



# Exploiting Depmap cancer dependency data using the depmap R package

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## Summary

The `depmap` package facilitates access in the R environment for data from the *Depmap* project, which maps genetic and chemical dependencies, and other molecular biological features for over 1700 cancer cell lines. The `depmap` package formats this data for use of popular R data analysis and visualization tools such as `dplyr` and `ggplot2`. In addition, the `depmap` package utilizes [ExperimentHub](#), storing versions of *Depmap* data accessible from the cloud.



## Introduction

Many contemporary cancer drug therapies are broadly toxic to cells. Precision cancer medicine, aims to avoid indiscriminate toxicity by exploiting cancer-specific vulnerabilities, termed *dependencies*. However, the exact nature of many of these dependencies in cancer cell lines is not completely understood. The *Depmap* project, a collaboration between the Broad Institute and Wellcome Sanger Institute, maps such dependencies in a broad range cancer cell lines, in the frame of searching for new targets in precision cancer medicine.

## Content of the package

The `depmap` package stores all *Depmap* datasets in the cloud on AWS, via [ExperimentHub](#) (EH). `depmap` accessor functions, such as `depmap_rnai()` can be used to retrieve the most current datasets and import them into R. It is also possible to download datasets of specific releases via the [EH](#) ID number. **Help files** with documentation are also provided for every data set.

```
1 ## automatically download the latest rnai dataset
2 rnai <- depmap::depmap_rnai()
3
4 ## or... download specific depmap rnai dataset
5 eh <- ExperimentHub()
6 query(eh, "depmap")
7 rnai <- eh[["EH3080"]]
8
9 ## obtain documentation on depmap rnai dataset
10 ?rnai
```

A table of the available datasets is shown below:

Dataset	Name
crispr	CRISPR Genetic Dependency (Depmap, Broad 2019)
rnai	RNAi Genetic Dependency (McFarland, et al. 2018)
copyNumber	Gene Level Copy Number (Depmap, Broad 2019)
TPM	TPM Gene Expression (Depmap, Broad 2019)
RPPA	Reverse Phase Protein Array (Ghandi, et al. 2019)
mutationCalls	CCLE Mutation Data (Depmap, Broad 2019)
metadata	Cancer Cell Line Metadata (Depmap, Broad 2019)
drug_dependency	PRISM Chemical Dependency (Corsello, et al. 2019)

## Use Case

A potential target in precision cancer medicine is gene *PIK3CA*. Oncogenic mutations of this gene increase dependency on the mRNA cap methyltransferase, *RNMT*, in breast cancer cells. A plot of the dependency scores for all cancer cell lines shows increased genetic dependency for this gene for breast cancer cell lines and that these mutations frequently appear in the COSMIC database. (Figure 1). The expression levels of this gene for all cancer cell lines are also illustrated (Figure 2)

## Discussion and Outlook

We hope that this package will serve as a reproducible research framework allowing researchers to easily mine, explore and illustrate dependency data taken from the *Depmap* project. The `depmap` R package will be maintained in line with biannual *Bioconductor* releases, in addition to incorporating quarterly releases of *Depmap* data. Feedback and questions from the community and contributions to the code are highly appreciated.

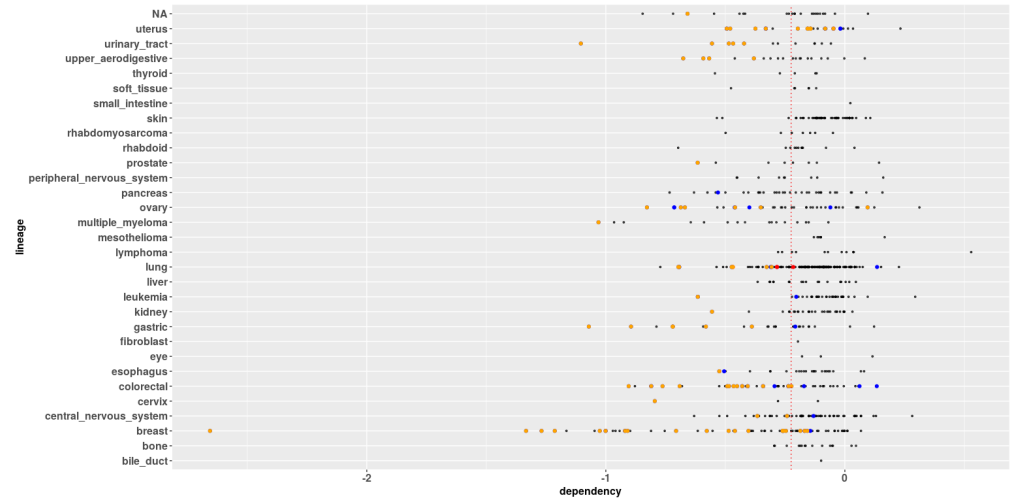


Figure 1: **Distribution of RNAi dependency scores for gene PIK3CA by lineage.** Types of mutations are highlighted: "damaging" (red), "other non-conserving" (blue), "is COSMIC hotspot" (orange), mean RNAi dependency scores for gene PIK3CA (dotted red line).

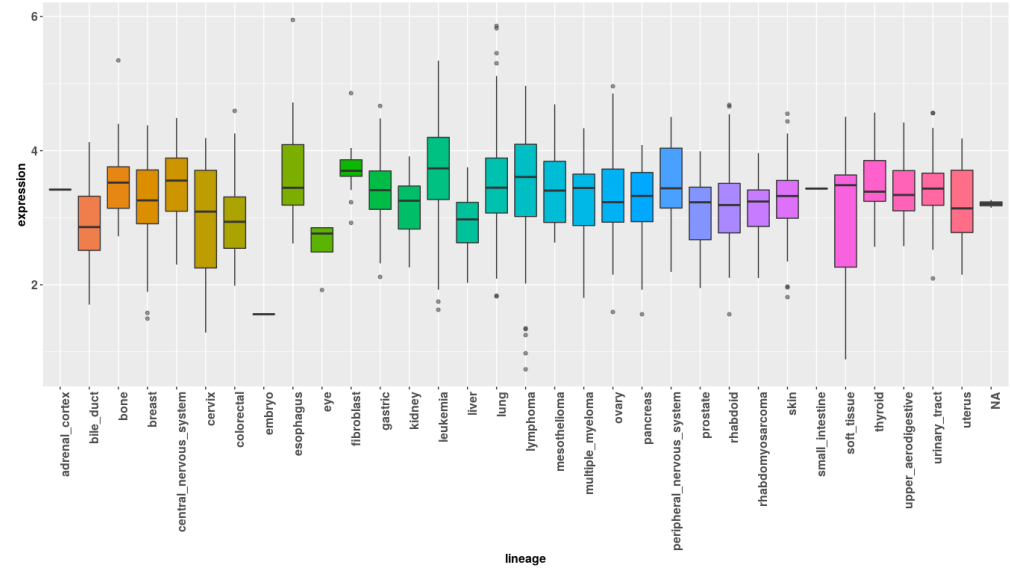


Figure 2: **Distribution of gene expression values for gene PIK3CA by lineage.** Log2+1 fold expression values for all major cancer diseases. Outliers shown in gray.

## Package Availability

The `depmap` package is available through *Bioconductor* (since v.3.8) and can be installed in the following manner:

```
1 BiocManager::install("depmap")
2 library("depmap")
```

## References

- [1] R. M. Meyers, J. G. Bryan, J. M. McFarland, B. A. Weir, A. E. Sizemore, H. Xu, N. V. Dharia, P. G. Montgomery, G. S. Cowley, S. Pantel, *et al.*, "Computational correction of copy number effect improves specificity of crispr-cas9 essentiality screens in cancer cells," *Nature genetics*, vol. 49, no. 12, p. 1779, 2017.
- [2] B. DepMap, "Depmap achilles 19q3 public," *FigShare version*, vol. 2, 2019.
- [3] J. M. McFarland, Z. V. Ho, G. Kugener, J. M. Dempster, P. G. Montgomery, J. G. Bryan, J. M. Krill-Burger, T. M. Green, F. Vazquez, J. S. Boehm, *et al.*, "Improved estimation of cancer dependencies from large-scale rnai screens using model-based normalization and data integration," *Nature communications*, vol. 9, 2018.
- [4] M. Ghandi, F. W. Huang, J. Jané-Valbuena, G. V. Kryukov, C. C. Lo, E. R. McDonald, J. Barretina, E. T. Gelfand, C. M. Bielski, H. Li, *et al.*, "Next-generation characterization of the cancer cell line encyclopedia," *Nature*, vol. 569, no. 7757, p. 503, 2019.
- [5] H. Li, S. Ning, M. Ghandi, G. V. Kryukov, S. Gopal, A. Deik, A. Souza, K. Pierce, P. Keskula, D. Hernandez, *et al.*, "The landscape of cancer cell line metabolism," *Nature medicine*, vol. 25, no. 5, p. 850, 2019.
- [6] S. M. Corsello, R. T. Nagari, R. D. Spangler, J. Rossen, M. Kocak, J. G. Bryan, R. Humeidi, D. Peck, X. Wu, A. A. Tang, *et al.*, "Non-oncology drugs are a source of previously unappreciated anti-cancer activity," *bioRxiv*, p. 730119, 2019.
- [7] J. M. Dempster, J. Rossen, M. Kazachkova, J. Pan, G. Kugener, D. E. Root, and A. Tsherniak, "Extracting biological insights from the project achilles genome-scale crispr screens in cancer cell lines," *BioRxiv*, 2019.
- [8] S. Dunn, O. Lombardi, R. Lukoszek, and V. H. Cowling, "Oncogenic pik3ca mutations increase dependency on the mrna cap methyltransferase, rnmt, in breast cancer cells," *Open biology*, vol. 9, no. 4, p. 190052, 2019.
- [9] A. Tsherniak, F. Vazquez, P. G. Montgomery, B. A. Weir, G. Kryukov, G. S. Cowley, S. Gill, W. F. Harrington, S. Pantel, J. M. Krill-Burger, *et al.*, "Defining a cancer dependency map," *Cell*, vol. 170, no. 3, pp. 564–576, 2017.