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☐ Initial submission ☐ Revised version ☒ Final submission

Life Sciences Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form is intended for publication with all accepted life science papers and provides structure for consistency and transparency in reporting. Every life science submission will use this form; some list items might not apply to an individual manuscript, but all fields must be completed for clarity.

For further information on the points included in this form, see Reporting Life Sciences Research. For further information on Nature Research policies, including our data availability policy, see Authors & Referees and the Editorial Policy Checklist.

Experimental design

1. Sample size

Describe how sample size was determined.

Sample size was based on prior reports by our group using these and similar animal models (e.g., Arlauckas, Science Translational Medicine, 2017). Power analysis used in the development of these models indicates that sample sizes of 6-7 animals are sufficient, given SD = 25% with a 99% difference between treatment and control groups; a = 0.05, b = 0.2.

2. Data exclusions

Describe any data exclusions.

No data were excluded in analysis.

3. Replication

Describe whether the experimental findings were reliably reproduced.

All attempts for replication were successful.

4. Randomization

Describe how samples/organisms/participants were allocated into experimental groups.

Mice were randomly assigned to the groups.

5. Blinding

Describe whether the investigators were blinded to group allocation during data collection and/or analysis.

Investigator were not blinded to group allocation in tumour measurement; however, efficacy of the treatments were apparent both in quantification and in representative images of outcomes. Survival endpoints were determined by blinded veterinary staff.

Note: all studies involving animals and/or human research participants must disclose whether blinding and randomization were used.

6. Statistical parameters

For all figures and tables that use statistical methods, confirm that the following items are present in relevant figure legends (or in the Methods section if additional space is needed).

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement (animals, litters, cultures, etc.)
☐	☒ A description of how samples were collected, noting whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒ A statement indicating how many times each experiment was replicated
☐	☒ The statistical test(s) used and whether they are one- or two-sided (note: only common tests should be described solely by name; more complex techniques should be described in the Methods section)
☐	☒ A description of any assumptions or corrections, such as an adjustment for multiple comparisons
☐	☒ The test results (e.g. *P* values) given as exact values whenever possible and with confidence intervals noted
☐	☒ A clear description of statistics including central tendency (e.g. median, mean) and variation (e.g. standard deviation, interquartile range)
☐	☒ Clearly defined error bars

See the web collection on statistics for biologists for further resources and guidance.

Software

Policy information about availability of computer code

7. Software

Describe the software used to analyze the data in this study.	All analysis was performed in GraphPad Prism v6. Image processing was performed in FIJI (ImageJ, NIH) as detailed in the Methods. Analysis of cell shape was performed in CellProfiler (Broad Institute) and the pipeline used in analysis is defined in the Supplementary Information.

For manuscripts utilizing custom algorithms or software that are central to the paper but not yet described in the published literature, software must be made available to editors and reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). *Nature Methods* guidance for providing algorithms and software for publication provides further information on this topic.

Materials and reagents

Policy information about availability of materials

8. Materials availability

Indicate whether there are restrictions on availability of unique materials or if these materials are only available for distribution by a for-profit company.	The rat IgG2a kappa anti-mouse PD1 29F.1A12 clone was kindly provided by Gordon Freeman (DFCI). All other reagents are commercially available.

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).	Antibodies used include those for 1) flow cytometry: anti-CD45 (30-F11, eBioscience), anti-CD11c (N418, BioLegend), anti-Ly6G (1A8, Biolegend), and anti-F4/80 (BM8, BioLegend) which were all used according to manufacturers instructions; 2) T-cell depletion: 200 ug anti-CD8 (BioXcell, clone 53-6.72) administered every 3 days via i.p. injection per the manufacturers instructions; and 3) tumor treatment: 200 ug of the rat IgG2a kappa anti-mouse PD1 (clone 29F.1A12) was administered via i.p. injection as per our previous reports (Arlauckas et al, Science Translational Medicine, 2017).

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.	Cell sources are defined in the Methods (cell models): RAW 264.7 and B16.F10 cells were sourced from ATCC. MC38 cell lines were provided by Mark Smyth (QIMR Berghofer Medical Research Institute). KP1.9 cells were provided by Dr. A. Zippelius (University Hospital Basel, Switzerland). Murine bone marrow-derived macrophages (BMDMs) were isolated and derived from C57BL/6 mice, and human macrophages were derived from peripheral blood mononuclear cells.
b. Describe the method of cell line authentication used.	Cell lines were used from the source without authentication.
c. Report whether the cell lines were tested for mycoplasma contamination.	Cells were tested monthly and found to be negative for mycoplasma contamination.
d. If any of the cell lines used are listed in the database of commonly misidentified cell lines maintained by ICLAC, provide a scientific rationale for their use.	No commonly misidentified cell lines were used.

Animals and human research participants

Policy information about studies involving animals; when reporting animal research, follow the ARRIVE guidelines

11. Description of research animals

Provide details on animals and/or animal-derived materials used in the study.	Studies were conducted in compliance with the Institutional Animal Care and Use Committees at Massachusetts General Hospital (MGH). Unless otherwise stated, experiments were performed using female C57BL/6 (#000664, Jackson) that were 6- to 8-weeks old at the start of the experiment. Examination of CDNP-VT680 distribution into macrophages was examined in recently developed NOD MerTKGFP/+ mice (Mohan, Proc Natl Acad Sci U S A, 2017), crossed into NOD SCID mice (#001303, Jackson). IL12 expression was examined in p40-IRES-eYFP IL12 reporter mice (#015864, Jackson) described previously (Reinhardt, J Immunol, 2006).

Policy information about studies involving human research participants

12. Description of human research participants

Describe the covariate-relevant population characteristics of the human research participants.	This study did not involve human research participants.

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Flow Cytometry Reporting Summary

Form fields will expand as needed. Please do not leave fields blank.

Data presentation

For all flow cytometry data, confirm that:

☒ 1. The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

☒ 2. 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).

☒ 3. All plots are contour plots with outliers or pseudocolor plots.

☒ 4. A numerical value for number of cells or percentage (with statistics) is provided.

Methodological details

5. Describe the sample preparation.	Sample preparation is described in detail in Methods.
6. Identify the instrument used for data collection.	LSR2
7. Describe the software used to collect and analyze the flow cytometry data.	FACS Diva and FlowJo vX.0.7
8. Describe the abundance of the relevant cell populations within post-sort fractions.	No cell sorting was performed.
9. Describe the gating strategy used.	Briefly, single cells were selected using forward and side scatter linearity. Live cells were selected as defined by 7AAD- negativity. Immune cell populations were gated from CD45+ cells, as defined in detail in Methods. The expression gating of TAM IL12-eYFP and CDNP-VT680 positive cells is indicated in Supplementary Fig. 12.

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