

Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our [Editorial Policies](#) and the [Editorial Policy Checklist](#).

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

- | n/a | Confirmed |
|-------------------------------------|--|
| <input type="checkbox"/> | <input checked="" type="checkbox"/> The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement |
| <input type="checkbox"/> | <input checked="" type="checkbox"/> A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly |
| <input type="checkbox"/> | <input checked="" type="checkbox"/> The statistical test(s) used AND whether they are one- or two-sided
<i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i> |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> A description of all covariates tested |
| <input type="checkbox"/> | <input checked="" type="checkbox"/> A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons |
| <input type="checkbox"/> | <input checked="" type="checkbox"/> A full description of the statistical parameters 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) |
| <input type="checkbox"/> | <input checked="" type="checkbox"/> For null hypothesis testing, the test statistic (e.g. F , t , r) with confidence intervals, effect sizes, degrees of freedom and P value noted
<i>Give P values as exact values whenever suitable.</i> |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Estimates of effect sizes (e.g. Cohen's d , Pearson's r), indicating how they were calculated |

Our web collection on [statistics for biologists](#) contains articles on many of the points above.

Software and code

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

Data collection

The morphology of the nanoparticles and vesicles: transmission electron microscope (HT7700, HITACHI, Tokyo, Japan);
The hydrodynamic size distribution, ζ potential and polydispersity index of ME-NPs: Zetasizer Nano ZS dynamic light scattering instrument (Malvern, UK);
Flow cytometry: BD Aria III cytometer (BD Biosciences);
ELISpot: Mabtech IRIS analyzer (Beijing Xingjianya Biotechnology Co., Ltd);
IgG titer detection: SpectraMax iD3;
Immunofluorescence assay: Olympus FV1000 confocal microscope

Data analysis

Statistical analysis: GraphPad Prism (v9.0);
Flow cytometry analysis: FlowJo Software (v10.9.0);
IgG titer analysis: SoftMax[®] Pro v7.1.2;
Immunofluorescence assay: ImageJ software;
Single-cell sequencing analysis: Cell Ranger (v3.0.0), Seurat package (v5.0.4), DoubleFinder package (v2.0.6), and Harmony package (v1.2.3);
Visualization: dplyr package (v1.1.4) and ggplot2 package (v3.5.1);
Cell-cell communication analysis: CellChat package (v1.6.1);
Gene set enrichment analysis: Molecular Signatures Database (v7.5.1);
Gene Ontology (GO) enrichment analysis: clusterProfiler R package (v3.8.1)

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 and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio [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 description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our [policy](#)

The data and materials that support the findings of this study are available from the corresponding author upon reasonable request. Single-cell RNA sequencing data of spleens derived from mice receiving PBS, LNP, or ME-NPs were submitted to Genome Sequence Archive (<https://ngdc.cncb.ac.cn/gsa/>) under the following accession number CRA043096. Proteomic data by mass spectrometry of Mtb inner membrane were submitted to Open Archive for Miscellaneous Data (<https://ngdc.cncb.ac.cn/omix/>) under the following accession number OMIX016941.

Research involving human participants, their data, or biological material

Policy information about studies with [human participants or human data](#). See also policy information about [sex, gender \(identity/presentation\), and sexual orientation](#) and [race, ethnicity and racism](#).

Reporting on sex and gender	<input type="text" value="n/a"/>
Reporting on race, ethnicity, or other socially relevant groupings	<input type="text" value="n/a"/>
Population characteristics	<input type="text" value="n/a"/>
Recruitment	<input type="text" value="n/a"/>
Ethics oversight	<input type="text" value="n/a"/>

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is 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/documents/nr-reporting-summary-flat.pdf](https://www.nature.com/documents/nr-reporting-summary-flat.pdf)

Life sciences study design

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

Sample size	<input type="text" value="Sample size was selected based on the standard practices in this field. For animal experiments, at least five mice per group were used. For cell culture experiments, at least five biological replicates per group were performed. No statistical methods were used to determine the sample size."/>
Data exclusions	<input type="text" value="No data were excluded from the analysis"/>
Replication	<input type="text" value="All experiments were independently replicated at least two times and similar results were generated."/>
Randomization	<input type="text" value="Mice used in this study is age and sex matched, and randomly assigned into each group."/>
Blinding	<input type="text" value="Data acquisition and analyses were not blinded because subjective assessment was not included."/>

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

- | | | |
|-------------------------------------|-------------------------------------|-------------------------------|
| n/a | <input type="checkbox"/> | Involved in the study |
| <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 and archaeology |
| <input type="checkbox"/> | <input checked="" type="checkbox"/> | Animals and other organisms |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Clinical data |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Dual use research of concern |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Plants |

Methods

- | | | |
|-------------------------------------|-------------------------------------|------------------------|
| n/a | <input type="checkbox"/> | Involved 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 used in this study were listed as below:
 Anti-TLR2 (Proteintech, 66645-1-Ig, clone 1C1D3, 1:2000)
 Anti-TLR4 (Proteintech, 66350-1-Ig, clone 3G9A4, 1:2000)
 Anti-TLR6 (Proteintech, 22240-1-AP, 1:2000)
 Anti-NF- κ B p65 (Proteintech, 80979-1-RR, clone 4C7, 1:5000)
 Anti-Phospho-NF- κ B p65 (Ser468) (Proteintech, 82335-1-RR, clone 6N1, 1:2000)
 Anti-Beta Actin (Proteintech, 20536-1-AP, 1:4000)
 Anti-CD11c-FITC (BD Biosciences, 561045, clone HL3, 1:500);
 Anti-CD11b-FITC (Biolegend, 101205, clone M1/70, 1:500);
 Anti-CD80-PE (BD Biosciences, 561955, clone 16-10A1, 1:500);
 Anti-CD86-APC (BD Biosciences, 561964, clone GL1, 1:500);
 Anti-CD3e RB705 (BD Biosciences, 570648, clone 145-2C11, 1:500);
 Anti-CD4 APC (BD Biosciences, 569845, clone GK1.5, 1:500);
 Anti-CD8 α APC-Cy7 (BD Biosciences, 561967, clone 53-6.7, 1:500);
 Anti-CD44 PE/Cy7 (BD Biosciences, 560569, clone IM7, 1:200);
 Anti-CD62L FITC (BD Biosciences, 553150, clone MEL-14, 1:200);
 Anti-IFN- γ Brilliant Violet 786 (BD Biosciences, 563773, clone XMG1.2, 1:200);
 Anti-TNF- α Brilliant Violet 650 (BD Biosciences, 563943, clone MP6-XT22, 1:200);
 Anti-IL-2 Brilliant Violet 421 (BD Biosciences, 566296, clone JES6-5H4, 1:200);
 Anti-Ki-67 PE (Biolegend, 652404, clone 16A8, 1:200);
 Anti-CD25 PE (Biolegend, 113704, clone A18246A, 1:200);
 Anti-CD69 Brilliant Violet 605 (Biolegend, 104530, clone H1.2F3, 1:200);
 Anti-CD40 PE (Biolegend, 157506, clone FGK45, 1:200)

Validation

All antibodies used in this study are commercially available. The validations have been performed by respective manufacturers and the validation data are available on their respective websites:
 Anti-TLR2: <https://www.ptgcn.com/products/TLR2-Antibody-66645-1-Ig.htm>
 Anti-TLR4: <https://www.ptgcn.com/products/TLR4-Antibody-66350-1-Ig.htm>
 Anti-TLR6: <https://www.ptgcn.com/products/TLR6-Antibody-22240-1-AP.htm>
 Anti-NF- κ B p65: <https://www.ptgcn.com/products/NF-B-p65-Antibody-80979-1-RR.htm>
 Anti-Phospho-NF- κ B p65 (Ser468): <https://www.ptgcn.com/products/Phospho-NF-B-p65-Ser468-Antibody-82335-1-RR.htm>
 Anti-Beta Actin: <https://www.ptgcn.com/products/ACTB-Antibody-20536-1-AP.htm>
 Anti-CD11c-FITC: https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/fitc-hamster-anti-mouse-cd11c.557400?tab=product_details
 Anti-CD11b-FITC: <https://www.biolegend.com/en-gb/products/fitc-anti-mouse-human-cd11b-antibody-347?GroupID=BLG10660>
 Anti-CD80-PE: https://www.bdbiosciences.com/zh-cn/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/pe-hamster-anti-mouse-cd80.561955?tab=product_details
 Anti-CD86-APC: https://www.bdbiosciences.com/zh-cn/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/apc-rat-anti-mouse-cd86.561964?tab=product_details
 Anti-CD3e RB705: https://www.bdbiosciences.com/zh-cn/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/rb705-hamster-anti-mouse-cd3e.570560?tab=product_details
 Anti-CD4 APC: https://www.bdbiosciences.com/zh-cn/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/apc-rat-anti-mouse-cd4.569845?tab=product_details
 Anti-CD8 α APC/Cy7: https://www.bdbiosciences.com/zh-cn/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/apc-cy-7-rat-anti-mouse-cd8a.561967?tab=product_details
 Anti-CD44 PE/Cy7: https://www.bdbiosciences.com/zh-cn/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/pe-cy-7-rat-anti-mouse-cd44.560569?tab=product_details
 Anti-CD62L FITC: https://www.bdbiosciences.com/zh-cn/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/fitc-rat-anti-mouse-cd62l.553150?tab=product_details
 Anti-IFN- γ Brilliant Violet 786: https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/bv786-rat-anti-mouse-ifn.563773?tab=product_details
 Anti-TNF- α Brilliant Violet 650: https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/bv650-rat-anti-mouse-tnf.563943?tab=product_details
 Anti-IL-2 Brilliant Violet 421: https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/bv421-rat-anti-mouse-il-2.566296?tab=product_details

Anti-Ki-67 PE: <https://www.biolegend.com/en-gb/products/pe-anti-mouse-ki-67-antibody-8134>
 Anti-CD25 PE: <https://www.biolegend.com/en-gb/products/pe-anti-mouse-cd25-antibody-22500>
 Anti-CD69 Brilliant Violet 605: <https://www.biolegend.com/en-gb/products/brilliant-violet-605-anti-mouse-cd69-antibody-7864>
 Anti-CD40 PE: <https://www.biolegend.com/en-gb/products/pe-anti-mouse-cd40-antibody-19117>

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s)	RAW 264.7 cell lines were obtained from the American Type Culture Collection (ATCC). Mouse bone marrow-derived dendritic cells (BMDcs) were induced by 10% FBS, 2 mM L-glutamine, 100 µg/mL penicillin, 100 µg/mL streptomycin, 0.05 mM 2-mercaptoethanol, 10 ng/mL murine IL-4 and 20 ng/mL murine GM-CSF using bone marrow cells derived from C57BL/6N mice.
Authentication	None of the cell lines were authenticated.
Mycoplasma contamination	All of the used cell lines were negative for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	None were used.

Animals and other research organisms

Policy information about [studies involving animals; ARRIVE guidelines](#) recommended for reporting animal research, and [Sex and Gender in Research](#)

Laboratory animals	6-8 week old female wild-type mice (C57BL/6N background) were used. All mice were housed under specific pathogen-free conditions, and maintained in a climate-controlled environment (22±2°C, humidity at 55±10%) under a 12 hours dark- 12 hours light cycle.
Wild animals	No wild animals were used.
Reporting on sex	Experiments were exclusively performed with female mice due to animal welfare concerns such as fighting, aggression, and social defeat with male mice in shared housing conditions.
Field-collected samples	The study did not involve samples collected from the field.
Ethics oversight	All animal experiments were performed in approval of animal ethics committee of Beijing Chest Hospital (No. XK2023-150). The study was compliant with all of the relevant ethical regulations regarding animal research.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Plants

Seed stocks	n/a
Novel plant genotypes	n/a
Authentication	n/a

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

For the separation of splenocytes, spleens were aseptically ground and resuspended in mouse lymphocyte isolation solution followed by density gradient centrifugation. After red blood cell lysis and filtration through 70 μm cell strainer, splenocytes were cultured in RPMI 1640 medium with 10% fetal bovine serum (FBS). Bone marrow-derived dendritic cells (BMDCs) were isolated from the femurs of C57BL/6N mice and cultured in complete RPMI-1640 medium. Cell pellets were resuspended in RPMI 1640 complete medium and counted for culture.

Cells were harvested and washed with cell staining buffer (Biolegend). For live/dead cell staining, Zombie NIR in cell staining buffer were added and incubated at room temperature for 30 min. Then cells were incubated with surface marker antibodies (CD11c-FITC, CD11b-FITC, CD80-PE, CD86-APC, CD3-RB705, CD4-APC, CD8-APC-Cy7, CD44-PE-Cy7, CD62L-FITC, CD40-PE, CD25-PE, CD69-BV605) for 30 min. For intracellular cytokine staining, cells were treated with Protein Transport Inhibition Cocktail for 5 hours before collection. After surface staining, cells were fixed with Fixation Buffer and permeabilized with Permeabilization Buffer, and then intracellular antibodies (IFN- γ -BV785, TNF- α -BV650, and IL-2-BV421) were added and incubated for 30 min. For intranuclear staining, cells were fixed and nuclear membrane was permeated via Transcription Factor Buffer Set (BD Bioscience) after cell surface staining, and then intranuclear antibodies (Ki-67-PE) were added and incubated for 50 min.

Instrument

Cells were collected and recorded on a BD Aria III cytometer (BD Biosciences).

Software

Data were analyzed via FlowJo Software (v10.9.0).

Cell population abundance

The purity of sorted CD4+ central memory T cells was >90% (confirmed by flow cytometry) .

Gating strategy

CD4+ central memory T cells: CD3+CD4+CD44+CD62L+;
Polyfunctional CD4+ T cells: CD3+CD4+IFN- γ +TNF- α +IL-2+.

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