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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 sizes for in vivo therapy studies were selected to achieve a 95% power to detect a difference in groups of at least 1 st. dev.

2. Data exclusions

Describe any data exclusions.

All the tested samples or animals are included.

3. Replication

Describe whether the experimental findings were reliably reproduced.

All the experiments were conducted at least twice and could be reliably reproduced.

4. Randomization

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

Animals in tumor studies were randomized to groups equalizing mean tumor size at start of treatment.

5. Blinding

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

The investigator was blinded to the group allocation during the tumor size measurement, tissue harvesting and processing.

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.	Sample size was calculated using G*Power. Statistical analyses were performed using GraphPad Prism software. FlowJo was used to process all the flow cytometry data. Living Image software Version 3.0 was used to process mouse images.

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.	ALT-803, a human IL-15 superagonist (Sa), was obtained from Altor BioScience Corporation (Miramar, FL, USA) or generated as described previously (ref 49).

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).	Anti-mouse CD45RB (clone: MB23G2) was purchased from BioXCell (West Lebanon, NH, USA). Anti-human CD45 (clone: MEM-28) was purchased from Abcam (Cambridge, United Kingdom). Anti-CD3/CD28 beads were purchased from Thermo Fisher Scientific. The antibodies were not validated before use.

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.	B16F10 melanoma cells and U-87 MG human glioblastoma cells were acquired from American Type Culture Collection (Manassas, VA, USA) and cultured in DMEM. Click Beetle Red luciferase (CBR-luc) was introduced into U-87 MG cells by lentiviral transduction for bioluminescence imaging.
b. Describe the method of cell line authentication used.	The cell lines used have not been authenticated.
c. Report whether the cell lines were tested for mycoplasma contamination.	All cell line used in this paper were tested negative for mycoplasma.
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.	There are no cell lines used in this paper listed in the database of commonly misidentified cell lines maintained by ICLAC.

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.	Experiments and handling of mice were conducted under federal, state, and local guidelines and with approval from the Massachusetts Institute of Technology IACUC. Six to eight week-old female Thy1.2+ C57Bl/6 mice, TCR-transgenic Thy1.1+ pmel-1 mice, and Nod/SCID/γ-/- (NSG) mice were from the Jackson Laboratory.

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.	No human research participants were involved in this study. Experiments with human cells fall under NIH exemption - anonymous donor samples.