



UCLouvain

UCLouvain

Institut de Duve - Computational Biology and Bioinformatics



Exploiting Depmap cancer dependency data using the depmap R package

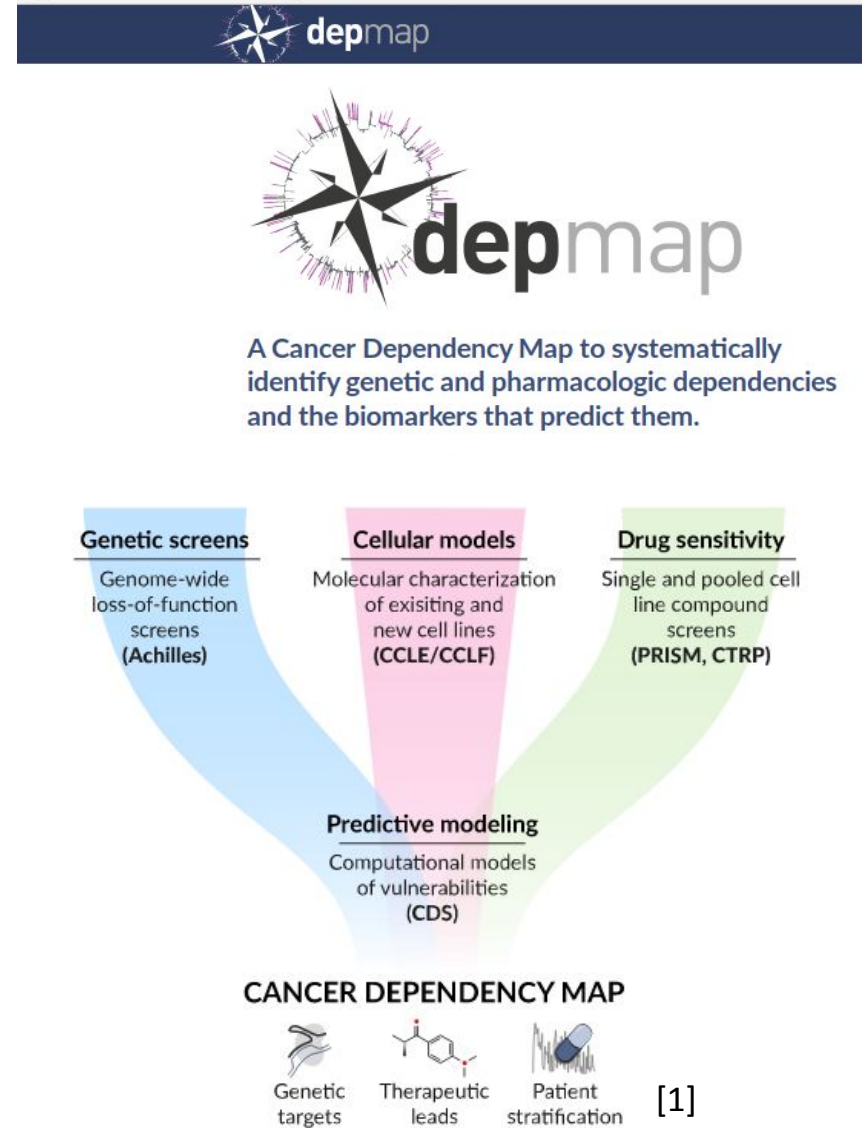
Theo Killian

Gatto Lab

Cancer Dependency Map

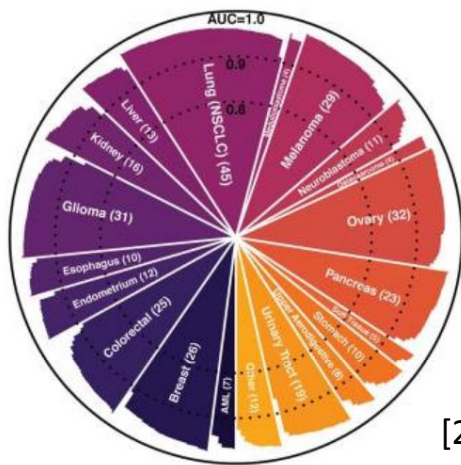
- Precision cancer medicine seeks to target dependencies
- For many cancers, the relationship between the genetic features of cancer and dependencies is not well understood.
- A “cancer dependency map” is needed: Depmap

<https://depmap.org/portal/download/> [1]



Depmap data

- In vitro characterization of cancer cell lines (~1700)
- Broadly represent “landscape” of cancer diseases
- New quarterly data releases (19Q1, 19Q2, etc.)
- Published under the Creative Commons license (CC BY 4.0)



[2]



[1]

Current Depmap Datasets (19Q3)

- *depmap* package imports Depmap data into R:
- “**rnai**” (RNAi genetic dependency)
- “**crispr**” (CRISPR genetic dependency)
- “**copyNumber**” (log fold copy number)
- “**TPM**” (protein-coding expression)
- “**RPPA**” (Reverse Phase Protein Array)
- “**mutationCalls**” (mutation calls)
- “**drug_sensitivity**” (chemical dependency)
- “**metadata**” (metadata about all cancer cell lines)

Value added to Depmap data in *depmap* package

- Data was cleaned, unique identifier *depmap_id* added for cell line entries in all datasets, *ENSEMBL_ID* added, etc.
- Data sets are comparable (e.g. consistent feature names)
- Datasets were converted to long format tibbles for use with popular R tools such as *dplyr* and *ggplot2*

Features of depmap R package

- Lightweight (data stored in the cloud via *ExperimentHub*)
- Accessor functions automatically download and cache data from cloud (e.g. `depmap_rnai()` downloads RNAi data)
- All past and future versions of Depmap data will be accessible to enhance research reproducibility

```
## accessor functions that download and cache the latest datasets
depmap::depmap_rnai() -> rnai

depmap::depmap_crispr() -> crispr

depmap::depmap_copyNumber() -> copyNumber

depmap::depmap_RPPA() -> RPPA

depmap::depmap_TPM() -> TPM

depmap::depmap_mutationCalls() -> mutationCalls

depmap::depmap_metadata() -> metadata

depmap::depmap_drug_sensitivity() -> drug_sensitivity
```

Use case for *depmap*

- Investigate cancer dependency target of interest in Depmap data
- Oncogenic PIK3CA mutations lead to increased genomic dependency in breast cancer cells
- Explore Depmap data for this gene and illustrating with *ggplot*

[Cell](#). Author manuscript; available in PMC 2018 Jul 27.
Published in final edited form as:
[Cell](#). 2017 Jul 27; 170(3): 564–576.e16.
doi: [10.1016/j.cell.2017.06.010](#)

PMCID: PMC5667678
NIHMSID: NIHMS886779
PMID: 28753430

Defining a Cancer Dependency Map

[Aviad Tsherniak](#)^{1,*}, [Francisca Vazquez](#)^{1,2,*}, [Phil G. Montgomery](#)¹, [Barbara A. Weir](#)^{1,2}, [Gregory Kryukov](#)^{1,2},
[Glenn S. Cowley](#)¹, [Stanley Gill](#)^{1,2}, [William F. Harrington](#)¹, [Sasha Pantel](#)¹, [John M. Krill-Burger](#)¹,
[Robin M. Meyers](#)¹, [Levi Ali](#)¹, [Amy Goodale](#)¹, [Yenarae Lee](#)¹, [Guozhi Jiang](#)¹, [Jessica Hsiao](#)¹, [William F. J. Gerath](#),
[Sara Howell](#)¹, [Erin Merkel](#)¹, [Mahmoud Chandi](#)¹, [Levi A. Garraway](#)^{1,2,3,4,5}, [David E. Root](#)^{1,*},
[Todd R. Golub](#)^{1,2,4,5,*}, [Jesse S. Boehm](#)^{1,*} and [William C. Hahn](#)^{1,2,3,4,*}#

► Author information ► Copyright and License information [Disclaimer](#)

[3]

[Open Biol.](#) 2019 Apr; 9(4): 190052.
Published online 2019 Apr 17. doi: [10.1098/rsob.190052](#)

PMCID: PMC6501644
PMID: 30991934

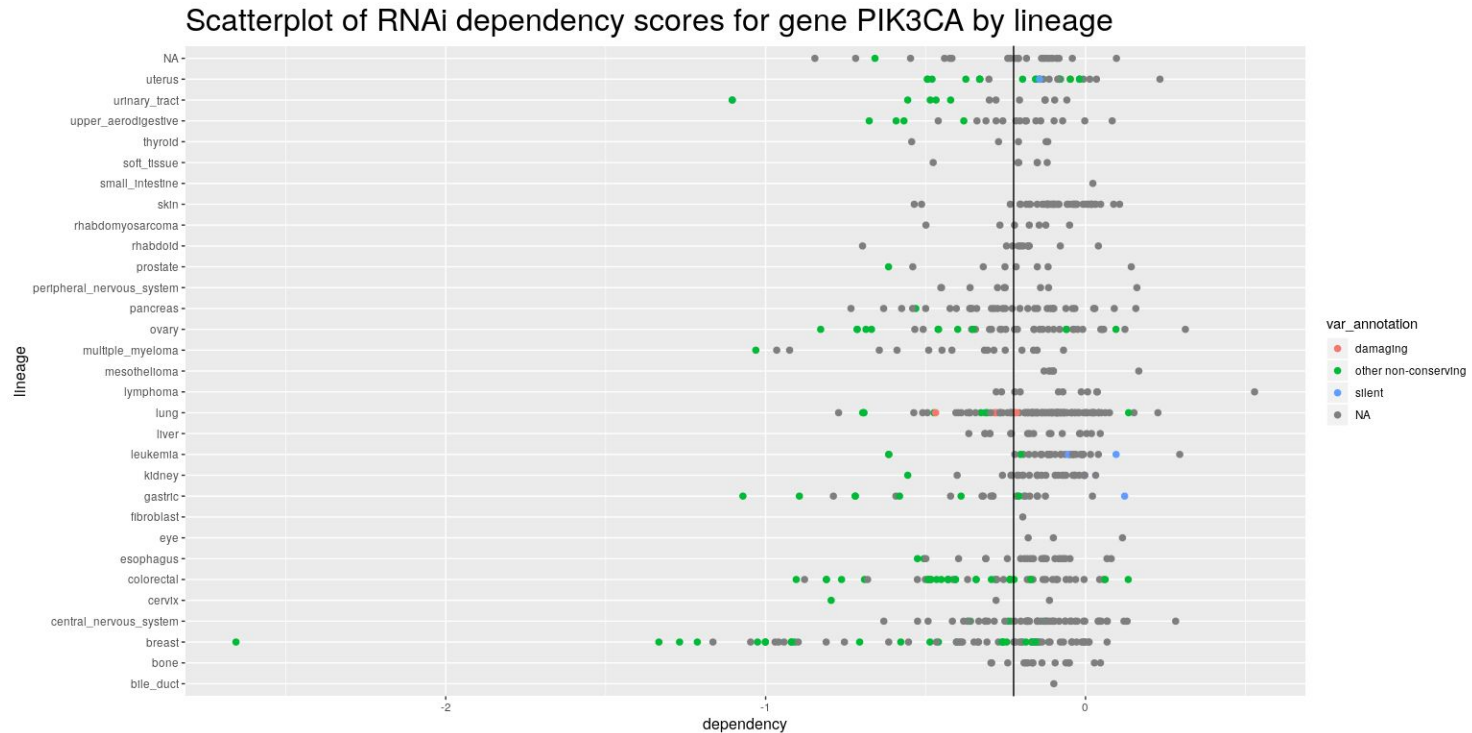
Oncogenic PIK3CA mutations increase dependency on the mRNA cap methyltransferase, RNMT, in breast cancer cells

[Sianadh Dunn](#)¹, [Olivia Lombardi](#)², [Radoslaw Lukoszek](#), and [Victoria H. Cowling](#)

► Author information ► Article notes ► Copyright and License information [Disclaimer](#)

[4]

Use Case Exploring Depmap Dependency Data

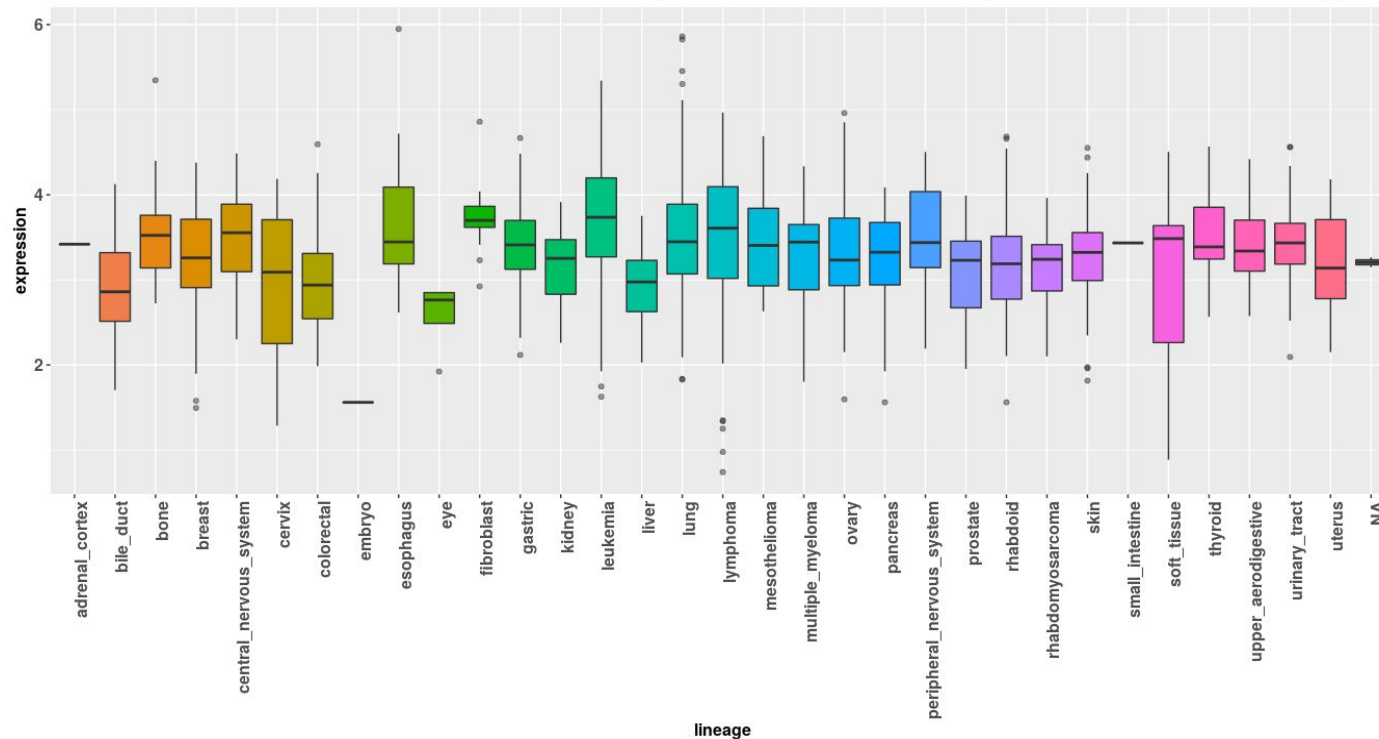


```
# join metadata and the rnai, select gene of interest and mutationcalls
meta_rnai <- metadata %>%
  select(depmap_id, lineage) %>%
  full_join(rnai, by = "depmap_id") %>%
  filter(gene_name == "PIK3CA") %>%
  left_join((mutationCalls %>% select(depmap_id, entrez_id, is_cosmic_hotspot, var_annotation)),
    by = c("depmap_id", "entrez_id"))

# feed to ggplot
meta_rnai %>%
  ggplot(aes(x=dependency, y=lineage, colour = var_annotation)) +
  geom_point(size = 2) +
  geom_vline(xintercept=mean(meta_rnai$dependency, na.rm = TRUE)) +
  ggtitle("Scatterplot of RNAi dependency scores for gene PIK3CA by lineage") +
  theme(axis.title = element_text(size = 12), plot.title = element_text(size = 24))
```


Use Case Exploring Depmap Expression Data

Plot of log2 + 1 transformed TPM expression values for gene PIK3CA by lineage



```
# join metadata and TPM, filter for gene of interest and feed to ggplot
metadata %>%
  select(depmap_id, lineage) %>%
  full_join(TPM, by = "depmap_id") %>%
  filter(gene_name == "PIK3CA") %>%
  ggplot(aes(x=lineage, y=expression, fill = lineage)) +
  geom_boxplot(outlier.alpha = 0.5) +
  ggtitle("Plot of log2 + 1 transformed TPM expression values for gene PIK3CA by lineage") +
  theme(axis.title = element_text(size = 12), plot.title = element_text(size = 24))
```

Some things to keep in mind

- RNAi and CRISPR datasets may have different dependency scores for the same gene and cell line (!) ^[5, 6]
- Imperative to take other features such as log copy number, expression into account
- We encourage you to combine Depmap data with other datasets of interest (TCGA, CCLE, etc)

depmap package requirements

Installation

To install this package, start R (version "3.6") and enter:

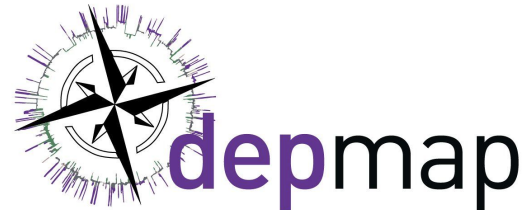
```
if (!requireNamespace("BiocManager", quietly = TRUE))
  install.packages("BiocManager")

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

For older versions of R, please refer to the appropriate [Bioconductor release](#).

Conclusion

- depmap will continue to be updated in line with future Bioconductor releases
- Additional Depmap data releases (>19Q4, etc) will continue to added in future *depmap* package versions
- If you have further questions, please check out my poster



References

- 1) DepMap, Broad. "DepMap Achilles 19Q3 public." *FigShare version 2* (2019).
- 2) Meyers, R. M., Bryan, J. G., McFarland, J. M., Weir, B. A., Sizemore, A. E., Xu, H., ... & Goodale, A. (2017). Computational correction of copy number effect improves specificity of CRISPR–Cas9 essentiality screens in cancer cells. *Nature genetics*, 49(12), 1779.
- 3) Tsherniak, A., Vazquez, F., Montgomery, P. G., Weir, B. A., Kryukov, G., Cowley, G. S., ... & Meyers, R. M. (2017). Defining a cancer dependency map. *Cell*, 170(3), 564-576.
- 4) Dunn, Sianadh, et al. "Oncogenic PIK3CA mutations increase dependency on the mRNA cap methyltransferase, RNMT, in breast cancer cells." *Open biology* 9.4 (2019): 190052.
- 5) McFarland, J. M., Ho, Z. V., Kugener, G., Dempster, J. M., Montgomery, P. G., Bryan, J. G., ... & Golub, T. R. (2018). Improved estimation of cancer dependencies from large-scale RNAi screens using model-based normalization and data integration. *Nature communications*, 9.
- 6) Aguirre, A. J., Meyers, R. M., Weir, B. A., Vazquez, F., Zhang, C. Z., Ben-David, U., ... & Kost-Alimova, M. (2016). Genomic copy number dictates a gene-independent cell response to CRISPR/Cas9 targeting. *Cancer discovery*, 6(8), 914-929.