

Welcome to

# ResistXplorer

- a web-based tool for visualization and exploratory analysis of resistome data

## The key features include:

- Support for a wide array of common as well as advanced methods for **composition profiling**, **visualization** and **exploratory data analysis**;
- Comprehensive support for various **data normalization** methods coupled with standard as well as more recent **statistical** and **machine learning algorithms**;
- Support for a variety of methods for performing **vertical data integrative analysis** on paired metagenomic datasets (i.e. taxonomic and resistome abundance profiles);
- Comprehensive support for **ARG functional annotations** along with their **microbe** and **phenotype** associations based on data collected from more than **10 reference and curated databases**;
- A powerful and fully featured **network visualization** for intuitive exploration of **ARG-microbial host** associations, incorporated with **functional annotations enrichment analysis** support.

In this manual, we will go through the analysis of resistome data using an **ARG list** as input.

## Please cite:

Dhariwal A, Junges R, Chen T, Petersen FC.

ResistoXplorer: a web-based tool for visualization and exploratory analysis of resistome data.

In this manual, you will encounter **blue** and **red** dialog boxes.



**Blue dialogs** indicate explanations and details for different functions in each page, while **red dialogs** indicate actions that will move forward with the analysis to a new screen or a download option for a visualization/analysis.

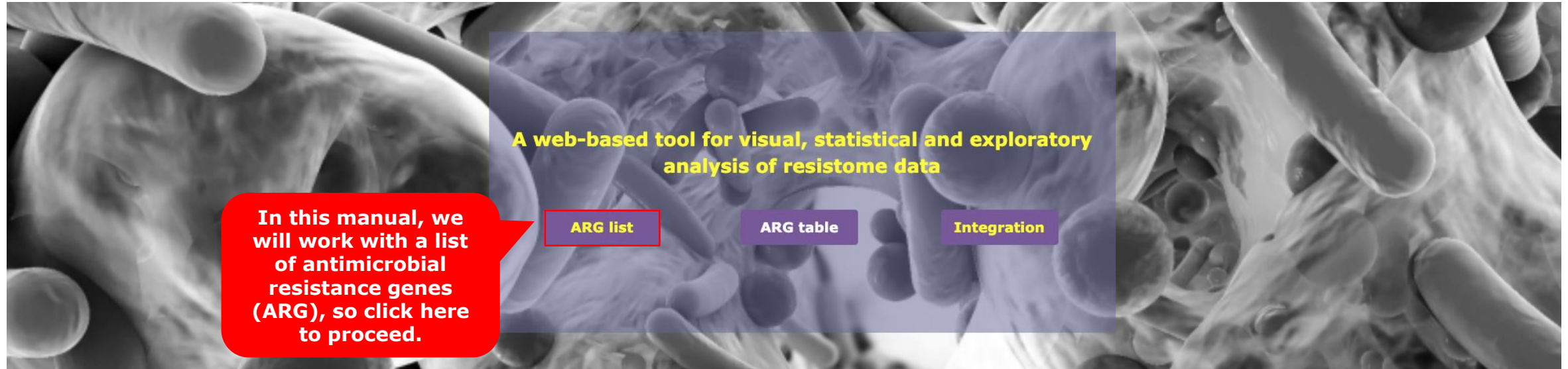


The question mark icons are available in ResistoXplorer. If you hove over it, a short explanation about that item will appear.

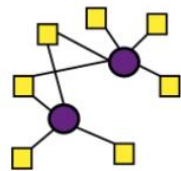


Throughout this manual you will also find additional explanations about the functionalities of ResistoXplorer following this icon.

In the front page of ResistoXplorer, you can select one of the three options for input data:  
ARG list      ///      ARG table      ///      Integration



## Features



ARG-MICROBE  
NETWORK  
EXPLORATION



INTERACTIVE  
EXPLORATION



COMPREHENSIVE  
DATABASE

You will be then directed to the upload screen where you can add your data.

🏠 ▶ Gene List

Please upload a list of antimicrobial resistance genes (ARGs)

**Database**

**Enter your data**  
You can enter a list of ARGs of interest with their optional fold change or abundance value

**Use example dataset:**  Gene list (source: Bengtsson-Palme, Johan, et al.)

Add your list of resistance genes in this text box.

*Optional: Add your list together with fold change or abundance values.*

*Optional: To explore the functionality of ResistoXplorer, you can use an example dataset.*

Choose your preferred database. Currently, ResistoXplorer supports six databases for this input: ResFinder; CARD; ARDB; BacMet; MARDy; and Antimicrobial peptide (AMP).

\*\*\*Please note that the input format is different depending on the selected database. More details are available in the next slide.

**In this manual, we will use the example database provided by ResistoXplorer. So tick the check box for example gene list dataset just above. To proceed with the analysis, finally click on 'Submit'**



## Data format

Each database can present a different data format, so please make sure that your gene list is in accordance with the database you will use. Otherwise you might not get any hits.

For instance, the example dataset used in ResistoXplorer is formatted according to ResFinder, so if you select a different database you might get fewer hits or none at all. For more information, please refer to the 'Data format' section in the homepage of ResistoXplorer.

Here below, we show how some of the formatting can look like:

### ResFinder

Name
aac(2')-Ia
aac(2')-Ib
aac(2')-Ic
aac(2')-Id
aac(2')-Ie
aac(2')-IIa
aac(3)-I
aac(3)-Ia
aac(3)-Ib
aac(3)-Ib-aac(6')-Ib'
aac(3)-Ic
aac(3)-Id

### CARD

Name
vanC
vanRA
vanSA
vanHA
vanA
vanXA
vanYA
vanZA
AAC(6'')-Ie-APH(2''''')-Ia
vanRB
vanSB

### ARDB

Name
aac2i
aac2i
aac2i
aac2ia
aac2ib
aac2ic
aac2ic
aac2ic
aac2ic
aac2ic
aac2ic
aac2ic

### BacMet

Name
acrA
acrB
acrD/yffA
acrE/envC
acrF/envD
actA
actR
actS
adeA
adeB
adeC
adel

### Antimicrobial peptide (AMP)

Name
acrB
almE
almF
almG
amiA
amiA
amiC
amiC
anrA
anrB
apsS
arnD



## **How do I my get a list of resistance genes for analysis?**

A list of resistance genes for analysis can be obtained in a variety of ways.

For instance, if the user has any genome or species of interest, it is possible to download the annotation directly from the databases and upload them into ResistoXplorer. If the interest is in a sequenced metagenomic sample, after upstream processing, the full list of genes can be uploaded into ResistoXplorer as well with the option of including abundance data.

Importantly, genes that are not involved with resistance or that are not included in the databases supported by ResistoXplorer do not need to be excluded by the user from the initial list of genes because they will be automatically excluded them from the analysis during data processing.

Of note, the list has to be formatted to the database of interest as seen in the previous slide. For more information, please refer to the 'Data format' section in the homepage of ResistoXplorer.

Based on your selections, a table will be shown containing all information regarding the list added during the upload step. See how it looks with the example dataset:

### Interaction table

Number of queries (ARGs):	14
Database:	ResFinder
Number of ARGs mapped to database:	14
Total number of taxa/host associations (initial):	68
Number of unique taxa/host:	38

Specific association (edge) can be deleted using **Delete** icon present below in the last column of table. Further, the interaction table can also be downloaded using the **Download** button.

You can download this data in .csv format by clicking here.

Class and mechanism of function for each ARG.

You can choose to exclude any ARGs from the analysis, and you can always go back to the start of the analysis by clicking on reset.

Reset Download

Gene (ARGs) ▾	Host (Microbe) ▾	Accession No. ▾	Class / Family ▾	Mechanism ▾	Reference	Action
ant(2'')-Ia	<a href="#">Acinetobacter baumannii</a>	<a href="#">DQ176450</a>	Aminoglycoside	Enzymatic modification	<a href="#">16304199</a>	
ant(2'')-Ia	<a href="#">Burkholderia cepacia</a>	<a href="#">HQ880250</a>	Aminoglycoside	Enzymatic modification	<a href="#">unpublished</a>	
ant(2'')-Ia	<a href="#">Citrobacter freundii</a>	<a href="#">AF458082</a>	Aminoglycoside	Enzymatic modification	<a href="#">12384364</a>	
ant(2'')-Ia	<a href="#">Corynebacterium asperum</a>	<a href="#">AJ871915</a>	Aminoglycoside	Enzymatic modification	<a href="#">unpublished</a>	
ant(2'')-Ia	<a href="#">Escherichia coli</a>	<a href="#">GQ466184, DQ018384</a>	Aminoglycoside	Enzymatic modification	<a href="#">unpublished, 15837385</a>	
ant(2'')-Ia	<a href="#">Klebsiella pneumoniae</a>	<a href="#">EF205594</a>	Aminoglycoside	Enzymatic modification	<a href="#">unpublished</a>	
ant(2'')-Ia	<a href="#">Morganella morganii</a>	<a href="#">HQ386848</a>	Aminoglycoside	Enzymatic modification	<a href="#">unpublished</a>	
ant(2'')-Ia	<a href="#">Pseudomonas aeruginosa</a>	<a href="#">DQ266447, JTTZ01000034, JF826500, AY920928</a>	Aminoglycoside	Enzymatic modification	<a href="#">unpublished, 22271862, 16048</a>	
ant(2'')-Ia	<a href="#">Salmonella oranienburg</a>	<a href="#">X74412</a>	Aminoglycoside	Enzymatic modification	<a href="#">unpublished</a>	
ant(2'')-Ia	<a href="#">Uncultured bacterium</a>	<a href="#">X04555, AY139594, AY139599</a>	Aminoglycoside	Enzymatic modification	<a href="#">3024112, 19719593</a>	
aph(3'')-Ib	<a href="#">Escherichia coli</a>	<a href="#">M28829, AF321550</a>	Aminoglycoside	Enzymatic modification	<a href="#">2653965, 12029529</a>	
aph(3'')-Ib	<a href="#">Pseudomonas aeruginosa</a>	<a href="#">AF313472, AF024602</a>	Aminoglycoside	Enzymatic modification	<a href="#">unpublished, 9687410</a>	
aph(3'')-Ib	<a href="#">Shigella flexneri</a>	<a href="#">AF321551</a>	Aminoglycoside	Enzymatic modification	<a href="#">12029529</a>	
aph(6)-Id	<a href="#">Actinobacillus pleuropneumoniae</a>	<a href="#">AB109805</a>	Aminoglycoside	Enzymatic modification	<a href="#">14711528</a>	
aph(6)-Id	<a href="#">Escherichia coli</a>	<a href="#">M28829, CP000971</a>	Aminoglycoside	Enzymatic modification	<a href="#">2653965, 18708504</a>	

(1 of 5)
1 2 3 4 5
15

Genes uploaded in the previous page.

Information regarding the microbial host for the referred gene.

Available literature

When ready, click here for the 'Network Builder' function.

This is the 'Network Builder' panel, where you get an overview of the interactions observed in the data uploaded into ResistoXplorer.

### Network Overview

Number of queries:	14
Number of nodes:	52 (ARGs: 14, Taxa: 38)
Number of edges:	68

In some cases, multiple isolated networks will be generated, with a big 'continent' containing most of queries, and several small 'islands' containing one or a few queries. These networks will be available for visual analysis in the next step.

[Network Filter](#) [Reset Network](#)

You can choose to filter the interactions to any desired cutoff. This is useful, for instance, if you want to focus on the strongest networks observed in the samples

Networks	Nodes	Edges	Queries	
ARGs-taxa1	48	66	12	<a href="#">Download</a>
ARGs-taxa2	2	1	1	<a href="#">Download</a>
ARGs-taxa3	2	1	1	<a href="#">Download</a>

By clicking here, you can download each interaction network.

Once you have filtered and selected the data you want to visualize, you can click here to be redirected to the customizable network visualization.



Network Customization

Network: ARGs-taxa1  
 Background: Black  
 View: Topology  
 Layout: Default Layout  
 Scope: -- Specify --  
 Download: -- Specify -- View Options

These drop-down menus can be used to customize the visualization of the data as preferred by you. Feel free to play around with the options

Function Explorer

Query: All genes  
 Algorithm: Hypergeometric test  
 Functional category: Class Submit

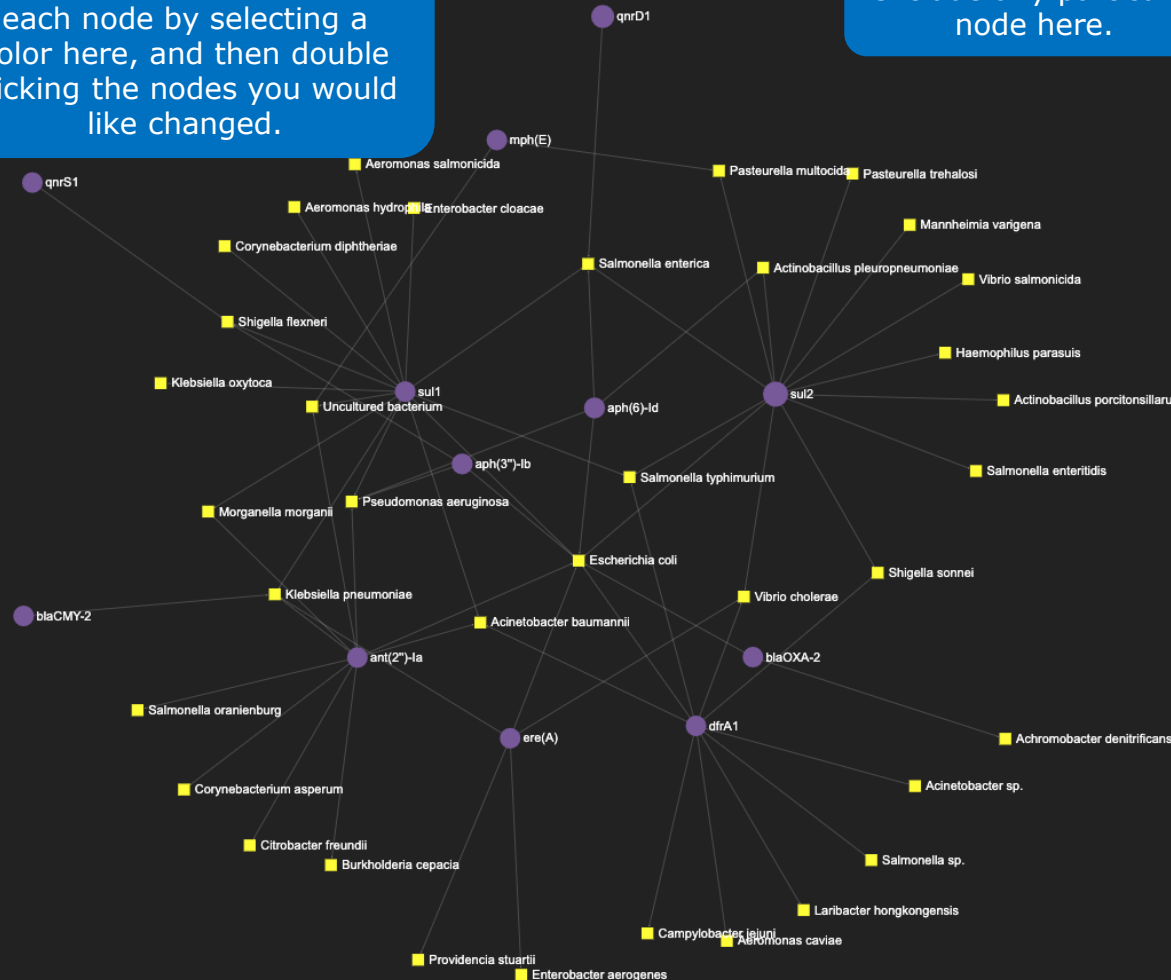
Name	Hits	Pval	Color
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Here you can explore the functions of the network. Remember to click submit after you make your selection.



You can change the color of each node by selecting a color here, and then double clicking the nodes you would like changed.

You can select and exclude any particular node here.



Node Explorer

ID:  Search  Delete

Highlight All interactions Submit

ID	Degree	Betweenness	Abundance
<input type="checkbox"/> sul1	14	399.4751	713
<input type="checkbox"/> sul2	13	364.5822	37332
<input type="checkbox"/> ant(2 <sup>-</sup> )-Ia	10	228.7985	27
<input type="checkbox"/> dfrA1	10	255.3126	36
<input type="checkbox"/> Escherichia coli	8	385.0485	-
<input type="checkbox"/> ere(A)	5	111.8352	45
<input type="checkbox"/> aph(6)-Id	4	30.42103	3221
<input type="checkbox"/> Klebsiella pneumon	4	82.44043	-
<input type="checkbox"/> Pseudomonas aerug	4	30.11349	-
<input type="checkbox"/> Salmonella enterica	4	87.44394	-
<input type="checkbox"/> aph(3 <sup>-</sup> )-Ib	3	21.27045	2595
<input type="checkbox"/> Acinetobacter baum	3	57.35209	-
<input type="checkbox"/> Uncultured bacteri	3	41.84167	-
<input type="checkbox"/> Shigella flexneri	3	49.6	-
<input type="checkbox"/> Salmonella typhimu	3	73.09144	-
<input type="checkbox"/> Vibrio cholerae	3	47.88507	-
<input type="checkbox"/> blaOXA-2	2	46	19
<input type="checkbox"/> mph(E)	2	8.304762	44
<input type="checkbox"/> Morganella morgan	2	7.916667	-
<input type="checkbox"/> Actinobacillus pleu	2	4.47381	-
<input type="checkbox"/> Shigella sonnei	2	16.4131	-
<input type="checkbox"/> Pasteurella multocic	2	18.37976	-
<input type="checkbox"/> blaCMY-2	1	0	778
<input type="checkbox"/> qnrD1	1	0	20603
<input type="checkbox"/> qnrS1	1	0	450
<input type="checkbox"/> Burkholderia cepaci	1	0	-
<input type="checkbox"/> Citrobacter freundii	1	0	-
<input type="checkbox"/> Corynebacterium as	1	0	-
<input type="checkbox"/> Salmonella oranien	1	0	-
<input type="checkbox"/> Achromobacter den	1	0	-

Current Selections



Network Customization

Network: ARGs-taxa1

Background: Black

View: Topology

Layout: Default Layout

Scope: -- Specify --

Download: -- Specify -- View Op

You can highlight nodes by double-clicking on them. As we seen before, this will select them and change their color to the one in the top panel.



To select a node, you can check its box in the right panel. If you uncheck the box, you will unselect the node.

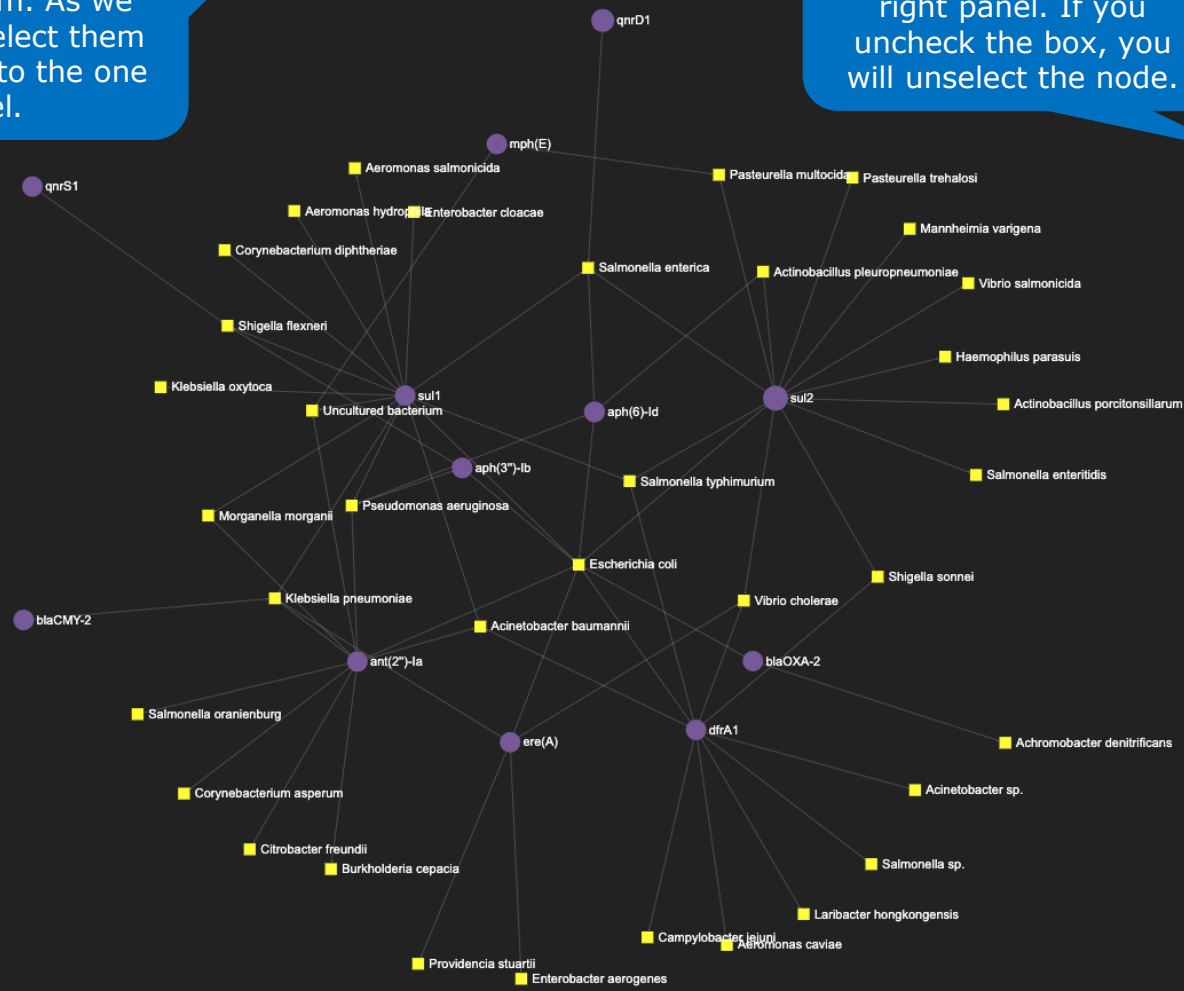
Function Explorer

Query: All genes

Algorithm: Hypergeometric test

Functional category: Class Submit

Name	Hits	Pval	Color
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Node Explorer

ID: Search Delete

Highlight All interactions Submit

<input type="checkbox"/>	ID	Degrec	Betweenness	Abundance
<input type="checkbox"/>	sul1	14	399.4751	713
<input type="checkbox"/>	sul2	13	364.5822	37332
<input type="checkbox"/>	ant(2 <sup>-</sup> )-Ia	10	228.7985	27
<input type="checkbox"/>	dfra1	10	255.3126	36
<input type="checkbox"/>	Escherichia coli	8	385.0485	-
<input type="checkbox"/>	ere(A)	5	111.8352	45
<input type="checkbox"/>	aph(6)-Id	4	30.42103	3221
<input type="checkbox"/>	Klebsiella pneumon	4	82.44043	-
<input type="checkbox"/>	Pseudomonas aerug	4	30.11349	-
<input type="checkbox"/>	Salmonella enterica	4	87.44394	-
<input type="checkbox"/>	aph(3 <sup>-</sup> )-Ib	3	21.27045	2595
<input type="checkbox"/>	Acinetobacter baum	3	57.35209	-
<input type="checkbox"/>	Uncultured bacteriu	3	41.84167	-
<input type="checkbox"/>	Shigella flexneri	3	49.6	-
<input type="checkbox"/>	Salmonella typhimu	3	73.09144	-
<input type="checkbox"/>	Vibrio cholerae	3	47.88507	-
<input type="checkbox"/>	blaOXA-2	2	46	19
<input type="checkbox"/>	mph(E)	2	8.304762	44
<input type="checkbox"/>	Morganella morgan	2	7.916667	-
<input type="checkbox"/>	Actinobacillus pleu	2	4.47381	-
<input type="checkbox"/>	Shigella sonnei	2	16.4131	-
<input type="checkbox"/>	Pasteurella multocic	2	18.37976	-
<input type="checkbox"/>	blaCMY-2	1	0	778
<input type="checkbox"/>	qnrD1	1	0	20603
<input type="checkbox"/>	qnrS1	1	0	450
<input type="checkbox"/>	Burkholderia cepaci	1	0	-
<input type="checkbox"/>	Citrobacter freundii	1	0	-
<input type="checkbox"/>	Corynebacterium as	1	0	-
<input type="checkbox"/>	Salmonella oranienl	1	0	-
<input type="checkbox"/>	Achromobacter den	1	0	-

Current Selections

Network Customization

Network: ARGs-taxa1  
 Background: Black  
 View: Topology  
 Layout: Default Layout  
 Scope: -- Specify --  
 Download: -- Specify -- View Options

Function Explorer

Query: All genes  
 Algorithm: Hypergeometric test  
 Functional category: Class Submit

Name	Hits	Pval	Color
------	------	------	-------



If you want to highlight the shared connections between two nodes, you can select them here and click on 'Shared' in the 'Highlight' drop-down menu. To finalize, click on 'Submit'.

Node Explorer

ID: Search Delete

Highlight All interactions Submit

ID	Degrec	Betweenness	Abundance
<input type="checkbox"/> sul1	14	399.4751	713
<input type="checkbox"/> sul2	13	364.5822	37332
<input type="checkbox"/> ant(2 <sup>-</sup> )-Ia	10	228.7985	27
<input type="checkbox"/> dfrA1	10	255.3126	36
<input type="checkbox"/> Escherichia coli	8	385.0485	-
<input type="checkbox"/> ere(A)	5	111.8352	45
<input type="checkbox"/> aph(6)-Id	4	30.42103	3221
<input type="checkbox"/> Klebsiella pneumon	4	82.44043	-
<input type="checkbox"/> Pseudomonas aerug	4	30.11349	-
<input type="checkbox"/> Salmonella enterica	4	87.44394	-
<input type="checkbox"/> aph(3 <sup>-</sup> )-Ib	3	21.27045	2595
<input type="checkbox"/> Acinetobacter baum	3	57.35209	-
<input type="checkbox"/> Uncultured bacteri	3	41.84167	-
<input type="checkbox"/> Shigella flexneri	3	49.6	-
<input type="checkbox"/> Salmonella typhimu	3	73.09144	-
<input type="checkbox"/> Vibrio cholerae	3	47.88507	-
<input type="checkbox"/> blaOXA-2	2	46	19
<input type="checkbox"/> mph(E)	2	8.304762	44
<input type="checkbox"/> Morganella morgan	2	7.916667	-
<input type="checkbox"/> Actinobacillus pleu	2	4.47381	-
<input type="checkbox"/> Shigella sonnei	2	16.4131	-
<input type="checkbox"/> Pasteurella multoci	2	18.37976	-
<input type="checkbox"/> blaCMY-2	1	0	778
<input type="checkbox"/> qnrD1	1	0	20603
<input type="checkbox"/> qnrS1	1	0	450
<input type="checkbox"/> Burkholderia cepaci	1	0	-
<input type="checkbox"/> Citrobacter freundii	1	0	-
<input type="checkbox"/> Corynebacterium as	1	0	-
<input type="checkbox"/> Salmonella oranien	1	0	-
<input type="checkbox"/> Achromobacter den	1	0	-

Current Selections

### Network Customization

Network: ARGs-taxa1

Background: Black

View: Topology

Layout: Default Layout

Scope: -- Specify --

Download: -- Specify -- [View Options](#)

### Function Explorer

Query: All genes

Algorithm: Hypergeometric test

Functional category: Class [Submit](#)

Name	Hits	Pval	Color
------	------	------	-------

You can also explore the function enrichment option. Click on 'Functional category', select 'Phenotype', and click on 'Submit'.



### Node Explorer

ID:  Search  Delete

Highlight All interactions Submit

ID	Degree	Betweenness	Abundance
<input type="checkbox"/> sul1	14	399.4751	713
<input type="checkbox"/> sul2	13	364.5822	37332
<input type="checkbox"/> ant(2 <sup>-</sup> )-Ia	10	228.7985	27
<input type="checkbox"/> dfrA1	10	255.3126	36
<input type="checkbox"/> Escherichia coli	8	385.0485	-
<input type="checkbox"/> ere(A)	5	111.8352	45
<input type="checkbox"/> aph(6)-Id	4	30.42103	3221
<input type="checkbox"/> Klebsiella pneumoniae	4	82.44043	-
<input type="checkbox"/> Pseudomonas aerug	4	30.11349	-
<input type="checkbox"/> Salmonella enterica	4	87.44394	-
<input type="checkbox"/> aph(3 <sup>-</sup> )-Ib	3	21.27045	2595
<input type="checkbox"/> Acinetobacter baum	3	57.35209	-
<input type="checkbox"/> Uncultured bacteri	3	41.84167	-
<input type="checkbox"/> Shigella flexneri	3	49.6	-
<input type="checkbox"/> Salmonella typhimu	3	73.09144	-
<input type="checkbox"/> Vibrio cholerae	3	47.88507	-
<input type="checkbox"/> blaOXA-2	2	46	19
<input type="checkbox"/> mph(E)	2	8.304762	44
<input type="checkbox"/> Morganella morgan	2	7.916667	-
<input type="checkbox"/> Actinobacillus pleu	2	4.47381	-
<input type="checkbox"/> Shigella sonnei	2	16.4131	-
<input type="checkbox"/> Pasteurella multoci	2	18.37976	-
<input type="checkbox"/> blaCMY-2	1	0	778
<input type="checkbox"/> qnrD1	1	0	20603
<input type="checkbox"/> qnrS1	1	0	450
<input type="checkbox"/> Burkholderia cepaci	1	0	-
<input type="checkbox"/> Citrobacter freundii	1	0	-
<input type="checkbox"/> Corynebacterium as	1	0	-
<input type="checkbox"/> Salmonella oranien	1	0	-
<input type="checkbox"/> Achromobacter den	1	0	-

### Current Selections





### Network Customization

Network: ARGs-taxa1  
 Background: Black  
 View: Topology  
 Layout: Default Layout  
 Scope: -- Specify --  
 Download: -- Specify -- View Options

### Function Explorer

Query: All genes  
 Algorithm: Hypergeometric test  
 Functional category: Phenotype Submit

Name	Hits	Pval	Color
Sulfamethoxazole	2	0.0113	<span style="background-color: yellow; border: 2px solid red;">■</span>
Streptomycin	2	0.594	■
Erythromycin	2	0.93	■
Amoxicillin	2	1	■
Amoxicillin+Clavulanic acid	2	1	■
Ampicillin	2	1	■
Ampicillin+Clavulanic acid	2	1	■
Cefotaxime	1	1	■
Cefoxitin	1	1	■
Ceftazidime	2	1	■
Ciprofloxacin	2	1	■
Gentamicin	1	1	■
Piperacillin	2	1	■
Piperacillin+Tazobactam	1	1	■
Ticarclillin	1	1	■
Ticarclillin+Clavulanic acid	1	1	■
Tobramycin	1	1	■
Trimethoprim	1	1	■



Now you see that the two genes connected to this phenotype are highlighted in the network.

### Node Explorer

ID:  Search

Highlight All interactions Submit

ID	Degree	Betweenness	Abundance
<input type="checkbox"/> sul1	14	399.4751	713
<input type="checkbox"/> sul2	13	364.5822	37332
<input type="checkbox"/> ant(2 <sup>+</sup> )-Ia	10	228.7985	27
<input type="checkbox"/> dfrA1	10	255.3126	36
<input type="checkbox"/> Escherichia coli	8	385.0485	-
<input type="checkbox"/> ere(A)	5	111.8352	45
<input type="checkbox"/> aph(6)-Id	4	30.42103	3221
<input type="checkbox"/> Klebsiella pneumon	4	82.44043	-
<input type="checkbox"/> Pseudomonas aerug	4	30.11349	-
<input type="checkbox"/> Salmonella enterica	4	87.44394	-
<input type="checkbox"/> aph(3 <sup>+</sup> )-Ib	3	21.27045	2595
<input type="checkbox"/> Acinetobacter baum	3	57.35209	-
<input type="checkbox"/> Uncultured bacteriu	3	41.84167	-
<input type="checkbox"/> Shigella flexneri	3	49.6	-
<input type="checkbox"/> Salmonella typhim	3	73.09144	-
<input type="checkbox"/> Vibrio cholerae	3	47.88507	-
<input type="checkbox"/> blaOXA-2	2	46	19
<input type="checkbox"/> mph(E)	2	8.304762	44
<input type="checkbox"/> Morganella morgan	2	7.916667	-
<input type="checkbox"/> Actinobacillus pleu	2	4.47381	-
<input type="checkbox"/> Shigella sonnei	2	16.4131	-
<input type="checkbox"/> Pasteurella multoci	2	18.37976	-
<input type="checkbox"/> blaCMY-2	1	0	778
<input type="checkbox"/> qnrD1	1	0	20603
<input type="checkbox"/> qnrS1	1	0	450
<input type="checkbox"/> Burkholderia cepaci	1	0	-
<input type="checkbox"/> Citrobacter freundii	1	0	-
<input type="checkbox"/> Corynebacterium as	1	0	-
<input type="checkbox"/> Salmonella oranien	1	0	-
<input type="checkbox"/> Achromobacter den	1	0	-

### Current Selections

- Sulfamethoxazole
  - sul1
  - sul2

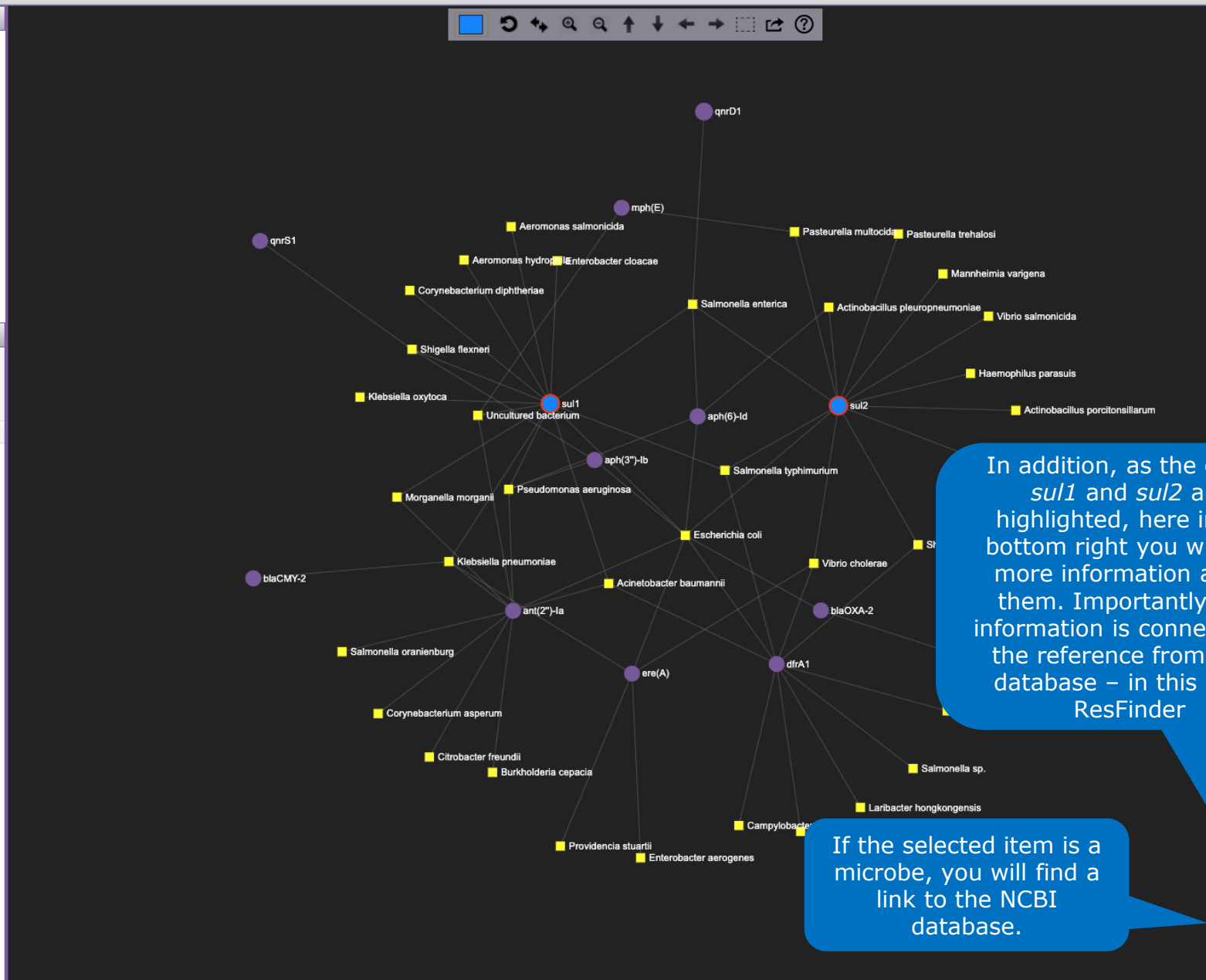
Network Customization

Network: ARGs-taxa1  
 Background: Black  
 View: Topology  
 Layout: Default Layout  
 Scope: -- Specify --  
 Download: -- Specify -- View Options

Function Explorer

Query: All genes  
 Algorithm: Hypergeometric test  
 Functional category: Phenotype Submit

Name	Hits	Pval	Color
Sulfamethoxazole	2	0.0113	<span style="background-color: #007bff; color: white; padding: 2px;">S</span>
Streptomycin	2	0.594	
Erythromycin	2	0.93	
Amoxicillin	2	1	
Amoxicillin+Clavulanic acid	2	1	
Ampicillin	2	1	
Ampicillin+Clavulanic acid	2	1	
Cefotaxime	1	1	
Cefoxitin	1	1	
Ceftazidime	2	1	
Ciprofloxacin	2	1	
Gentamicin	1	1	
Piperacillin	2	1	
Piperacillin+Tazobactam	1	1	
Ticarillin	1	1	
Ticarillin+Clavulanic acid	1	1	
Tobramycin	1	1	
Trimethoprim	1	1	



Node Explorer

ID:  Search

Highlight All interactions Submit

ID	Degree	Betweenness	Abundance
<input type="checkbox"/> sul1	14	399.4751	713
<input type="checkbox"/> sul2	13	364.5822	37332
<input type="checkbox"/> ant(2'')-Ia	10	228.7985	27
<input type="checkbox"/> dfrA1	10	255.3126	36
<input type="checkbox"/> Escherichia coli	8	385.0485	-
<input type="checkbox"/> ere(A)	5	111.8352	45
<input type="checkbox"/> aph(6)-Id	4	30.42103	3221
<input type="checkbox"/> Klebsiella pneumon	4	82.44043	-
<input type="checkbox"/> Pseudomonas aerug	4	30.11349	-
<input type="checkbox"/> Salmonella enterica	4	87.44394	-
<input type="checkbox"/> aph(3'')-Ib	3	21.27045	2595
<input type="checkbox"/> Acinetobacter baum	3	57.35209	-
<input type="checkbox"/> Uncultured bacteriu	3	41.84167	-
<input type="checkbox"/> Shigella flexneri	3	49.6	-
<input type="checkbox"/> Salmonella typhimur	3	73.09144	-
<input type="checkbox"/> blaCMY-2	3	47.88507	-
<input type="checkbox"/> blaOXA-2	2	46	19
<input type="checkbox"/> blaSHV-1	2	8.304762	44
<input type="checkbox"/> blaTEM-1	2	7.916667	-
<input type="checkbox"/> blaOXA-1	2	4.47381	-
<input type="checkbox"/> blaOXA-3	2	16.4131	-
<input type="checkbox"/> blaOXA-4	2	18.37976	-
<input type="checkbox"/> blaOXA-5	1	0	778
<input type="checkbox"/> blaOXA-6	1	0	20603
<input type="checkbox"/> blaOXA-7	1	0	450
<input type="checkbox"/> blaOXA-8	1	0	-
<input type="checkbox"/> blaOXA-9	1	0	-
<input type="checkbox"/> blaOXA-10	1	0	-
<input type="checkbox"/> blaOXA-11	1	0	-
<input type="checkbox"/> blaOXA-12	1	0	-
<input type="checkbox"/> blaOXA-13	1	0	-
<input type="checkbox"/> blaOXA-14	1	0	-
<input type="checkbox"/> blaOXA-15	1	0	-
<input type="checkbox"/> blaOXA-16	1	0	-
<input type="checkbox"/> blaOXA-17	1	0	-
<input type="checkbox"/> blaOXA-18	1	0	-
<input type="checkbox"/> blaOXA-19	1	0	-
<input type="checkbox"/> blaOXA-20	1	0	-
<input type="checkbox"/> blaOXA-21	1	0	-
<input type="checkbox"/> blaOXA-22	1	0	-
<input type="checkbox"/> blaOXA-23	1	0	-
<input type="checkbox"/> blaOXA-24	1	0	-
<input type="checkbox"/> blaOXA-25	1	0	-
<input type="checkbox"/> blaOXA-26	1	0	-
<input type="checkbox"/> blaOXA-27	1	0	-
<input type="checkbox"/> blaOXA-28	1	0	-
<input type="checkbox"/> blaOXA-29	1	0	-
<input type="checkbox"/> blaOXA-30	1	0	-
<input type="checkbox"/> blaOXA-31	1	0	-
<input type="checkbox"/> blaOXA-32	1	0	-
<input type="checkbox"/> blaOXA-33	1	0	-
<input type="checkbox"/> blaOXA-34	1	0	-
<input type="checkbox"/> blaOXA-35	1	0	-
<input type="checkbox"/> blaOXA-36	1	0	-
<input type="checkbox"/> blaOXA-37	1	0	-
<input type="checkbox"/> blaOXA-38	1	0	-
<input type="checkbox"/> blaOXA-39	1	0	-
<input type="checkbox"/> blaOXA-40	1	0	-
<input type="checkbox"/> blaOXA-41	1	0	-
<input type="checkbox"/> blaOXA-42	1	0	-
<input type="checkbox"/> blaOXA-43	1	0	-
<input type="checkbox"/> blaOXA-44	1	0	-
<input type="checkbox"/> blaOXA-45	1	0	-
<input type="checkbox"/> blaOXA-46	1	0	-
<input type="checkbox"/> blaOXA-47	1	0	-
<input type="checkbox"/> blaOXA-48	1	0	-
<input type="checkbox"/> blaOXA-49	1	0	-
<input type="checkbox"/> blaOXA-50	1	0	-
<input type="checkbox"/> blaOXA-51	1	0	-
<input type="checkbox"/> blaOXA-52	1	0	-
<input type="checkbox"/> blaOXA-53	1	0	-
<input type="checkbox"/> blaOXA-54	1	0	-
<input type="checkbox"/> blaOXA-55	1	0	-
<input type="checkbox"/> blaOXA-56	1	0	-
<input type="checkbox"/> blaOXA-57	1	0	-
<input type="checkbox"/> blaOXA-58	1	0	-
<input type="checkbox"/> blaOXA-59	1	0	-
<input type="checkbox"/> blaOXA-60	1	0	-
<input type="checkbox"/> blaOXA-61	1	0	-
<input type="checkbox"/> blaOXA-62	1	0	-
<input type="checkbox"/> blaOXA-63	1	0	-
<input type="checkbox"/> blaOXA-64	1	0	-
<input type="checkbox"/> blaOXA-65	1	0	-
<input type="checkbox"/> blaOXA-66	1	0	-
<input type="checkbox"/> blaOXA-67	1	0	-
<input type="checkbox"/> blaOXA-68	1	0	-
<input type="checkbox"/> blaOXA-69	1	0	-
<input type="checkbox"/> blaOXA-70	1	0	-
<input type="checkbox"/> blaOXA-71	1	0	-
<input type="checkbox"/> blaOXA-72	1	0	-
<input type="checkbox"/> blaOXA-73	1	0	-
<input type="checkbox"/> blaOXA-74	1	0	-
<input type="checkbox"/> blaOXA-75	1	0	-
<input type="checkbox"/> blaOXA-76	1	0	-
<input type="checkbox"/> blaOXA-77	1	0	-
<input type="checkbox"/> blaOXA-78	1	0	-
<input type="checkbox"/> blaOXA-79	1	0	-
<input type="checkbox"/> blaOXA-80	1	0	-
<input type="checkbox"/> blaOXA-81	1	0	-
<input type="checkbox"/> blaOXA-82	1	0	-
<input type="checkbox"/> blaOXA-83	1	0	-
<input type="checkbox"/> blaOXA-84	1	0	-
<input type="checkbox"/> blaOXA-85	1	0	-
<input type="checkbox"/> blaOXA-86	1	0	-
<input type="checkbox"/> blaOXA-87	1	0	-
<input type="checkbox"/> blaOXA-88	1	0	-
<input type="checkbox"/> blaOXA-89	1	0	-
<input type="checkbox"/> blaOXA-90	1	0	-
<input type="checkbox"/> blaOXA-91	1	0	-
<input type="checkbox"/> blaOXA-92	1	0	-
<input type="checkbox"/> blaOXA-93	1	0	-
<input type="checkbox"/> blaOXA-94	1	0	-
<input type="checkbox"/> blaOXA-95	1	0	-
<input type="checkbox"/> blaOXA-96	1	0	-
<input type="checkbox"/> blaOXA-97	1	0	-
<input type="checkbox"/> blaOXA-98	1	0	-
<input type="checkbox"/> blaOXA-99	1	0	-
<input type="checkbox"/> blaOXA-100	1	0	-

In addition, as the genes *sul1* and *sul2* are highlighted, here in the bottom right you will find more information about them. Importantly, the information is connected to the reference from each database – in this case, ResFinder

If the selected item is a microbe, you will find a link to the NCBI database.

Current Selections

- Sulfamethoxazole
- [sul1](#)
- [sul2](#)



Network Customization

Network: ARGs-taxa1

Background: Black

View: Topology

Layout: Default Layout

Scope: -- Specify --

Download: -- Specify -- View Options

Function Explorer

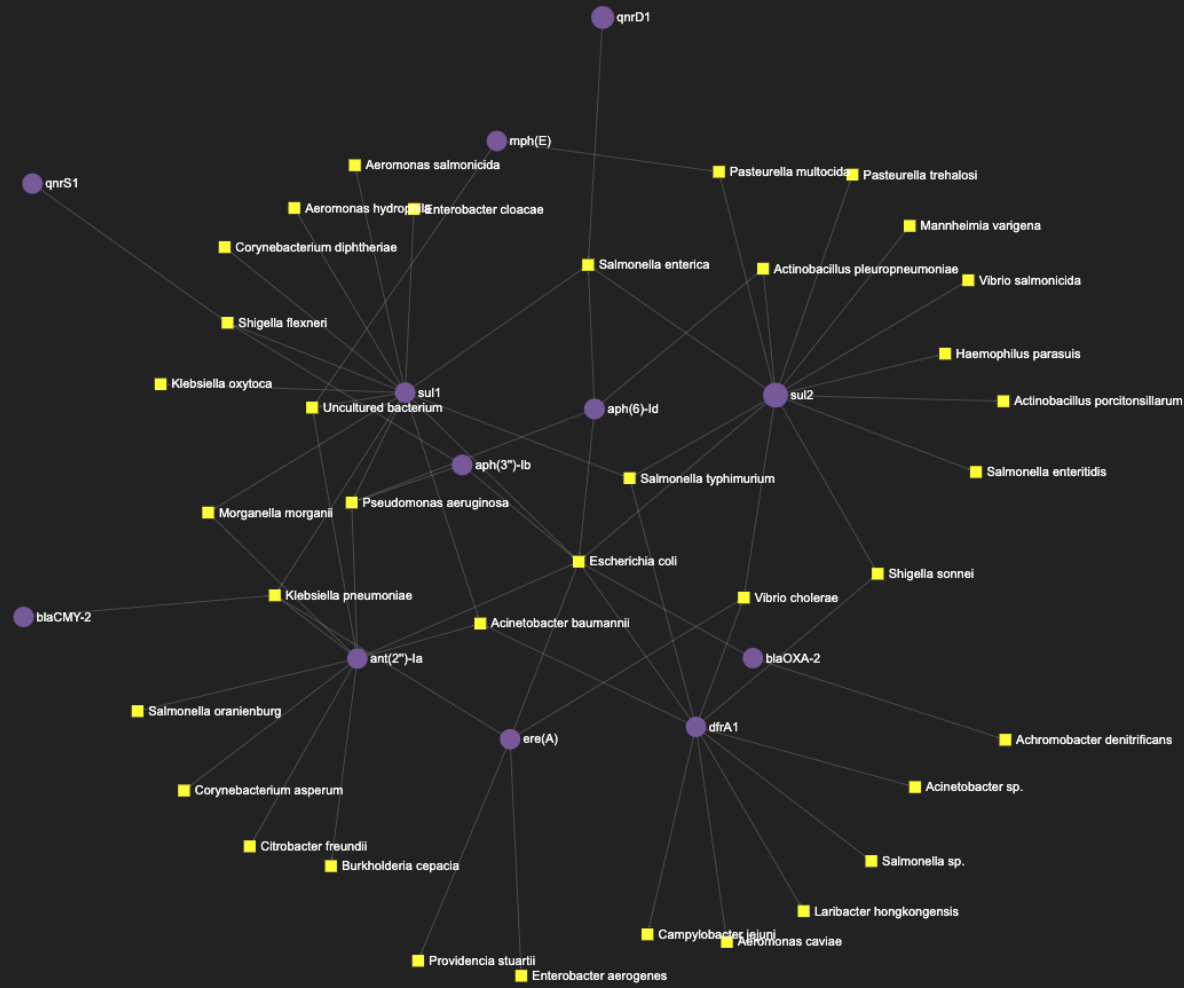
Query:

Algorithm: Hypergeometric test

Functional category: Class Submit

Name	Hits	Pval	Color
------	------	------	-------

Let's try to change the background color to white, and look at the expression values since we added the optional abundance data at the start of this manual.



Node Explorer

ID:  Search

Highlight All interactions Submit

ID	Degree	Betweenness	Abundance
<input type="checkbox"/> sul1	14	399.4751	713
<input type="checkbox"/> sul2	13	364.5822	37332
<input type="checkbox"/> ant(2'')-Ia	10	228.7985	27
<input type="checkbox"/> dfrA1	10	255.3126	36
<input type="checkbox"/> Escherichia coli	8	385.0485	-
<input type="checkbox"/> ere(A)	5	111.8352	45
<input type="checkbox"/> aph(6)-Id	4	30.42103	3221
<input type="checkbox"/> Klebsiella pneumon	4	82.44043	-
<input type="checkbox"/> Pseudomonas aerug	4	30.11349	-
<input type="checkbox"/> Salmonella enterica	4	87.44394	-
<input type="checkbox"/> aph(3'')-Ib	3	21.27045	2595
<input type="checkbox"/> Acinetobacter baum	3	57.35209	-
<input type="checkbox"/> Uncultured bacteriu	3	41.84167	-
<input type="checkbox"/> Shigella flexneri	3	49.6	-
<input type="checkbox"/> Salmonella typhimu	3	73.09144	-
<input type="checkbox"/> Vibrio cholerae	3	47.88507	-
<input type="checkbox"/> blaOXA-2	2	46	19
<input type="checkbox"/> mph(E)	2	8.304762	44
<input type="checkbox"/> Morganella morgan	2	7.916667	-
<input type="checkbox"/> Actinobacillus pleu	2	4.47381	-
<input type="checkbox"/> Shigella sonnei	2	16.4131	-
<input type="checkbox"/> Pasteurella multocic	2	18.37976	-
<input type="checkbox"/> blaCMY-2	1	0	778
<input type="checkbox"/> qnrD1	1	0	20603
<input type="checkbox"/> qnrS1	1	0	450
<input type="checkbox"/> Burkholderia cepaci	1	0	-
<input type="checkbox"/> Citrobacter freundii	1	0	-
<input type="checkbox"/> Corynebacterium as	1	0	-
<input type="checkbox"/> Salmonella ororient	1	0	-
<input type="checkbox"/> Achromobacter den	1	0	-

Current Selections

Network Customization

Network: ARGs-taxa1  
 Background: White  
 View: Expression  
 Layout: Default Layout  
 Scope: -- Specify --  
 Download: -- Specify -- View Options

Now the color of the background has changed to white and we can see the expression values for the antibiotic resistance genes.



The expression values are in a green-red gradient, meaning that higher values will be shown in red. This can be confirmed by looking at the uploaded ARG list.

Function Explorer

Query: All genes  
 Algorithm: Hypergeometric test  
 Functional category: Class Submit

Name	Hits	Pval	Color
------	------	------	-------



Node Explorer

ID	Degree	Betweenness	Abundance
light	All	interactions	Submit
Search			Delete
ant(2 <sup>+</sup> )-Ia	10	228.7985	27
dfrA1	10	255.3126	36
Escherichia coli	8	385.0485	-
ere(A)	5	111.8352	45
aph(6)-IId	4	30.42103	3221
Klebsiella pneumos	4	82.44043	-
Pseudomonas aeru	4	30.11349	-
Salmonella enteric	4	87.44394	-
aph(3 <sup>+</sup> )-Ib	3	21.27045	2595
Acinetobacter baur	3	57.35209	-
Uncultured bacteri	3	41.84167	-
Shigella flexneri	3	49.6	-
Salmonella typhim	3	73.09144	-
Vibrio cholerae	3	47.88507	-
blaOXA-2	2	46	19
mph(E)	2	8.304762	44
Morganella morga	2	7.916667	-
Actinobacillus ple	2	4.47381	-
Shigella sonnei	2	16.4131	-
Pasteurella multoci	2	18.37976	-
blaCMY-2	1	0	778
qnrD1	1	0	20603
qnrS1	1	0	450
Burkholderia cepac	1	0	-
Citrobacter freund	1	0	-
Corynebacterium a	1	0	-
Salmonella oranien	1	0	-
Achromobacter dei	1	0	-

Current Selections



**Network Customization**

Network: ARGs-taxa1  
 Background: White  
 View: Expression  
 Layout: Default Layout  
 Scope: -- Specify --  
 Download: -- Specify -- View Options

There is also a variety of different layouts that can be employed, such as the Fruchterman-Reingold.

**Function Explorer**

Query: All genes  
 Algorithm: Hypergeometric test  
 Functional category: Class Submit

Name	Hits	Pval	Color
------	------	------	-------



**Node Explorer**

ID: Search Delete

ID	Degree	Betweenness	Abundance
<input type="checkbox"/> sul1	14	399.4751	713
<input type="checkbox"/> sul2	13	364.5822	37332
<input type="checkbox"/> ant(2 <sup>+</sup> )-Ia	10	228.7985	27
<input type="checkbox"/> dfrA1	10	255.3126	36
<input type="checkbox"/> Escherichia coli	8	385.0485	-
<input type="checkbox"/> ere(A)	5	111.8352	45
<input type="checkbox"/> aph(6)-Ib	4	30.42103	3221
<input type="checkbox"/> Klebsiella pneumo	4	82.44043	-
<input type="checkbox"/> Pseudomonas aeru	4	30.11349	-
<input type="checkbox"/> Salmonella enteric	4	87.44394	-
<input type="checkbox"/> aph(3 <sup>+</sup> )-Ib	3	21.27045	2595
<input type="checkbox"/> Acinetobacter baur	3	57.35209	-
<input type="checkbox"/> Uncultured bacteri	3	41.84167	-
<input type="checkbox"/> Shigella flexneri	3	49.6	-
<input type="checkbox"/> Salmonella typhim	3	73.09144	-
<input type="checkbox"/> Vibrio cholerae	3	47.88507	-
<input type="checkbox"/> blaOXA-2	2	46	19
<input type="checkbox"/> mph(E)	2	8.304762	44
<input type="checkbox"/> Morganella morgar	2	7.916667	-
<input type="checkbox"/> Actinobacillus plet	2	4.47381	-
<input type="checkbox"/> Shigella sonnei	2	16.4131	-
<input type="checkbox"/> Pasteurella multoci	2	18.37976	-
<input type="checkbox"/> blaCMY-2	1	0	778
<input type="checkbox"/> qnrD1	1	0	20603
<input type="checkbox"/> qnrS1	1	0	450
<input type="checkbox"/> Burkholderia cepac	1	0	-
<input type="checkbox"/> Citrobacter freundii	1	0	-
<input type="checkbox"/> Corynebacterium a	1	0	-
<input type="checkbox"/> Salmonella oranien	1	0	-
<input type="checkbox"/> Achromobacter dei	1	0	-

**Current Selections**

Network Customization

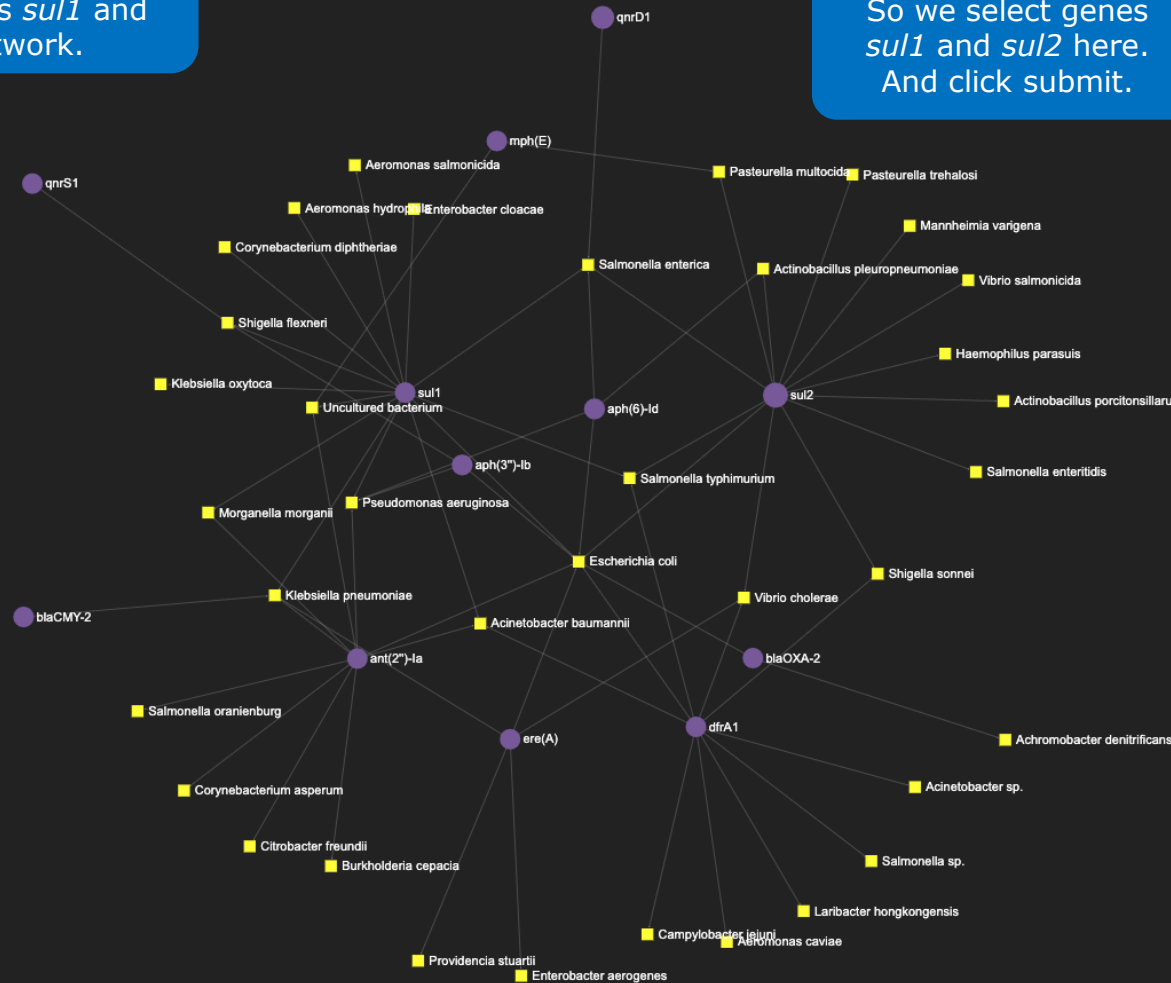
Network: ARGs-taxa1  
 Background: Black  
 View: Topology  
 Layout: Default Layout  
 Scope: -- Specify --  
 Download: -- Specify -- View Options

Function Explorer

Query: All genes  
 Algorithm: Hypergeometric test  
 Functional category: Class Submit

Name	Hits	Pval	Color
------	------	------	-------

Let's go back to the start say we want to isolate all the nodes connected to genes *sul1* and *sul2* in the network.



So we select genes *sul1* and *sul2* here. And click submit.

Node Explorer

ID:  Search  Delete

Highlight All interactions Submit

<input type="checkbox"/> ID	Degrec	Betweenness	Abundance
<input checked="" type="checkbox"/> sul1	14	399.4751	713
<input checked="" type="checkbox"/> sul2	13	364.5822	37332
<input type="checkbox"/> ant(2'')-Ia	10	228.7985	27
<input type="checkbox"/> dfrA1	10	255.3126	36
<input type="checkbox"/> Escherichia coli	8	385.0485	-
<input type="checkbox"/> ere(A)	5	111.8352	45
<input type="checkbox"/> aph(6)-Id	4	30.42103	3221
<input type="checkbox"/> Klebsiella pneumon	4	82.44043	-
<input type="checkbox"/> Pseudomonas aerug	4	30.11349	-
<input type="checkbox"/> Salmonella enterica	4	87.44394	-
<input type="checkbox"/> aph(3'')-Ib	3	21.27045	2595
<input type="checkbox"/> Acinetobacter baum	3	57.35209	-
<input type="checkbox"/> Uncultured bacteri	3	41.84167	-
<input type="checkbox"/> Shigella flexneri	3	49.6	-
<input type="checkbox"/> Salmonella typhimu	3	73.09144	-
<input type="checkbox"/> Vibrio cholerae	3	47.88507	-
<input type="checkbox"/> blaOXA-2	2	46	19
<input type="checkbox"/> mph(E)	2	8.304762	44
<input type="checkbox"/> Morganella morgan	2	7.916667	-
<input type="checkbox"/> Actinobacillus pleu	2	4.47381	-
<input type="checkbox"/> Shigella sonnei	2	16.4131	-
<input type="checkbox"/> Pasteurella multoci	2	18.37976	-
<input type="checkbox"/> blaCMY-2	1	0	778
<input type="checkbox"/> qnrD1	1	0	20603
<input type="checkbox"/> qnrS1	1	0	450
<input type="checkbox"/> Burkholderia cepaci	1	0	-
<input type="checkbox"/> Citrobacter freundii	1	0	-
<input type="checkbox"/> Corynebacterium as	1	0	-
<input type="checkbox"/> Salmonella oranien	1	0	-
<input type="checkbox"/> Achromobacter den	1	0	-

Current Selections



**Network Customization**

Network: module6  
 Background: Black  
 View: Topology  
 Layout: Default Layout  
 Scope: -- Specify --  
 Download: -- Specify -- View Options

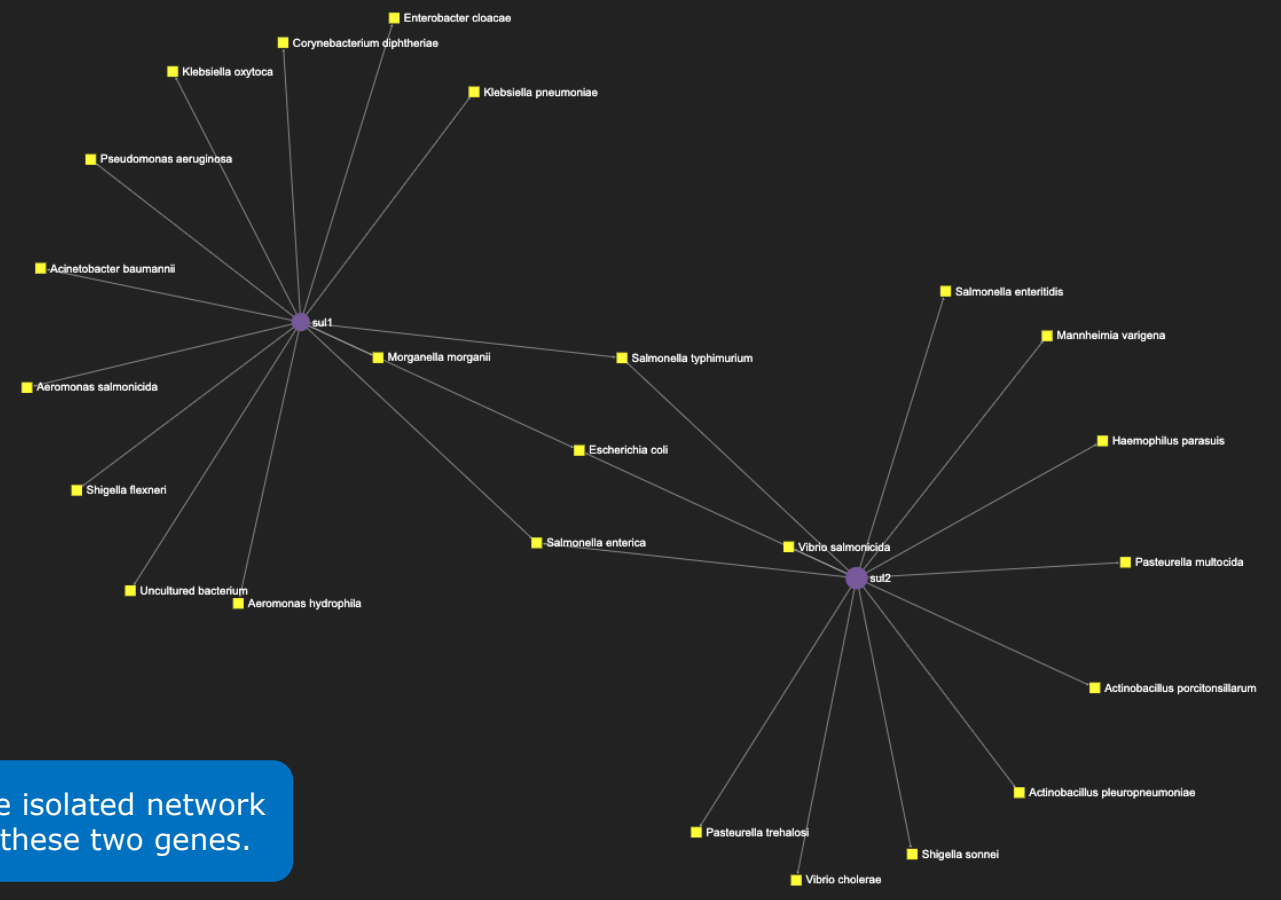
The image can be downloaded here in several formats.

**Function Explorer**

Query: All genes  
 Algorithm: Hypergeometric test  
 Functional category: Class Submit

Name	Hits	Pval	Color
------	------	------	-------

This is the isolated network map for these two genes.



**Node Explorer**

ID: Search Delete

Highlight All interactions Submit

ID	Degree	Betweenness	Abundance
<input type="checkbox"/> sul1	14	210.5	713
<input type="checkbox"/> sul2	13	196.5	37332
<input type="checkbox"/> Escherichia coli	2	44	-
<input type="checkbox"/> Salmonella enterica	2	44	-
<input type="checkbox"/> Salmonella typhim	2	44	-
<input type="checkbox"/> Acinetobacter baur	1	0	-
<input type="checkbox"/> Klebsiella pneumo	1	0	-
<input type="checkbox"/> Morganella morgan	1	0	-
<input type="checkbox"/> Pseudomonas aeru	1	0	-
<input type="checkbox"/> Uncultured bacteri	1	0	-
<input type="checkbox"/> Shigella flexneri	1	0	-
<input type="checkbox"/> Actinobacillus plet	1	0	-
<input type="checkbox"/> Shigella sonnei	1	0	-
<input type="checkbox"/> Vibrio cholerae	1	0	-
<input type="checkbox"/> Pasteurella multoci	1	0	-
<input type="checkbox"/> Aeromonas hydrop	1	0	-
<input type="checkbox"/> Aeromonas salmon	1	0	-
<input type="checkbox"/> Corynebacterium d	1	0	-
<input type="checkbox"/> Enterobacter cloaci	1	0	-
<input type="checkbox"/> Klebsiella oxytoca	1	0	-
<input type="checkbox"/> Actinobacillus por	1	0	-
<input type="checkbox"/> Haemophilus paras	1	0	-
<input type="checkbox"/> Mannheimia varige	1	0	-
<input type="checkbox"/> Pasteurella trehalo	1	0	-
<input type="checkbox"/> Salmonella enteriti	1	0	-
<input type="checkbox"/> Vibrio salmonicida	1	0	-

- Current Selections**
- Node: sul2
  - ResFinder
  - A1830714
  - A1877041
  - A1830710
  - F1968160



## How do I identify important nodes in my network?

The position of the nodes within the network will reveal their importance in terms of connection with other antibiotic resistance genes and microbial hosts.

Consequently, changes in the most important positions of the network will have more impact as opposed to less important or more peripheral positions. This means that if you try to 'click and drag' an important node, it will carry several other smaller nodes with it. Their position will not change, but you will see that the lines connecting them follow the more important node.

The degree centrality indicates the number of connections to other nodes (the node with the highest degree of centrality will act as a hub of the network), while the betweenness centrality measures the number of shortest paths going through the node considering the whole network (the node with the highest betweenness centrality controls the flow of information in the network). Each of the measures is independent.

In addition, you can also double click several nodes to select them, and extract them to a new network. With this, you can focus on your ARGs of interest. Or you can use this to analyze parts of the network separately.



**THIS MANUAL IS FINISHED.**

To explore more features of ResistoXplorer based on different input data, please check our manuals for **ARG table** and **Integration**.

Thank you for using

**Resist****st** **Xplorer**

**Please cite:**

Dhariwal A, Junges R, Chen T, Petersen FC.

ResistoXplorer: a web-based tool for visualization and exploratory analysis of resistome data.