darkly-colored portions of the histograms show the proportion of individuals with that antibody levels who had a *P. vivax* episode (>500 parasites/μL). (a) Antigens that need low antibody levels to show an association with 50% of protection against clinical malaria. (b) Antigens that need medium antibody levels to show an association with 50% of protection against clinical malaria. (c) Antigens that need high/very high antibody levels to show an association with 50% of protection against clinical malaria.

DOI: https://doi.org/10.7554/eLife.28673.012