

## Reporting Summary

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### Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. figure legend, table legend, main text, or Methods section).

n/a Confirmed

- The exact sample size ( $n$ ) for each experimental group/condition, given as a discrete number and unit of measurement
- An indication of whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
- The statistical test(s) used AND whether they are one- or two-sided  
*Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
- A description of all covariates tested
- A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
- A full description of the statistics including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
- For null hypothesis testing, the test statistic (e.g.  $F$ ,  $t$ ,  $r$ ) with confidence intervals, effect sizes, degrees of freedom and  $P$  value noted  
*Give  $P$  values as exact values whenever suitable.*
- For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
- For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
- Estimates of effect sizes (e.g. Cohen's  $d$ , Pearson's  $r$ ), indicating how they were calculated
- Clearly defined error bars  
*State explicitly what error bars represent (e.g. SD, SE, CI)*

*Our web collection on [statistics for biologists](#) may be useful.*

### Software and code

Policy information about [availability of computer code](#)

Data collection

Standard default instrument software for was used for raw data collection

Data analysis

Excel and GraphPad Prism6 were used for data analysis and plotting. FlowJo was used for flow cytometry analysis. Image Lab software were used for Native PAGE and SDS PAGE. Coreldraw was used to arrange figures.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research [guidelines for submitting code & software](#) for further information.

### Data

Policy information about [availability of data](#)

All manuscripts must include a [data availability statement](#). This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

All raw data are available upon request.

## Field-specific reporting

Please select the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

Life sciences  Behavioural & social sciences  Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see [nature.com/authors/policies/ReportingSummary-flat.pdf](https://www.nature.com/authors/policies/ReportingSummary-flat.pdf)

## Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	We did not predetermine sample size using software. For in vivo studies, sample sizes are indicated in the methods and/or figures captions. For mouse immunization and functional assays, each group used n=10 mice, as this sample size was chosen based on previous papers. For example, reference: Sci Rep. 2016 Jan 8;6:18848 and Infect Immun. 2015 May;83(5):1799-808. For other studies, sample sizes are described in each figure legend. From past experience, we expected the number of mice required for the local reactogenicity was n=3 and for adjuvant experiment, n=4. Because we assumed our liposomal adjuvant can induced higher titer and low local reactogenicity, and n=3-4 mice are effective size for these experiment. Toxicity studies and draining lymph node studies (uptake, germinal center B cells, follicular helper T cells and cell recruitment), used n=5 mice and for antibody durability studies n=6 mice per group were used. From past experience, n=5-6 mice per group is an appropriate size for those experiments. For rabbit immunization studies, each group contained n=3-4 rabbits. The sample size were chosen based on previous reference: BMC Biotechnol. 2015 Dec 1;15:108.
Data exclusions	No data were excluded.
Replication	Experiments were repeated in at least three independent experiments. Details are provided in the figure captions. Antigen/liposomes binding assays in this study correspond to separately setup experiments. Binding has been tested separately by two individuals in our lab according to standard protocol. Serum from immunized mice has been checked by two independent labs after shipping (NIAID and SUNY at Buffalo).ELISA results were consistent in two independent labs .
Randomization	There was no randomization in these experiments, beyond randomly grouping mice into varying groups without a formal protocol. The samples for injection were not randomized, each adjuvant has a different appearance. Rabbits were randomly separated into groups for vaccination.
Blinding	Blinding was not used in our experiments. ELISA and SMFA results were performed in the NIAID lab using shipped serum, with no or minimal knowledge of sample identification, however samples were not formally blinded.

## Reporting for specific materials, systems and methods

### Materials & experimental systems

n/a	Involvement in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> Unique biological materials
<input type="checkbox"/>	<input checked="" type="checkbox"/> Antibodies
<input type="checkbox"/>	<input checked="" type="checkbox"/> Eukaryotic cell lines
<input checked="" type="checkbox"/>	<input type="checkbox"/> Palaeontology
<input type="checkbox"/>	<input checked="" type="checkbox"/> Animals and other organisms
<input checked="" type="checkbox"/>	<input type="checkbox"/> Human research participants

### Methods

n/a	Involvement in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> ChIP-seq
<input type="checkbox"/>	<input checked="" type="checkbox"/> Flow cytometry
<input checked="" type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging

## Antibodies

### Antibodies used

Antibodies were purchased from BioLegend, and were diluted 400 times prior to use.  
 I. For flow cytometry  
 I-a. Immune cell recruitment in lymph nodes, Biolegend (Fig 3C, Fig S8)  
 CD11c\_APC Cy7 (Clone: N418; Cat. 117323; Lot B237078)  
 CD3 PerCP/Cy5.5 (Clone: 17A2; Cat. 100217; Lot B233419)  
 I-A/I-E Alex Fluor 700 (Clone: M5/114.15.2; Cat. 107621; Lot B24168)  
 F4/80 Pacific Blue (Clone: BM8; Cat. 123123; Lot B217177)  
 Ly-6G PE (Clone: 1A8; Cat. 127607; Lot B235376)

Ly-6C (Clone: HK1.4; Cat. 128021; Lot B221000)  
 CD11b PE/Cy7 (Clone: M1/70; Cat. 101215; Lot B249267)  
 I-b. Antigen uptake into draining lymph node immune cells Biolegend\_(Fig 3F, , Fig S11)  
 I-A/I-E Pacific Blue (Clone: M5/114.15.2; Cat. 107619; Lot: B252426)  
 CD11c APC (Clone: N418; Cat. 117310; Lot: B253461)  
 F4/80 PE (Clone: BM8; Cat. 123109; Lot: B251636)  
 I-c. GC B cells staining (Fig 3H, Fig S13)  
 GL7 Pacific Blue (Clone: GL7; Cat. 144613; Lot: B244647)  
 CD95 PE (Clone: SA367H8; Cat. # 152607; Lot: B239352)  
 B220 APC (Clone: RA3-6B2; Cat # 103211; Lot: B205878)  
 I-d. Tfh cells, Biolegend (Fig 3I , Fig S14)  
 CXCR5 APC (Clone: L138D7 Cat. # 145505; Lot B243491)  
 PD-1 PE (Clone: 29F.1A12; Cat 135205; Lot: B251877)  
 Alexa Fluor 488 CD4 (Clone: GK1.5; Cat # 100425; Lot: B238433)  
 I-e. Assessing long-lived plasma cells, Biolegend (Fig 4B, Fig S15)  
 B220 APC (Clone: RA3-6B2; Cat # 103211; Lot: B205878)  
 CD138 PE (Clone: 281-2; Cat # 142503; Lot: B246402)  
 I-f. BMDC activation (Fig 3G, Fig S12)  
 CD11c FITC (Clone: N418; Cat. 117313; Lot: B230157)  
 CD80 APC (Clone: 16-10A1; Cat. 104713; Lot: B248973)  
 CD40 Pacific Blue (Clone: 3/23; Cat. 124625; Lot: B242315)  
 I-A/I-E PE (Clone: M5/114.15.2; Cat. 107607; B221907)  
 II. For Immunoprecipitationclonal (Fig1F)  
 II-a. monoclonal Antibody 4B7 Anti-Plasmodium falciparum 25 kDa Gamete Surface Protein (Pfs25) (Cat MRA-28; Lot 60673339)  
 III. For Indirect immunofluorescence assay (IFA) (Fig6F, Fig S19)  
 III-a. Goat anti-Mouse IgG (H&L) - Affinity Pure, DyLight®488 Conjugate (Cat. GtxMu-003-D488NHSX; Lot 61-69-031618)

## Validation

The validation of the antibodies are provided on their manufacturer website (<https://www.biolegend.com/>)  
 I-a. Immune cell recruitment in lymph nodes, Biolegend (Fig 3C, Fig S8)  
 CD11c\_APC Cy7 <https://www.biolegend.com/en-us/products/apc-cy7-anti-mouse-cd11c-antibody-3931>  
 CD3 PerCP/Cy5.5 <https://www.biolegend.com/en-us/products/percp-cy5-5-anti-mouse-cd3-antibody-5596>  
 A/I-E Alex Fluor 700 <https://www.biolegend.com/en-us/products/alexa-fluor-700-anti-mouse-i-a-i-e-antibody-3413>  
 F4/80 Pacific Blue <https://www.biolegend.com/en-us/products/pacific-blue-anti-mouse-f4-80-antibody-4075>  
 Ly-6G PE <https://www.biolegend.com/en-us/products/pe-anti-mouse-ly-6g-antibody-4777>  
 Ly-6C <https://www.biolegend.com/en-us/products/alexa-fluor-488-anti-mouse-ly-6c-antibody-6756>  
 CD11b PE/Cy7 <https://www.biolegend.com/en-us/products/pe-cy7-anti-mouse-human-cd11b-antibody-1921>  
 I-b. Antigen uptake into draining lymph node immune cells Biolegend\_(Fig 3F, , Fig S11)  
 A/I-E Pacific Blue <https://www.biolegend.com/en-us/products/pacific-blue-anti-mouse-i-a-i-e-antibody-3136>  
 CD11c APC <https://www.biolegend.com/en-us/products/apc-anti-mouse-cd11c-antibody-1813>  
 F4/80 PE <https://www.biolegend.com/en-us/products/pe-anti-mouse-f4-80-antibody-4068>  
 I-c. GC B cells staining (Fig 3H, Fig S13)  
 GL7 Pacific Blue <https://www.biolegend.com/en-us/products/pacific-blue-anti-mouse-human-gl7-antigen-t-and-b-cell-activation-marker-antibody-9580>  
 CD95 PE <https://www.biolegend.com/en-us/products/pe-anti-mouse-cd95-fas-antibody-13907>  
 B220 APC <https://www.biolegend.com/en-us/products/apc-anti-mouse-human-cd45r-b220-antibody-442>  
 I-d. Tfh cells, Biolegend (Fig 3I , Fig S14)  
 CXCR5 APC <https://www.biolegend.com/en-us/products/apc-anti-mouse-cd185-cxcr5-antibody-8456>  
 PD-1 PE <https://www.biolegend.com/en-us/products/pe-anti-mouse-cd279-pd-1-antibody-6170>  
 Alexa Fluor 488 CD4 <https://www.biolegend.com/en-us/products/alexa-fluor-488-anti-mouse-cd4-antibody-2695>  
 I-e. Assessing long-lived plasma cells, Biolegend (Fig 4B, Fig S15)  
 B220 APC <https://www.biolegend.com/en-us/products/apc-anti-mouse-human-cd45r-b220-antibody-442>  
 CD138 PE <https://www.biolegend.com/en-us/products/pe-anti-mouse-cd138-syndecan-1-antibody-7519>  
 I-f. BMDC activation (Fig 3G, Fig S12)  
 CD11c FITC <https://www.biolegend.com/en-us/products/alexa-fluor-488-anti-mouse-cd11c-antibody-2702>  
 CD80 APC <https://www.biolegend.com/en-us/products/apc-anti-mouse-cd80-antibody-2340>  
 CD40 Pacific Blue <https://www.biolegend.com/en-us/products/pacific-blue-anti-mouse-cd40-antibody-8104>  
 I-A/I-E PE <https://www.biolegend.com/en-us/products/pe-anti-mouse-i-a-i-e-antibody-367>  
 II. For Immunoprecipitationclonal (Fig1F)  
 II-a. Monoclonal antibody 4B7 Anti-Plasmodium falciparum 25 kDa Gamete Surface Protein (Pfs25)  
<https://www.beiresources.org/Catalog/BEIMonoclonalAntibodies/MRA-28.aspx>  
 III. For Indirect immunofluorescence assay (IFA) (Fig6F, Fig S19)  
 III-a. Goat anti-Mouse IgG (H&L) - Affinity Pure, DyLight®488 Conjugate <https://www.immunoreagents.com/products/view/1018-goat-anti-mouse-igg-hl-affinity-pure>

## Eukaryotic cell lines

Policy information about [cell lines](#)

Cell line source(s)

RAW264.7 cells were from ATCC. Bone-marrow cells were collected fresh from ICR mice.

Authentication	No authentication was carried out. Cell morphology and adhesion was consistent with expectations.
Mycoplasma contamination	Cell lines were not tested for mycoplasma.
Commonly misidentified lines (See <a href="#">ICLAC</a> register)	No commonly misidentified cell lines were used in this study.

## Animals and other organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research

Laboratory animals	8-week-old female CD-1 mice, 10-12 week old female New Zealand white rabbits.
Wild animals	This study did not involved wild animals.
Field-collected samples	This study did not involved field-collected samples.

## Flow Cytometry

### Plots

Confirm that:

- The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).
- The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).
- All plots are contour plots with outliers or pseudocolor plots.
- A numerical value for number of cells or percentage (with statistics) is provided.

### Methodology

Sample preparation	<p>For immune cell recruitment in lymph nodes, (Fig 3C, Fig S8) Mice were injected intramuscularly with CoPoP/PHAD liposomes or Alum with 100 ng of Pfs25. 48 hr after injection, mice were sacrificed and lymph nodes were collected for cell extraction. Cells were fixed with 4% PFA for 15 min at room temperature, and washed with PBS for 3 times. Cells were stained with combination antibodies against Ly6C, CD11b, Ly6G, CD11c, CD3, I-A/I-E and F4/80, for 1 hr on ice.</p> <p>For antigen uptake into draining lymph node immune cells (Fig 3F, Fig S11) Cells collected from the lymph node were from mice injected with Pfs25 oyster-488, after 2 days of injection the mice were sacrificed and lymph node were collected and pass through cell strainer. The cells were later fix with 4% PFA and stained with fluorescence-labeled antibodies. Cells (5X10<sup>5</sup> cells per tube) were aliquot into each tube for staining with specific antibodies, including I-A/I-E (MHCII), PE F4/80, APC CD11c, APC CD45R/B220. The cells were stained for 30 min at room temperature, and followed by 3 time washing with PBS.</p> <p>For GC B cells staining (Fig 3H, Fig S13) and Tfh cells (Fig 3I, Fig S14) For GC cells and Tfh cell populations, mice received 1 µg Pfs25 adjuvanted with CoPoP/PHAD or Alum. 14 days after immunization, mice were sacrificed and the inguinal LN were collected. Cells extracted from the lymph nodes were fixed with 4% paraformaldehyde for 15 min at room temperature, washed three times with 3 mL PBS with centrifugation at 500 rcf for 5 min. 5×10<sup>5</sup> cells per tube were than stained for 1 hr on ice with antibodies against B220, CD95, GL7. CD4, CXCR5 or PD-1 prior to flow cytometry.</p> <p>For assessing long-lived plasma cells (Fig 4B, Fig S15) Bone marrow cells collected from mice, the cells were collected and pass through cell strainer. Red blood cells were lysis using commercial lysis buffer. Later the cells were fix with 4% PFA and stained with fluorescence-labeled antibodies, followed by intracellular staining with intracellular marker. Cell (5X10<sup>5</sup> cells per tube) were aliquot into each tube for staining with specific antibodies, including APC CD45R/B220 and PE CD138. The cells were stained for 30 min at room temperature, and followed by 3 time washing with PBS. . Cells were later permeabilized with 0.1% Triton X-100 and stained with Pfs25-oyster488, followed by 3 times washing with 0.1% Triron X-100, and 3 time washing with PBS.</p> <p>For BMDC activation (Fig 3G, Fig S12) After cells incubated for 24 hr with CoPoP/PHAD, CoPoP, and PBS mixed at 1 µg/mL Pfs25, with a fixed 4:1 mass ratio of CoPoP to Pfs25. Cells were washed with PBS containing 0.1% BSA for 3 times, and stained with antibodies against CD11c, CD40, CD80 and MHC-II for 1 hr on ice prior to flow cytometry.</p>
Instrument	The instrument we used for data collection is the BD LSRFortessa X-20.
Software	The software we used for flow analysis is FlowJo V10.
Cell population abundance	<p>For the lymph node, there are 7.5% of B220 positive cells, 4.5% of MHCII cells, 1.5% of CD 11c positive cells, and 2.5% of F4/80 positive cells.</p> <p>For Bone marrow cells, there are 0.8% of CD138 positive and B220 negative cells.</p> <p>For GC B cells, ~10% of B220+ cells and 2.43% of CD95+GL7+ cells in CoPoP treated groups and 1% in control.</p> <p>For Tfh cells, ~65% of CD4+ cells with 0.85% of CXCR5+PD1+ cells in CoPoP treated group and 0.065% in control.</p> <p>For BMDC cells, there are 85% CD11c+ cells and ~18% MHCII + cells for both control and CoPoP group. 88% of CD40+ cells in CoPoP group, and 42% of CD40+ cells in control. 82.2% of CD80+ cells in CoPoP group, and 51.1% of CD80+ cells in control.</p>

## Gating strategy

## I. For immune cell recruitment in lymph nodes, (Fig 3C, Fig S8)

Cells were first gated with CD11c and CD11b (Fig S8A). Then immune cells were identified based on surface marker in CD11chigh and CD11blow, neutrophils (Ly6Ghigh)(Fig S8D), eosinophils (Ly6Gint, F4/80int, SSC)(Fig S8E), monocytes (Ly6C high)(Fig S8C) and macrophage (F4/80 high)(Fig S8B). Three types of DC cells were gated (Fig S8F), for myeloid DC, we first gate Cd11chigh and CD11bhgh, then gated MHC-II positive cells.

## II. For antigen uptake into draining lymph node immune cells (Fig 3F, , Fig S11)

The cells were first gated with SSC/FSC, then compared to the unstained cells, the population of cells were gated with B220 positive, I-A/I-E positive, CD 11c positive and F4/80 positive. Later on, by comparing the groups of Pfs25-oyster 488 injected mice to the group of untreated mice, the Pfs25 positive cells were gated.

## III. For GC B cells staining (Fig 3H, Fig S13) and Tfh cells (Fig 3I , Fig S14)

GC B cells: The cells were gated with SSC/FSC, then gated with B220 + cells, and finally gated with GL7+CD95+ cells.

Tfh cells: The cells were gated with SSC/FSC, then gated with CD4 + cells, and finally gated with CXCR5+PD-1+ cells.

For assessing long-lived plasma cells (Fig 4B, Fig S15)

The cells were first gated with SSC/FSC, then compared to the unstained cells, the population of cells were gated with CD138 positive and B220 negative. Pfs25 positive cells were gated by comparing control mice to immunized mice.

## IV. For BMDC activation (Fig 3G, Fig S12)

The cells were first gate with SSC/FSC, then gated with CD40, CD80, MHCII or CD11c positive cells.

Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.