

Exploiting Depmap cancer dependency data using the depmap R package

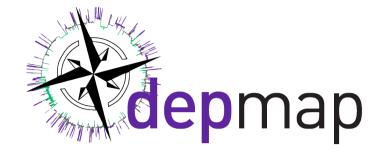


Theo Killian, Laurent Gatto

Computational biology and bioinformatics lab, de Duve Institute, UCLouvain

theodore.killian@uclouvain.be





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, providing a reproducible research framework for these datasets.

Introduction

Many contemporary cancer drug therapies are broadly toxic to cells. Precision cancer medicine, aims to avoid indescriminate toxicity by exploiting cancerspecific 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

depmap package stores all Depmap datasets in the Cloud on AWS. depmap accessor functions, such as depmap_rnai() that utilize ExperimentHub can be used to retrieve the most current datasets and import them into the R environment. 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.

```
\textit{## automatically download the latest rnai dataset}
rnai <- depmap::depmap_rnai()</pre>
## or... download specific depmap rnai dataset
eh <- ExperimentHub()</pre>
query(eh, "depmap")
rnai <- eh[["EH3080"]]</pre>
## obtain documentation on depmap rnai dataset
```

A table of the available datasets is shown below:

| Dataset | Name |
|-----------------|--|
| crispr | CRISPR (Avana) Genetic Dependency (Depmap, Broad 2019) |
| rnai | RNAi (Broad, Novartis, Marcotte) 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 Screens (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)

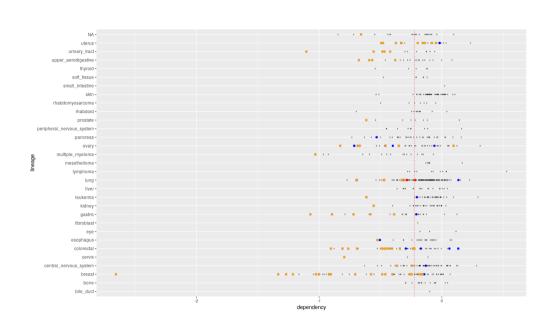


Figure 1: Distribution of RNAi dependency scores for gene PIK3CA by lineage. Types of mutations are highlighted: "damaging" (red), "other non-conserving" (blue), "is COSMIC hotspot" (orange), mean RNAi dependency scores for gene PIK3CA (dotted red line).

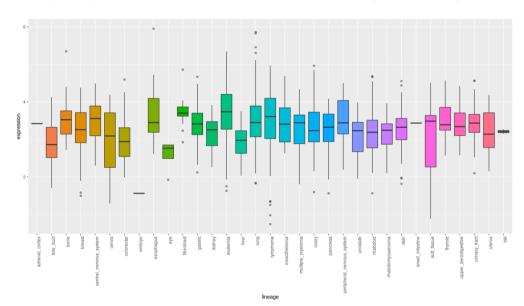


Figure 2: Distribution of gene expression values for gene PIK3CA by lineage. Log2+1 fold expression values for all major cancer diseases. Outliers shown in gray.

Discussion and Outlook

We hope that this package will allow researchers to more easily mine, explore and visually illustrate dependency data taken from the *Depmap* project. The depmap R package will continue to be maintained in line with biannual *Bioconductor* releases, in addition to incorporating quarterly releases of Depmap data. Feedback and questions from the community are most welcome and contributions to the code are highly appreciated.

Package Availability

The depmap package is available through Bioconductor (v.3.10) and can be installed in the following manner:

BiocManager::install("depmap") 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.

 B. DepMap, "Depmap achilles 19q3 public," FigShare version, vol. 2, 2019.

 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. 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,
- 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, p. 720243.
- [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,