

# User Manual: KSEA App

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*The KSEA App computationally infers relative kinase activity from quantitative phosphoproteomics data.*

Version: 1.0 (February 2017)

URL: <https://casecpb.shinyapps.io/ksea/>

*Please cite the following papers if using this tool:*

1. Wiredja D.D., Koyutürk M., Chance M.R. (2017) The KSEA App: a web-based tool for kinase activity inference from quantitative phosphoproteomics. *Submitted for review.*
2. Casado, P., Rodriguez-Prados, J.-C., Cosulich, S. C., Guichard, S., Vanhaesebroeck, B., Joel, S., and Cutillas, P. R. (2013) Kinase-substrate enrichment analysis provides insights into the heterogeneity of signaling pathway activation in leukemia cells. *Sci. Signal.* 6, rs6-rs6

*Current specifications for the Kinase-Substrate Database:*

- PhosphoSitePlus Database: July 2016 Release, restricted to human proteins
- NetworkKIN predictions: pre-computed dataset from Human ENSEMBL version 59, restricted to predictions with scores 1 or greater

***Version 1.0 only supports human protein analysis!***

Thank you for using the KSEA App!

Any questions? Please email [ddw34@case.edu](mailto:ddw34@case.edu).

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# Instructions

## 1) Format the Data File

The KSEA App only accepts an experimental data file that adheres to the following specific format.

The data must be a comma delimited .csv file containing these columns with the **exact** header (in bold) and order:

- **Protein**: the Uniprot ID for the parent protein [optional]
- **Gene**: the HUGO gene symbol for the parent protein
- **Peptide**: the sequence of the peptide [optional]
- **Residue.Both**: the modified site (multiple sites are supported but must be separated by semicolons without spaces)
- **p**: the p-value of the differential phosphorylation between the two groups [optional]
- **FC**: the fold change between the two groups' peptide intensities (not log-transformed); only numeric values are allowed, and there can be no character values or blank cells

Sample dataset correctly formatted for input into the KSEA App interface:

|    | A       | B        | C                           | D            | E        | F        |
|----|---------|----------|-----------------------------|--------------|----------|----------|
| 1  | Protein | Gene     | Peptide                     | Residue.Both | p        | FC       |
| 2  | P62263  | RPS14    | IEDVTPIPSDSTR               | S139         | 2.84E-05 | 0.423607 |
| 3  | Q9H4L7  | SMARCA1  | KLSSSEPYEEDEFNDDQSIK        | Y217;S214    | 4.51E-05 | 0.591793 |
| 4  | Q8N5I9  | C12orf45 | IEVLDSPLASK                 | S178         | 0.000082 | 0.502393 |
| 5  | P29375  | KDM5A    | VEPEVLSTDTQTSPPEPTR         | S204         | 0.000222 | 0.476324 |
| 6  | Q5UIP0  | RIF1     | SPQRPSDWSK                  | S782         | 0.000353 | 0.523072 |
| 7  | Q86W50  | METTL16  | EGEAAAVEGPCPSQESLSQEENPEPTE | S455         | 0.000424 | 1.776738 |
| 8  | O75400  | PRPF40A  | SDSPESDAEREK                | S888         | 0.000439 | 0.718616 |
| 9  | Q6PL18  | ATAD2    | NNSNTCNIENELEDSRK           | S1243        | 0.000623 | 0.416637 |
| 10 | P10588  | NR2F6    | AAEDDSASPPGAASDAEPGDEERPGL  | S40          | 0.000793 | 0.407655 |
| 11 | P31641  | SLC6A6   | SPGTRPEDEAEGKPPQR           | T28          | 0.000829 | 0.326469 |

### Important notes:

- The Gene, Residue.Both, and FC values are necessary for the calculations.
- The Protein, Peptide, and p values are optional, but the columns and headers must be present in the input file. You can leave the rest of the column as "NULL" but not blank.
- **DO NOT** leave cells blank or as **NA**, or else the entire row will be discarded!
- Rows with FC = 0 will be discarded since  $\log_2(0)$  cannot be calculated.
- FC values must use a period to indicate the decimal point, not a comma.
- *This current KSEA application only compares two groups at a time; therefore, if a dataset contains multiple conditions, the user must submit separate input files, each with a single fold change column, for every pairwise comparison.*

A sample data file input is provided at the top of the website's left panel.

## 2) Upload the Data

Click on the **Browse** button on the left panel.

This will allow you to select your formatted data file.

## 3) Select the Analysis and Plotting Parameters

### Select kinase-substrate dataset

- Choose the kinase-substrate (K-S) dataset that the algorithm will use to extract substrates for each kinase
- **PhosphoSitePlus** alone is the more conservative choice since it only uses curated annotations.
- **PhosphoSitePlus + NetworkKIN** allows users to include K-S predictions generated from NetworkKIN; this option is recommended if you want to score more kinases or improve the coverage of experimental phosphosites used for KSEA calculations.

### Set NetworkKIN score cutoff

- This option only appears if you select **PhosphoSitePlus + NetworkKIN** in the previous parameter.
- Choose the minimum NetworkKIN score to decide which predicted K-S relationships to discard.
- A higher number corresponds to a more confident K-S prediction.
- The minimum cutoff is 1.

-----The following two parameters are for annotating the bar plot output-----

### [for plot] Set p-value cutoff

1. Decide which kinases in the bar plot would get marked for being statistically significant.
2. Kinases with significant negative scores will be marked blue, whereas those that have significant positive scores will be red.
3.  $p < 0.05$  is the default setting.

### [for plot] Set substrate count cutoff

- Decide the minimum number of detected substrates a kinase must have to be included in the bar plot.
- A lower cutoff thus allows more kinases into the bar plot.
- Kinases that don't pass the cutoff will be excluded from the bar plot but will still be in the two table outputs.

## 4) Click GO!

Then click on the **Plot**, **KSEA Kinase Scores**, and **Kinase-Substrate Links** tabs to see the results.

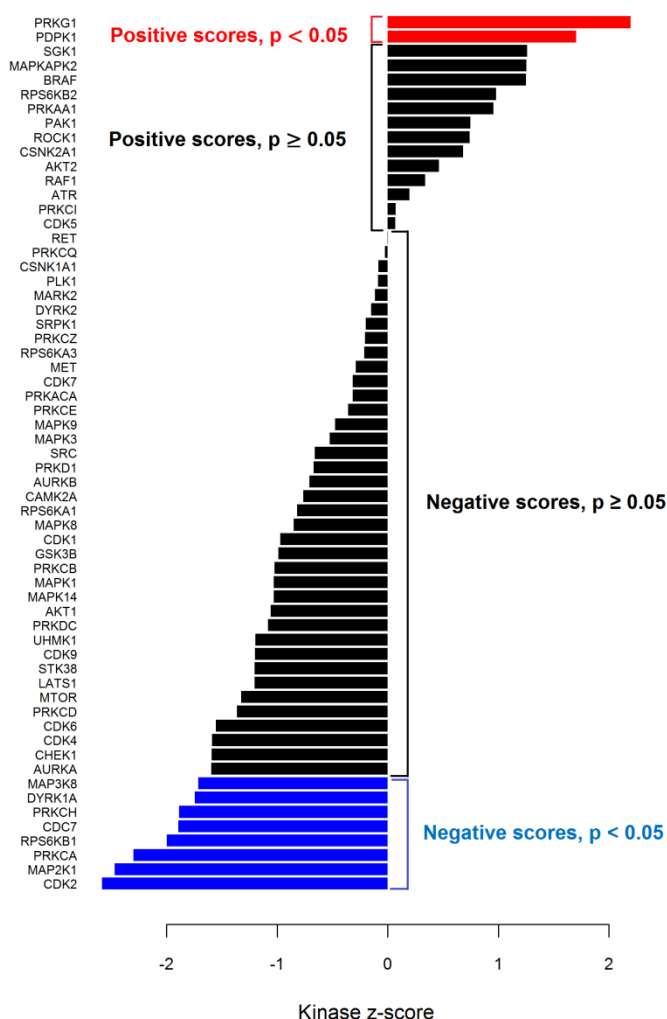
## 5) Download the Results

The KSEA results could be saved by downloading the individual outputs under the **Downloads** tab.

### Plot

- This is the bar plot that summarizes the KSEA results.
- Note that not all kinases are included. The kinase substrate count cutoff, set in the left panel, decides which kinases to include in this plot.
- The p-value cutoff, set in the left panel, decides which kinases to color blue/red for visual annotation of kinases that reach statistical significance.
- Kinases with non-significant scores will be black.
- Do not worry if the preview bar plot under the **Plot** tab appears squished. The file that is available under the **Downloads** tab offers a clearer, well-proportioned .tif image.

Below is a bar plot, generated from phosphoproteomics data from Kim *et al.*, *Mol. Cancer Res*, 2016.



Plotting parameters:

- [for plot] Set p-value cutoff: 0.05
- [for plot] Set substrate count cutoff: 4

## KSEA Kinase Scores

- This is a complete table listing *ALL* the kinases, including those that are not featured in the bar plot, that have at least one identified substrate in the input dataset.
- Please refer to the original Casado *et al.* publication for detailed description of these columns and what they represent.
- **Kinase.Gene** indicates the gene name\* for each kinase.
- **mS** represents the mean log2(fold change) of all the kinase's substrates.
- **Enrichment** is the background-adjusted value of the kinase's mS.
- **m** is the total amount of detected substrates from the experimental dataset for each kinase.
- **z.score** is the normalized score for each kinase, weighted by the number of identified substrates.
- **p.value** represents the statistical assessment for the z.score.
- **FDR** is the p-value adjusted for multiple hypothesis testing using the Benjamini & Hochberg method.

*This table is useful if you want to 1) look at all the scored kinases, not just the filtered ones from the bar plot, and 2) generate custom graphs to supplement the KSEA App's default bar plot.*

*Note: the KSEA Kinase Scores table will NOT be altered if you change the bar plot's p-value cutoff and the kinase substrate count cutoff. However, this table will be altered if you adjust the NetworkKIN score cutoff for the K-S dataset parameter.*

## Kinase-Substrate Links

- This is a complete table listing *ALL* the K-S relationships identified from the experimental dataset. This includes relationships for kinases that are not featured in the bar plot.
- For each kinase, every substrate identified from the dataset was used for the KSEA calculations (in other words, there was no filtering of the substrates).
- **Kinase.Gene** represents the gene name\* for each kinase.
- **Substrate.Gene** indicates the gene name for each substrate linked to that kinase.
- **Substrate.Mod** is the substrate's specific amino acid residue that was modified.
- **Source** shows the database where the K-S annotation was derived from.
- **log2FC** is the log2(fold change) value of that particular substrate phosphosite from the experiment. If that same site was detected across multiple peptides that map to the same protein, the average log2FC is reported.

*This table is useful if you want the specific substrates that contributed to each kinase's score.*

*Note: the Kinase-Substrate Links table will NOT be altered if you change the bar plot's p-value cutoff and the kinase substrate count cutoff. However, this table will be altered if you adjust the NetworkKIN score cutoff for the K-S dataset parameter.*

**\*WARNING:** The *PDK1* gene name is often mistaken for the wrong protein. The KSEA App follows the assignments in this table, which are based on the PhosphoSitePlus and UniprotKB convention.

| Kinase.Gene | Uniprot ID | Protein Name                                  |
|-------------|------------|---|
| PDK1        | Q15118     | pyruvate dehydrogenase kinase isoform 1       |
| PDPK1       | O15530     | 3-phosphoinositide-dependent protein kinase 1 |

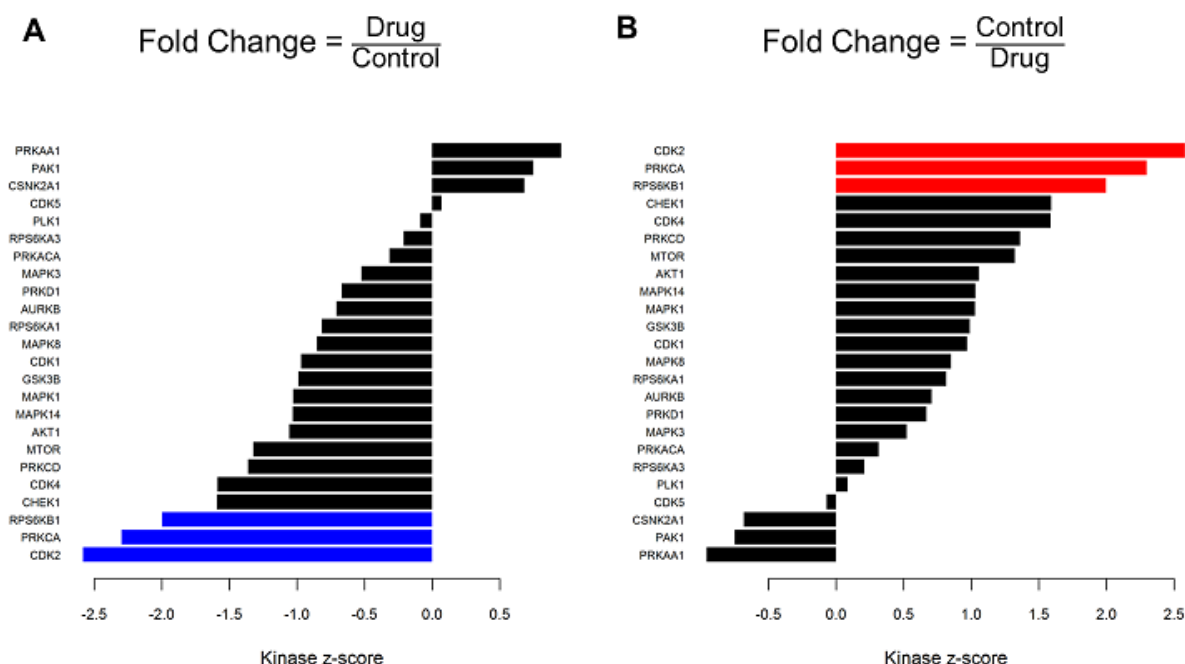
# How to Interpret the Results

*Interpretation of the kinase scores depends on how the fold change values were calculated!*

We will demonstrate using a sample case study:

Take, for instance, a phosphoproteomics experiment looking at two groups:  
Control vs. Drug-Treated.

The following plots are generated by KSEA using the same dataset, but the fold change values were calculated differently.



- A.** Bar plot of the kinase scores calculated from the dataset in which the fold change was determined by **Drug/Control**. In this case, phosphosites with decreased phosphorylation in the drug-treated group will have a fold change ratio that is **less than one**, leading to a  $\log_2(\text{fold change})$  that is **negative**. Thus, if a kinase (in this case, like CDK2, PRKCA, or RPS6KB1) has substrates that are collectively dephosphorylated with drug, its normalized score will be **negative** in value. In turn, this kinase is deemed downregulated with drug because its signaling output is decreased in that group relative to control.
- B.** Bar plot of the kinase scores calculated from the same experimental dataset, but this time the fold change was calculated as **Control/Drug**. The ratio is basically the inverse of A. Note how the kinases from **A** have the same magnitude of the kinase z-scores as in **B**, but the directionality is opposite (negative score in **A** becomes positive in **B**). In this case, phosphosites

with decreased phosphorylation in the drug-treated group will have a fold change ratio that is **greater than one**, leading to a  $\log_2(\text{fold change})$  that is **positive**. Thus, if a kinase has a high proportion of substrates dephosphorylated with drug, its normalized score will be **positive** in value. Regardless, the final interpretation is the same as in **A**: this kinase is deemed downregulated with drug because its signaling output is decreased in that group relative to control.

**Take-away message: the fold change setup determines whether a downregulated kinase has a negative or positive score!**

**We recommend keeping the reference/control group at the denominator of the fold change ratio. This makes interpretation more logical, given the bar plot's built-in coloring scheme.**



# Troubleshooting

An incorrectly-formatted dataset input is the most common cause for errors.

Below are examples of unacceptable inputs:

|    | A        | B       | C                        | D            | E      | F     |
|----|----------|---------|--------------------------|--------------|--------|-------|
| 1  | Gene     | Protein | Peptide                  | Residue.both | p      | fc    |
| 2  | YWHAE    | P62258  | AAFDDAIAELDTLSEESYK      | S210         | 0.0095 | 1.19  |
| 3  | SFN      | P31947  | DNLTWTADNAGEEGGEAPQEPQS  | S248         | 0.0017 | 3.89  |
| 4  | YWHAQ    | P27348  | DNLTWTSDSAGEECDAAEGAEN   | S232         | 0.0019 | 1.83  |
| 5  | YWHAZ    | P63104  | TAFDEAIAELDTLSEESYK      | S207         | 0.0026 | 0.996 |
| 6  | YWHAZ    | P63104  | NLLSVAYK                 | S45          | 0.0028 | 1.07  |
| 7  | YWHAZ    | P63104  | DNLTWTSDTQGDEAEAGEGGEN   | T232         | 0.0029 | 2.75  |
| 8  | TNKS1BP1 | Q9C0C2  | RFSEGVQLQSPSQDQEK        | S429         | 0.003  | 0.805 |
| 9  | TNKS1BP1 | Q9C0C2  | YESQEPLAQESPLPLATR       | S601         | 0.0031 | 1.27  |
| 10 | TNKS1BP1 | Q9C0C2  | SFGTRPLSSGFSPEEAQQQDEEFK | S984         | 0.0032 | 0.815 |
| 11 | TNKS1BP1 | Q9C0C2  | VSGAGFSPSSK              | S1138        | 0.0033 | 0.872 |



- A. The columns are in the incorrect order; it must follow the exact order as specified in p. 3.
- B. The column titles are case-sensitive; the highlighted headers should be “Residue.Both” rather than “Residue.both” and “FC” instead of “fc”.

|    | A       | B          | C                        | D            | E  | F          |
|----|---------|------------|--------------------------|--------------|----|------------|
| 1  | Protein | Gene       | Peptide                  | Residue.Both | p  | FC         |
| 2  | P62258  | YWHAE      | AAFDDAIAELDTLSEESYK      | S210         | NA | 1.19       |
| 3  | P31947  | SFN        | DNLTWTADNAGEEGGEAPQEPQS  | S248         | NA | 3.89       |
| 4  | P27348  | YWHAQ      | DNLTWTSDSAGEECDAAEGAEN   | S232         | NA | 1.83       |
| 5  | P63104  | YWHAZ      | TAFDEAIAELDTLSEESYK      | S207         | NA | 0.996      |
| 6  | P63104  | YWHAZ      | NLLSVAYK                 | S45          | NA | 1.07       |
| 7  | P63104  | YWHAZ      | DNLTWTSDTQGDEAEAGEGGEN   | T232         | NA | 2.75       |
| 8  | Q9C0C2  | HGNC:19081 | VPSSDEEVVEEPQSR          | S1620;S1621  | NA | 1.28; 3.12 |
| 9  | Q9C0C2  | HGNC:19081 | VPSSDEEVVEEPQSR          | S1620        | NA | 1.72       |
| 10 | Q9C0C2  | HGNC:19081 | YSSQDADEQDWEFQK          | S919         | NA | 1.51       |
| 11 | Q9C0C2  | HGNC:19081 | RESAASGLGLLEEGAGAGAAQEEV | S1473;S1476  | NA | 1.81       |



- C. These gene identifiers are not supported, so these rows will be missed when the algorithm searches against the K-S dataset. The application only accepts the HUGO Gene Symbol format.
- D. These cells contain **NA**, which will lead to deletion of these rows in the analysis. Instead, write, “NULL” in these cells; do not remove the entire column or leave the cells empty. Remember: only the **Gene**, **Residue.Both**, and **FC** values are absolutely required for KSEA calculations, but the other three columns must still be present.
- E. The fold change (FC) column incorrectly contains multiple values. There can only be one. See example K for another variation of this problem.

|    | A       | B     | C                            | D              | E      | F        |
|----|---------|-------|------------------------------|----------------|--------|----------|
| 1  | Protein | Gene  | Peptide                      | Residue.Both   | p      | FC       |
| 2  | Q15019  | 2-Sep | IYHLPDAESDEDEDFK             | S218           | 0.4766 | 0.163499 |
| 3  | Q16181  | 7-Sep | ILEQQNSSRTLEK                | T426           | 0.4768 | -0.29513 |
| 4  | Q9UHD8  | 9-Sep | LGDSGGPALKR                  | S22            | 0.4774 | -0.30579 |
| 5  | Q9UHD8  | 9-Sep | RLGDSSGPALK                  | S22            | 0.4775 | 0.042644 |
| 6  | Q9NRG9  | AAAS  | FSPVLGR                      | S495           | 0.0315 | 0.250962 |
| 7  | Q13685  | AAMP  | GTEGHQGPLTCVAANQDGSILITGSVIT | T290,T291      | 0.0362 | 0.124328 |
| 8  | Q9NY61  | AATF  | YLVDGTPKNAGSEEISSEDELVEEK    | S316,S320,S321 | 0.3946 | 0.536053 |
| 9  | Q9NY61  | AATF  | YLVDGTPKNAGSEEISSEDELVEEK    | S320,S321      | 0.3947 | 0.464668 |
| 10 | Q9BZC7  | ABCA2 | ALVADEPEDLDTEDEGLISFEEER     | T2412          | 0.0509 | 0.163499 |
| 11 | P33527  | ABCC1 | HHNSTAELQK                   | S930           | 0.2906 | -2.34373 |
| 12 | O15439  | ABCC4 | DNEESEQPPVPGTPTLR            | T646           | 0.2907 | -0.33825 |

- F.** Be careful! If this datasheet was opened in MS Excel, some gene names that resemble months will be automatically converted to calendar dates. These genes will be missed when the algorithm searches against the K-S database. To avoid this, import the file into Excel by going to **Data > From Text**. After choosing the file to upload, pick **Delimited** under the file type, select **Comma** as the delimiter, and click **Next**. In the final step, click on the column with the gene names, and select **Text** under “Column data format.” Click **Finish**.
- G.** The FC values are log-transformed, which will introduce errors. The correct FC values must be positive ratios ranging from 0 to infinity. However, the algorithm removes FC = 0 entries to avoid errors when these ratios are log-transformed in downstream analyses.
- H.** These residues are separated by commas, so these entries will be missed during the K-S search. While the application accepts multiple modification entries under **Residue.Both**, they must be separated by semicolons.

|    | A       | B       | C            | D      | E       | F     |
|----|---------|---------|--------------|--------|---------|-------|
| 1  | Protein | Gene    | Residue.Both | p      | FC      | FC    |
| 2  | Q7Z7B0  | FILIP1  | T1205        | 0.1755 | 0.00297 | 0.869 |
| 3  | Q64303  | Pak2    | S206         | 0.2641 | 0.00789 | 1.98  |
| 4  | Q68D20  | PMS2CL  | S50          | 0.4215 | 0.00831 | 0.794 |
| 5  | Q3B726  | TWISTNB | S316         | 0.1312 | 0.0174  | 0.687 |
| 6  | Q96I15  | SCLY    | S129         | 0.3415 | 0.0245  | 0.669 |
| 7  | P05455  | SSB     | T362         | 0.2643 | 0.0331  | 3.11  |
| 8  | Q02040  | AKAP17A | S633         | 0.0305 | 0.0419  | 1.26  |
| 9  | O14683  | TP53I11 | S14          | 0.5635 | 0.0677  | 1.2   |
| 10 | Q8IVP5  | FUNDC1  | S13          | 0.1802 | NULL    | 0.94  |
| 11 | Q8N3D4  | EHBP1L1 | S1273        | 0.1472 | 0.0873  | 0.978 |

- I.** The **Peptide** column is missing completely. The header must be present in the file; just leave the subsequent cells as “NULL.” *DO NOT* include **NA** or leave the cells empty/blank.
- J.** This protein/gene is from rats. The KSEA App currently supports only human protein analysis.
- K.** There are two **FC** columns where there can only be one. The current application only does two-group comparisons at a time. If the experimental dataset has 3+ conditions, you must create a new data file for each pairwise comparison.
- L.** This cell contains “NULL,” which is a character value. This will create errors. Only positive numeric values are allowed under the **FC** column, so peptides/phosphosites with no FC measurements must be entirely discarded from the dataset.

**Below are examples of acceptable inputs:**

|    | A       | B        | C                            | D            | E        | F        |
|----|---------|----------|------------------------------|--------------|----------|----------|
| 1  | Protein | Gene     | Peptide                      | Residue.Both | p        | FC       |
| 2  | P62263  | RPS14    | IEDVTPIPSDSTR                | S139         | 2.84E-05 | 0.423607 |
| 3  | Q9H4L7  | SMARCA1  | KLSSSEPYEEDEFNDDQSIK         | Y217;S214    | 4.51E-05 | 0.591793 |
| 4  | Q8N5I9  | C12orf45 | IEVLDSKASK                   | S178         | 0.000082 | 0.502393 |
| 5  | P29375  | KDM5A    | VEPEVLSTDTQTSPEPGTR          | S204         | 0.000222 | 0.476324 |
| 6  | Q5UIP0  | RIF1     | SPQRPSDWSK                   | S782         | 0.000353 | 0.523072 |
| 7  | Q86W50  | METTL16  | EGEAAAVEGPCPSQESLSQEEENPEPTE | S455         | 0.000424 | 1.776738 |
| 8  | O75400  | PRPF40A  | SDSPESDAEREK                 | S888         | 0.000439 | 0.718616 |
| 9  | Q6PL18  | ATAD2    | NNSNTCNIELEDSRK              | S1243        | 0.000623 | 0.416637 |
| 10 | P10588  | NR2F6    | AAEDDSASPPGAASDAEPGDEERPGL   | S40          | 0.000793 | 0.407655 |
| 11 | P31641  | SLC6A6   | SPGTRPEDEAEGKPPQR            | T28          | 0.000829 | 0.326469 |



|    | A       | B        | C       | D            | E    | F          |
|----|---------|----------|---------|--------------|------|------------|
| 1  | Protein | Gene     | Peptide | Residue.Both | p    | FC         |
| 2  | NULL    | E2F8     | NULL    | S71          | NULL | 1.7076724  |
| 3  | NULL    | ESYT2    | NULL    | S691         | NULL | 1.42234314 |
| 4  | NULL    | ESYT2    | NULL    | S755         | NULL | 1.62779682 |
| 5  | NULL    | ESYT2    | NULL    | S758         | NULL | 1.45135416 |
| 6  | NULL    | ESYT2    | NULL    | S761         | NULL | 1.3213071  |
| 7  | NULL    | MED19    | NULL    | S226         | NULL | 1.01828943 |
| 8  | NULL    | KIAA1598 | NULL    | S101         | NULL | 2.29095562 |
| 9  | NULL    | KIAA1598 | NULL    | S249         | NULL | 2.05053696 |
| 10 | NULL    | KIAA1598 | NULL    | S375         | NULL | 0.82156758 |
| 11 | NULL    | KIAA1598 | NULL    | S506         | NULL | 0.0807036  |



# Source Code and Local Access

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## Source Code

The source code for the KSEA App and other dependent files are stored at our GitHub site: <https://github.com/casecpb/KSEA>.

Files will be updated as newer versions are released.

## Local Access via GitHub

**We encourage you to run the app locally on your computer when analyzing sensitive files.**

Locally running the KSEA App requires installation of the R programming language and the Shiny package. These are all free packages that require no login/registration. No coding experience is needed to launch the local version of this app.

Instructions are listed below but can also be found at the GitHub page (link above):

1. Download and install the R programming software [here](#). We recommend you have version 3.0.3 or newer installed. This app has not been tested on older versions.
2. Download and install the free R Studio software [here](#). This provides a useful interface for R programming.  
(This step is optional; if you choose to skip it, steps 3-6 can be done exactly as described within the R program's basic console.)
3. Open R Studio, and install the Shiny package by typing in the following command into your console, and then hit **Enter**. This may take up to a minute for completion.

```
install.packages("shiny")
```

4. Once the ">" symbol and cursor reappear, type in the following code, and then hit **Enter**.

```
shiny::runGitHub('KSEA', 'casecpb')
```

5. The KSEA App should then automatically launch in a new window/browser tab. This step may take a few seconds.
6. When finished with the analysis, just exit the interface. Then, if needed, hit the escape (Esc) key within the R studio console to terminate the KSEA App. Ignore the warning messages that may appear, and exit from R Studio.

*Note: steps 1-3 only need to be done once if you are using the same computer. If you wish to access the KSEA App again after the first time, just reopen R Studio, and go straight to step 4.*

# Warnings!

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1. The KSEA App does not store any of the data once the site is reloaded or disconnected. Please download all the results before exiting!
2. To conserve server run time, the site disconnects automatically after 10 minutes of inactivity.
3. Our current server has a 25-hour cap for active run time per month. Once the max is reached, the online KSEA App is unavailable till the next cycle, which restarts around the 15<sup>th</sup> day of each month. If you cannot access the website, please run the app locally by sourcing the code and dependent files through our GitHub page: <https://github.com/casecpb/KSEA>.
4. The KSEA App is on a public website hosted by RStudio's shinyapps.io online service (the "RStudio Service"). Please read their Terms of Use: <https://www.rstudio.com/about/shinyapps-terms-use/>.

DO NOT upload confidential files, such as identifiable patient data:

RSTUDIO IS NOT RESPONSIBLE FOR THE CONFIDENTIALITY, AVAILABILITY, SECURITY, LOSS, MISUSE OR MISAPPROPRIATION OF ANY DATA YOU SUBMIT TO THE RSTUDIO SERVICE OR ANY APPLICATION MADE AVAILABLE VIA THE RSTUDIO SERVICE.

If you wish to run KSEA on sensitive files, consider running it locally on your computer (see the **Source Code and Local Access** section of the manual).