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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.

Records of 1058 pts with advanced melanoma treated with anti-PD1/PDL1 therapy were reviewed across ten institutions to identify those with a diagnosis of DM. Each institution conducted its own search to find patients who fit these criteria.

2. Data exclusions

Describe any data exclusions.

From the 60 identified advanced DM patients, those without tumor tissue available were not included in the IHC or WES analyses.

3. Replication

Describe whether the experimental findings were reliably reproduced.

The IHC analyses were replicated twice. The WES was done once.

4. Randomization

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

Samples were not randomized as this was not relevant to this study.

5. Blinding

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

Blinding was not relevant for this study, as clinical data and tumor tissue was from patients all known to have desmoplastic melanoma. However, personnel who performed the IHC staining and sequencing of the tumor tissue did not know the clinical data (response, survival, etc) of the patients.

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.	Analysis of IHC data was done with HALO software (Indica Labs). GraphPad Prism and R were used for statistical analyses. For WES, the UCSC hg19 reference, BWA-mem, Genome Analysis Toolkit (GATK) Best Practices Workflow v3, PicardTools, MuTect, and VarScan2 software were used. Published software tools were used as cited in the text. No unpublished custom algorithms were used.

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.	No restrictions

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 included rabbit polyclonal S100 (DAKO, 1/1000 dilution, low pH retrieval), CD8 clone C8/144B (Dako, 1/100, low pH retrieval), and PD-L1 (Sp142, 1/200 dilution with High pH retrieval Spring Biosciences, Pleasanton, CA).

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.	N/A
b. Describe the method of cell line authentication used.	N/A
c. Report whether the cell lines were tested for mycoplasma contamination.	N/A
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.	N/A

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.	N/A

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.	Patients were diagnosed with advanced desmoplastic melanoma.