

# Package ‘GmicR’

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**Type** Package

**Title** Combines WGCNA and xCell readouts with bayesian network learning to generate a Gene-Module Immune-Cell network (GMIC)

**Version** 1.2.0

**Author** Richard Virgen-Slane

**Maintainer** Richard Virgen-Slane <RVS.BioTools@gmail.com>

**Description** This package uses bayesian network learning to detect relationships between Gene Modules detected by WGCNA and immune cell signatures defined by xCell. It is a hypothesis generating tool.

**License** GPL-2 + file LICENSE

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Auto_WGCNA	<i>Carries out WGCNA with default settings or custom settings</i>
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## Description

Carries out WGCNA with default settings or custom settings

## Usage

```
Auto_WGCNA(
  datExpr,
  colname_correct = TRUE,
  minModuleSize = 10,
  deepSplit = 4,
  networkType = "signed hybrid",
  TOMType = "unsigned",
  corFnc = "bicor",
  mergeCutHeight = 0.25,
  sft_RsquaredCut = 0.85,
  removeFirst = FALSE,
  reassignThreshold = 1e-06,
  maxBlockSize = 25000,
  nThreads = NULL
)
```

## Arguments

<code>datExpr</code>	Expression data. A matrix (preferred) or data frame in which columns are genes and rows are samples. NAs are allowed, but not too many. See <code>checkMissingData</code> below and details.
<code>colname_correct</code>	a logical value. If TRUE (default), "." in gene names will be replaced with "-". This corrects a name change that is induced by R when creating a data.frame. If FALSE, no changes will be made.
<code>minModuleSize</code>	minimum module size for module detection. See <a href="#">cutreeDynamic</a> for more details.
<code>deepSplit</code>	integer value between 0 and 4. Provides a simplified control over how sensitive module detection should be to module splitting, with 0 least and 4 most sensitive. See <a href="#">cutreeDynamic</a> for more details.

networkType	network type. Allowed values are (unique abbreviations of) "unsigned", "signed", "signed hybrid". See <a href="#">adjacency</a> .
TOMType	one of "none", "unsigned", "signed". If "none", adjacency will be used for clustering. If "unsigned", the standard TOM will be used (more generally, TOM function will receive the adjacency as input). If "signed", TOM will keep track of the sign of correlations between neighbors.
corFnc	the correlation function to be used in adjacency calculation.
mergeCutHeight	dendrogram cut height for module merging.
sft_RsquaredCut	desired minimum scale free topology fitting index $R^2$ . Default is 0.80.
removeFirst	should the first bin be removed from the connectivity histogram?
reassignThreshold	p-value ratio threshold for reassigning genes between modules. See Details.
maxBlockSize	integer giving maximum block size for module detection. Ignored if blocks above is non-NULL. Otherwise, if the number of genes in <code>datExpr</code> exceeds <code>maxBlockSize</code> , genes will be pre-clustered into blocks whose size should not exceed <code>maxBlockSize</code> .
nThreads	non-negative integer specifying the number of parallel threads to be used by certain parts of correlation calculations. This option only has an effect on systems on which a POSIX thread library is available (which currently includes Linux and Mac OSX, but excludes Windows). If zero, the number of online processors will be used if it can be determined dynamically, otherwise correlation calculations will use 2 threads.

**Value**

Returns a lists containing network input parameters used for WGCNA, WGCNA module information, and quality control plots.

**Note**

This is a wrapper for WGCNA.

**See Also**

[blockwiseModules](#)

[adjacency](#)

**Examples**

```
sample_dat_dir<-system.file("extdata", "sample_dat.Rdata",
package = "GmicR", mustWork = TRUE)
load(sample_dat_dir)
GMIC_Builder<-Auto_WGCNA(sample_dat, mergeCutHeight = 0.35,
minModuleSize = 10)
```

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Batch_Net	<i>Generates a subgraph from query nodes</i>
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**Description**

Generates a subgraph from query nodes

**Usage**

```
Batch_Net(bn_output, Node_ids, relationship_type = "nbr")
```

**Arguments**

bn_output	R object output from bn_tabu_gen function
Node_ids	vector containing the nodes for subgraph generation.
relationship_type	the relationship to be returned for the specified query nodes. The options are "mb", "nbr", "parents", "children". Default setting is "nbr".

**Value**

a subgraph containing the selected nodes and relationships.

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bn_tabu_gen	<i>Uses tabu search algorithm to learn the structure of discretized data.</i>
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**Description**

Uses tabu search algorithm to learn the structure of discretized data.

**Usage**

```
bn_tabu_gen(  
  Auto_WGCNA_OUTPUT,  
  whitelist = NULL,  
  blacklist = NULL,  
  score = "bde",  
  tabu = 50,  
  iss = 10,  
  cluster = NULL,  
  debug = TRUE,  
  bootstraps_replicates = 500  
)
```

**Arguments**

Auto_WGCNA_OUTPUT	an R object generated by Auto_WGCNA and discretized using the Data_Prep function.
whitelist	a data frame with two columns (optionally labeled "from" and "to"), containing a set of arcs to be included in the graph.
blacklist	a data frame with two columns (optionally labeled "from" and "to"), containing a set of arcs not to be included in the graph.
score	character string indicating the score used for structure learning. If "bde" (default), prior is set to "uniform". If bds is used, the prior is set to "marginal".
tabu	a positive integer number, the length of the tabu list used in the tabu function.
iss	the imaginary sample size, used by the Bayesian Dirichlet scores (bde and bds) It is also known as "equivalent sample size". The default value is equal to 10.
cluster	an optional cluster object from package <b>parallel</b> .
debug	a boolean value. If TRUE a lot of debugging output is printed; otherwise the function is completely silent.
bootstraps_replicates	an integer for the number of bootstraps_replicates used for structure learning. Default value is 500

**Value**

The learned bayesian network

**See Also**

[arc.strength](#)

[hc](#)

[score](#)

**Examples**

```
GMIC_Builder_disc_dir<-system.file("extdata", "GMIC_Builder_disc.Rdata",
package = "GmicR", mustWork = TRUE)
load(GMIC_Builder_disc_dir)

no_cores<-1
cl<-parallel::makeCluster(no_cores)

GMIC_net<-bn_tabu_gen(GMIC_Builder_disc,
cluster = cl,
bootstraps_replicates = 50, score = "bds")
parallel::stopCluster(cl)
```

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Data_Prep	<i>Discretizes biological assay data in preparation for bayesian network learning</i>
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### Description

Discretizes biological assay data in preparation for bayesian network learning

### Usage

```
Data_Prep(
  Auto_WGCNA_OUTPUT = NULL,
  Remove_ME0 = FALSE,
  Numeric_Pheno_scores = NULL,
  xCell_Signatures = NULL,
  ibreaks = 60
)
```

### Arguments

Auto_WGCNA_OUTPUT	R object generated from Auto_WGCNA function.
Remove_ME0	a logical value. If FALSE (default), ME0 is not removed. If TRUE the eigengene for module 0 is removed prior to analysis.
Numeric_Pheno_scores	a data.frame with rows indicating sample ID and columns representing additional phenotype data to be included in BN learning. If NULL (default) no data will be included. If provided, the data.frame will be merged with MEs and discretized into three levels.
xCell_Signatures	the name of the text file generated by xCell that contains the cell signature scores. If NULL (default) the only module eigenegnes will be processed. If not NULL and if Auto_WGCNA_OUTPUT is NULL, cell signature scores will be discretized.
ibreaks	an integer that indicates the number of ibreaks used for discretization. The default value is 60.

### Value

a list containing a data.frame with module eigenegnes merged with Xcell signature scores and discretized into three levels: L, M, H. If Auto\_WGCNA\_OUTPUT is NULL, both scaled and discretized cell signatures will be return.

### Note

Please verify that the sample name formatting is consistent between both datasets. Rownames in the module eigenegnes data.frame and the column names of xCell signatures scores text file are matched for merging. Only samples that are present in both will be processed!

**Examples**

```
file_dir<-system.file("extdata", "IRIS_xCell_sig.txt",
package = "GmicR", mustWork = TRUE)
Disc_Xcell_sig<-Data_Prep(xCell_Signatures=file_dir, ibreaks = 10)
Disc_Xcell_sig$disc_data
```

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Gmic_viz	<i>Visualized network</i>
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**Description**

Visualized network

**Usage**

```
Gmic_viz(Auto_WGCNA_Output, Filter_unconnected_ME = TRUE)
```

**Arguments**

Auto\_WGCNA\_Output

R object with GMIC bayesian network

Filter\_unconnected\_ME

a logical value. If TRUE, the default, unconnected modules will be removed from the final network. If FALSE, all modules will be shown.

**Value**

a shiny object for network visualization.

**Examples**

```
GMIC_Final_dir<-system.file("extdata", "GMIC_Final.Rdata",
package = "GmicR", mustWork = TRUE)
load(GMIC_Final_dir)
if(interactive()){
Gmic_viz(GMIC_Final)}
```

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GO_Module_NameR	<i>GO enrichment for module names</i>
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**Description**

GO enrichment for module names

**Usage**

```
GO_Module_NameR(Auto_WGCNA_OUTPUT, cutoff_size = NULL)
```

**Arguments**

Auto\_WGCNA\_OUTPUT  
 object returned by GSEAGO\_Builder function

cutoff\_size  
 integer indication the GO size cut off. If NULL (default) the term with the smallest Pvalue will be returned.

**Value**

a data.frame listing the GO name for each module. Additionally, a table similar to the output of Query\_Pre function is returned, appended with module GO names.

**Examples**

```
GMIC_Builder_dir<-system.file("extdata", "GMIC_Builder.Rdata",
package = "GmicR", mustWork = TRUE)
load(GMIC_Builder_dir)
GMIC_Builder<-GO_Module_NameR(GMIC_Builder, cutoff_size = 100)
```

---

GSEAGO\_Builder                    *GO enrichment for module names*

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**Description**

GO enrichment for module names

**Usage**

```
GSEAGO_Builder(
  Auto_WGCNA_OUTPUT,
  species = "Homo sapiens",
  no_cores = 4,
  ontology = "BP",
  GO_conditional = FALSE,
  colname_correct = TRUE
)
```

**Arguments**

Auto\_WGCNA\_OUTPUT  
 output from Auto\_WGCNA function.

species  
 either 'Homo sapiens' (default) or 'Mus musculus'.

no\_cores  
 Number of cores to use. Default = 4.

ontology  
 string either 'BP'(Biological Process; default), 'CC'(Cellular Component), or 'MF' (Molecular Function).

GO\_conditional  
 A logical indicating whether the calculation should condition on the GO structure. will not be carried out. If TRUE,

colname\_correct  
 a logical value. If TRUE (default), "." in gene names will be replaced with "-". This corrects a name change that is induced by R when creating a data.frame. If FALSE, no changes will be made.



**Value**

Lists with gene ontology enrichment analysis, performed using GOstats, for each module.

**Note**

gene names must be official gene symbol

**Examples**

```
GMIC_Builder_dir<-system.file("extdata", "GMIC_Builder.Rdata",
                             package = "GmicR", mustWork = TRUE)
load(GMIC_Builder_dir)
GMIC_Builder$GSEAGO_Builder_Output<-NULL
Test_GMIC_Builder<-GSEAGO_Builder(GMIC_Builder, no_cores = 1)
summary(Test_GMIC_Builder$GSEAGO_Builder_Output)
```

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InverseARCs

*Identifies arcs between nodes with inverse relationships*

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**Description**

Identifies arcs between nodes with inverse relationships

**Usage**

```
InverseARCs(Output, threshold = -0.3)
```

**Arguments**

Output	a data frame containing the output of BN_Conditions function.
threshold	number indicating the maximum slope for defining negative relationships. Default level is -0.3.

**Value**

arcs with inverse relationships

**Examples**

```
GMIC_net_dir<-system.file("extdata", "GMIC_net.Rdata",
                          package = "GmicR", mustWork = TRUE)
load(GMIC_net_dir)
GMIC_Final<-InverseARCs(GMIC_net, threshold = -0.3)
```

---

 Query\_Prep

*Query Prep*


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### Description

Query Prep

### Usage

```
Query_Prep(
  Auto_WGCNA_OUTPUT,
  numGenes = 500,
  Find_hubs = FALSE,
  nThreads = NULL,
  calculate_intramodularConnectivity = TRUE
)
```

### Arguments

Auto_WGCNA_OUTPUT	R object generated by Auto_WGCNA function.
numGenes	integer indicating the number of random genes to test for hub gene detection. Default is 500.
Find_hubs	logical value. If TRUE, module hub genes will be returned. If FALSE (default), intramodularConnectivity will be returned without hub gene identification.
nThreads	non-negative integer specifying the number of parallel threads to be used by certain parts of correlation calculations. This option only has an effect on systems on which a POSIX thread library is available (which currently includes Linux and Mac OSX, but excludes Windows). If zero, the number of online processors will be used if it can be determined dynamically, otherwise correlation calculations will use 2 threads.
calculate_intramodularConnectivity	a logical value. If TRUE (default), the intramodularConnectivity will be calculated using the intramodularConnectivity function from WGCNA. If FALSE, a table of modules and genes will be returned without intramodularConnectivity values.

### Value

a data.frame detailing the gene symbols for each module. Gene intramodularConnectivity may also be returned. If detected, hub genes are annotated.

### Examples

```
GMIC_Builder_dir<-system.file("extdata", "GMIC_Builder.Rdata",
  package = "GmicR", mustWork = TRUE)
load(GMIC_Builder_dir)
GMIC_Builder<-Query_Prep(GMIC_Builder, Find_hubs = TRUE)
head(GMIC_Builder$Query)
```

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xCell_loader	<i>Scales and centers data by sample/row in preparation for discretization</i>
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**Description**

Scales and centers data by sample/row in preparation for discretization

**Usage**

```
xCell_loader(File = NULL)
```

**Arguments**

File                   the name of the text file generated by xCell that contains the cell signature scores.

**Value**

xCell signatures scaled and centered by sample. For GMIC, ImmuneScore, StromaScore, and MicroenvironmentScore are removed.

**Examples**

```
file_dir<-system.file("extdata", "IRIS_xCell_sig.txt",  
package = "GmicR", mustWork = TRUE)  
Xcell_sig<-xCell_loader(file_dir)  
plot(Xcell_sig$Bcells)
```

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