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eLife's transparent reporting form

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Sample-size estimation
- You should state whether an appropriate sample size was computed when the study was being designed
- You should state the statistical method of sample size computation and any required assumptions
- If no explicit power analysis was used, you should describe how you decided what sample (replicate) size (number) to use

Please outline where this information can be found within the submission (e.g., sections or figure legends), or explain why this information doesn't apply to your submission:

For cell culture experiments (figures 1-3 and supplemental figures 1-4) n=3 biological replicates and n=3 technical replicates were used.
For animal experiments, number of animals were decided based on previous experience with the *Nf1 fl/fl DhhCre* neurofibroma mouse model.

Replicates
- You should report how often each experiment was performed
- You should include a definition of biological versus technical replication
- The data obtained should be provided and sufficient information should be provided to indicate the number of independent biological and/or technical replicates
- If you encountered any outliers, you should describe how these were handled
- Criteria for exclusion/inclusion of data should be clearly stated
- High-throughput sequence data should be uploaded before submission, with a private link for reviewers provided (these are available from both GEO and ArrayExpress)

Please outline where this information can be found within the submission (e.g., sections or figure legends), or explain why this information doesn't apply to your submission:

For all experiments described in this manuscript, n numbers are specified in figure legends, in text and/or in materials and methods section of the manuscript. A biological replicate is data from an individual mouse and a technical replicate is the number of sections analyzed per mouse or the number of cell cultures studied from a single mouse.

For cell culture experiments (figures 1-3 and supplemental figures 1-4) n=3 biological replicates and n=3 technical replicates were used.

-In shRNA cell culture experiments, 3 different P2RY14 shRNAs were tested in 3 biological replicates with 3 technical replicates, each.

For animal experiments (figures 4-6 and supplemental figures 5-6), the breakdown of n numbers is as follows:

-Survival study: *Nf1 fl/fl DhhCre* n=8 biological replicates; *P2RY14+/- fl/fl DhhCre* n=14 biological replicates*; P2RY14-/- Nf1 fl/fl DhhCre* n=13 biological replicates; *Nf1 fl/+ DhhCr*e n=11 biological replicates. This number is based on our prior use of the *Nf1 fl/fl DhhCre* neurofibroma model in survival studies.

-Tumor quantification and diameter measurements at 7-months of age: *Nf1 fl/fl DhhCre* n=8 biological replicates; 48 tumors and *P2RY14-/- Nf1 fl/flDhhCre* n=8 biological replicates; 11 tumors.

- Ki67 cell quantification at 7-months of age: *WT* n=3 biological replicates; *Nf1 fl/fl DhhCre* n=3 biological replicates; *P2RY14 -/- Nf1 fl/fl DhhCre* n=3 biological replicates.

-Rolipram treatment experiment: vehicle n=21 biological replicates and rolipram treated n=6 biological replicates.

-Ki67 cell quantification: vehicle n=3 biological replicates and rolipram n=3 biological replicates.

- Tumor quantification and diameter measurements at 4-months of age: *Nf1 fl/fl DhhCre* n=5 biological replicates; 19 tumors and *P2RY14-/- Nf1 fl/flDhhCre* n=5 biological replicates; 5 tumors.

- Ki67 cell quantification at 7-months of age: *Nf1 fl/fl DhhCre* n=3 biological replicates; *P2RY14 -/- Nf1 fl/fl DhhCre* n=3 biological replicates.

- Electron microscopy at 4-months and 7 months of age: *WT* n=3 biological replicates; *Nf1 fl/fl DhhCre* n=3 biological replicates; *P2RY14 -/- Nf1 fl/fl DhhCre* n=3 biological replicates.

Statistical reporting

- Statistical analysis methods should be described and justified
- Raw data should be presented in figures whenever informative to do so (typically when N per group is less than 10)
- For each experiment, you should identify the statistical tests used, exact values of N, definitions of center, methods of multiple test correction, and dispersion and precision measures (e.g., mean, median, SD, SEM, confidence intervals; and, for the major substantive results, a measure of effect size (e.g., Pearson's r, Cohen's d)
- Report exact p-values wherever possible alongside the summary statistics and 95% confidence intervals. These should be reported for all key questions and not only when the p-value is less than 0.05.

Please outline where this information can be found within the submission (e.g., sections or figure legends), or explain why this information doesn't apply to your submission:

Information can be found in each figure legend.

(For large datasets, or papers with a very large number of statistical tests, you may upload a single table file with tests, Ns, etc., with reference to sections in the manuscript.)

Group allocation

- Indicate how samples were allocated into experimental groups (in the case of clinical studies, please specify allocation to treatment method); if randomization was used, please also state if restricted randomization was applied
- Indicate if masking was used during group allocation, data collection and/or data analysis

Please outline where this information can be found within the submission (e.g., sections or figure legends), or explain why this information doesn't apply to your submission:

Samples were randomly assigned to the treatment groups.

Additional data files ("source data")

- We encourage you to upload relevant additional data files, such as numerical data that are represented as a graph in a figure, or as a summary table
- Where provided, these should be in the most useful format, and they can be uploaded as "Source data" files linked to a main figure or table
- Include model definition files including the full list of parameters used
- Include code used for data analysis (e.g., R, MatLab)
- Avoid stating that data files are "available upon request"

Please indicate the figures or tables for which source data files have been provided:

All the data used for figure preparations will be available at Synapse Project (https://www.synapse.org/). Currently they have not been released yet.