

Exploiting Depmap cancer dependency data using the depmap R package



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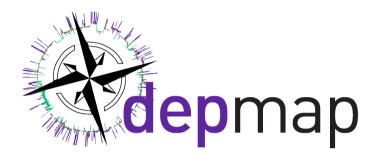
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Summary

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 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

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.

```
## automatically download the latest rnai dataset
rnai <- depmap::depmap_rnai()</pre>
## or... download specific depmap rnai dataset
eh <- ExperimentHub()
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 Genetic Dependency (Depmap, Broad 2019)
$_{ m rnai}$	RNAi Genetic Dependency (McFarland, et al. 2018)
$\operatorname{copyNumber}$	Gene Level Copy Number (Depmap, Broad 2019)
TPM	TPM Gene Expression (Depmap, Broad 2019)
RPPA	Reverse Phase Protein Array (Ghandi, et al. 2019)
${ m mutation Calls}$	CCLE Mutation Data (Depmap, Broad 2019)
$\operatorname{metadata}$	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.

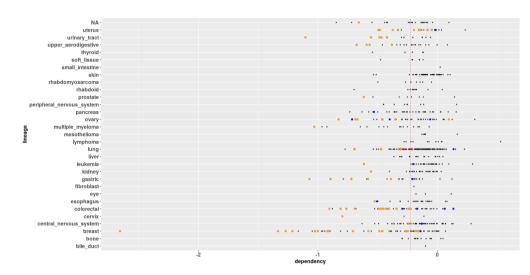


Figure 1: Distribution of RNAi dependency scores for gene PIK3CA by lineage. Types of mutations are highlighted: "damaging" (red), "other non-conserving" (blue), "is COSMIC hotspot" (orange), mean RNAi dependency scores for gene PIK3CA (dotted red line).

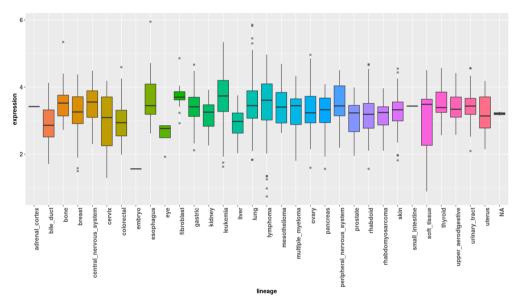


Figure 2: Distribution of gene expression values for gene PIK3CA by lineage. Log2+1 fold expression values for all major cancer diseases. Outliers shown in gray.

Package Availability

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

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

References

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