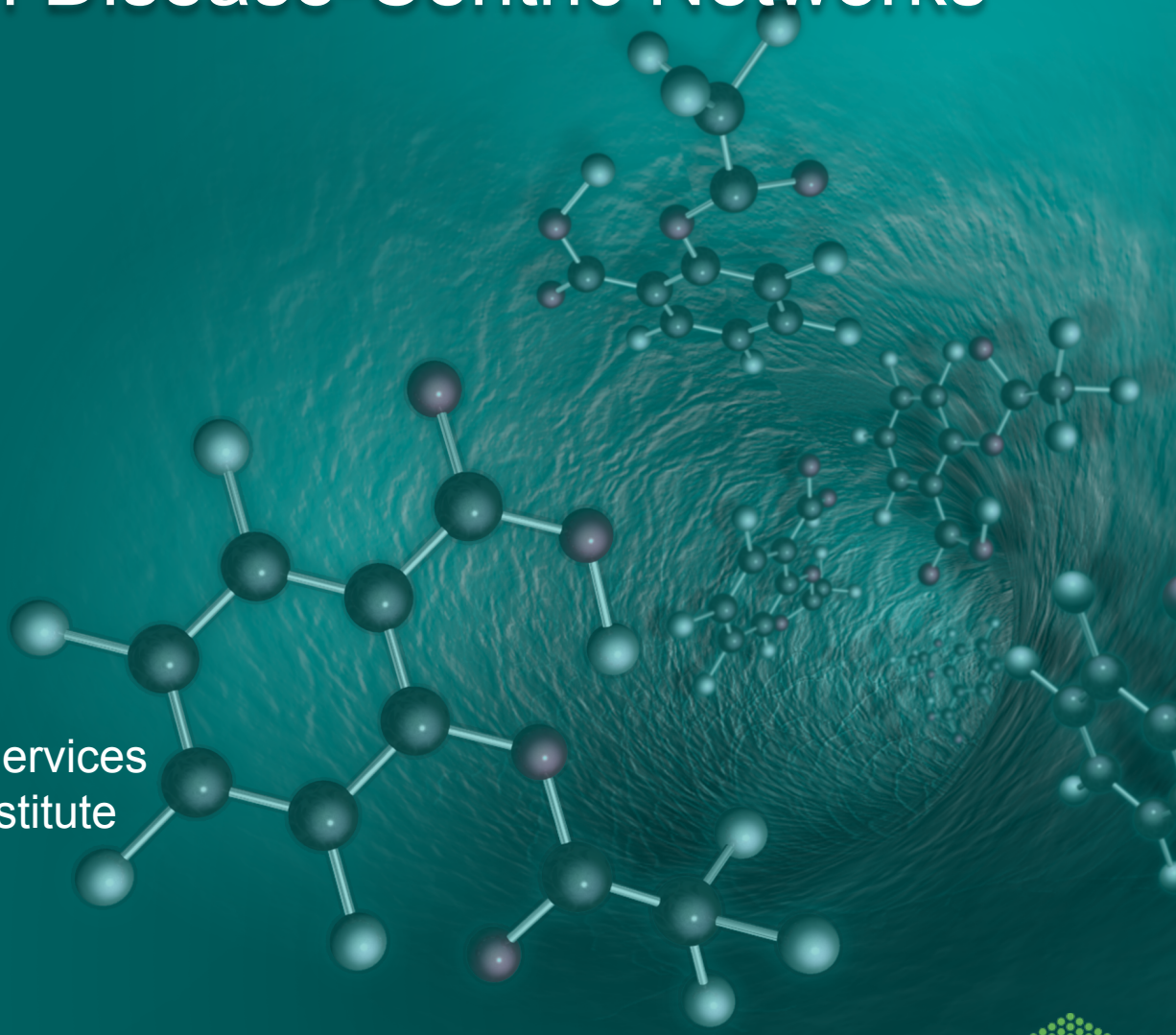
IntAct
High Resolution Disease-Centric Networks



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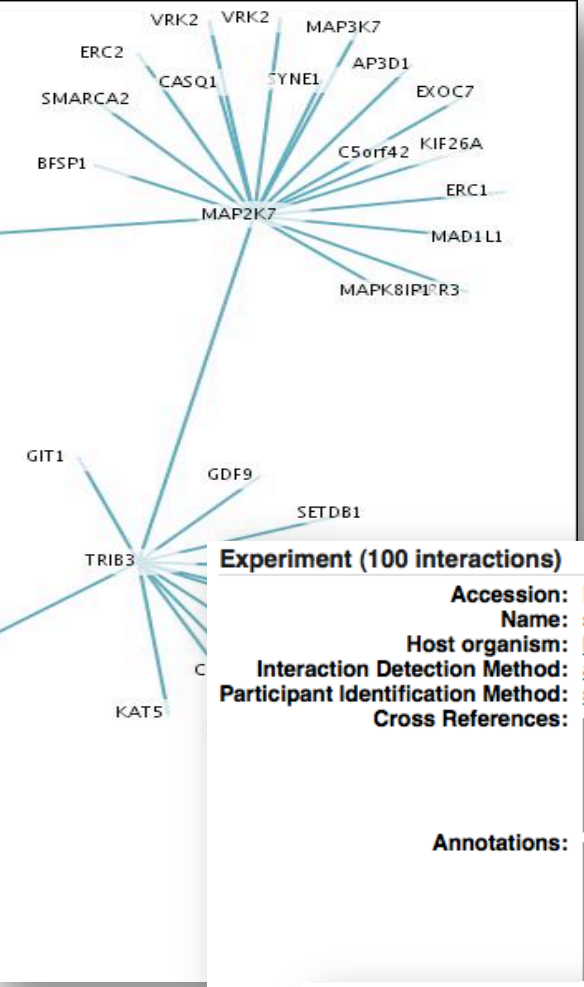
EMBL-EBI



- 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:

imex	IM-12079	-	imex-primary
pubmed	19615732	-	primary-reference
newt	9606	human	target-species

Annotations:

curation request	Harper Wade: 28th Oct 2009, Department of Pathology, Harvard Medical School, 77 Avenue Louis Pasteur, NRB 940, Boston, MA 02115
confidence-mapping	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

POSITIONAL FEATURES

1 70 140 210 280 350 420 490 560 630 700 770

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

www.ebi.ac.uk/intact

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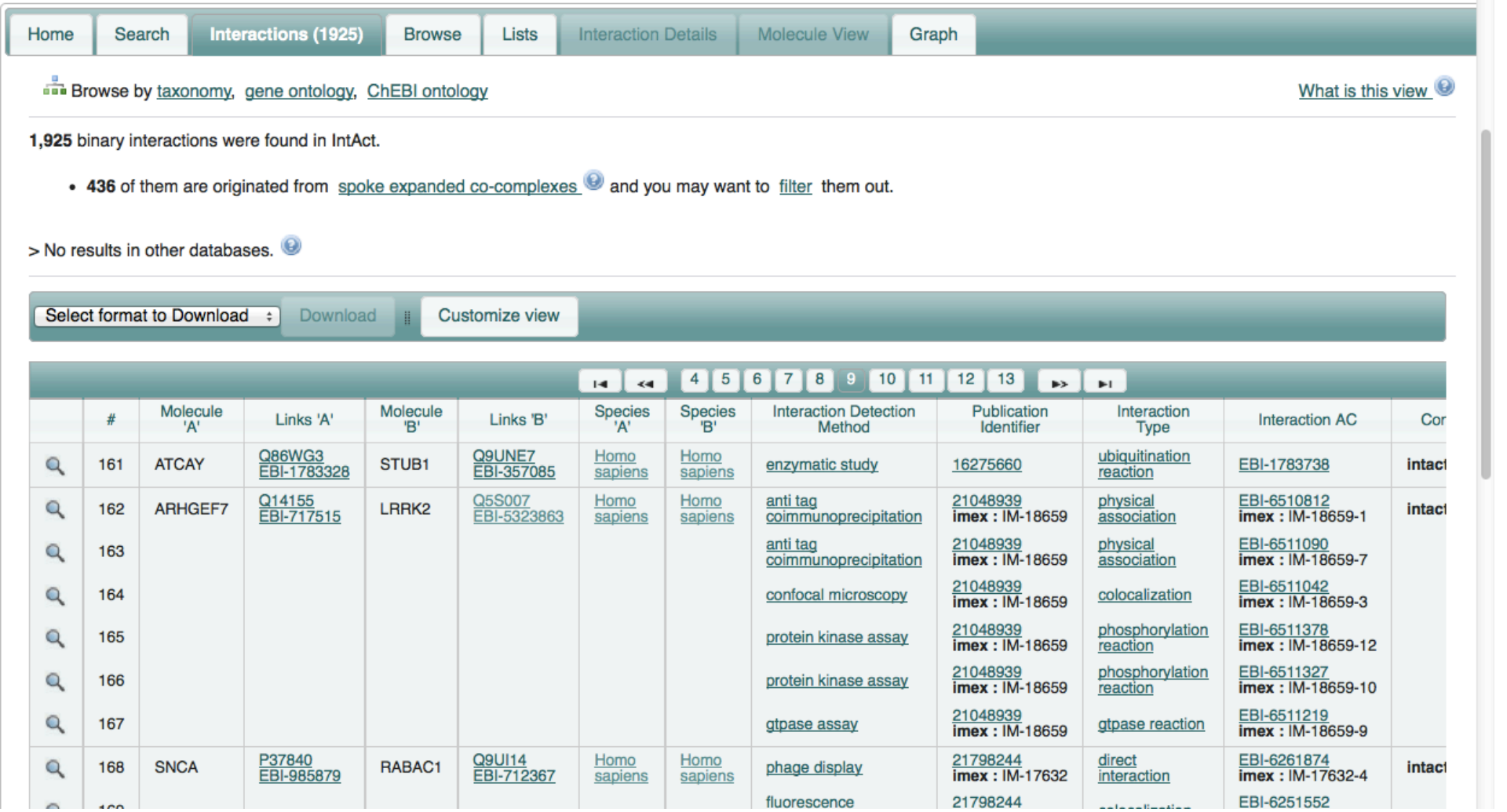
Tabular view



Home | Search | Interactions (1925) | Browse | Lists | Interaction Details | Molecule View | Graph

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

4 5 6 7 8 9 10 11 12 13

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

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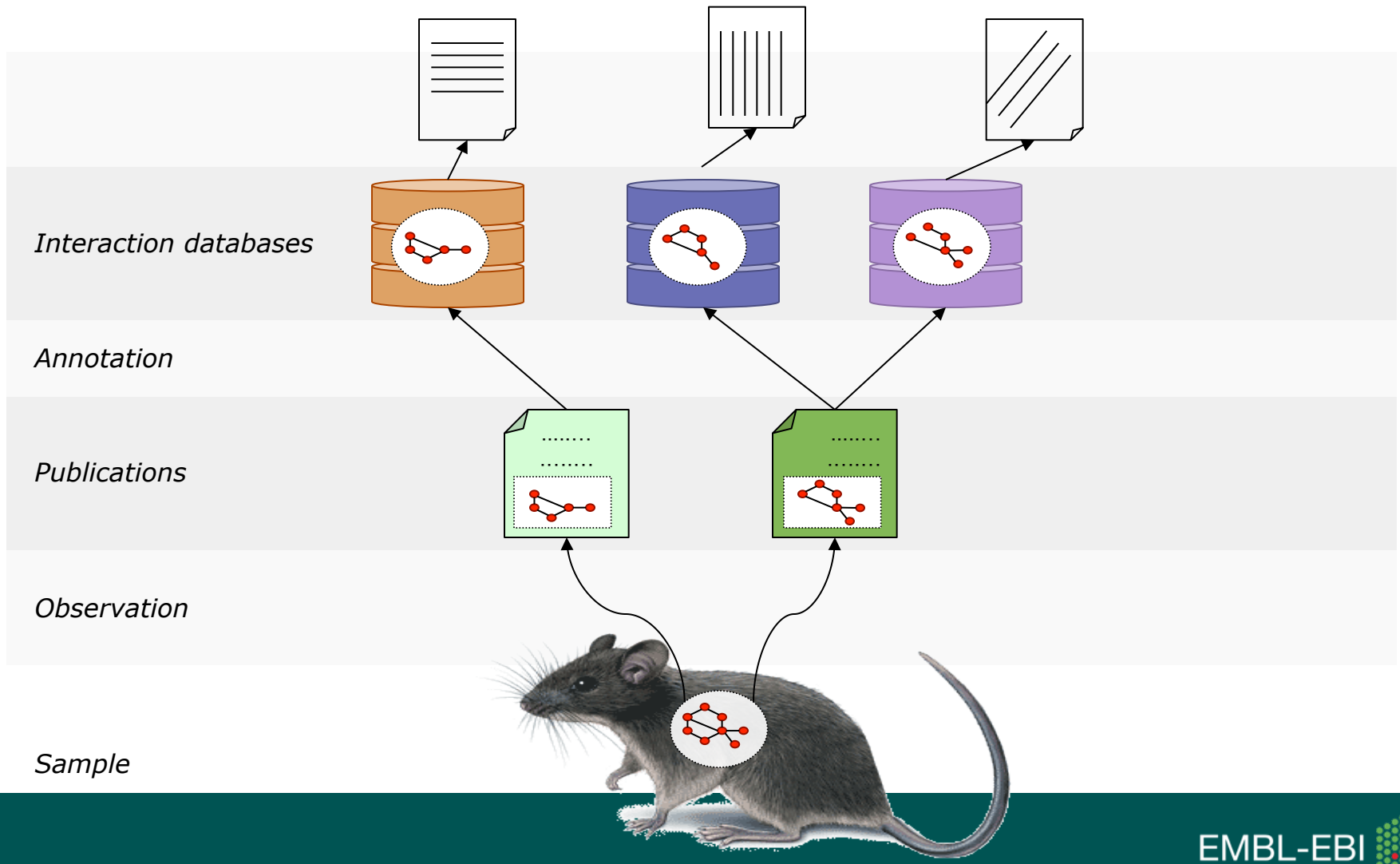
Detailed Sequence view

- LRRK2_human in IntAct molecule view
- http://www.ebi.ac.uk/intact/molecule/EBI-5323863

Molecular Interactions 2002



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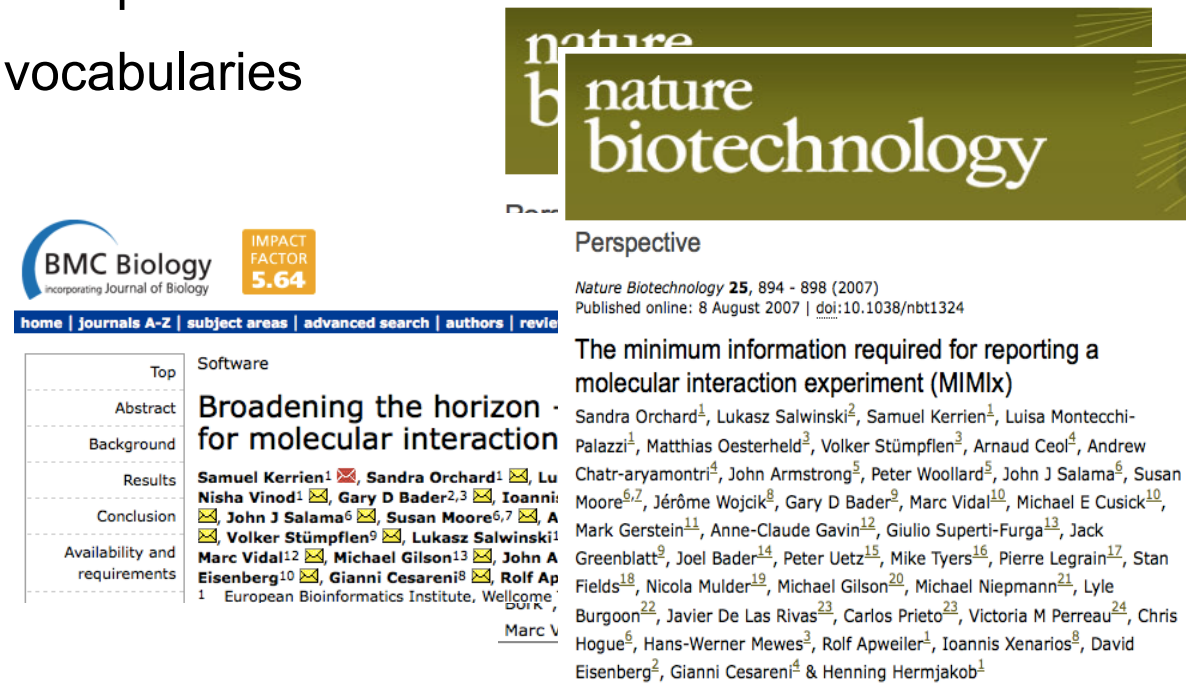
PSI-MI

- 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)



www.psidev.info/MI

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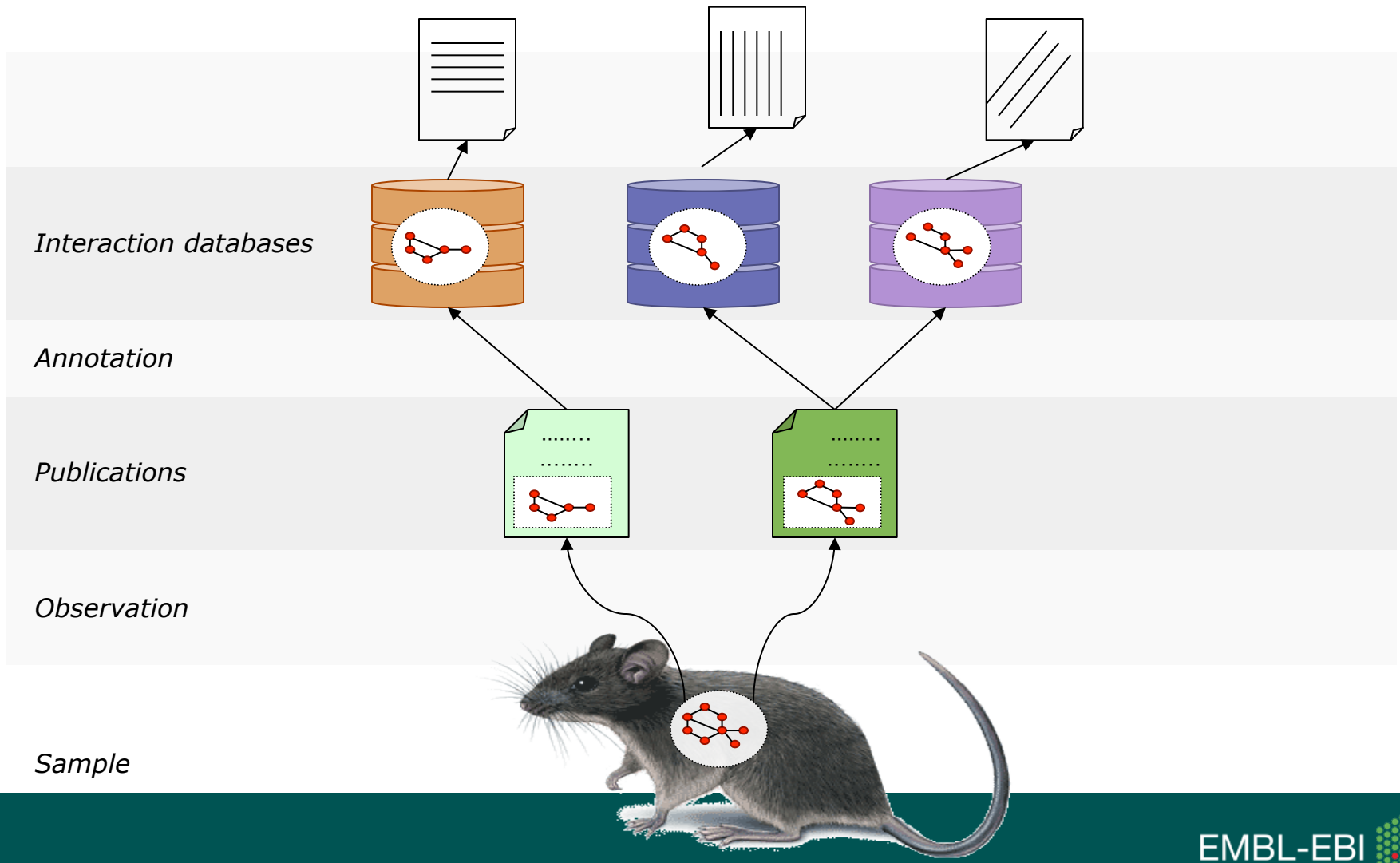
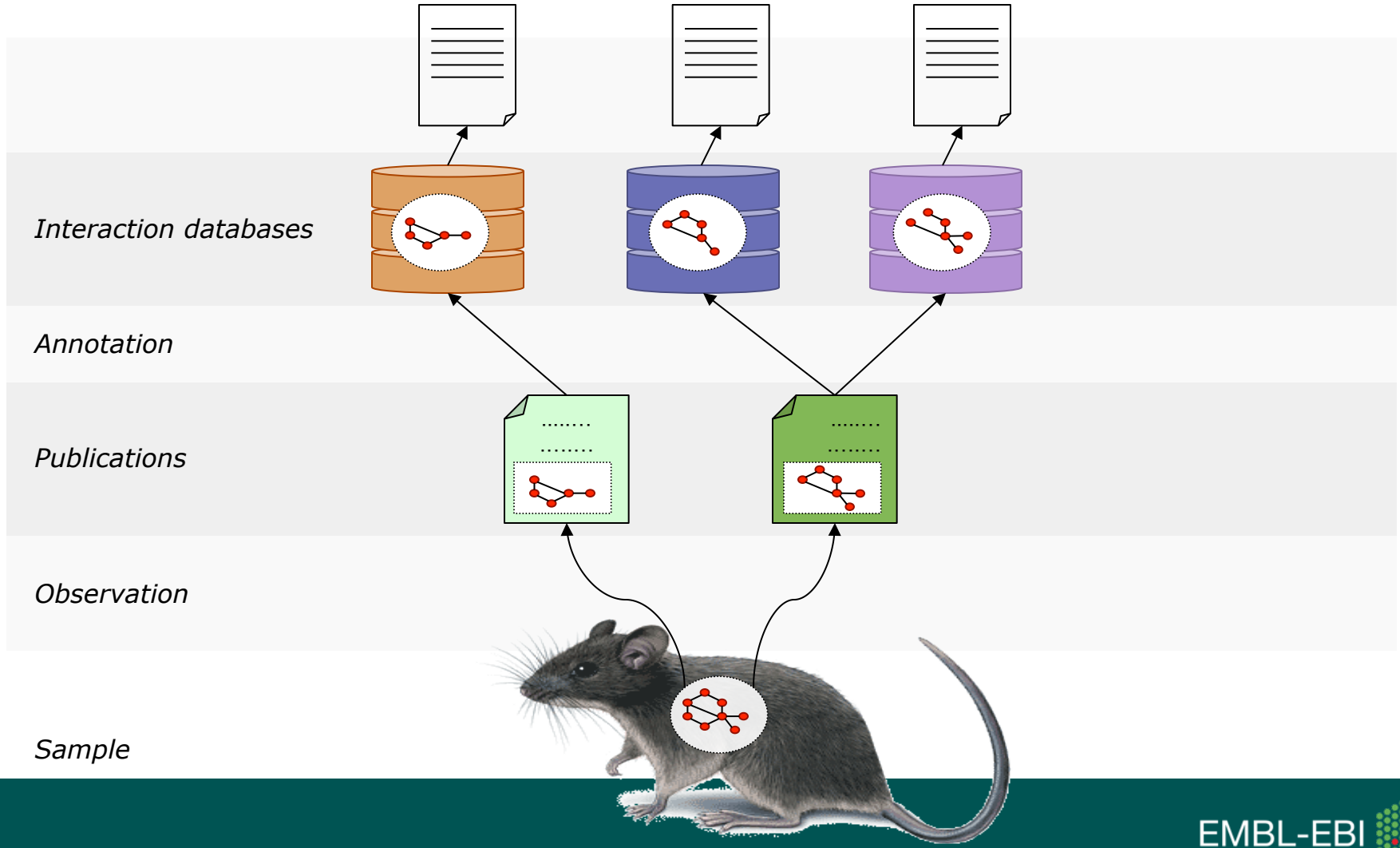
PSI-MI


Interaction databases
Annotation
Publications
Observation
Sample

PSI-MI


Interaction databases
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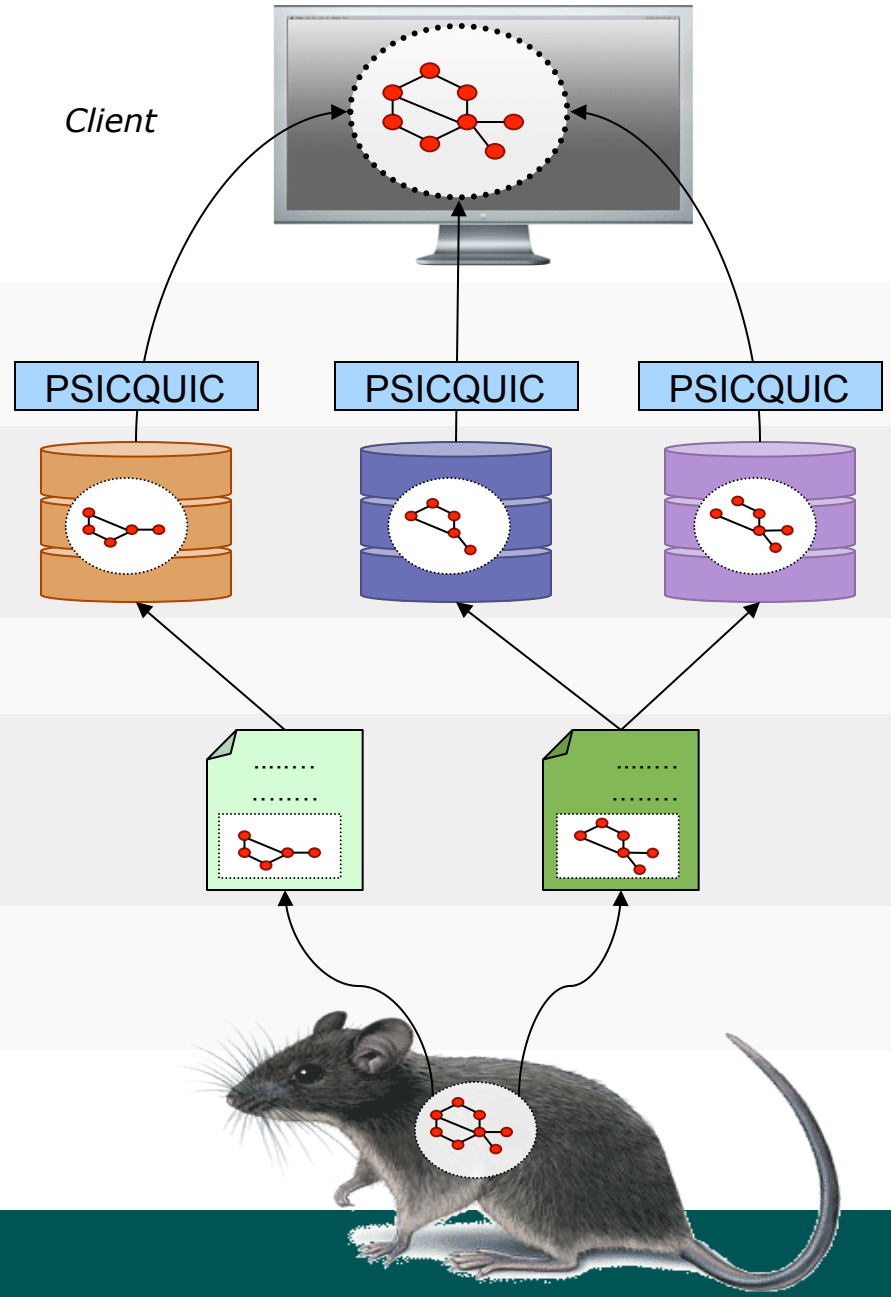
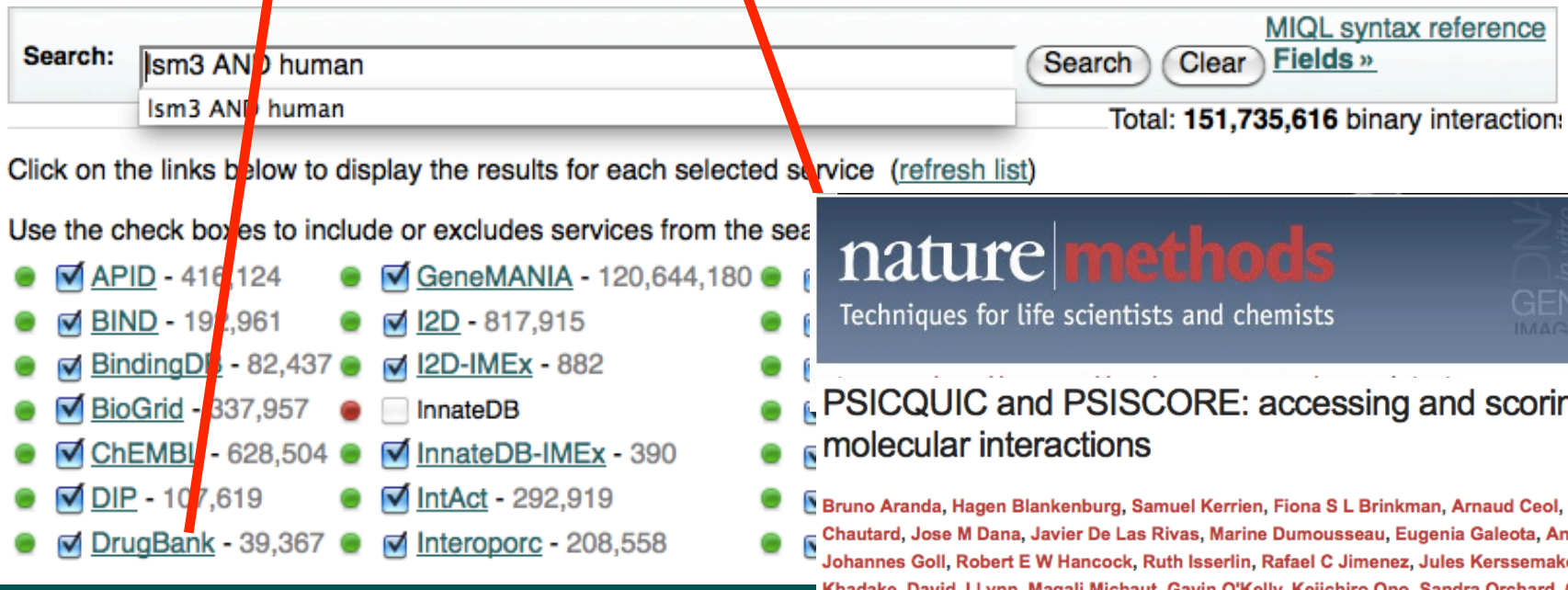
Sample


Client
PSICQUIC servers
PSICQUIC
PSICQUIC
PSICQUIC
Interaction databases
Annotation
Publications
Observation
Sample

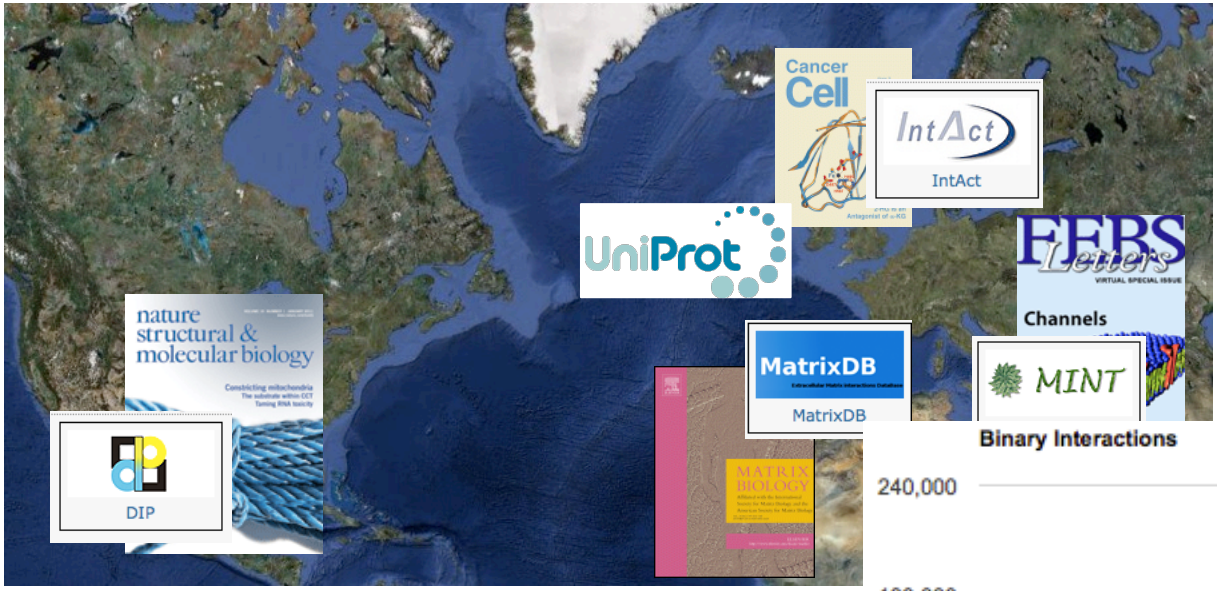
The PSI Common Query Interface: PSICQUIC

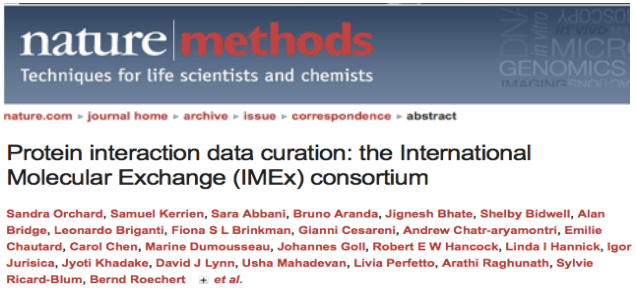
- Common computational interface for querying molecular interaction databases
  - Not limited to protein-protein interactions, also e.g.
    - Drug-target interactions
    - Simplified pathway data



http://www.ebi.ac.uk/Tools/webservices/psicquic/view/

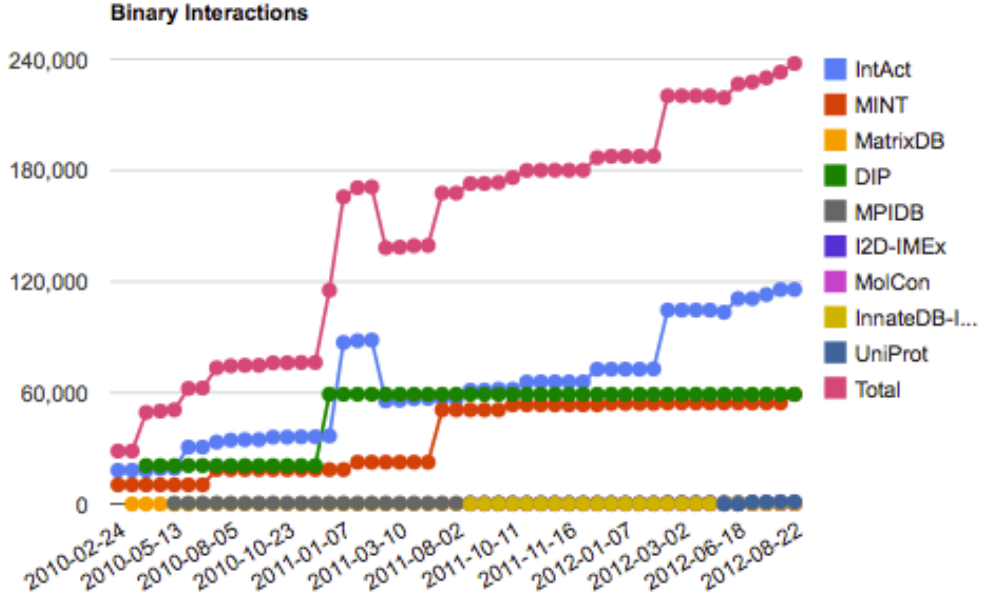
The International Molecular Exchange Consortium (IMEx)





- Non-redundant curation
- Common curation standards

- EU CA PSIMEx grant 2009-2014
- In production since 2/2010



http://www.imexconsortium.org/

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Community collaboration

IntAct

Genome Biology IMPACT FACTOR 6.63

Search *Genome Biology* for

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Conclusion
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The Plant Cell, Vol. 22: 997–1005, April 2010, www.plantcell.org © 2010 American Society of Plant Biologists

PERSPECTIVE
Special Series on Large-Scale Biology

THE PLANT CELL

Mappin
Predict

Research Article

A domain level interaction network of amyloid precursor protein and Aβ of Alzheimer's disease

KiYoung Lee
[a] Department
[b] Departments
[c] European Mo

Victoria M. Perreau[1,2,3,*], Sandra Orchard[4],
Paul A. Ad
Roberto Ca
Tiffany F. C
James A. D
G. Faux[3],
Simon A. J
Mok[3,7], De
White[2,7], A
Hermjakob

Issue

Most cellular proteome. The article informs they can be u set as an exan our efforts to locations.

Article first

nature
International weekly journal of science

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Archive > Volume 480 > Issue 7376 > Articles > Article

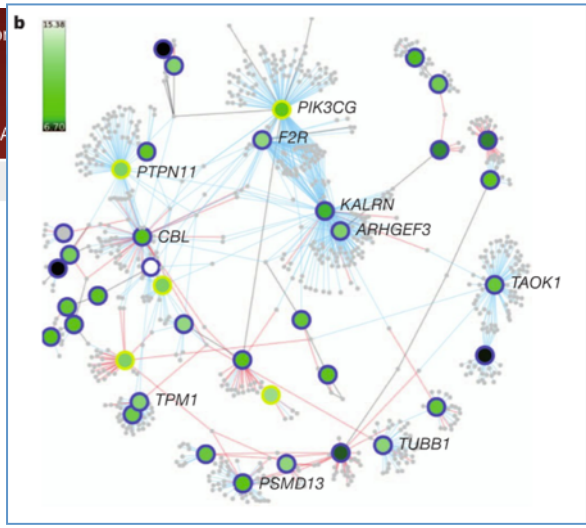
NATURE | ARTICLE

◂ previous article next article ▸

New gene functions in megakaryopoiesis and platelet formation

Jovana Serbanovic-Canic, Ulrich Elling, Alison H. Goodall, Yann Labrune, 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 Ellinghaus, 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, Bev
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 Falchi, 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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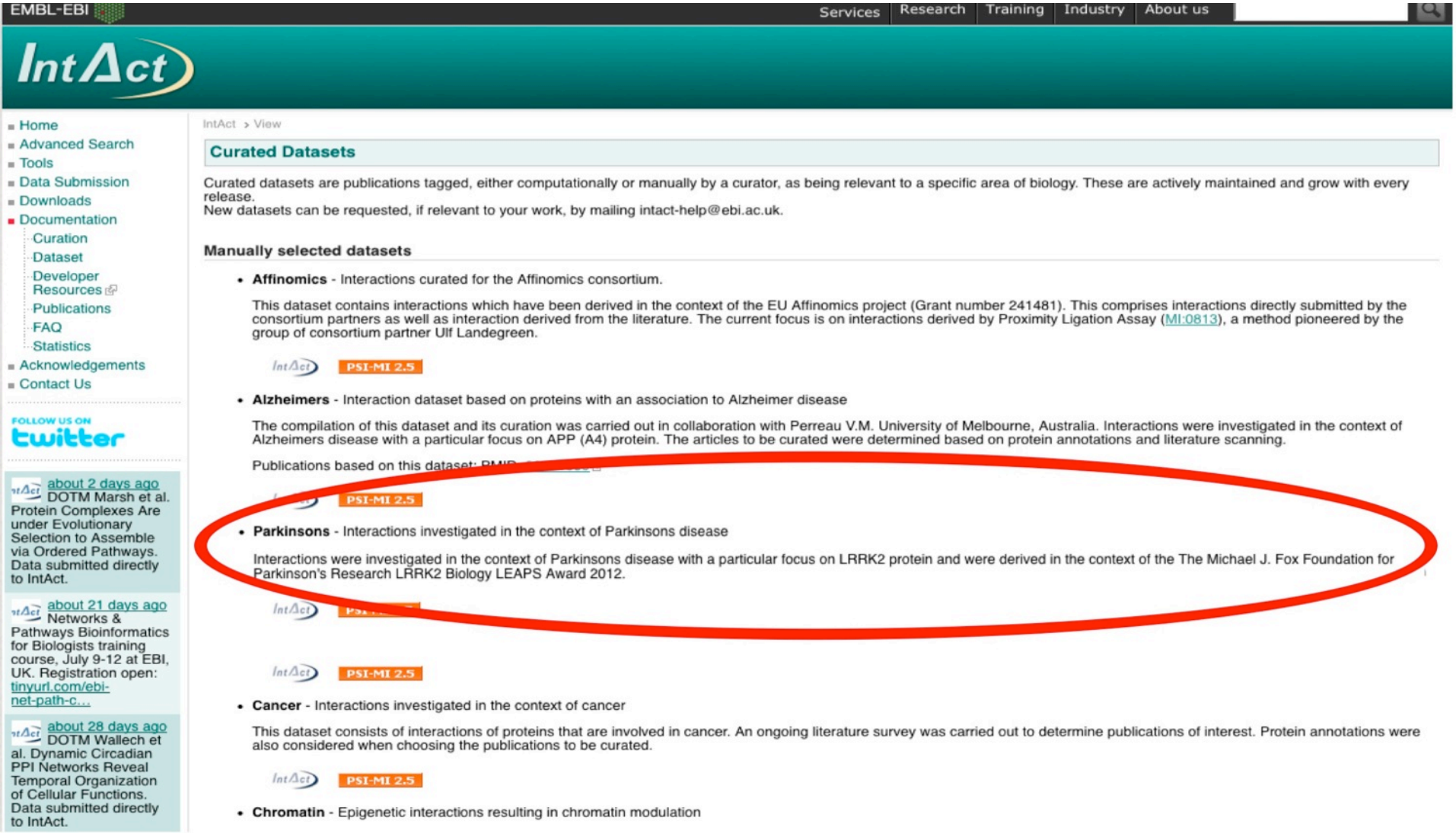
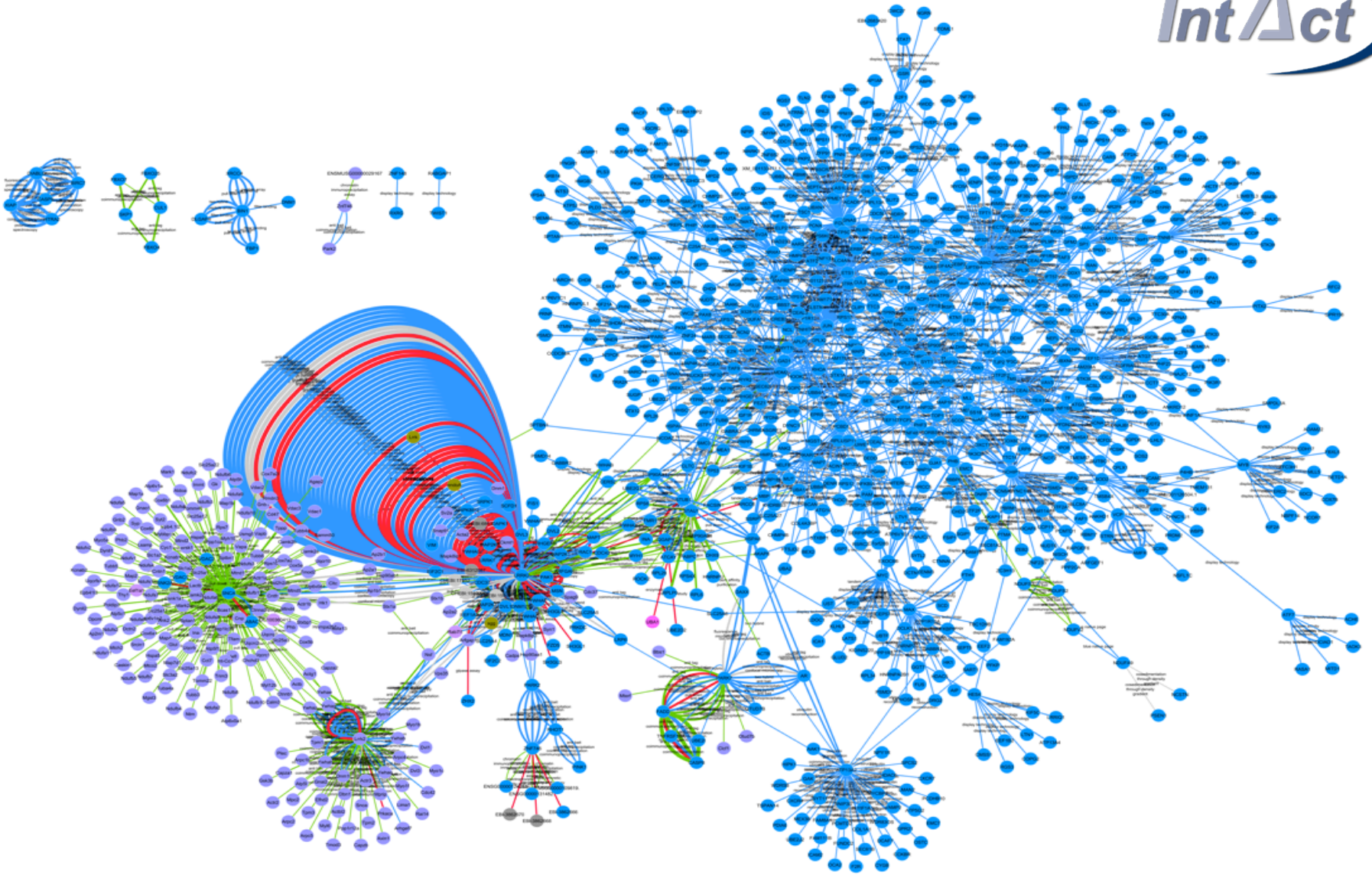
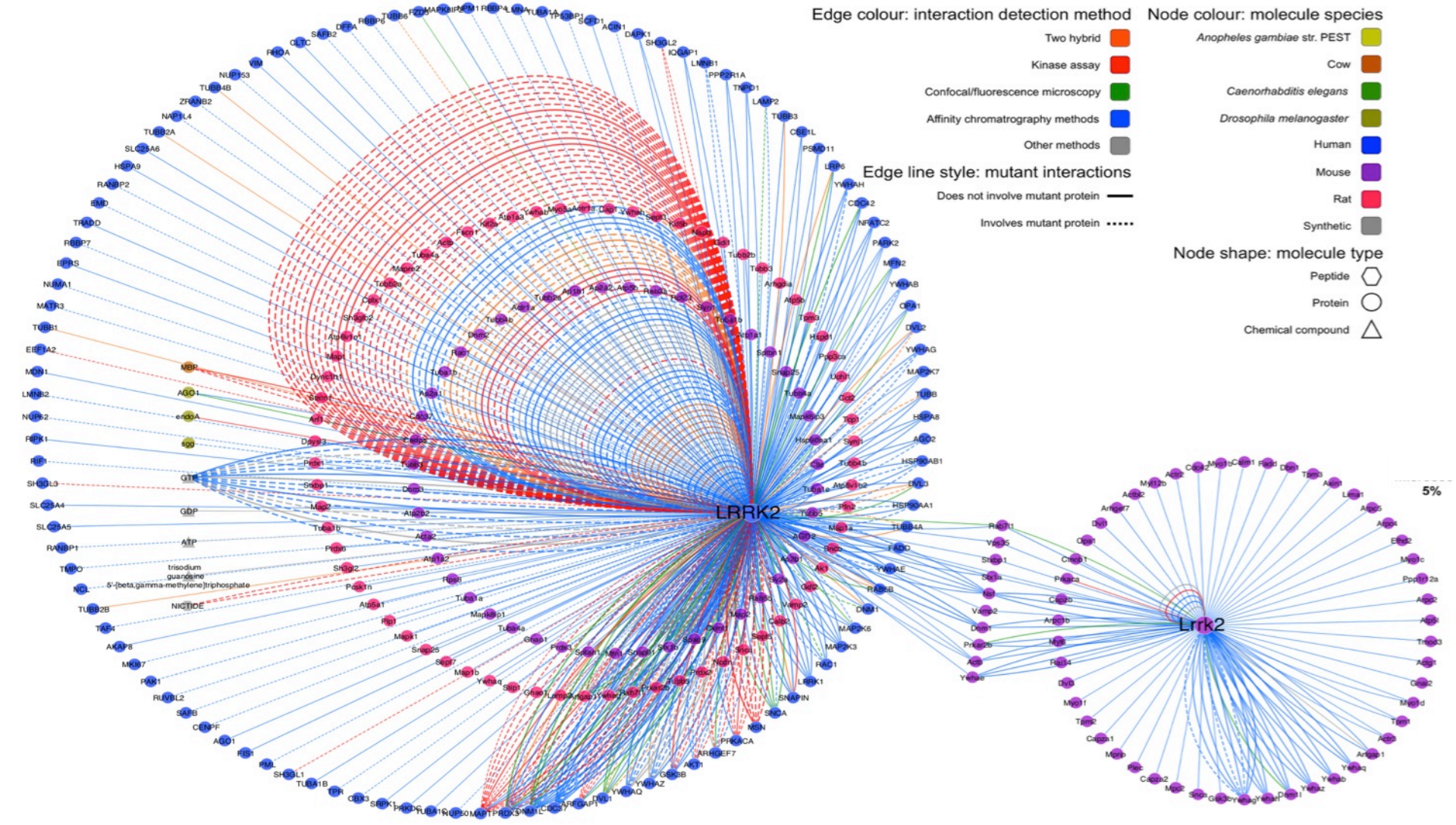


The LRRK2 Interactome

- 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



Porras et al, submitted

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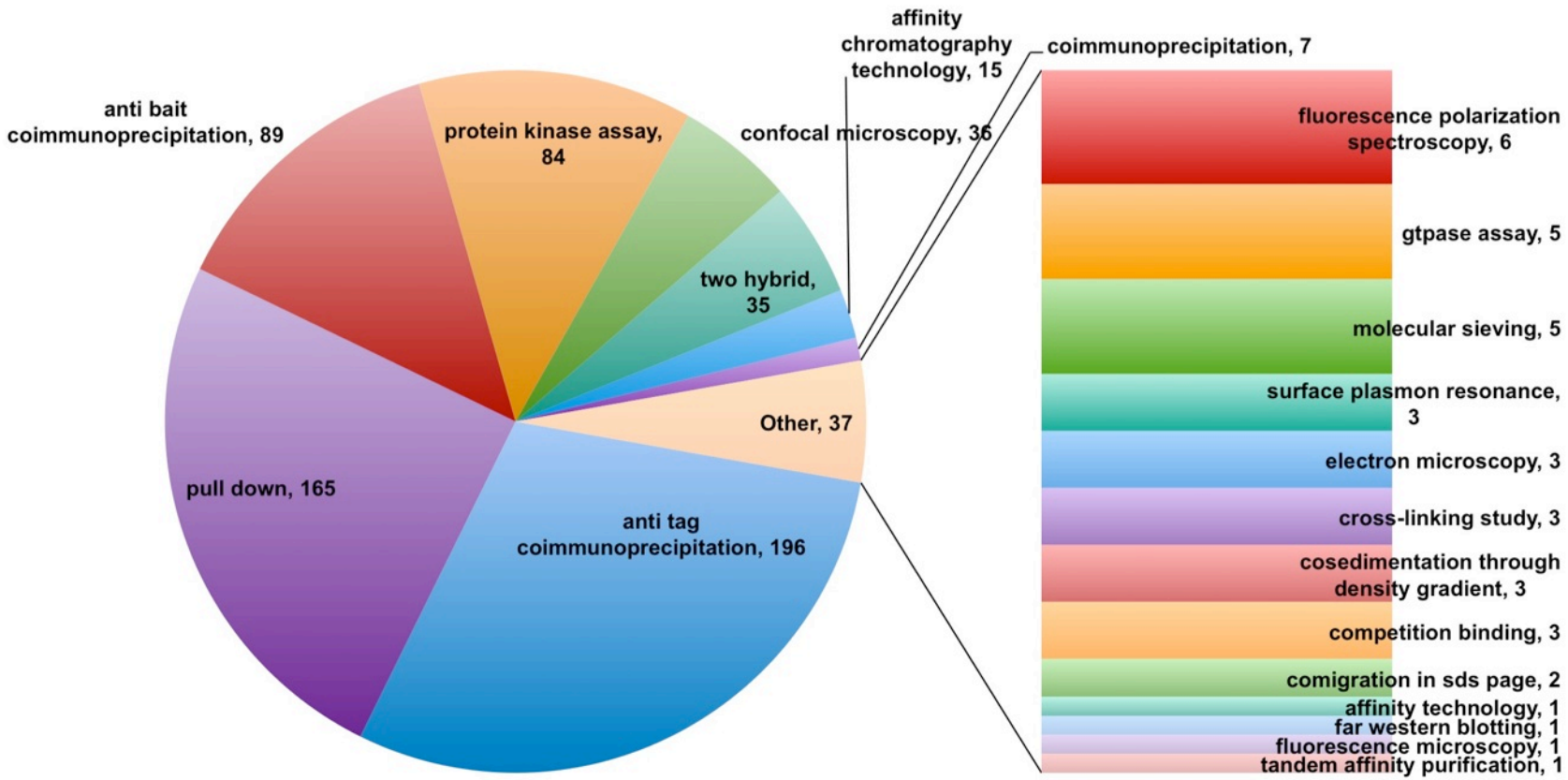
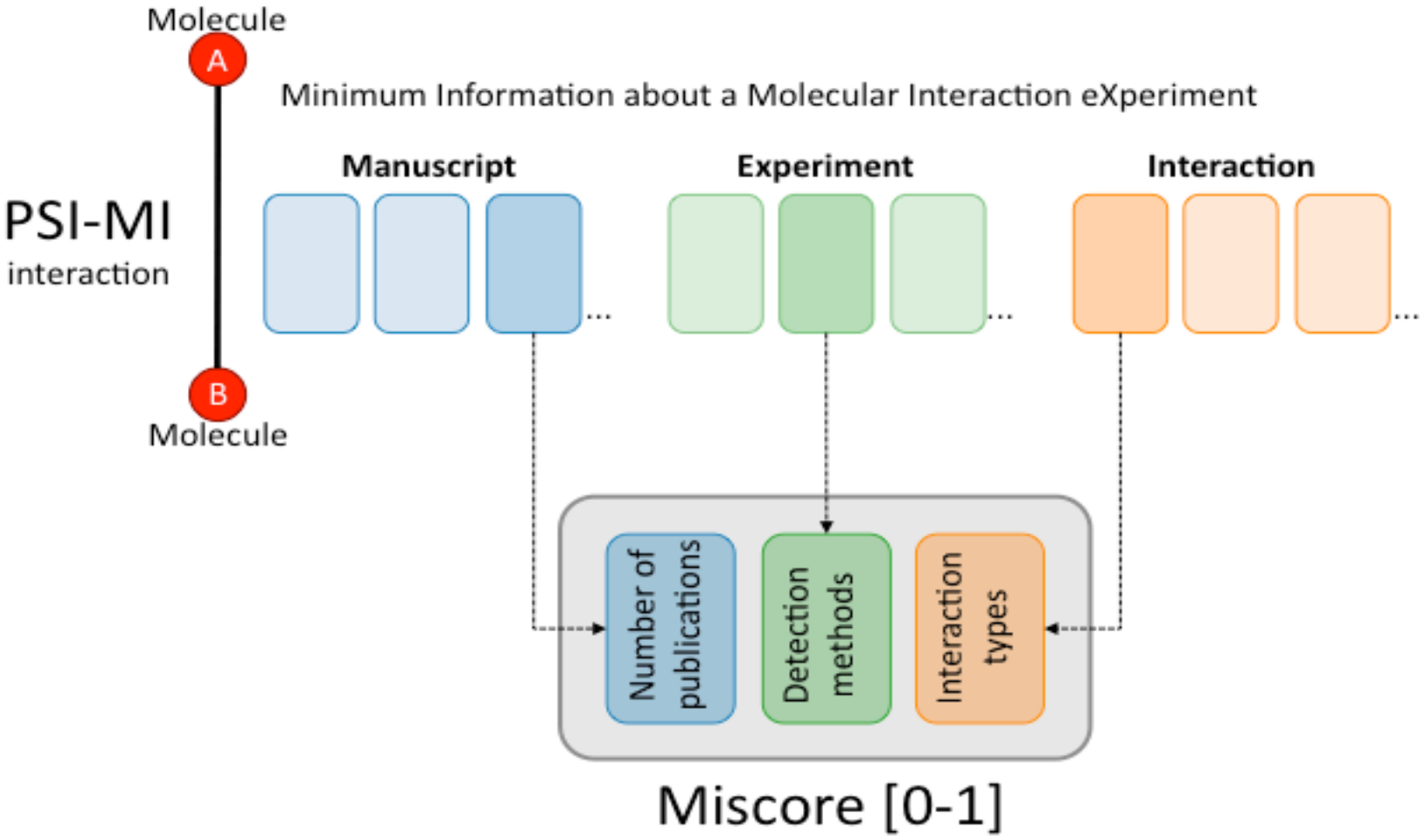
Interaction Detection Methods

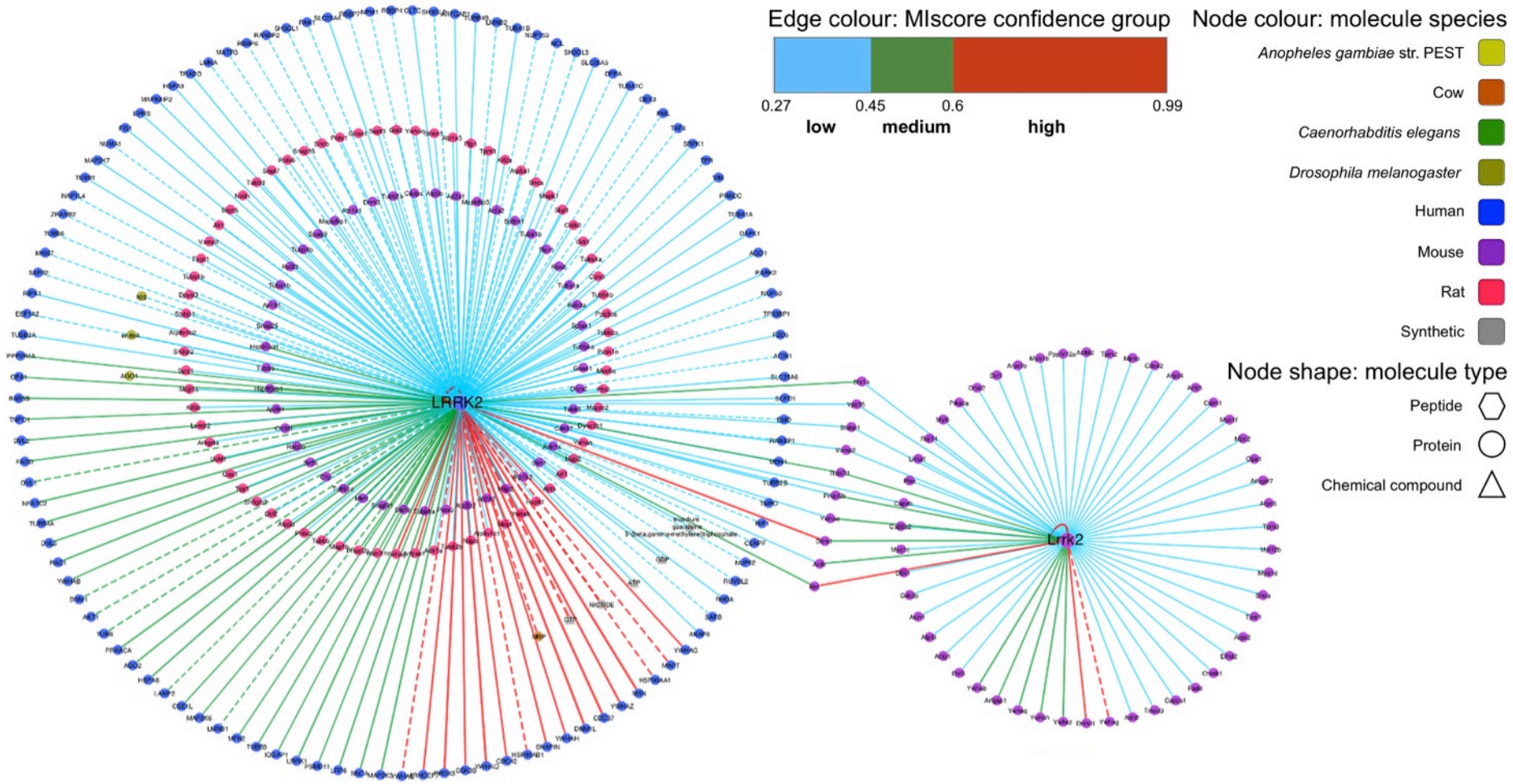


Miscore – Evidence scoring



Villaveces et al, submitted

Evidence Merge and Scoring



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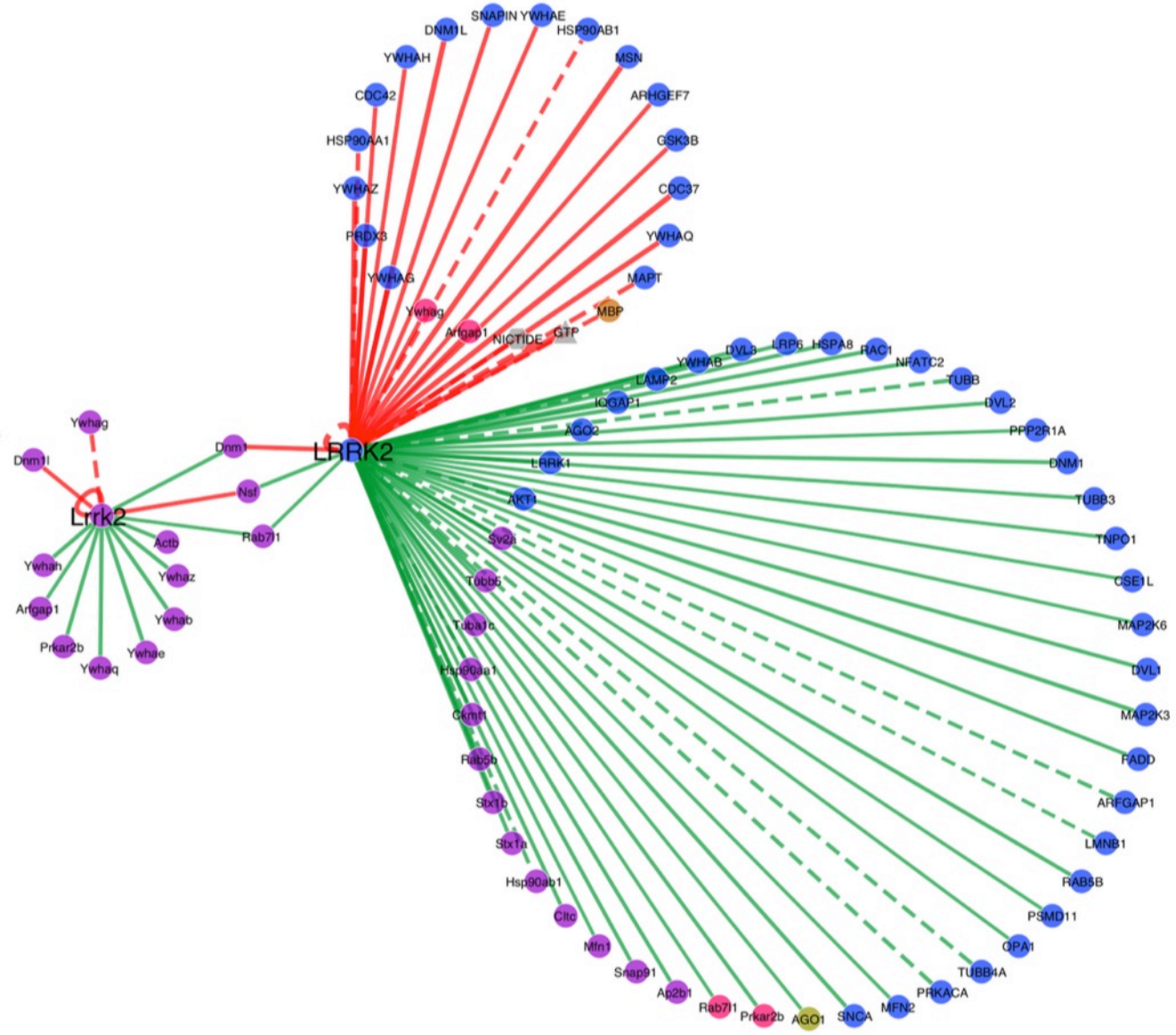
High confidence subnetwork



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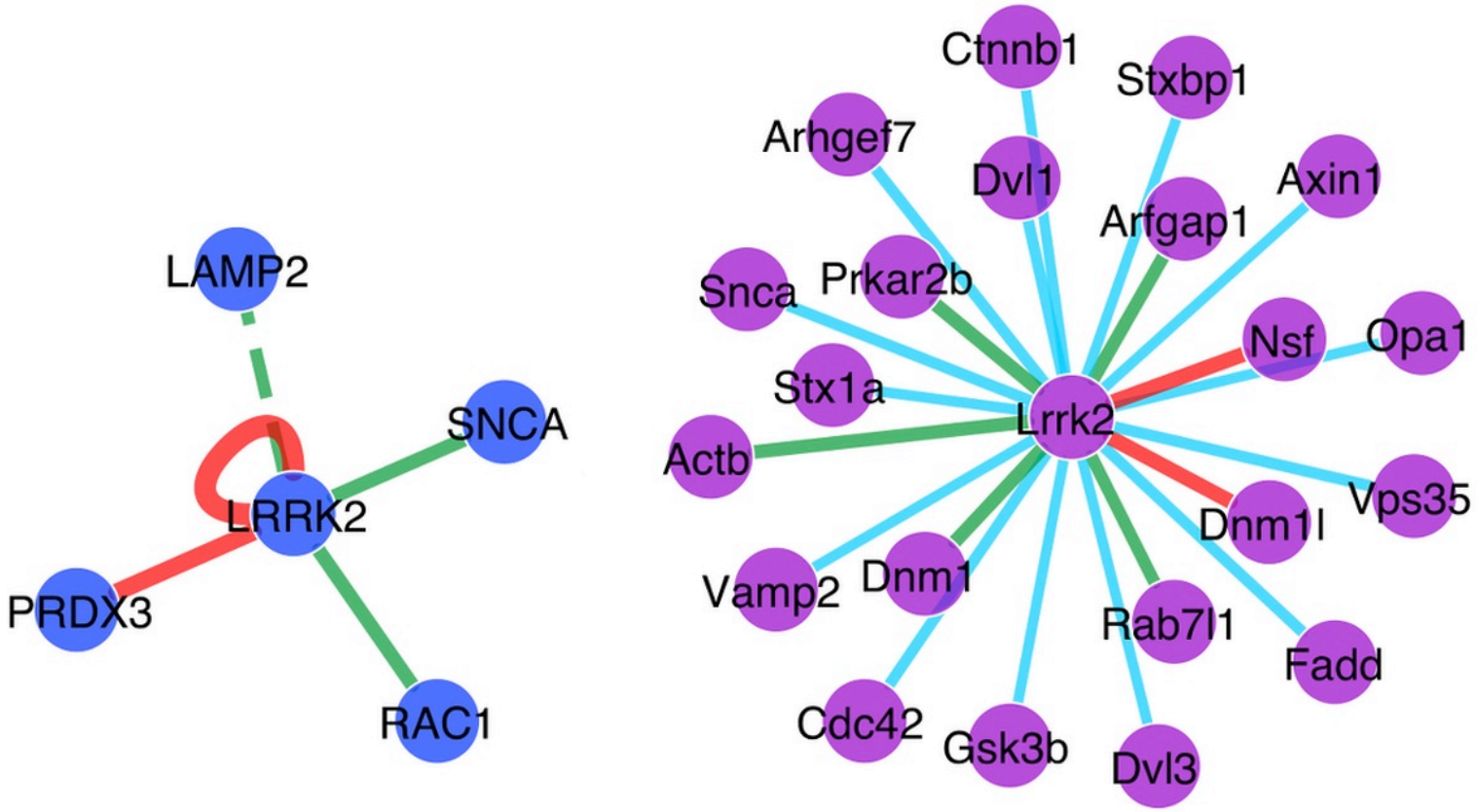
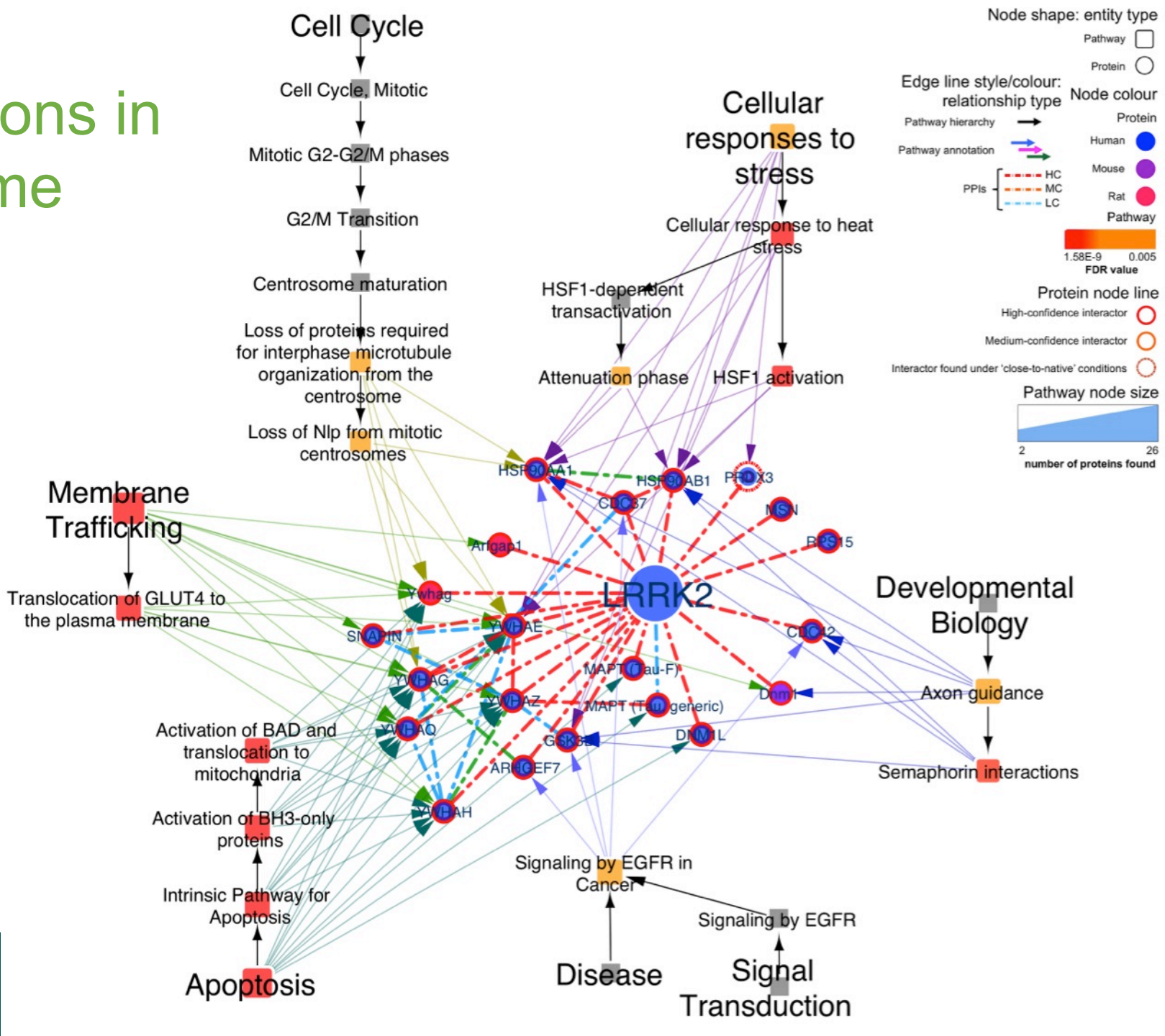
The LRRK2 Interactome – Native conditions



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/

Meldal et al, submitted

Complex Portal

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

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 CO2 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 Fe2+ or Fe3+ ion. Oxygen only binds to Fe2+ ions, not Fe3+ ions. CO2 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

Please send annotation suggestions!

Hemoglobin HbA complex

Species: Homo sapiens; 9606
Accession number: EBI-9008420

Participants

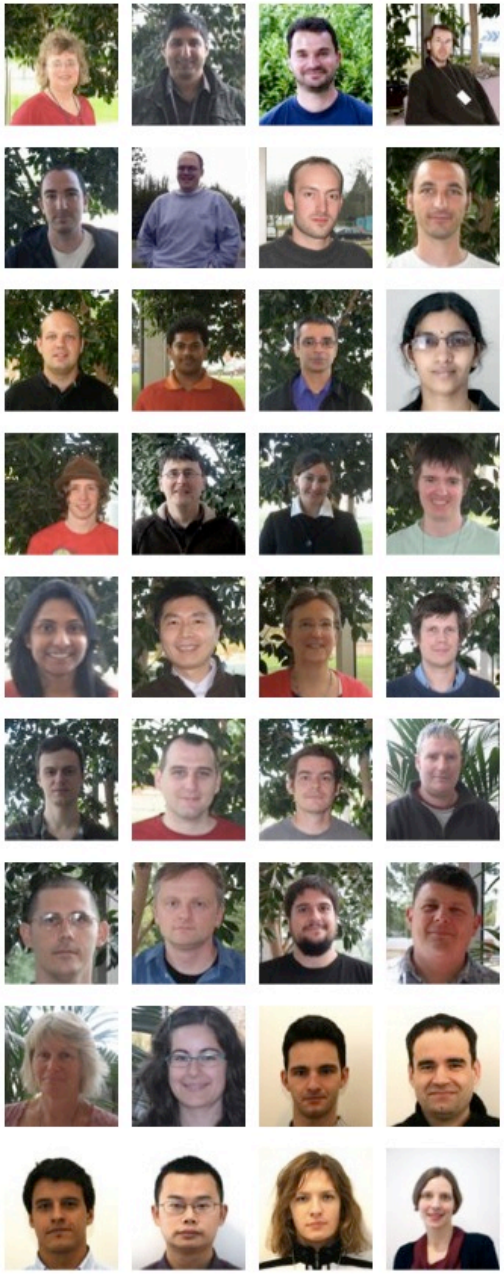
ID	Name	Description	Stochiometry	Biological Role	Interactor Type	Linked Features	Other Features
P69905 EBI-714680	HBA1	Hemoglobin subunit alpha	2	unspecified role	protein	binding-associated region CHEBI:30413 [?-?] binding-associated region P68871 [?-?]	
P68871 EBI-715554	HBB	Hemoglobin subunit beta	2	unspecified role	protein	binding-associated region CHEBI:30413 [?-?] binding-associated region P69905 [?-?]	
CHEBI:30413 EBI-6880399	heme	heme	4	cofactor	small molecule	binding-associated region P69905 [?-?] binding-associated region P68871 [?-?]	

Cross References

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

Acknowledgements

- PSIMEx partners, particularly:
  - Gianni Cesareni, U Tor Vergata, Rome
  - Lukasz Salvinski, UCLA
  - Johannes Goll, JCVI
  - Silvie Ricard-Blum, U Lyon
  - Ioannis Xenarios, UniProt
- Editors
  - Mike Dunn, Proteomics
  - Achim Kraus, Proteomics
  - Ralph Bradshaw, MCP
- Funding
  - NHLBI Contract 268201000035C: Proteome Biology of Cardiovascular Disease.
  - NIH Reactome P41 HG003751
  - EU FW7 PSIMEx
  - EU FW7 AgedBrainSysBio
  - BBSRC MIDAS BB/L024179/1
- IntAct team
  - Sandra Orchard
  - Marine Dumousseau
  - Oscar Forner Martinez
  - Margaret Duesbury
  - Birgit Meldal
  - Pablo Porras Milan
  - (Rafael Jimenez)
- MPI Martinsried
  - Bianca Haberman
  - Jose Villaveces
- Reactome team
  - Steve Jupe
  - David Croft
  - Antonio Fabregat
  - Phani Garapati
  - Bijay Jassal
  - Lincoln Stein, OICR
  - Peter D'Eustachio, NYU
  - Robin Haw, OICR
- **All data providers!**



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