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☐ Initial submission ☐ Revised version ☒ Final submission

Life Sciences Reporting Summary

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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.

   We determined sample size based on the sufficient statistics. The sample size should be more than 4 across the manuscript. Specifically, for mouse implanted tumor assays, the numbers of mice were included in the figure legends of Fig 2k; Fig. 3j, k, l; Fig. 4k,l; Extended Data Fig. 3c; Extended Data Fig. 6j,k,l,m,n.o,p,q,r,s. For MMTV-oncogene induced breast tumor samples in the presence or absence of Cyclin D1-/-, the numbers of mice were included in the figure legends of Fig. 2d and Extended data Fig. 2g. For Cdk4/6 inhibitor treatment of mice, mice numbers are included in figure legends of Extended data Fig. 3d,e.

2. Data exclusions

   Describe any data exclusions.

   No data was excluded from the experiments.

3. Replication

   Describe whether the experimental findings were reliably reproduced.

   Yes, the experimental findings were reliably reproduced.

4. Randomization

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

   Yes, for the xenografted mice assay or mice with palbociclib treatment, mice (from the Jackson Laboratory) were randomized into different groups.

5. Blinding

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

   Yes. The lab technician help to treat mice using the vehicle or CDK4 inhibitor palbociclib. However, to minimize the likelihood of differential treatment or assessments of outcomes during data collection and analysis, animals were pooled and randomly divided into four groups with comparable average tumor size. Moreover, the lab technician who measured the mice were blinded to the treatment groups.

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.	We used the ImageJ software to quantify the protein bands intensity and used the GraphPad and Excel to do the graph figures and statistics.

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 restriction.

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).	All commercial antibodies used in this study were provided with information regarding the dilution, vendor and catalog number (described in the methods/ antibody section). We also used the CRISPR KO or shRNAs to specifically deplete endogenous protein to verify anti-PD-L1, anti-SPOP, anti-Cdh1 and anti-CD8 antibodies.

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.	The source of the cell lines was included in the Methods/Cell Culture section.
b. Describe the method of cell line authentication used.	No
c. Report whether the cell lines were tested for mycoplasma contamination.	Yes, cell lines used in this study were routinely tested to be 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.	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.

C57BL/6J mice (Jackson lab) were used for the B16-F10 and MC38 implanted tumor assays as well as for the CDK4 inhibitor treatment. Balb/c mice (Jackson lab) were used for the CT26 and 4T1 cells implanted tumor assays. cyclin D1+/+/MMTV-Wnt-1 or c-Myc and MMTV-ErbB2 induced mouse mammary tumor models were generated in house.

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 subject was involved in this study.

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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.	The source of cells and processing steps were clearly described below: Single Cell Generation from Tumor Tissue and Flow Cytometry analysis. Tumor tissues were minced and digested with 5 ml of 2 mg/ml collagenase (Sigma) in DMEM for 1 hour at 37°C. Cells were then collected by centrifuge and filtered through a 70 µm strainer in DMEM. Cell pellets were suspended and lysed in red blood cell lysis buffer for 5 min. The cells were then filtered through a 40 µm strainer in 1 X PBS with 2% BSA. The fixed cells were suspended in Intracellular Staining Perm Wash Buffer (421002, Biolegend) after centrifuge for two times to permeabilize the cells. Cells were then co-stained with antibodies against CD3 (100236, APC conjugated, Biolegend), Granzyme B (515403, FITC conjugated, Biolegend), IFN-γ (505808, PE conjugated, Biolegend) to check the activities of T cells. Or cells were co-stained with antibodies against CD3 (100236, APC conjugated, Biolegend), CD4 (100510, FITC conjugated, Biolegend), CD8 (100708, PE conjugated, Biolegend). The corresponding isotype IgG1 controls were used for controls. The cells were incubated with corresponding antibodies for 30 minutes at room temperature. Cells were washed by 1 × PBS with 2% BSA and analyzed by flow cytometry.
6. Identify the instrument used for data collection.	We used the BD LSRFortessa with 4 lasers machine to collect and analyze all the FACS results in the manuscript.
7. Describe the software used to collect and analyze the flow cytometry data.	We used the FASCDiva software version 8.0.2 to collect and analyze the flow cytometry data.
8. Describe the abundance of the relevant cell populations within post-sort fractions.	N/A
9. Describe the gating strategy used.	FSC/SSC gates are exemplified in Supplementary figures. APC- conjugated corresponding isotype IgG stained cells were used as a negative control. The boundaries between “positive” and “negative” staining are also indicated in Supplementary figures.

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