**Materials Design Analysis Reporting (MDAR)**

**Checklist for Authors**

The [MDAR framework](https://osf.io/xfpn4/) establishes a minimum set of requirements in transparent reporting mainly applicable to studies in the life sciences.

*eLife* asks authors to **provide detailed information within their article** to facilitate the interpretation and replication of their work. Authors can also upload supporting materials to comply with relevant reporting guidelines for health-related research (see [EQUATOR Network](http://www.equator-network.org/%20)), life science research (see the [BioSharing Information Resource](http://biosharing.org/)), or animal research (see the [ARRIVE Guidelines](http://www.plosbiology.org/article/info:doi/10.1371/journal.pbio.1000412) and the [STRANGE Framework](https://doi.org/10.1038/d41586-020-01751-5); for details, see *eLife*’s [Journal Policies](https://reviewer.elifesciences.org/author-guide/journal-policies)). Where applicable, authors should refer to any relevant reporting standards materials in this form.

For all that apply, please note **where in the article** the information is provided. Please note that we also collect information about data availability and ethics in the submission form.

**Materials:**

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| **Newly created materials** | **Indicate where provided: section/figure legend** | **N/A** |
| The manuscript includes a dedicated "materials availability statement" providing transparent disclosure about availability of newly created materials including details on how materials can be accessed and describing any restrictions on access. | RNAseq section under Materials and methods.  Data availability section under Additional information. |  |
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| **Antibodies** | **Indicate where provided: section/figure legend** | **N/A** |
| For commercial reagents, provide supplier name, catalogue number and [RRID](https://scicrunch.org/resources), if available. | All information regarding the commercial reagents are provided in the Materials and methods section, and  Key Resource Table. |  |
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| **DNA and RNA sequences** | **Indicate where provided: section/figure legend** | **N/A** |
| Short novel DNA or RNA including primers, probes: Sequences should be included or deposited in a public repository. | Transcript sequences for the designed alleles is provided in the ***Figure 1­–figure supplement 2***.  All primers are provided in ***Appendix 1***. |  |
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| **Cell materials** | **Indicate where provided: section/figure legend** | **N/A** |
| Cell lines: Provide species information, strain. Provide accession number in repository OR supplier name, catalog number, clone number, OR RRID. | HEK-HT cells were created and maintained in the Counter Lab ([***Counter et al., 1992***](#_ENREF_10)). HEK-HT cells were authenticated by immunoblot against SV40 large T antigen and tested negative for mycoplasma. |  |
| Primary cultures: Provide species, strain, sex of origin, genetic modification status. | Mouse embryonic fibroblasts (MEFs) derived from the designed *KrasLSL-natG12D/+*, *Kras LSL-natQ61R/+*, *Kras LSL-comG12D/+*, and *Kras LSL-comQ61R/+* mice validated with genotyping PCR. MEF cultures were tested negative for mycoplasma. |  |
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| **Experimental animals** | **Indicate where provided: section/figure legend** | **N/A** |
| Laboratory animals or Model organisms: Provide species, strain, sex, age, genetic modification status. Provide accession number in repository OR supplier name, catalog number, clone number, OR RRID. | Mus musculus: *KrasLSL-natG12D/+*, *Kras LSL-natQ61R/+*, *Kras LSL-comG12D/+*, *Kras LSL-comQ61R/+* , *Kras LSL-rareG12D/+* designed in this paper. *ACTBFLPe/FLPe* (Jackson Laboratory, #003800), *Rosa26CreERT2 CreERT2* (Jackson Laboratory, #008463), and *CC10CreER/CreER;Rosa26CAG-fGFP/CAG-fGFP* (gift from Mark Onaitis).Also provided in Materials and methods section and ***Key resources table***. |  |
| Animal observed in or captured from the field: Provide species, sex, and age where possible. |  | X |
|  |  |  |
| **Plants and microbes** | **Indicate where provided: section/figure legend** | **N/A** |
| Plants: provide species and strain, ecotype and cultivar where relevant, unique accession number if available, and source (including location for collected wild specimens). |  | X |
| Microbes: provide species and strain, unique accession number if available, and source. |  | X |
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| **Human research participants** | **Indicate where provided: section/figure legend) or state if these demographics were not collected** | **N/A** |
| If collected and within the bounds of privacy constraints report on age, sex, gender and ethnicity for all study participants. |  | **X** |

**Design:**

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| **Study protocol** | **Indicate where provided: section/figure legend** | **N/A** |
| If the study protocol has been pre-registered, provide DOI. For clinical trials, provide the trial registration number OR cite DOI. |  | X |
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| **Laboratory protocol** | **Indicate where provided: section/figure legend** | **N/A** |
| Provide DOI OR other citation details if detailed step-by-step protocols are available. |  | X |
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| **Experimental study design (statistics details) \*** | | |
| **For in vivo studies: State whether and how the following have been done** | **Indicate where provided: section/figure legend. If it could have been done, but was not, write “not done”** | **N/A** |
| Sample size determination | Materials and methods sections:  RNAseq  Reverse phase protein microarray (RPPA)  Tumorigenesis studies  Tissue analysis |  |
| Randomisation | Materials and methods sections:  Ras activity on lung tissue  RNAseq  Reverse transcription quantitative real-time PCR (qRT-PCR)  Reverse phase protein microarray (RPPA)  Tumorigenesis studies |  |
| Blinding | Materials and methods sections: Tumorigenesis studies  Tissue analysis |  |
| Inclusion/exclusion criteria | Materials and methods sections:  Reverse transcription quantitative real-time PCR (qRT-PCR)  Reverse phase protein microarray (RPPA)  Tumorigenesis studies |  |
|  |  |  |
| **Sample definition and in-laboratory replication** | **Indicate where provided: section/figure legend** | **N/A** |
| State number of times the experiment was replicated in the laboratory. | Materials methods sections: Ectopic expression, immunoblots, and Ras activity assay  Immunoblot and Ras activity assays in MEF cultures  Ras activity assay on lung tissue |  |
| Define whether data describe technical or biological replicates. | Figure legends for ***Figure 1B-C***, ***Figure 1–figure supplement 3***, ***Figure 1–figure supplement 5***, ***Figure 1–figure supplement 6***, and ***Figure 3–figure supplement 7***.  Materials and methods sections:  Ectopic expression, immunoblots, and Ras activity assay  Immunoblot and Ras activity assays in MEF cultures  Reverse phase protein microarray (RPPA)  Reverse transcription quantitative real-time PCR (qRT-PCR) |  |
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| **Ethics** | **Indicate where provided: section/submission form** | **N/A** |
| Studies involving human participants: State details of authority granting ethics approval (IRB or equivalent committee(s), provide reference number for approval. |  | X |
| Studies involving experimental animals: State details of authority granting ethics approval (IRB or equivalent committee(s), provide reference number for approval. | All animal experiments were approved by Duke IACUC (Protocol #A195-19-09). |  |
| Studies involving specimen and field samples: State if relevant permits obtained, provide details of authority approving study; if none were required, explain why. |  | X |
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| **Dual Use Research of Concern (DURC)** | **Indicate where provided: section/submission form** | **N/A** |
| If study is subject to dual use research of concern regulations, state the authority granting approval and reference number for the regulatory approval. |  | X |

**Analysis:**

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| **Attrition** | **Indicate where provided: section/figure legend** | **N/A** |
| Describe whether exclusion criteria were pre-established. Report if sample or data points were omitted from analysis. If yes, report if this was due to attrition or intentional exclusion and provide justification. | For qRT-PCR analysis for the second biological replicate, one of two negative controls did not have numerical data for two transcripts and hence was not used for plotting.  RPPA analysis of one of the *Rosa26CreERT2/+*;*KrasLSL-natG12D/+* mouse lungs was deemed an outlier, as it shared little commonality with the other three biological replicates. As such, the RPPA analysis of this mouse was not included. |  |
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| **Statistics** | **Indicate where provided: section/figure legend** | **N/A** |
| Describe statistical tests used and justify choice of tests. | All statistical tests are provided in the Materials and methods section, and corresponding figure legends.  ***Figure 1–figure supplement 5***: One-way ANOVA multiple pairwise comparison with Tukey testing.  Figure 4–figure supplement 2: One-way ANOVA with Bonferroni’s multiple comparisons test with a single pooled variance and a 95% CI.  ***Figure 4–figure supplement 2***: One-way ANOVA with Bonferroni’s multiple comparisons test with a single pooled variance and a 95% CI.  ***Figure 4–figure supplement 4***: pairwise comparisons of the survival curves via Log-rank Mantel-Cox test.  ***Figure 4–figure supplement 6***: Two-way ANOVA multiple comparisons with Sidak testing and one-way ANOVA multiple comparisons with Tukey testing. |  |
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| **Data availability** | **Indicate where provided: section/submission form** | **N/A** |
| For newly created and reused datasets, the manuscript includes a data availability statement that provides details for access (or notes restrictions on access). | RNAseq under Materials and methods section, and Data availability statement provided under Additional information |  |
| When newly created datasets are publicly available, provide accession number in repository OR DOI and licensing details where available. | RNAseq under Materials and methods section, and Data availability statement provided under Additional information |  |
| If reused data is publicly available provide accession number in repository OR DOI, OR URL, OR citation. | Citations for TRANSFAC database and druggable kinases are provided in Transcriptome analysis under Materials and methods section. |  |
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| **Code availability** | **Indicate where provided: section/figure legend** | **N/A** |
| For any computer code/software/mathematical algorithms essential for replicating the main findings of the study, whether newly generated or re-used, the manuscript includes a data availability statement that provides details for access or notes restrictions. | Software and algorithms are available in the ***Key resource table*** as stated in the Data availability under Additional information section. |  |
| Where newly generated code is publicly available, provide accession number in repository, OR DOI OR URL and licensing details where available. State any restrictions on code availability or accessibility. |  | X |
| If reused code is publicly available provide accession number in repository OR DOI OR URL, OR citation. | Citations for all reused codes and algorithms are provided in the ***Key resource table***. |  |

**Reporting:**

The MDAR framework recommends adoption of discipline-specific guidelines, established and endorsed through community initiatives.

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| **Adherence to community standards** | **Indicate where provided: section/figure legend** | **N/A** |
| State if relevant guidelines (e.g., ICMJE, MIBBI, ARRIVE, STRANGE) have been followed, and whether a checklist (e.g., CONSORT, PRISMA, ARRIVE) is provided with the manuscript. |  | X |

\* We provide the following guidance regarding transparent reporting and statistics; we also refer authors to [Ten common statistical mistakes to watch out for when writing or reviewing a manuscript](https://doi.org/10.7554/eLife.48175).

**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

**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)

**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.

**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