

PAGnet: an integrated regulatory network in *Pseudomonas aeruginosa*

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Abstract

PAGnet is an R package to perform Master Regulator Analysis (MRA) for identification of key transcription factors mediating a biological process or pathway in *Pseudomonas aeruginosa* Genomic netork (PAGnet).

Package

PAGnet 0.1.0

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1 Overview

Regulatory networks including virulence-related transcriptional factors (TFs) determine bacterial pathogenicity in response to different environmental cues. *Pseudomonas aeruginosa*, a Gram-negative opportunistic pathogen of humans, recruits numerous TFs in quorum sensing (QS) system, type III secretion system (T3SS) and Type VI secretion system (T6SS) to mediate the pathogenicity. Although many virulence-related TFs have been illustrated individually, very little is known about their crosstalks and regulatory network. Here, based on chromatin immunoprecipitation coupled with high-throughput sequencing (ChIP-seq) and transcriptome profiling (RNA-seq), we primarily focused on understanding the crosstalks of 19 virulence-related TFs, which led to construction of a virulence regulatory network named PAGnet (*Pseudomonas aeruginosa* Genomic network) including 48 crosstalk targets.

The PAGnet uncovered the intricate mechanism of virulence regulation and revealed master regulators in QS, T3SS and T6SS pathways. The package **PAGnet** is designed for Master Regulator Analysis (MRA) over a list of regulons from PAGnet. We also provide an online PAGnet platform was established to provide the analysis for these TFs and more virulence factors.

```
## loading packages
library(PAGnet)
```

2 Quick Start

2.0.1 Master Regulator Analysis

The user can choose to use the default PAVIRnet or to upload their own regulatory network in a predefined format.

```
library(PAGnet)
data(PAGnet)

#Use PAGnet as regulatory network
#Select T3SS related genes as signatures
#run MRA
head(PAGnet)
##   TranscriptionFactor Target
## 1          PA5261 PA2523
## 2          PA5261 PA1727
## 3          PA5261 PA4396
## 4          PA5261 PA2189
## 5          PA5261 PA1736
## 6          PA5261 PA3763
head(tf)
## [1] "PA5261" "PA3385" "PA4101" "PA2588" "PA1713" "PA2586"
head(qs)
## [1] "PA1130" "PA3387" "PA3476" "PA3477" "PA3479" "PA3478"
```

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The function `pagnet.mra` is used to perform MRA in PAGnet or user uploaded network. The MRA computes the overlap between the transcriptional regulatory unities (regulons) and the input signature genes using the hypergeometric distribution. Having completed master regulator analysis, a table will be returned.

```
mra_results <- pagnet.mra(rnet=PAGnet,tflist=tf,signature = qs,
                          pValueCutoff = 0.05,pAdjustMethod="BH")

mra_results
##      TF network.size regulon.size signature.size observed.signature.size
## 7 PA1430           422           45           20              10
## 9 PA1003           422           21           20              7
## 12 PA3477          422            7           20              5
## 14 PA1431          422            9           20              5
## 10 PA1898          422            6           20              3
## 11 PA2593          422            2           20              2
## 18 PA2227          422            7           20              3
##      Pvalue adjust.Pvalue
## 7 < 1e-4      < 1e-4
## 9 < 1e-4      < 1e-4
## 12 < 1e-4     < 1e-4
## 14 < 1e-4     < 1e-4
## 10 0.0017     0.0065
## 11 0.0021     0.0066
## 18 0.0028     0.0076
```

To output the MRA results, the user can use `write.csv` to output csv file.

```
## write.csv(mra_results,"MRA_results.csv")
```

3 Need helps?

If you have any question/issue, please feel free to contact us.

4 Session Information

```
## R version 3.5.2 (2018-12-20)
## Platform: x86_64-w64-mingw32/x64 (64-bit)
## Running under: Windows 10 x64 (build 17763)
##
## Matrix products: default
##
## locale:
## [1] LC_COLLATE=Chinese (Simplified)_China.936
## [2] LC_CTYPE=Chinese (Simplified)_China.936
## [3] LC_MONETARY=Chinese (Simplified)_China.936
## [4] LC_NUMERIC=C
## [5] LC_TIME=Chinese (Simplified)_China.936
##
## attached base packages:
## [1] stats      graphics  grDevices  utils      datasets  methods   base
```

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```
##  
## other attached packages:  
## [1] PAGnet_0.1.0    BiocStyle_2.8.2  
##  
## loaded via a namespace (and not attached):  
## [1] Rcpp_0.12.18    bookdown_0.7    digest_0.6.17   rprojroot_1.3-2  
## [5] backports_1.1.2 magrittr_1.5     evaluate_0.11   stringi_1.2.4  
## [9] rmarkdown_1.10  tools_3.5.2     stringr_1.3.1   xfun_0.3  
## [13] yaml_2.2.0      compiler_3.5.2  htmltools_0.3.6 knitr_1.20
```

5 References
