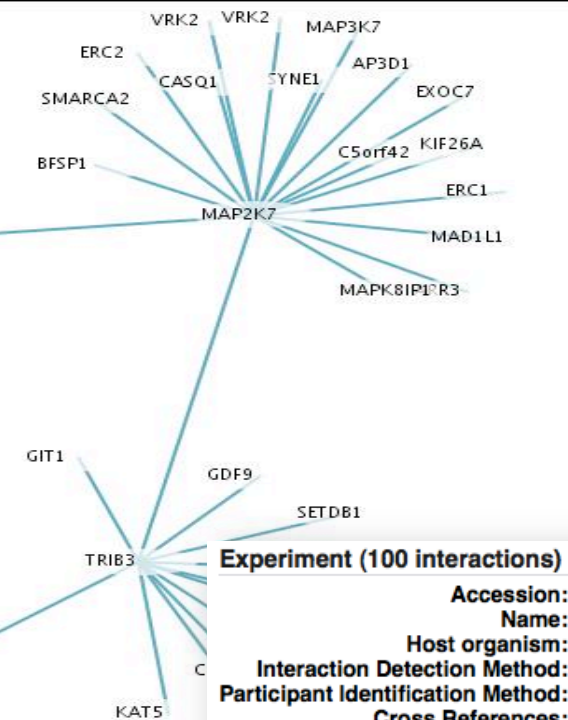


# IntAct

## High Resolution Disease-Centric Networks

Henning Hermjakob  
Team Leader Proteomics Services  
European Bioinformatics Institute  
[hhe@ebi.ac.uk](mailto:hhe@ebi.ac.uk)



- Manually curated molecular interaction DB
- 454.515 binary interaction evidences
- Detailed, “deep” curation model

### Experiment (100 interactions)

**Accession:** EBI-2509892  
**Name:** sowa-2009-1  
**Host organism:** [human-293t](#)  
**Interaction Detection Method:** [anti tag coip](#)  
**Participant Identification Method:** [sequence tag](#)

#### Cross References:

|                        |                          |       |                                   |
|------------------------|--------------------------|-------|-----------------------------------|
| <a href="#">imex</a>   | <a href="#">IM-12079</a> | -     | <a href="#">imex-primary</a>      |
| <a href="#">pubmed</a> | <a href="#">19615732</a> | -     | <a href="#">primary-reference</a> |
| <a href="#">newt</a>   | <a href="#">9606</a>     | human | <a href="#">target-species</a>    |

#### Annotations:

|                                    |   |
|------------------------------------|---|
| <a href="#">curation request</a>   | Harper Wade: 28th Oct 2009, Department of Pathology, Harvard Medical School, 77 Avenue Louis Pasteur, NRB 940, Boston, MA 02115   |
| <a href="#">confidence-mapping</a> | High-confidence candidate interaction proteins were identified using CompPASS, an automated MS/MS data-processing component, a protein function/annotation component, and an interaction network analysis component. Interactors scored using the D score which incorporates the uniqueness, the abundance of the interactor (TSC), and the reproducibility of the interaction to assign a score to each protein within each IP (the same protein in two different IPs may have distinct D scores since its TSC |

### POSITIONAL FEATURES

| FEATURE TYPE          | LABELS          | FEATURE ANNOTATIONS | SERVER NAME | EVIDENCE (Category)  |
|-----------------------|-----------------|---------------------|-------------|----------------------|
| signal peptide        | UNIPROTKB P0... |                     | uniprot     | inferred by curator  |
| mature protein region | Amyloid beta... |                     | uniprot     | inferred by curator  |
| sufficient to bind    | 711-770, 683... |                     | intact      | inferred from direct |
| sufficient to bind    | 672-713         |                     | intact      | inferred from direct |
| active peptide        | P3 (42)         |                     | uniprot     | inferred by curator  |
| extramembrane         | Extracellula... |                     | uniprot     | inferred by curator  |
| transmembrane         | Helical;        |                     | uniprot     | inferred by curator  |
| alpha helix           | UNIPROTKB P0... |                     | uniprot     | inferred by curator  |
| beta strand           | UNIPROTKB P0... |                     | uniprot     | inferred by curator  |
| turn                  | UNIPROTKB P0... |                     | uniprot     | inferred by curator  |

# Tabular view

Browse by [taxonomy](#), [gene ontology](#), [ChEBI ontology](#)

[What is this view](#)

1,925 binary interactions were found in IntAct.

- 436 of them are originated from [spoke expanded co-complexes](#) and you may want to [filter](#) them out.

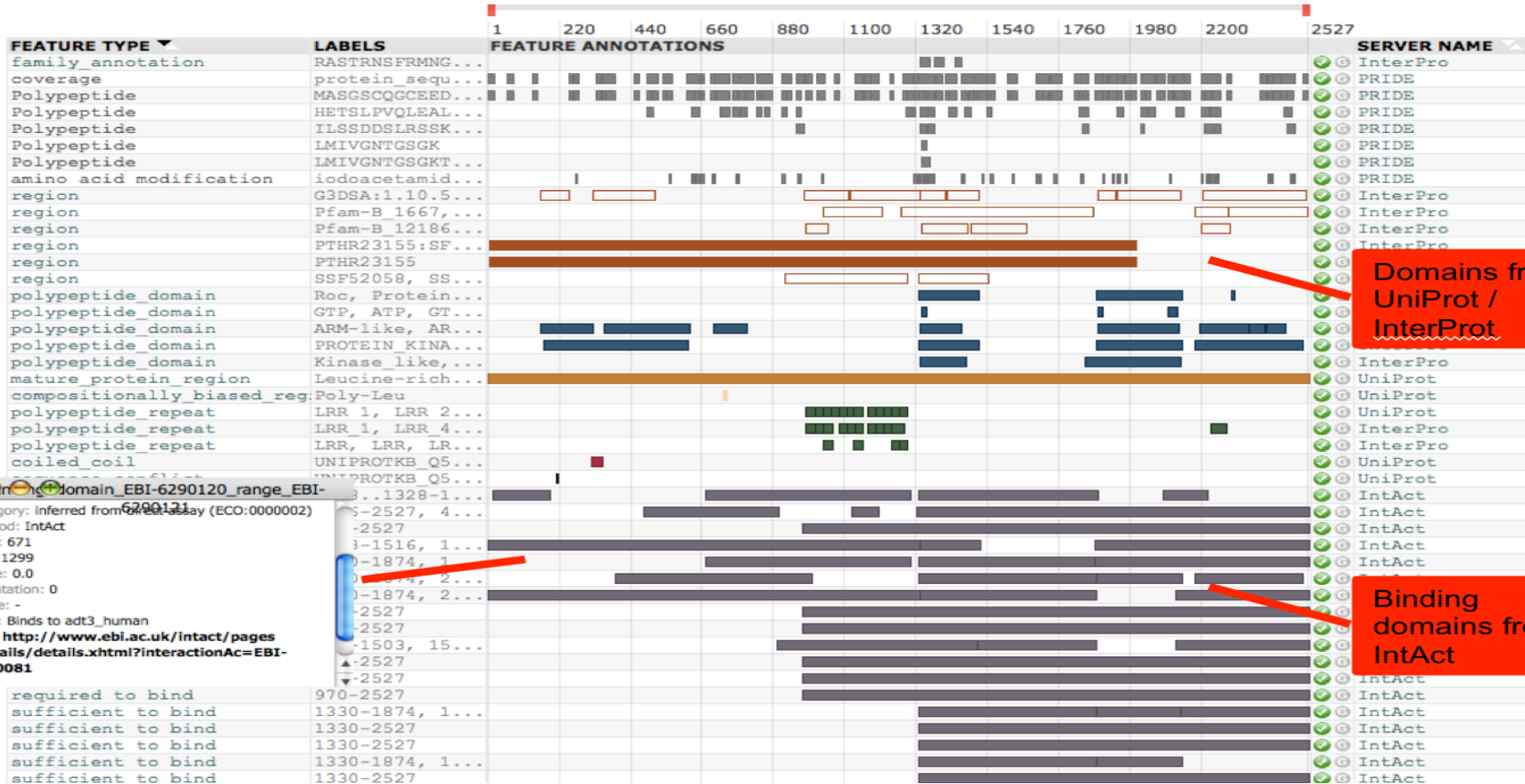
> No results in other databases.

Select format to Download Download Customize view

| #   | Molecule 'A' | Links 'A'   | Molecule 'B' | Links 'B'   | Species 'A'                  | Species 'B'                  | Interaction Detection Method                                | Publication Identifier                                      | Interaction Type   | Interaction AC  | Cor    |
|-----|--------------|---|--------------|---|------------------------------|------------------------------|---|---|--|---|--------|
| 161 | ATCAY        | <a href="#">Q86WG3</a><br><a href="#">EBI-1783328</a> | STUB1        | <a href="#">Q9UNE7</a><br><a href="#">EBI-357085</a>  | <a href="#">Homo sapiens</a> | <a href="#">Homo sapiens</a> | <a href="#">enzymatic study</a>                             | <a href="#">16275660</a>                                    | <a href="#">ubiquitination reaction</a>                          | <a href="#">EBI-1783738</a>                                       | intact |
| 162 | ARHGEF7      | <a href="#">Q14155</a><br><a href="#">EBI-717515</a>  | LRRK2        | <a href="#">Q5S007</a><br><a href="#">EBI-5323863</a> | <a href="#">Homo sapiens</a> | <a href="#">Homo sapiens</a> | <a href="#">anti tag coimmunoprecipitation</a>              | <a href="#">21048939</a><br><a href="#">imex : IM-18659</a> | <a href="#">physical association</a>                             | <a href="#">EBI-6510812</a><br><a href="#">imex : IM-18659-1</a>  | intact |
| 163 |              |   |              |   |                              |                              | <a href="#">anti tag coimmunoprecipitation</a>              | <a href="#">21048939</a><br><a href="#">imex : IM-18659</a> | <a href="#">physical association</a>                             | <a href="#">EBI-6511090</a><br><a href="#">imex : IM-18659-7</a>  |        |
| 164 |              |   |              |   |                              |                              | <a href="#">confocal microscopy</a>                         | <a href="#">21048939</a><br><a href="#">imex : IM-18659</a> | <a href="#">colocalization</a>                                   | <a href="#">EBI-6511042</a><br><a href="#">imex : IM-18659-3</a>  |        |
| 165 |              |   |              |   |                              |                              | <a href="#">protein kinase assay</a>                        | <a href="#">21048939</a><br><a href="#">imex : IM-18659</a> | <a href="#">phosphorylation reaction</a>                         | <a href="#">EBI-6511378</a><br><a href="#">imex : IM-18659-12</a> |        |
| 166 |              |   |              |   |                              |                              | <a href="#">protein kinase assay</a>                        | <a href="#">21048939</a><br><a href="#">imex : IM-18659</a> | <a href="#">phosphorylation reaction</a>                         | <a href="#">EBI-6511327</a><br><a href="#">imex : IM-18659-10</a> |        |
| 167 |              |   |              |   |                              | <a href="#">gtpase assay</a> | <a href="#">21048939</a><br><a href="#">imex : IM-18659</a> | <a href="#">gtpase reaction</a>                             | <a href="#">EBI-6511219</a><br><a href="#">imex : IM-18659-9</a> |   |        |
| 168 | SNCA         | <a href="#">P37840</a><br><a href="#">EBI-985879</a>  | RABAC1       | <a href="#">Q9UI14</a><br><a href="#">EBI-712367</a>  | <a href="#">Homo sapiens</a> | <a href="#">Homo sapiens</a> | <a href="#">phage display</a>                               | <a href="#">21798244</a><br><a href="#">imex : IM-17632</a> | <a href="#">direct interaction</a>                               | <a href="#">EBI-6261874</a><br><a href="#">imex : IM-17632-4</a>  | intact |
| 169 |              |   |              |   |                              | <a href="#">fluorescence</a> | <a href="#">21798244</a>                                    | <a href="#">colocalization</a>                              | <a href="#">EBI-6251552</a>                                      |   |        |

# Detailed Sequence view

## POSITIONAL FEATURES



LRRK2\_human in IntAct molecule view

<http://www.ebi.ac.uk/intact/molecule/EBI-5323863>

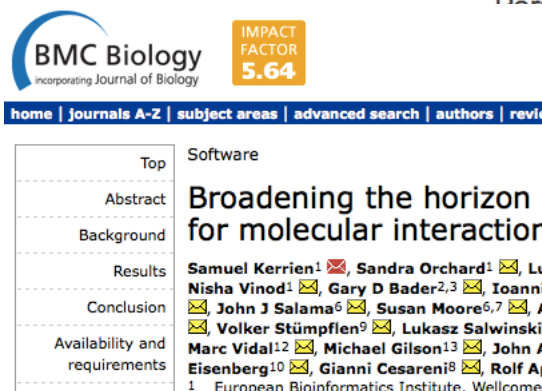


# Molecular Interactions 2002



# PSI-MI

- Community format for the representation of interaction data
- XML format, controlled vocabularies
- 2004
  - Protein interactions
- 2007
  - Molecular interactions
  - Minimum requirements
- 2010
  - Widely implemented
  - 890 Google Scholar citations (2014)



BMC Biology  
incorporating Journal of Biology

IMPACT FACTOR 5.64

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Top Software

Abstract **Broadening the horizon for molecular interaction**

Background

Results **Samuel Kerrien<sup>1</sup>**, Sandra Orchard<sup>1</sup>, Lu Nisha Vinod<sup>1</sup>, Gary D Bader<sup>2,3</sup>, Ioanni: John J Salama<sup>6</sup>, Susan Moore<sup>6,7</sup>, A: Volker Stümpflen<sup>9</sup>, Lukasz Salwinski<sup>1</sup>, Marc Vidal<sup>12</sup>, Michael Gilson<sup>13</sup>, John A Eisenberg<sup>10</sup>, Gianni Cesareni<sup>8</sup>, Rolf Ap

Availability and requirements

1 European Bioinformatics Institute, Wellcome



## Perspective

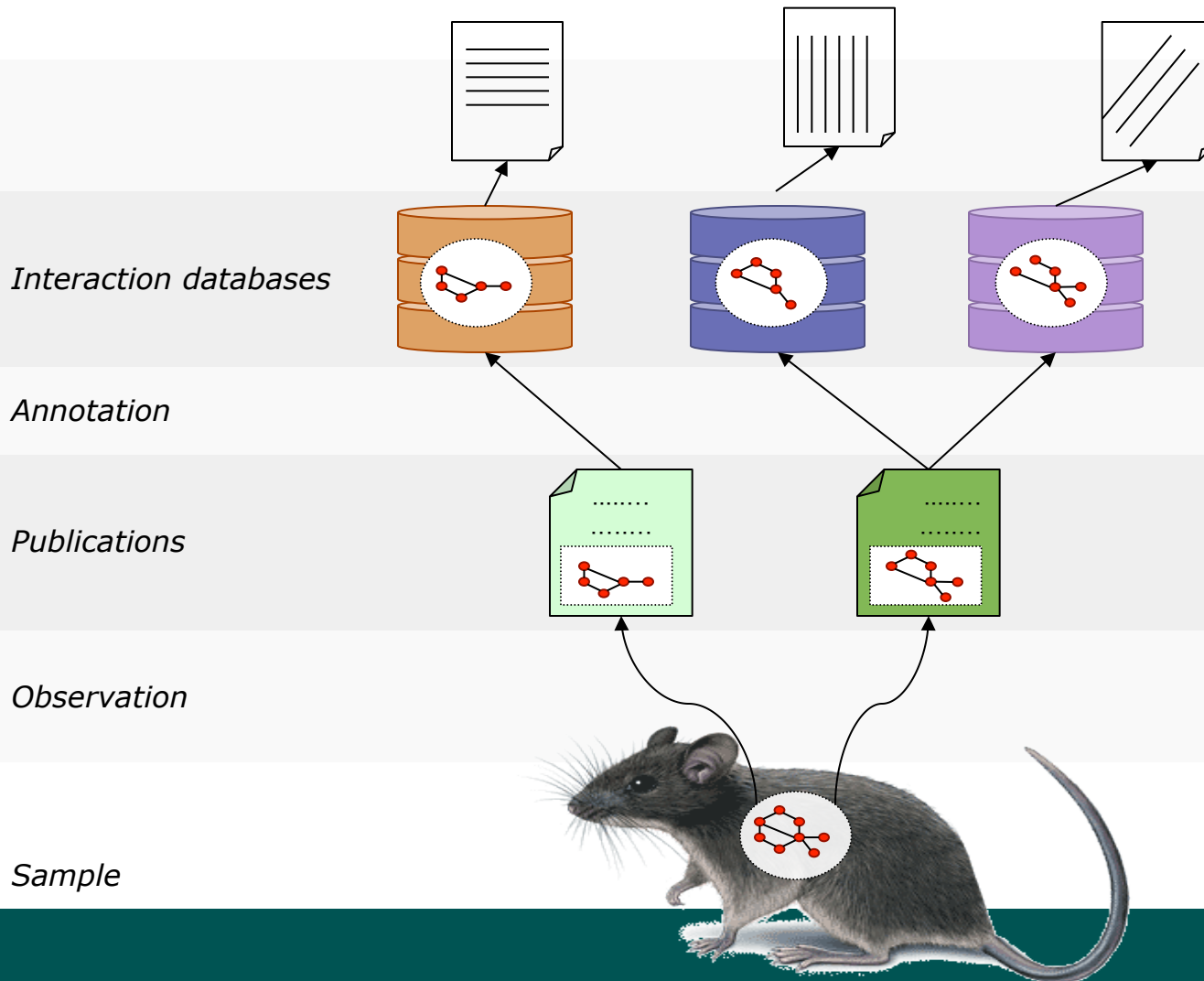
*Nature Biotechnology* **25**, 894 - 898 (2007)  
Published online: 8 August 2007 | doi:10.1038/nbt1324

### The minimum information required for reporting a molecular interaction experiment (MIMIx)

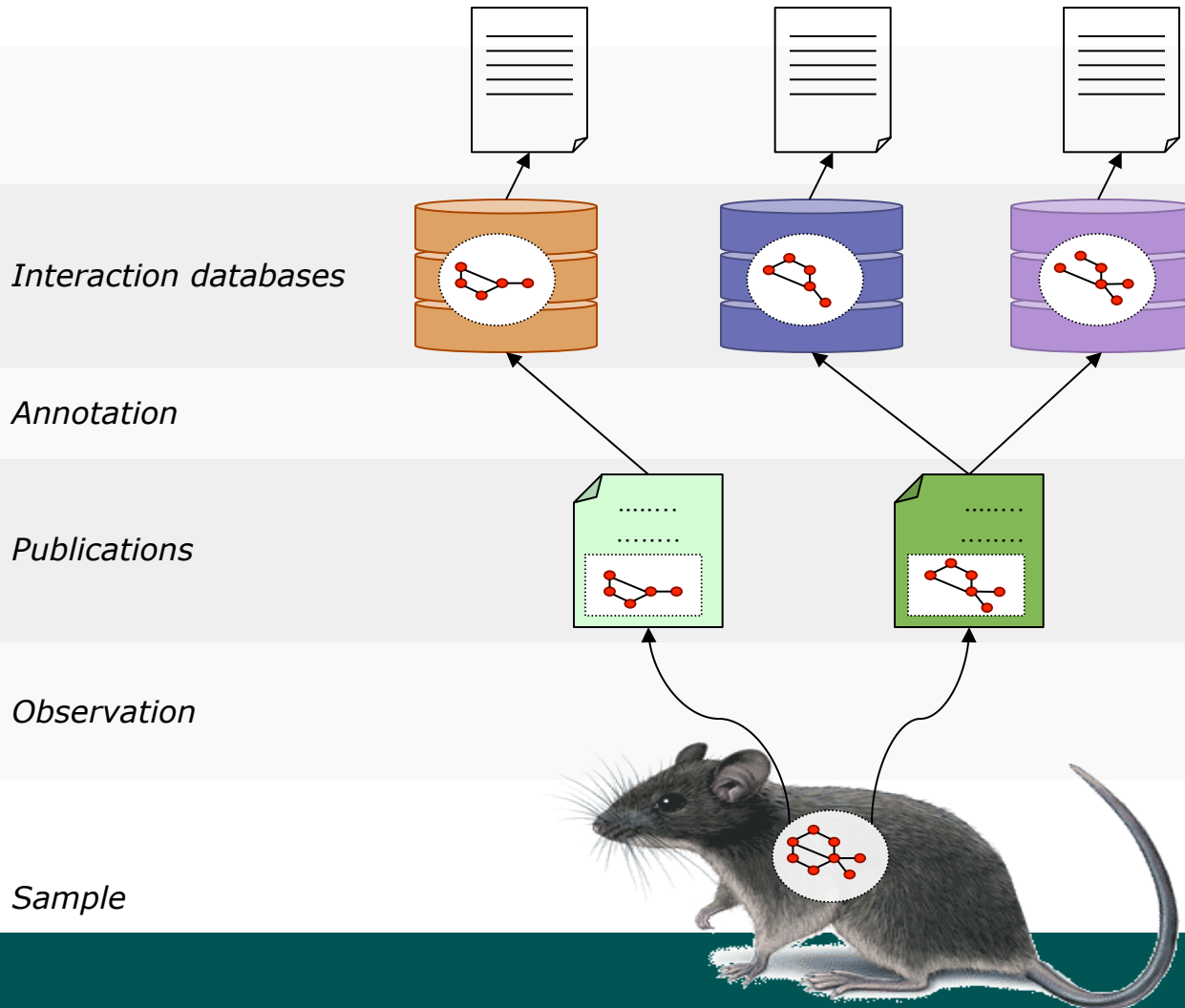
Sandra Orchard<sup>1</sup>, Lukasz Salwinski<sup>2</sup>, Samuel Kerrien<sup>1</sup>, Luisa Montecchi-Palazzi<sup>1</sup>, Matthias Oesterheld<sup>3</sup>, Volker Stümpflen<sup>3</sup>, Arnaud Ceol<sup>4</sup>, Andrew Chatr-aryamontri<sup>4</sup>, John Armstrong<sup>5</sup>, Peter Woollard<sup>5</sup>, John J Salama<sup>6</sup>, Susan Moore<sup>6,7</sup>, Jérôme Wojcik<sup>8</sup>, Gary D Bader<sup>9</sup>, Marc Vidal<sup>10</sup>, Michael E Cusick<sup>10</sup>, Mark Gerstein<sup>11</sup>, Anne-Claude Gavin<sup>12</sup>, Giulio Superti-Furga<sup>13</sup>, Jack Greenblatt<sup>9</sup>, Joel Bader<sup>14</sup>, Peter Uetz<sup>15</sup>, Mike Tyers<sup>16</sup>, Pierre Legrain<sup>17</sup>, Stan Fields<sup>18</sup>, Nicola Mulder<sup>19</sup>, Michael Gilson<sup>20</sup>, Michael Niepmann<sup>21</sup>, Lyle Burgoon<sup>22</sup>, Javier De Las Rivas<sup>23</sup>, Carlos Prieto<sup>23</sup>, Victoria M Perreau<sup>24</sup>, Chris Hogue<sup>9</sup>, Hans-Werner Mewes<sup>3</sup>, Rolf Apweiler<sup>1</sup>, Ioannis Xenarios<sup>9</sup>, David Eisenberg<sup>2</sup>, Gianni Cesareni<sup>4</sup> & Henning Hermjakob<sup>1</sup>



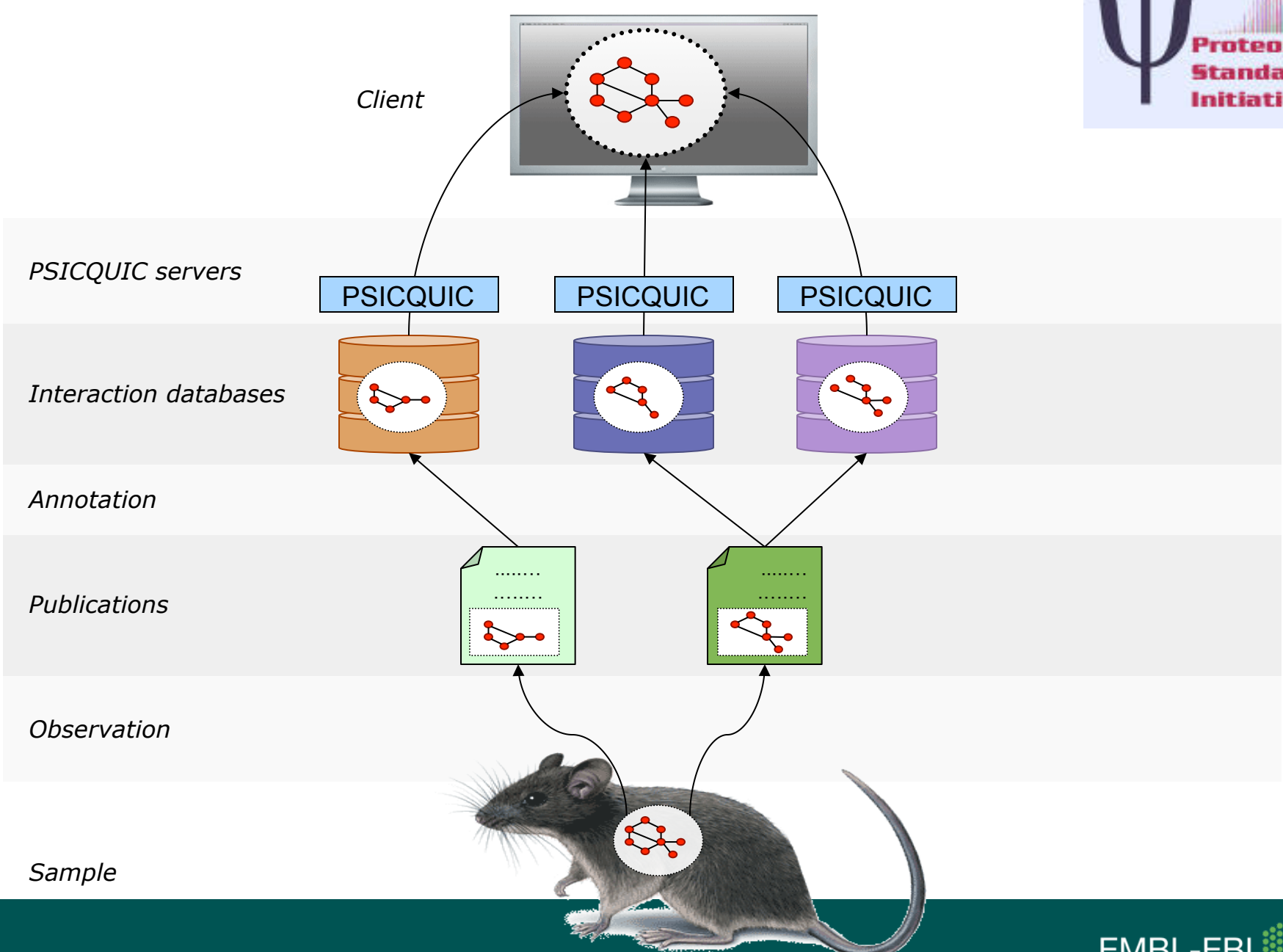
# PSI-MI



# PSI-MI







# The PSI Common Query Interface: PSICQUIC



- Common computational interface for querying molecular interaction databases
  - Not limited to protein-protein interactions, also e.g.
    - Drug-target interactions
    - Simplified pathway data

Search:    [MIQL syntax reference Fields »](#)

Total: **151,735,616** binary interaction:

Click on the links below to display the results for each selected service ([refresh list](#))

Use the check boxes to include or excludes services from the search

- |  |   |
|--|---|
| <input checked="" type="checkbox"/> <a href="#">APID</a> - 416,124     | <input checked="" type="checkbox"/> <a href="#">GeneMANIA</a> - 120,644,180 |
| <input checked="" type="checkbox"/> <a href="#">BIND</a> - 192,961     | <input checked="" type="checkbox"/> <a href="#">I2D</a> - 817,915           |
| <input checked="" type="checkbox"/> <a href="#">BindingDB</a> - 82,437 | <input checked="" type="checkbox"/> <a href="#">I2D-IMEx</a> - 882          |
| <input checked="" type="checkbox"/> <a href="#">BioGrid</a> - 337,957  | <input type="checkbox"/> InnateDB   |
| <input checked="" type="checkbox"/> <a href="#">ChEMBL</a> - 628,504   | <input checked="" type="checkbox"/> <a href="#">InnateDB-IMEx</a> - 390     |
| <input checked="" type="checkbox"/> <a href="#">DIP</a> - 107,619      | <input checked="" type="checkbox"/> <a href="#">IntAct</a> - 292,919        |
| <input checked="" type="checkbox"/> <a href="#">DrugBank</a> - 39,367  | <input checked="" type="checkbox"/> <a href="#">Interoporc</a> - 208,558    |

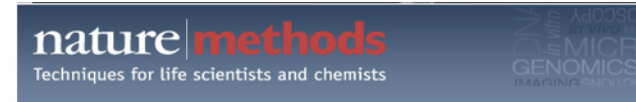
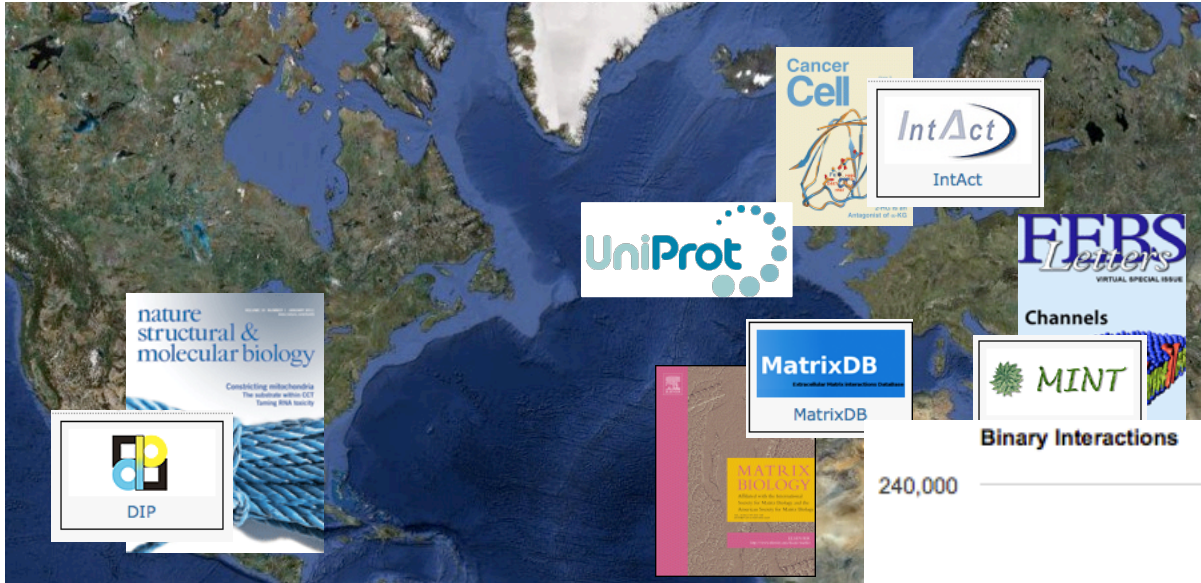
**nature** **methods**

Techniques for life scientists and chemists

## PSICQUIC and PSISCORE: accessing and scoring molecular interactions

Bruno Aranda, Hagen Blankenburg, Samuel Kerrien, Fiona S L Brinkman, Arnaud Ceol, Emilie Chautard, Jose M Dana, Javier De Las Rivas, Marine Dumousseau, Eugenia Galeota, Anna Gaulton, Johannes Goll, Robert E W Hancock, Ruth Isserlin, Rafael C Jimenez, Jules Kerssemakers, Jyoti Khadake, David J Lynn, Magali Michaut, Gavin O'Kelly, Keiichiro Ono, Sandra Orchard, Carlos Prieto, Sabry Razick, Olga Rigina *et al.*

# The International Molecular Exchange Consortium (IMEx)

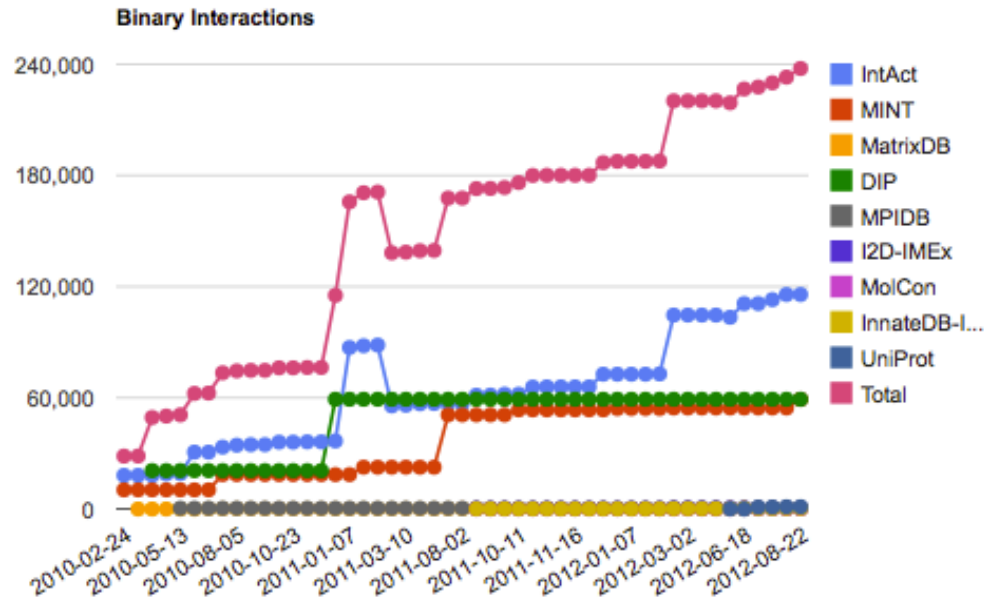


nature.com > Journal home > archive > issue > correspondence > abstract

## Protein interaction data curation: the International Molecular Exchange (IMEx) consortium

Sandra Orchard, Samuel Kerrien, Sara Abbani, Bruno Aranda, Jignesh Bhate, Shelby Bidwell, Alan Bridge, Leonardo Briganti, Fiona S L Brinkman, Gianni Cesareni, Andrew Chatr-aryamontri, Emilie Chautard, Carol Chen, Marine Dumousseau, Johannes Goll, Robert E W Hancock, Linda I Hannick, Igor Jurisica, Jyoti Khadake, David J Lynn, Usha Mahadevan, Livia Perfetto, Arathi Raghunath, Sylvie Ricard-Blum, Bernd Roechert *et al.*

- Non-redundant curation
- Common curation standards
- EU CA PSIMEx grant 2009-2014
- In production since 2/2010





- Top
- Abstract
- Background
- Results and discussion
- Conclusion
- Materials and methods
- Abbreviations

**PERSPECTIVE**  
*Special Series on Large-Scale Biology*

**Mapping and Predicting** **Research Article**  
**A domain level interaction network of amyloid precursor protein and A $\beta$  of Alzheimer's disease**

KiYoung Lee, Victoria M. Perreau<sup>1,2,3,7</sup>, Sandra Orchard<sup>4</sup>, Issue

<sup>a</sup> Department of  
<sup>b</sup> Departments  
<sup>c</sup> European Molecular

Paul A. Adame  
Roberto Casadevall  
Tiffany F. O'Neil

**nature**

International weekly journal of science

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Archive > Volume 480 > Issue 7376 > Articles > Article

NATURE | ARTICLE

< previous article next article >

**Most cellular proteome. The article informs they can be used as an example of our efforts to map locations.**

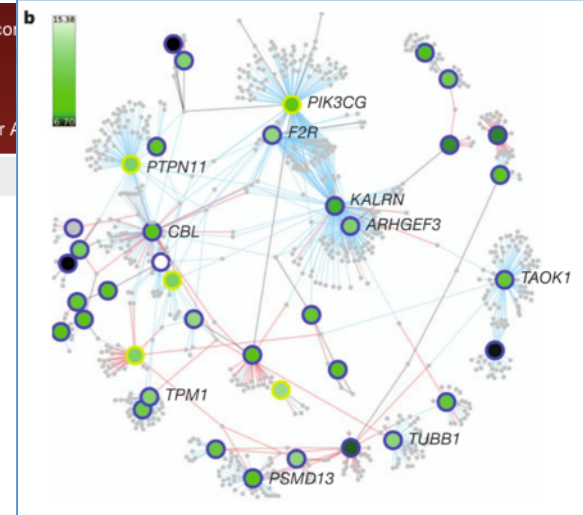
James A. Drenth, G. Faux<sup>3</sup>, Simon A. Johnston, Mok<sup>3,7</sup>, DeNew gene functions in megakaryopoiesis and platelet White<sup>2,7</sup>, A formation

Hermjakob

Article first

Jovana Serbanovic-Canic, Ulrich Elling, Alison H. Goodall, Yann Labruere, Lorna M. Lopez, Reedik Mägi, Stuart Meacham, Yukinori Okada, Nicola Pirastu, Rossella Sorice, Alexander Teumer, Katrin Voss, Weihua Zhang, Ramiro Ramirez-Solis, Joshua C. Bis, David Elinghaus, Martin Gögele, Jouke-Jan Hottenga, Claudia Langenberg, Peter Kovacs, Paul F. O'Reilly, So-Youn Shin, Tõnu Esko, Jaana Hartiala, Stavroula Kanoni, Federico Murgia, Afshin Parsa, Jonathan Stephens, Pim van der Harst, C. Ellen van der Schoot, Hooman Allayee, Antony Attwood, Bevil Bastardot, Saonli Basu, Sebastian E. Baumeister, Ginevra Biino, Loren François Cambien, John C. Chambers, Francesco Cucca, Pio D'Adamo, Boer, Eco J. C. de Geus, Angela Döring, Paul Elliott, Jeanette Erdmann, David M. Evans, Mario Fasani, Wei Feng, Aaron R. Folsom, Ian H. Frazer, Quince D. Gibson, Nicole L. Glazer, Chris Hammond, Anna-Liisa Hartikainen, Susan R. Heckbert, Christian Hengstenberg, Micha Hersch, Thomas Illig, Ruth J. F. Loos, Jennifer Jolley, Kay Tee Khaw, Brigitte Kühnel, Marie-Christine Kyrtsonis, Vasiliki Lagou, Heather Lloyd-Jones, Thomas Lumley, Massimo Mangino, Andrea Maschio, Irene Mateo Leach, Barbara McKnight, Yasin Memari, Braxton D. Mitchell, Grant W. Montgomery, Yusuke

**Jyoti Khadake**  
**Steven Jupe**



[Nature](#). 2011 Nov 30;480(7376):201-8.



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about 2 days ago  
DOTM Marsh et al.  
Protein Complexes Are under Evolutionary Selection to Assemble via Ordered Pathways. Data submitted directly to IntAct.

about 21 days ago  
Networks & Pathways Bioinformatics for Biologists training course, July 9-12 at EBI, UK. Registration open: [tinyurl.com/ebi-net-path-c...](http://tinyurl.com/ebi-net-path-c...)

about 28 days ago  
DOTM Wallech et al. Dynamic Circadian PPI Networks Reveal Temporal Organization of Cellular Functions. Data submitted directly to IntAct.

IntAct > View

## Curated Datasets

Curated datasets are publications tagged, either computationally or manually by a curator, as being relevant to a specific area of biology. These are actively maintained and grow with every release. New datasets can be requested, if relevant to your work, by mailing [intact-help@ebi.ac.uk](mailto:intact-help@ebi.ac.uk).

### Manually selected datasets

- Affinomics** - Interactions curated for the Affinomics consortium.

This dataset contains interactions which have been derived in the context of the EU Affinomics project (Grant number 241481). This comprises interactions directly submitted by the consortium partners as well as interaction derived from the literature. The current focus is on interactions derived by Proximity Ligation Assay ([MI:0813](#)), a method pioneered by the group of consortium partner Ulf Landegreen.

- Alzheimers** - Interaction dataset based on proteins with an association to Alzheimer disease

The compilation of this dataset and its curation was carried out in collaboration with Perreau V.M. University of Melbourne, Australia. Interactions were investigated in the context of Alzheimers disease with a particular focus on APP (A4) protein. The articles to be curated were determined based on protein annotations and literature scanning.

Publications based on this dataset: [PMID: 22411111](#)

- Parkinsons** - Interactions investigated in the context of Parkinsons disease

Interactions were investigated in the context of Parkinsons disease with a particular focus on LRRK2 protein and were derived in the context of the The Michael J. Fox Foundation for Parkinson's Research LRRK2 Biology LEAPS Award 2012.

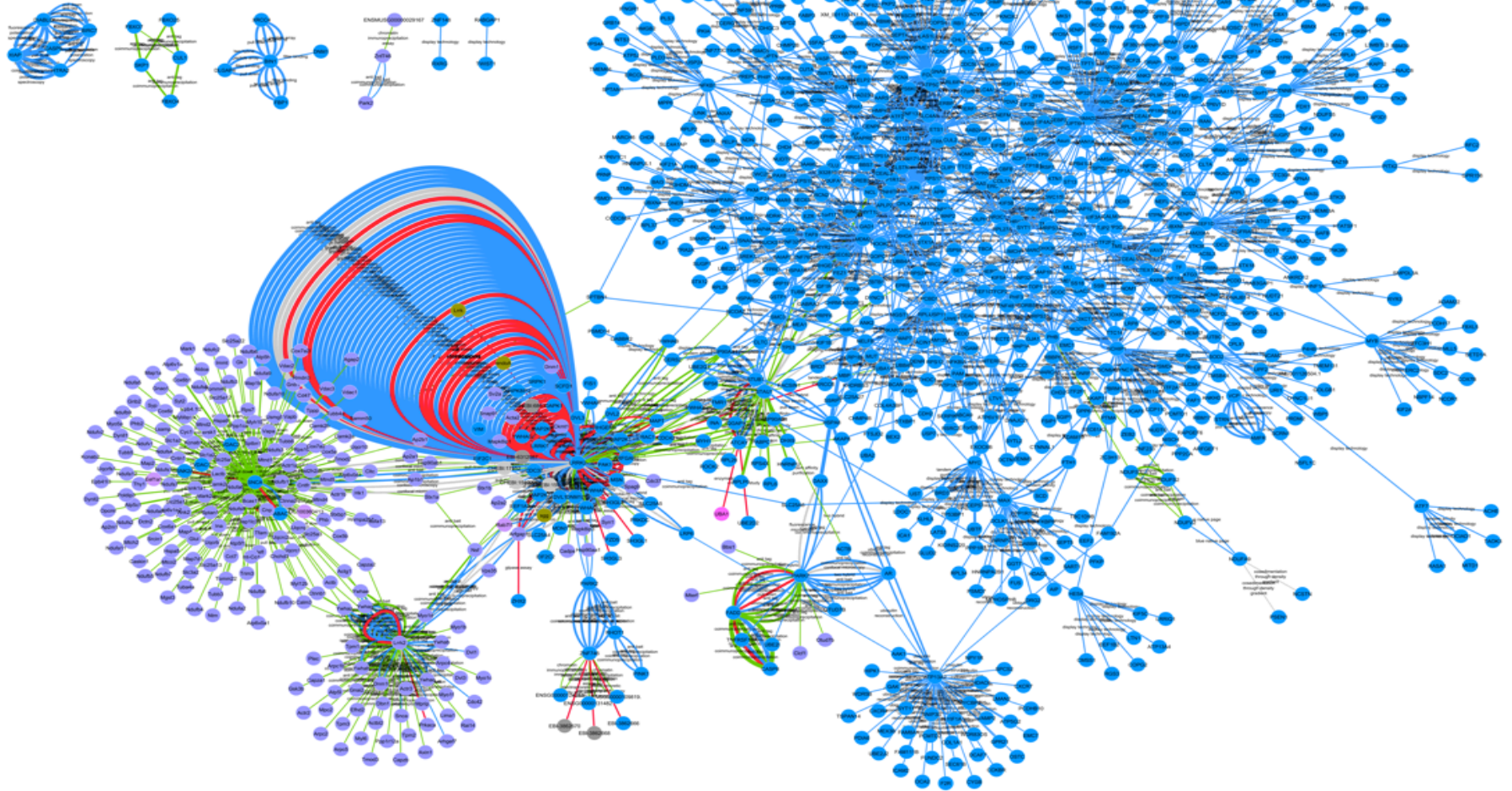
- Cancer** - Interactions investigated in the context of cancer

This dataset consists of interactions of proteins that are involved in cancer. An ongoing literature survey was carried out to determine publications of interest. Protein annotations were also considered when choosing the publications to be curated.

- Chromatin** - Epigenetic interactions resulting in chromatin modulation

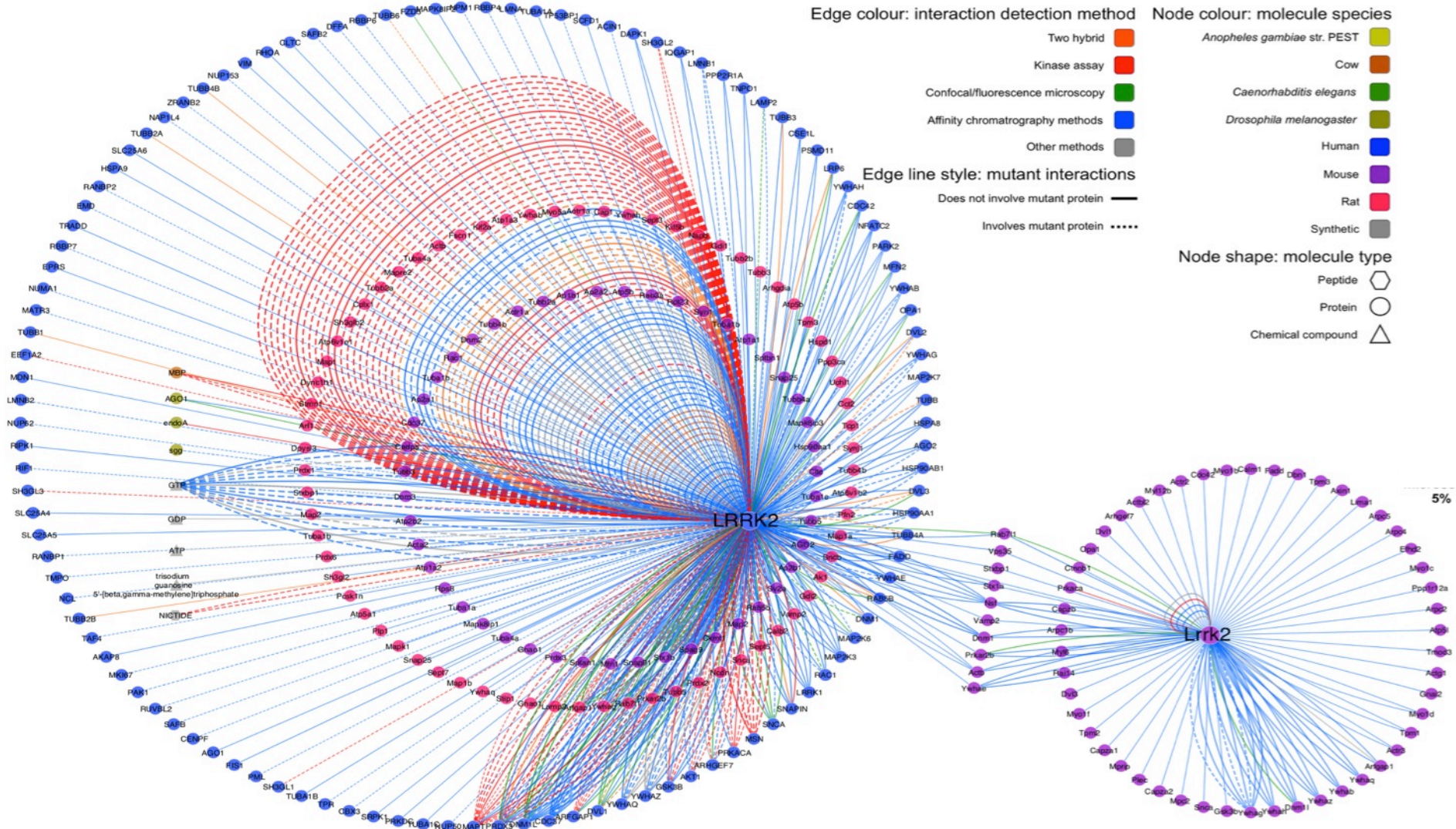
# The LRRK2 Interactome

- LRRK2 is a protein strongly implied in Parkinson's disease by genetic evidence
- Large, multidomain protein, kinase activity, unknown physiological function
- IntAct does targeted curation of LRRK2 interactions
- currently 3133 binary interaction evidences
  - ≠ 3133 interactions!
- Reached saturation of network and near completeness in terms of papers
  - “Saturation”: new publications curated rarely add new information



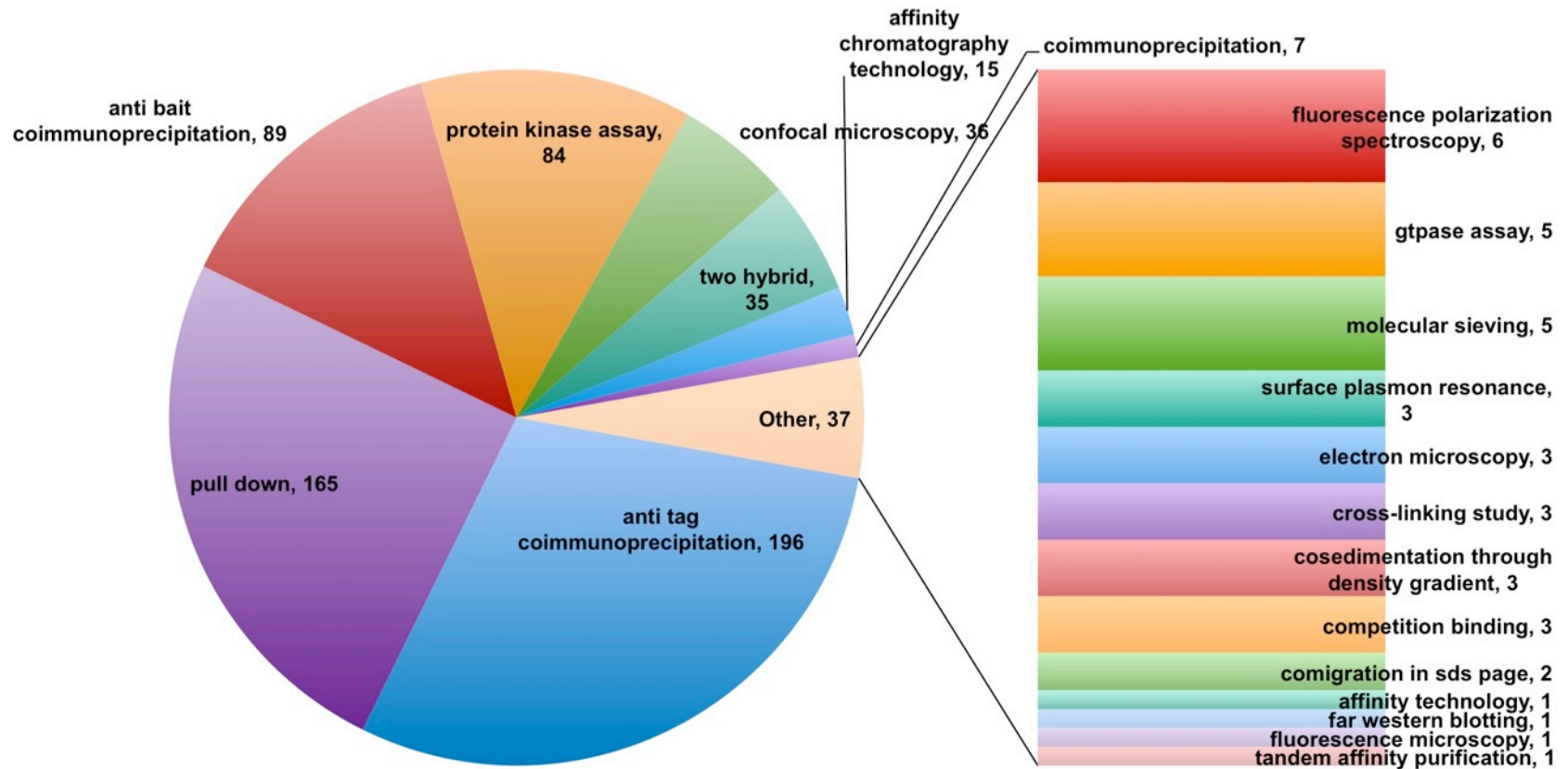


# The LRRK2 interactome

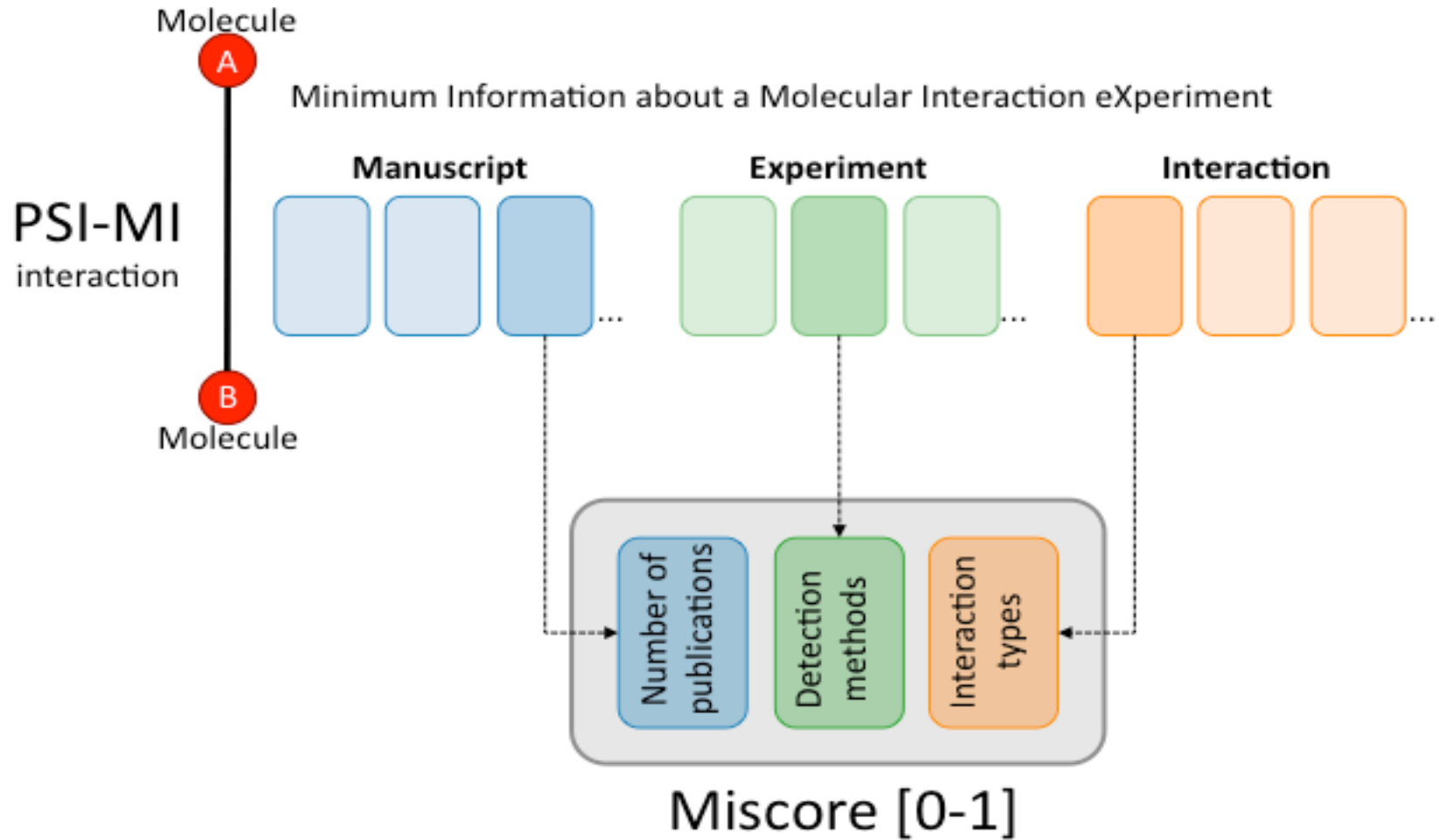




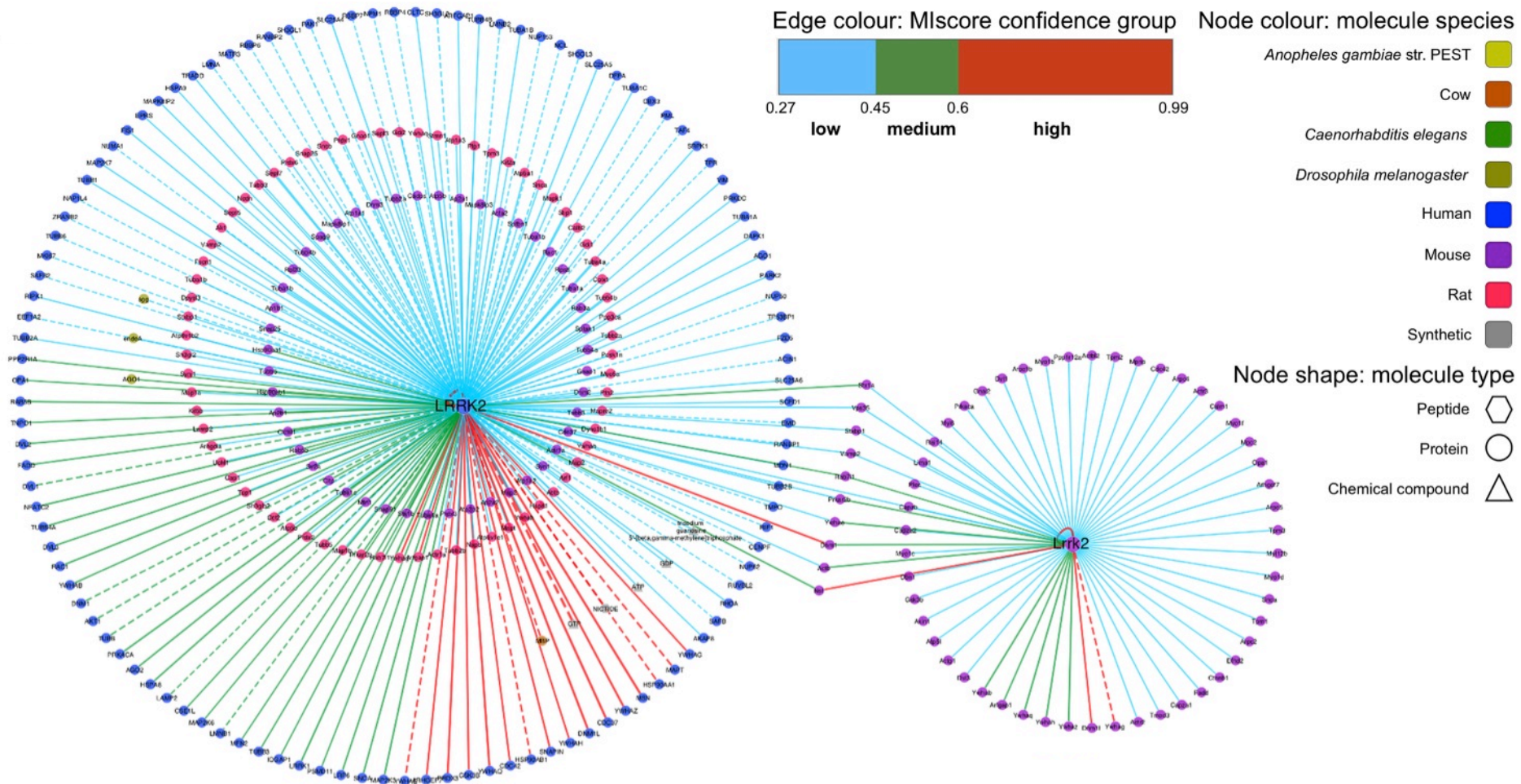
# Interaction Detection Methods



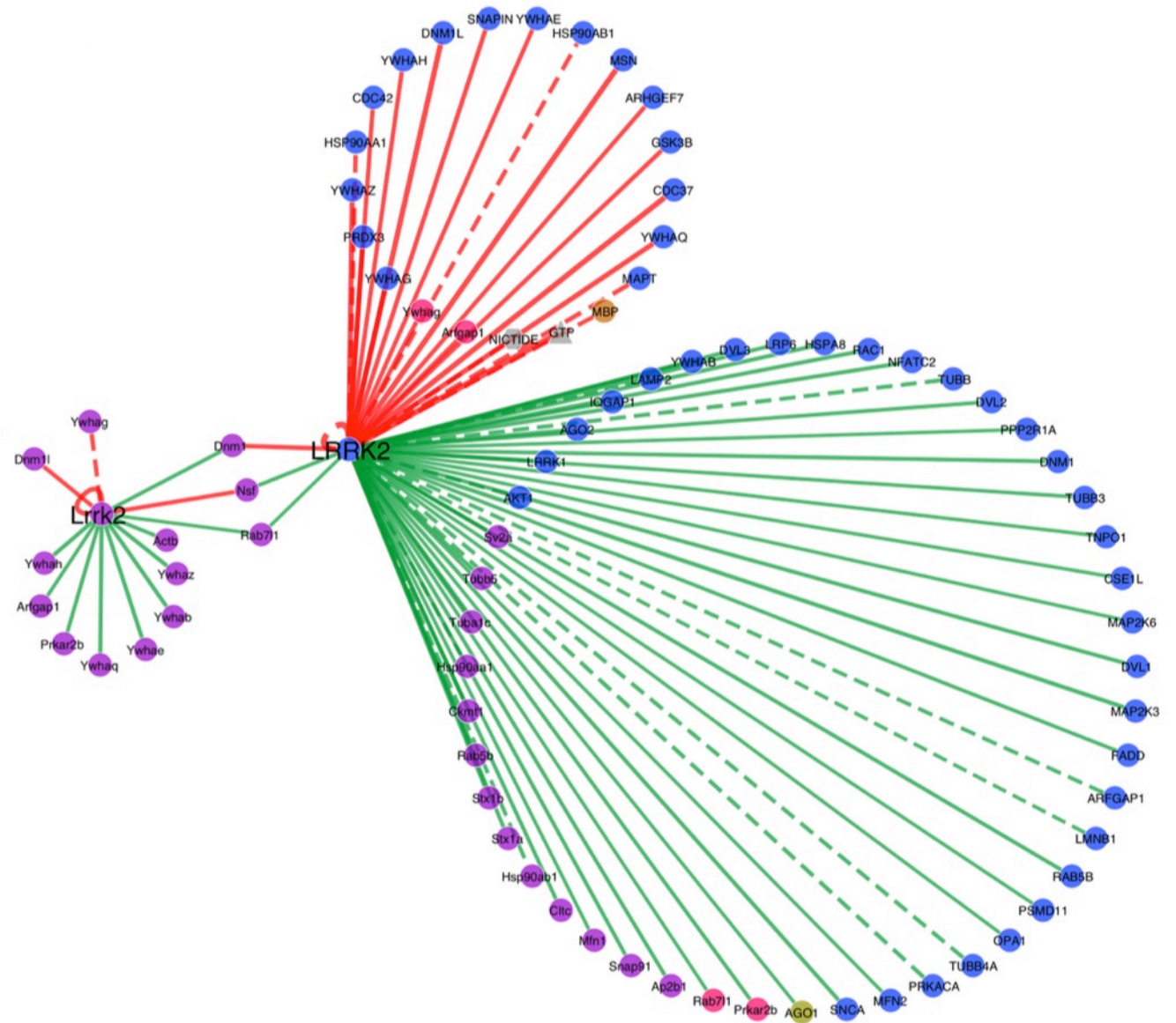
# Miscore – Evidence scoring



# Evidence Merge and Scoring

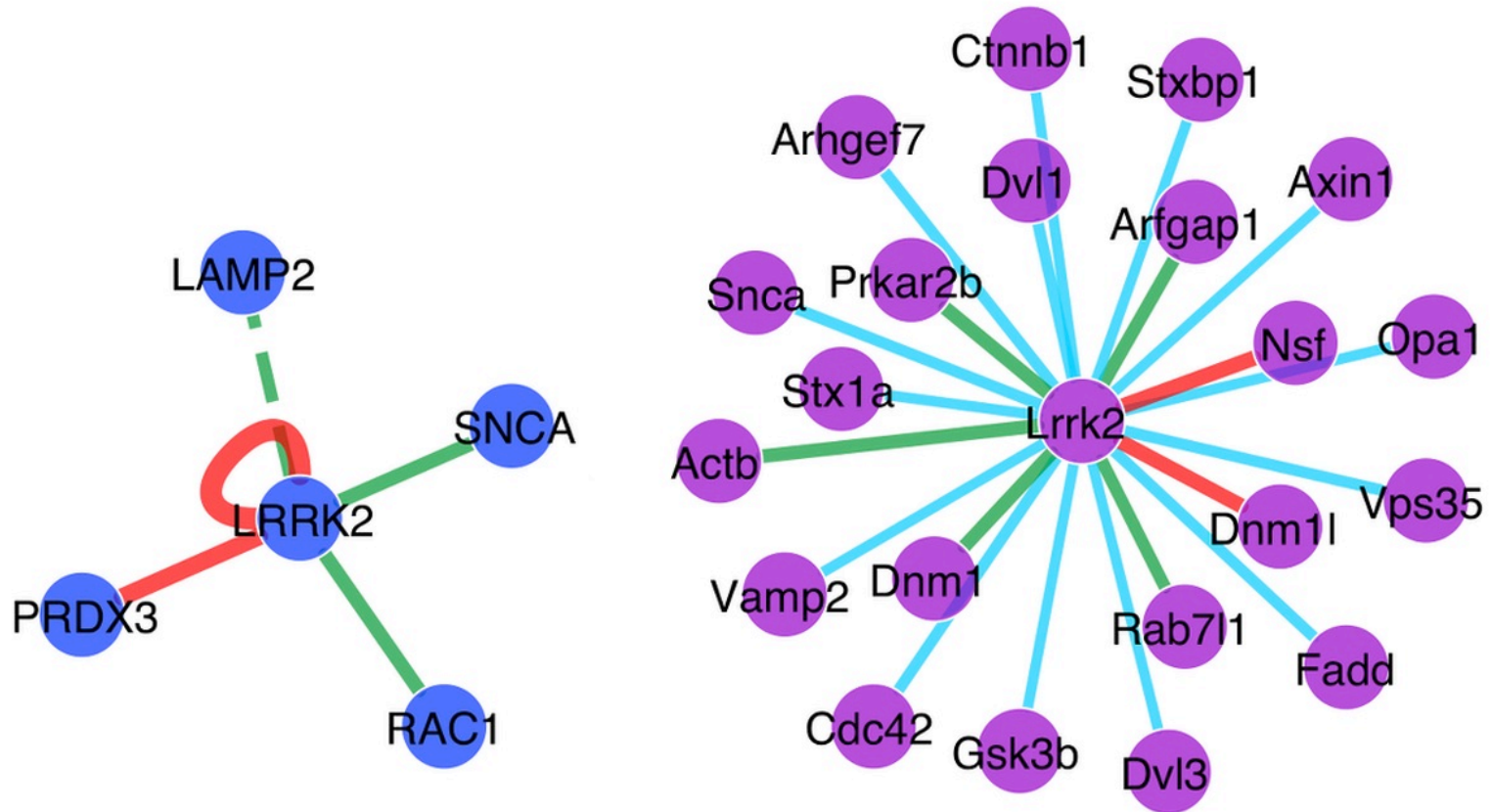


# High confidence subnetwork

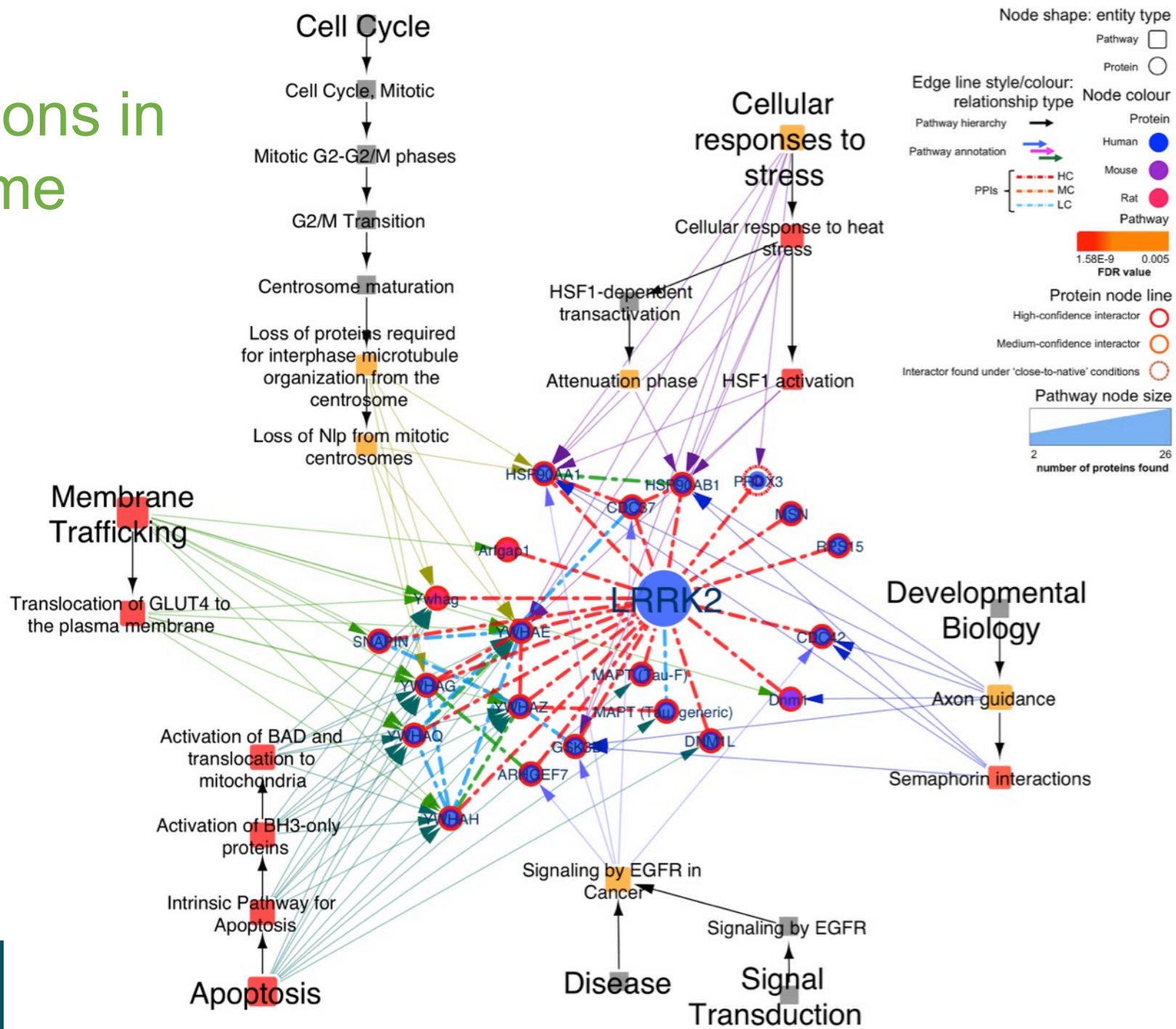




# The LRRK2 Interactome – Native conditions



# LRRK2 interactions in Reactome context



# The EBI Complex Portal

- Aims to be a reference resource for stable molecular complexes
  - “UniProt for Complexes”
- Detailed, manual annotation
- Active collaboration with UniProt, Reactome, Gene Ontology
- Currently 917 annotated complexes, mainly
  - Human
  - Yeast
  - Mouse
- <http://www.ebi.ac.uk/intact/complex/>

[Complex Portal](#) > [Details](#)

# Hemoglobin HbA complex

Species: Homo sapiens; 9606

Accession number: EBI-9008420

## Summary

Systematic Name:

2xHBA1:2xHBB

Synonyms:

|                         |                         |                              |
|-------------------------|-------------------------|------------------------------|
| HBA-HBB complex         | HBA1-HBB complex        | HBA2-HBB complex             |
| HBA1-HBB heterotetramer | HBA2-HBB heterotetramer | adult hemoglobin HbA complex |
| HBA-HBB heterotetramer  | Haemoglobin HbA complex |                              |



[Complex Portal](#) > [Details](#)

## Hemoglobin HbA complex

Species: Homo sapiens; 9606

Accession number: EBI-9008420

### Function:

Adult hemoglobin A (HbA) is expressed in erythrocytes in the bone marrow. Binds oxygen in the lungs and transports it to the various peripheral tissues. Transports CO<sub>2</sub> from cells back to the lungs. It appears in late pregnancy and becomes the dominant hemoglobin type in adults, replacing fetal hemoglobin (EBI-9108045 & EBI-9108218).

### Properties:

Two alpha chains and two beta chains. Each chain has a heme b group attached to it containing either an Fe<sup>2+</sup> or Fe<sup>3+</sup> ion. Oxygen only binds to Fe<sup>2+</sup> ions, not Fe<sup>3+</sup> ions. CO<sub>2</sub> binds directly to the protein chains and therefore does not compete with oxygen binding. MW = 64 kD

### Disease:

Mutations in hemoglobin alpha chain can result in a range of diseases, including alpha-thalassemia, Heinz body anemias and hemoglobin H (HBH) disease. Mutations in hemoglobin beta chain can result in a range of diseases, including sickle-cell anemia, beta-thalassemia and Heinz body anemias.



# Complex Portal

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## Hemoglobin HbA complex

Species: Homo sapiens; 9606

Accession number: EBI-9008420

### Participants

| ID   | Name | Description              | Stoichiometry | Biological Role  | Interactor Type | Linked Features   | Other Features |
|--|------|--------------------------|---------------|------------------|-----------------|---|----------------|
| <a href="#">P69905</a><br><a href="#">EBI-714680</a>       | HBA1 | Hemoglobin subunit alpha | 2             | unspecified role | protein         | binding-associated region CHEBI:30413 [?/?]<br>binding-associated region P68871 [?/?] |                |
| <a href="#">P68871</a><br><a href="#">EBI-715554</a>       | HBB  | Hemoglobin subunit beta  | 2             | unspecified role | protein         | binding-associated region CHEBI:30413 [?/?]<br>binding-associated region P69905 [?/?] |                |
| <a href="#">CHEBI:30413</a><br><a href="#">EBI-6880399</a> | heme | heme                     | 4             | cofactor         | small molecule  | binding-associated region P69905 [?/?]<br>binding-associated region P68871 [?/?]      |                |

Please send annotation suggestions!

### Cross References

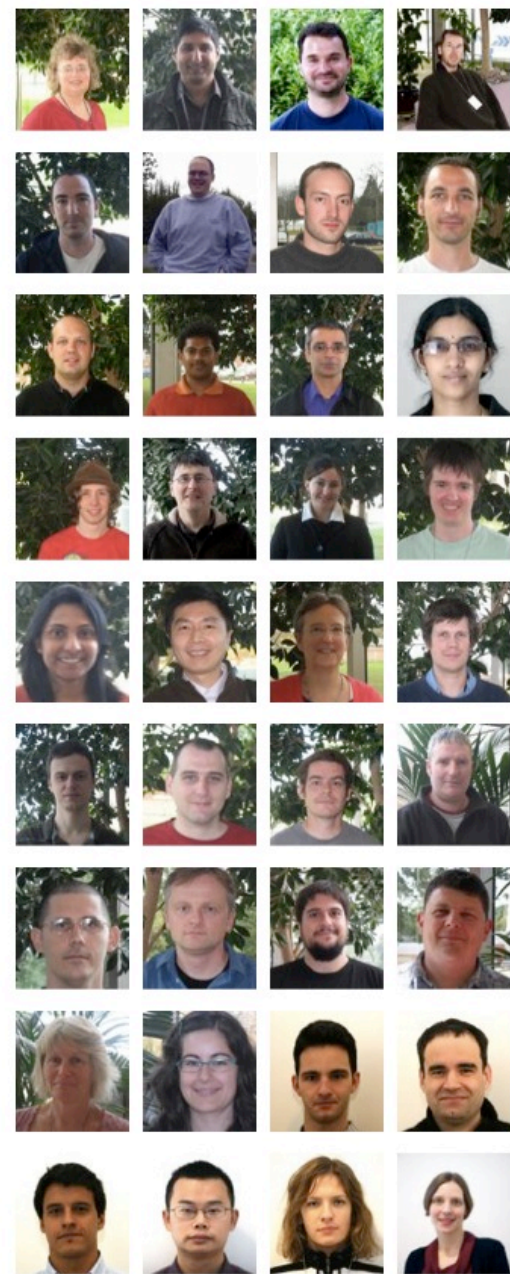
| Type                                     | Database          | Identifier                    | Description                       |
|--|-------------------|-------------------------------|-----------------------------------|
| identical object in an external resource | chembl            | <a href="#">CHEMBL2095168</a> |                                   |
|  | evidence ontology | ECO:0000353                   |                                   |
| biological process                       | gene ontology     | <a href="#">GO:0006788</a>    | heme oxidation                    |
| biological process                       | gene ontology     | <a href="#">GO:0010942</a>    | positive regulation of cell death |
| biological process                       | gene ontology     | <a href="#">GO:0015670</a>    | carbon dioxide transport          |
| biological process                       | gene ontology     | <a href="#">GO:0015671</a>    | oxygen transport                  |
| biological process                       | gene ontology     | <a href="#">GO:0030185</a>    | nitric oxide transport            |
| cellular component                       | gene ontology     | <a href="#">GO:0005833</a>    | hemoglobin complex                |

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**If the Human Genome Project had not followed an open data release policy, what would we be searching our spectra against today?**

