

# PSICQUIC

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## 1 Introduction

PSICQUIC (the Proteomics Standard Initiative Common QUery InterfaCe, pronounced “psy-kick”) is “an effort from the HUPO Proteomics Standard Initiative (HUPO-PSI) to standardise the access to molecular interaction databases programmatically”. The Bioconductor PSICQUIC package provides a traditional R function-calling (S4) interface layered on top of the PSICQUIC REST interface, to obtain a data.frame of annotated interactions between specified proteins, each of which is typically described by the HUGO symbol of the gene which codes for the protein of interest.

PSICQUIC is loose association of web accessible databases, “providers”, linked explicitly only by virtue of being listed at the central PSICQUIC web site. Each provider supports the **MIQL** (molecular interaction query language), and each of which returns standard columns in tab-delimited text. In typical use one queries for all of the interactions in which a protein participates. Equally typical are queries for all known interactions between two specified proteins. These queries are easily constrained by **provider** (e.g., BioGrid or IntAct), by **detectionMethod**, by interaction **type**, and/or by **publicationID**.

Interactions among a set of three or more genes may also be requested. The combinations of possible pairs grows non-linearly with the number of genes, so use this option with care.

PSICQUIC may therefore be best suited to the close study of a few dozen genes or proteins of interest, rather than for obtaining interactions for hundreds or thousands of genes or proteins. For bulk interactions, we recommend that you directly download databases from individual PSICQUIC (or other) providers.

Approximately thirty databases currently implement PSICQUIC. They all

- Support the molecular interaction query language (MIQL)
- Use a controlled vocabulary describing interactions and detection methods
- Communicate via SOAP or REST
- Return results in XML or a tab-delimited form
- May be interrogated programmatically or via a URL in a web browser

```
> library(PSICQUIC)
> psicquic <- PSICQUIC()
> providers(psicquic)
```

```
[1] "APID"          "bhf-uc1"      "ChEMBL"       "DIP"
[5] "HPIDb"        "InnateDB"     "IntAct"       "mentha"
[9] "MPIDb"        "MatrixDB"     "MINT"         "Reactome"
[13] "Reactome-FIs" "STRING"       "BIND"         "Interporc"
[17] "I2D-IMEx"     "InnateDB-IMEx" "MolCon"       "UniProt"
[21] "MBInfo"       "BindingDB"    "VirHostNet"   "Spike"
[25] "BAR"
```

## 2 Quick Start: find interactions between Myc and Tp53

A simple example is the best introduction to this package. Here we discover that BioGrid, Intact, Reactome, STRING and BIND each report one or more interactions between human Myc and Tp53:

```
> library(Psicquic)
> psicquic <- Psicquic()
> providers(psicquic)

[1] "APID"          "bhf-uc1"      "ChEMBL"       "DIP"
[5] "HPIDb"        "InnateDB"     "IntAct"       "mentha"
[9] "MPIDb"        "MatrixDB"     "MINT"         "Reactome"
[13] "Reactome-FIs" "STRING"       "BIND"         "Interporc"
[17] "I2D-IMEx"     "InnateDB-IMEx" "MolCon"       "UniProt"
[21] "MBInfo"       "BindingDB"    "VirHostNet"   "Spike"
[25] "BAR"

> tbl <- interactions(psicquic, id=c("TP53", "MYC"), species="9606")
> dim(tbl)
```

```
[1] 7 16
```

Note that the several arguments to the *interactions* method are unspecified. They maintain their default values, and act as wildcards in the query.

How many of the approximately twenty-five data sources reported interactions?

```
> table(tbl$provider)

      BIND      IntAct Reactome-FIs      STRING      mentha
      1         1         1         2         2
```

What kind of interactions, detection methods and references were reported? (Note that the terms used in the controlled vocabularies used by the PSICQUIC data sources are often quite long, complicating the display of extractions from our data.frame. To get around this here, we extract selected columns in small groups so that the results will fit on the page.)

```
> tbl[, c("provider", "type", "detectionMethod")]

  provider                                type
1   IntAct      psi-mi:MI:0914(association)
2   mentha      psi-mi:MI:0914(association)
3   mentha      psi-mi:MI:0915(physical association)
4 Reactome-FIs      -
5   STRING      -
6   STRING      psi-mi:MI:0190
7   BIND      -
  detectionMethod
1   psi-mi:MI:0676(tandem affinity purification)
2   psi-mi:MI:0676(tandem affinity purification)
3   psi-mi:MI:0004(affinity chromatography technology)
4   psi-mi:MI:0046(experimental knowledge based)
5   psi-mi:MI:0364(inferred by curator)
6   psi-mi:MI:0087(predictive text mining)
7   psi-mi:MI:0030(crosslink)
```

These are quite heterogeneous. The well-established “tandem affinity purification” proteomics method probably warrants more weight than “predictive text mining”. Let’s focus on them:

```

> tbl[grep("affinity", tbl$detectionMethod),
+      c("type", "publicationID", "firstAuthor", "confidenceScore", "provider")]

```

	type	publicationID	
1	psi-mi:MI:0914(association)	pubmed:21150319 imex:IM-16995	
2	psi-mi:MI:0914(association)	pubmed:21150319	
3	psi-mi:MI:0915(physical association)	pubmed:21150319	
	firstAuthor	confidenceScore	provider
1	Agrawal et al. (2010)	intact-miscore:0.35	IntAct
2	-	mentha-score:0.236	mentha
3	-	mentha-score:0.236	mentha

This result demonstrates that different providers report results from the same paper in different ways, sometimes omitting confidence scores, and sometimes using different (though related) terms from the PSI controlled vocabularies.

### 3 Retrieve all Myc interactions found by Agrawal et al, 2010, using tandem affinity purification

These reports of TP53/Myc interactions by detection methods variously described as “affinity chromatography technology” and “tandem affinity purification”, both accompanied by a reference to the same recent paper (“**Proteomic profiling of Myc-associated proteins**”, Agrawal et al, 2010), suggests the next task: obtain all of the interactions reported in that paper.

```

> tbl.myc <- interactions(psicquic, "MYC", species="9606", publicationID="21150319")

```

How many were returned? From what sources? Any confidence scores reported?

```

> dim(tbl.myc)
[1] 974 16

```

```

> table(tbl.myc$provider)

```

IntAct	mentha
452	522

```

> table(tbl.myc$confidenceScore)

```

intact-miscore:0.35	intact-miscore:0.53	intact-miscore:0.56	intact-miscore:0.60
403	29	9	1
intact-miscore:0.67	intact-miscore:0.69	intact-miscore:0.79	intact-miscore:0.96
3	3	1	3
mentha-score:0.126	mentha-score:0.236	mentha-score:0.309	mentha-score:0.332
292	173	1	12
mentha-score:0.354	mentha-score:0.416	mentha-score:0.49	mentha-score:0.623
1	27	6	1
mentha-score:0.731	mentha-score:0.891	mentha-score:0.945	mentha-score:0.999
1	2	1	2
mentha-score:1			
3			

### 4 Gene symbols for input, “native” identifiers for results

PSICQUIC queries apparently expect HUGO gene symbols for input. These are translated by each provider into each provider’s native identifier type, which is nearly always a protein id of some sort. The results returned use the protein identifier native to each provider – but see notes on the use of our IDMapper class for converting these protein identifiers to gene symbols and entrez geneIDs. If you submit a protein identifier in a query, it is apparently used without translation, and the interactions returned are limited to those which use exactly the protein identifier you supplied. Thus the use of gene symbols is recommended for all of your calls to the *interactions* method.

Here is a sampling of the identifiers returned by the PSICQUIC providers:

- refseq:NP\_001123512

- uniprotkb:Q16820
- string:9606.ENSPP00000373992—uniprotkb:Q9UMJ4
- entrez gene/locuslink:2041—BIOGRID:108355

## 5 Add Entrez GeneIDs and HUGO Gene Symbols

Though informative, this heterogeneity along with the frequent absence of entrez geneIDs and gene symbols limits the immediate usefulness of these results for many prospective users. We attempt to remedy this with the `IDMapper` class, which uses `biomaRt` and some simple parsing strategies to map these lengthy identifiers into both geneID and gene symbol. At this point in the development of the `PSICQUIC` package, this step – which adds four columns to the results data.frame – must be done explicitly, and is currently limited to human identifiers only. Support for additional species will be added.

```
> idMapper <- IDMapper("9606")
> tbl.myc <- addGeneInfo(idMapper, tbl.myc)
> print(head(tbl.myc$A.sym))

[1] "MYC" "MYC" "MYC" "MYC" "MYC" "MYC"

> print(head(tbl.myc$B.sym))

[1] "NAV2"      "RAB11FIP5" "TTN"      "DOCK7"      "IKZF2"      "SDK1"
```

## 6 Retrieve Interactions Among a Set of Genes

If the `id` argument to the `interactions` method contains two or more gene symbols, then all interactions among all possible pairs of those genes will be retrieved. Keep in mind that the number of unique combinations grows larger non-linearly with the number of genes supplied, and that each unique pair becomes a distinct query to each of the specified providers.

```
> tbl.3 <- interactions(psicquic, id=c("ALK", "JAK3", "SHC3"),
+                       species="9606", quiet=TRUE)
> tbl.3g <- addGeneInfo(idMapper, tbl.3)
> tbl.3gd <- with(tbl.3g, as.data.frame(table(detectionMethod, type, A.sym, B.sym, provider)))
> print(tbl.3gd <- subset(tbl.3gd, Freq > 0))
```

```

      detectionMethod
86  psi-mi:MI:0006(anti bait coimmunoprecipitation)
90      psi-mi:MI:0113(western blot)
162      psi-mi:MI:0113(western blot)
244      psi-mi:MI:0046(experimental knowledge based)
268      psi-mi:MI:0046(experimental knowledge based)
483 psi-mi:MI:0045(experimental interaction detection)
491      psi-mi:MI:0087(predictive text mining)
507 psi-mi:MI:0045(experimental interaction detection)
515      psi-mi:MI:0087(predictive text mining)
739 psi-mi:MI:0004(affinity chromatography technology)
811 psi-mi:MI:0004(affinity chromatography technology)
      type A.sym B.sym provider Freq
86      psi-mi:MI:0914(association) ALK JAK3 APID 1
90      psi-mi:MI:0914(association) ALK JAK3 APID 1
162      psi-mi:MI:0914(association) ALK SHC3 APID 1
244      - JAK3 ALK Reactome-FIs 1
268      - SHC3 ALK Reactome-FIs 1
483      - SHC3 ALK STRING 1
491      psi-mi:MI:0190 SHC3 ALK STRING 1
507      - ALK JAK3 STRING 1
515      psi-mi:MI:0190 ALK JAK3 STRING 1
739 psi-mi:MI:0915(physical association) ALK JAK3 mentha 2
811 psi-mi:MI:0915(physical association) ALK SHC3 mentha 1
```

## 7 References

- Aranda, Bruno, Hagen Blankenburg, Samuel Kerrien, Fiona SL Brinkman, Arnaud Ceol, Emilie Chautard, Jose M. Dana et al. "PSICQUIC and PSISCORE: accessing and scoring molecular interactions." *Nature methods* 8, no. 7 (2011): 528-529.
- Agrawal, Pooja, Kebing Yu, Arthur R. Salomon, and John M. Sedivy. "Proteomic profiling of Myc-associated proteins." *Cell Cycle* 9, no. 24 (2010): 4908-4921.