

Throwing down the gauntlet...

Bio-Ontologies SIG 2011



If you believe *the hype* around wikis in biology, show us what you can do with ‘wiki’-derived content...

When: July 15-16, 2011 (co-located with ISMB/ECCB)

Where: Vienna, Austria

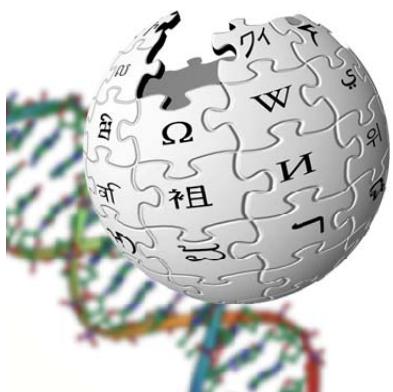
Info: <http://www.bio-ontologies.org.uk>

Organizers: Nigam Shah, Larisa Soldatova, Susie Stephens, Susanna Sansone

The Gene Wiki: Cultivating and mining community intelligence in biology

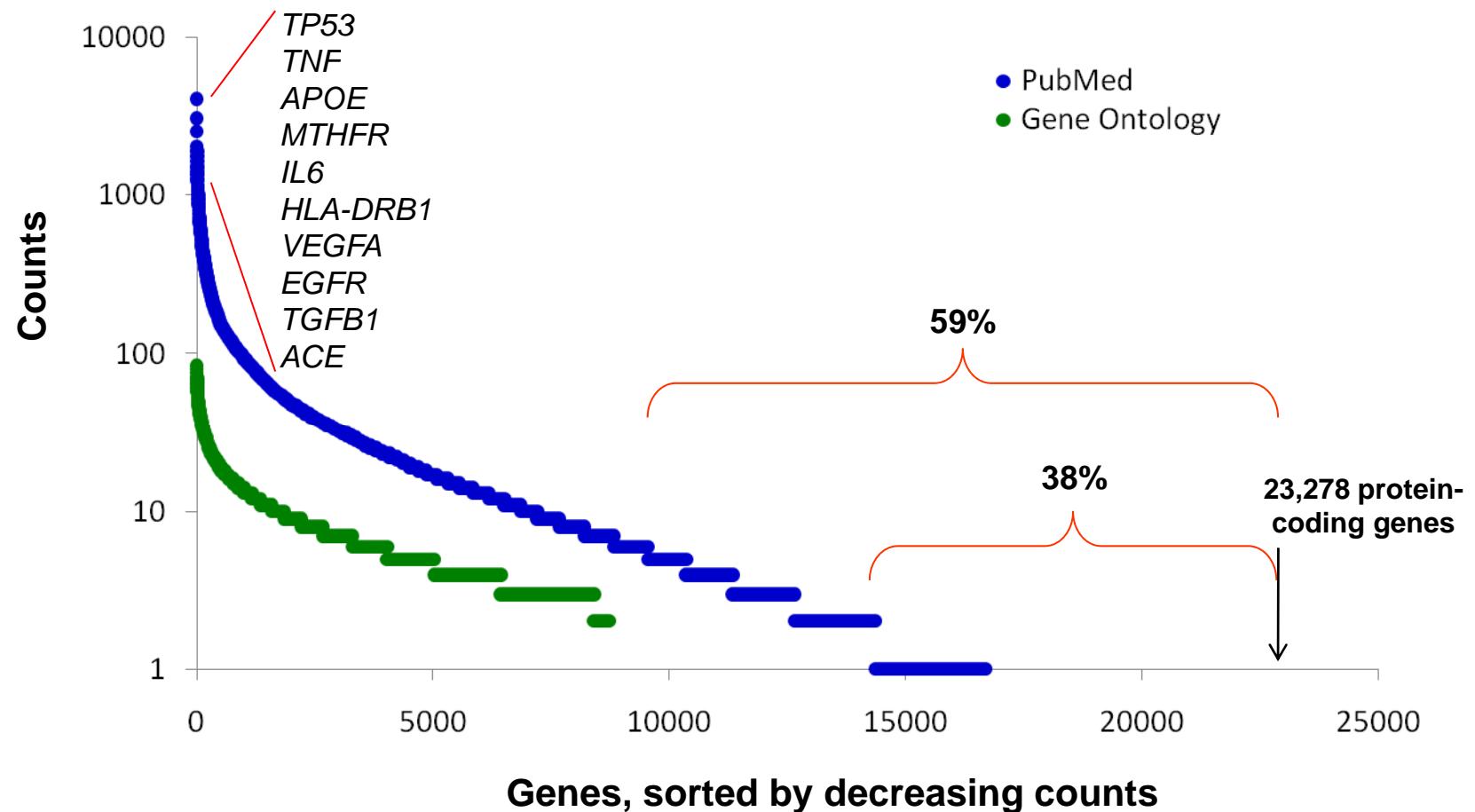
NETTAB 2010
November 30, 2010

Andrew Su

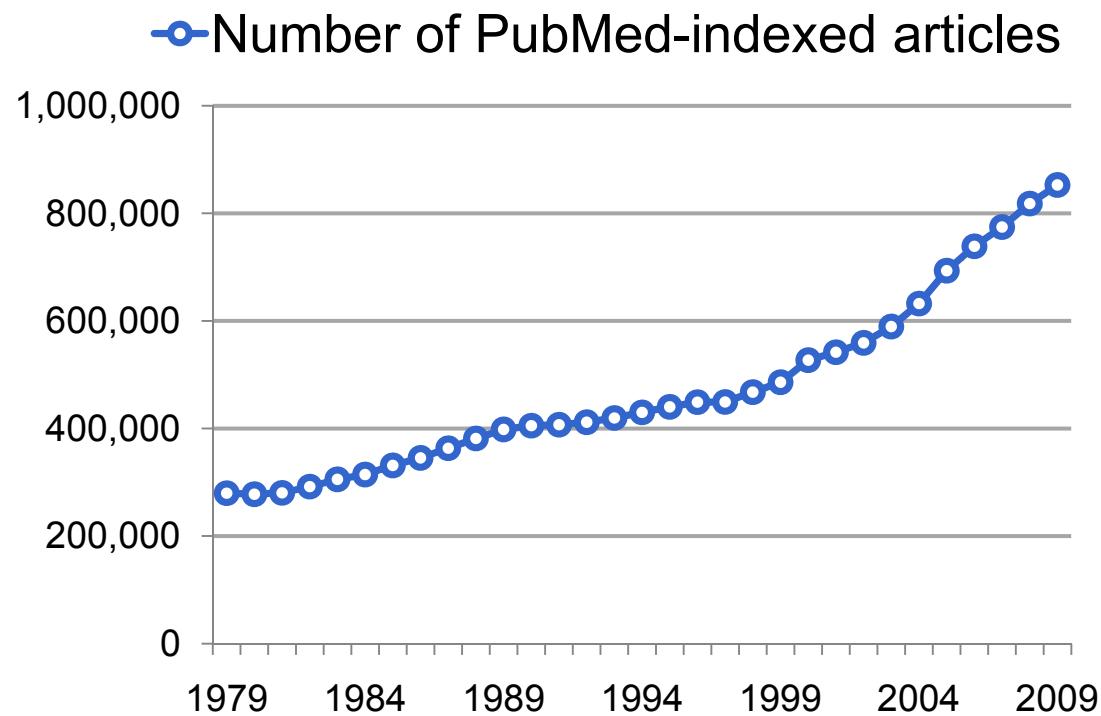


Genomics Institute of the
Novartis Research
Foundation

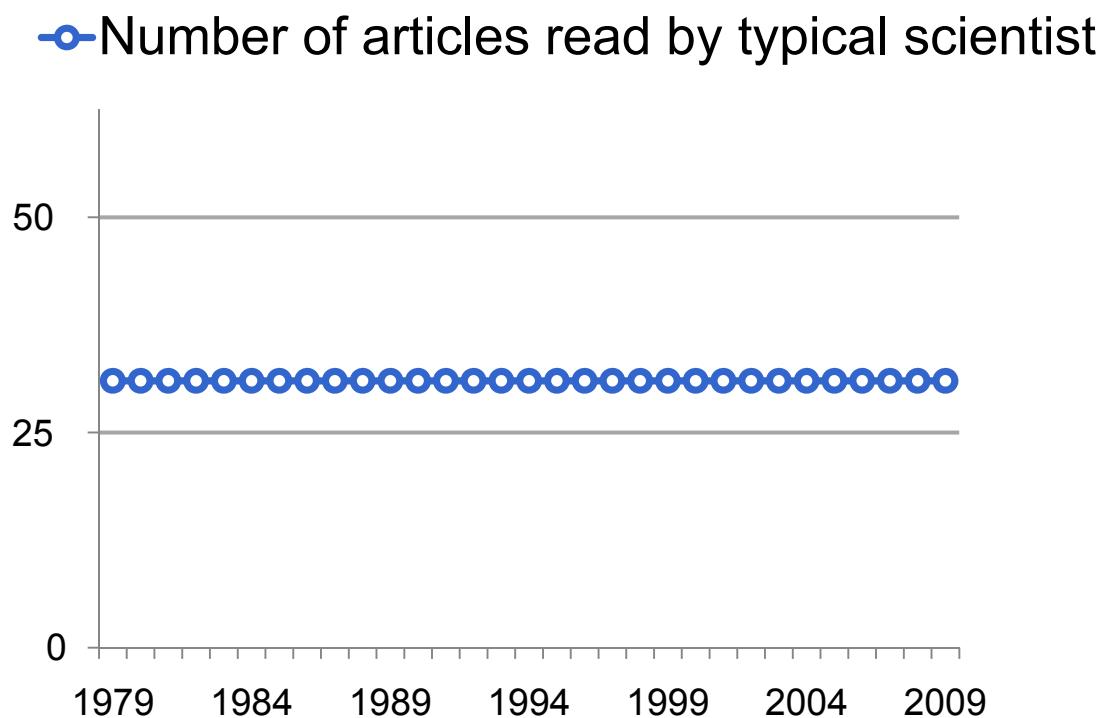
Few genes are well annotated...



... because the literature is sparsely curated?



... because the literature is sparsely curated?





82,063 articles (0.4% of PubMed)
have been cited by GO annotations

FEATURE

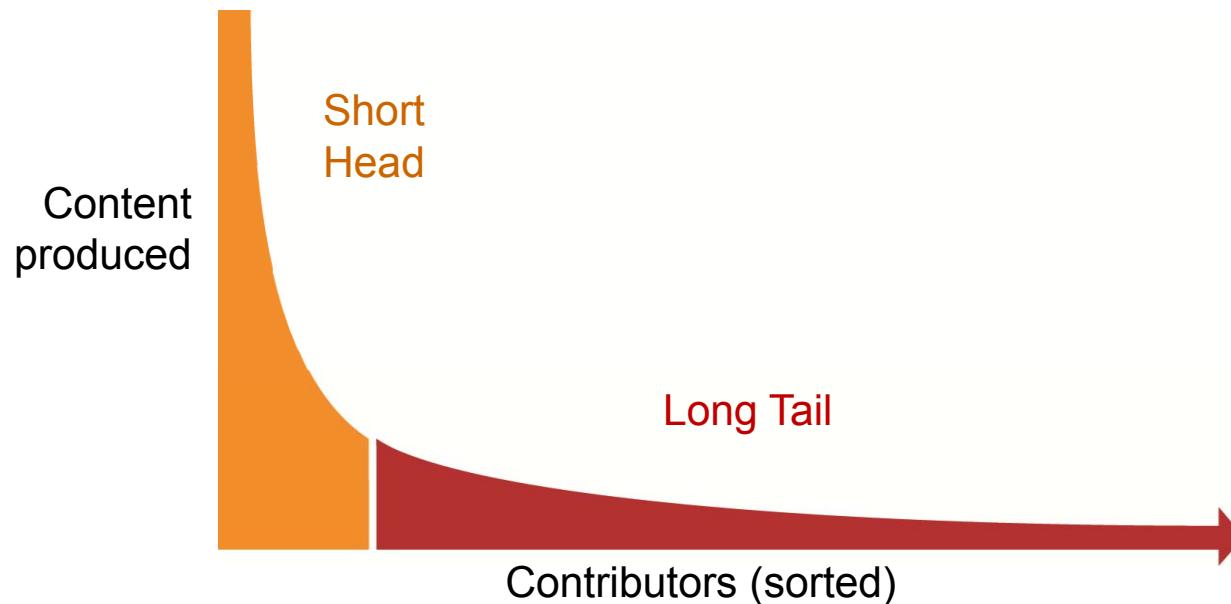
The future of biocuration

To thrive, the field that links biologists and their data urgently needs structure, recognition and support

“Sooner or later, the research community will need to be involved in the annotation effort to scale up to the rate of data generation.



The Long Tail is a prolific source of content



News reporting:	Newspapers	Blogs
Video:	TV/Hollywood	YouTube
Product reviews:	Consumer reports	Amazon reviews
Food reviews:	Food critics	Yelp
Judging:	Olympics	American Idol

Wikipedia is reasonably accurate

nature

Vol 438 | 15 December 2005

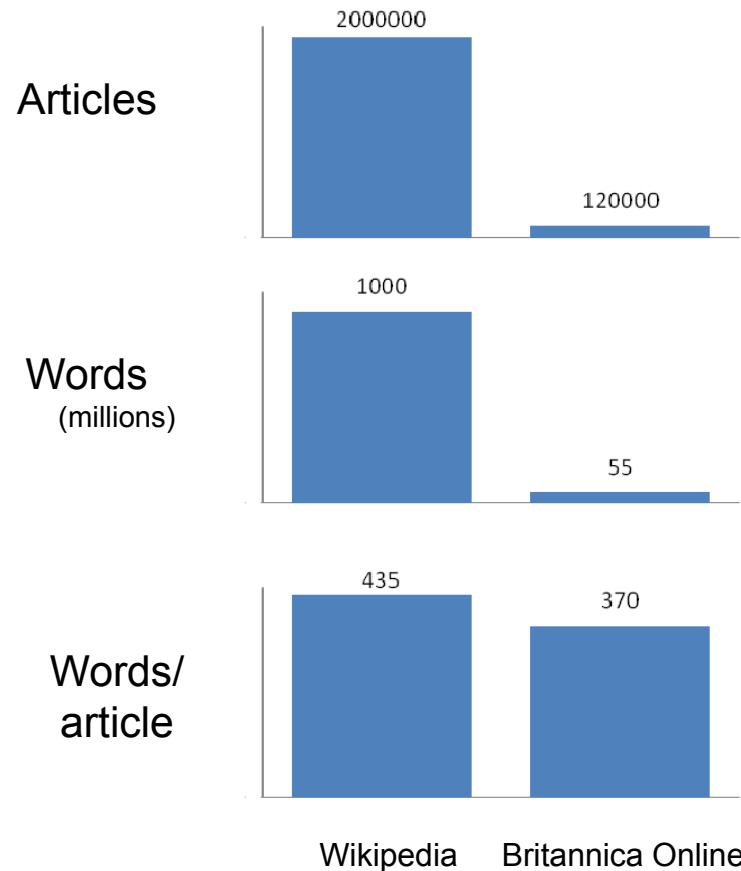
SPECIAL REPORT

Internet encyclopaedias go head to head

Jimmy Wales' Wikipedia comes close to Britannica in terms of the accuracy of its science entries, a *Nature* investigation finds.



Wikipedia has breadth and depth





We can harness the
Long Tail of scientists
to directly participate in
the gene annotation
process.

Gene “stubs” seed community contributions

Gene summary

Protein interactions

Linked references

Idea: Jan 2007
 Prototype: Mar 2007
 Ver 1.0 bot: Nov 2007

WIKIPEDIA The Free Encyclopedia

Navigation Main page Contents Featured content Current events Random article Interaction About Wikipedia Community portal Recent changes Contact Wikipedia Donate to Wikipedia Help Toolbox What links here Related changes Upload file Special pages Permanent link Cite this page Print/export Create a book Download as PDF Printable version

Article Discussion WikiTrust

Read Edit View history Go Search

ITK (gene)

From Wikipedia, the free encyclopedia

IL2-inducible T-cell kinase, also known as ITK, is a protein which in humans is encoded by the *ITK* gene.^[1]

Contents [hide]

- 1 Function
- 2 Structure
- 3 Interactions
- 4 References
- 5 Further reading

Function

This gene encodes an intracellular tyrosine kinase expressed in T-cells. The protein is thought to play a role in T-cell proliferation and differentiation.^{[2][3]}

Structure

This protein contains the following domains, which are often found in intracellular kinases:^[4]

- N-terminus – PH (pleckstrin homology domain)
- BTK – Bruton's tyrosine kinase Cys-rich motif
- SH3 – (Src homology 3)
- SH2 – (Src homology 2)
- C-terminus – tyrosine kinase, catalytic domain

Interactions

ITK (gene) has been shown to interact with FYN^{[5][6]} Wiskott-Aldrich syndrome protein,^{[7][8]} KHDRBS1,^{[8][9][10]} PLCG1,^{[10][11]} Lymphocyte cytosolic protein 2,^{[11][12]} Linker of activated T cells,^{[12][13]} Karyopherin alpha 2,^[14] Grb2^{[5][9]} and Peptidylprolyl isomerase A.^[15]

References

1. ^ Gibson S, Leung B, Squire JA, Hill M, Arima N, Goss P, Hogg D, Mills GB (September 1993). "Identification, cloning, and characterization of a novel human T-cell-specific tyrosine kinase located at the hematopoietin complex on chromosome 5q". *Blood* 82 (5): 1561–72. PMID 8364206.
2. ^ Kosaka Y, Felices M, Berg LJ (October 2006). "Itk and Th2 responses: action but no reaction". *Trends Immunol.* 27 (10): 453–60. doi:10.1016/j.tibbio.2006.08.006. PMID 16931156.
3. ^ "Entrez Gene: ITK IL2-inducible T-cell kinase".
4. ^ Hawkins J, Marcy A (July 2001). "Characterization of Itk tyrosine kinase: contribution of noncatalytic domains to enzymatic activity". *Protein Expr Purif.* 22 (2): 211–9. doi:10.1006/pepb.2001.1447. PMID 11437596.
5. ^ a b c Bunnell, S C, Diehn M, Yaffe M B, Findell P R, Cantley L C, Berg L J (Jan. 2000). "Biochemical interactions integrating Itk with the T cell receptor-initiated signaling cascade". *J. Biol. Chem.* (UNITED STATES) 275 (3): 2219–30. ISSN 0021-9258. PMID 10636929.
6. ^ a b c Okenveil C, O'Halloran T A, Knoll J, Standaert
- intramolecular association in a tyrosine kinase of the Tec family". *Nature (ENGLAND)* 385 (6611): 93–7. doi:10.1038/385093a0. ISSN 0028-0836. PMID 8985255.
7. ^ Perez-Villar, J, Kanner B (Dec. 1999). "Regulated association between the tyrosine kinase Emt/Itk/Tsk and phospholipase-C gamma 1 in human T lymphocytes". *J. Immunol. (UNITED STATES)* 163 (12): 6435–41. ISSN 0021-1767. PMID 10586033.
8. ^ Shim, Eun Kyung; Moon Chang Suk; Lee Gi Yeon; Ha Yun Jung; Chae Suhn-Kee; Lee Jong Ran (Sep. 2004). "Association of the Src homology 2 domain-containing leukocyte phosphoprotein of 76 kD (SLP-76) with the p85 subunit of phosphoinositide 3-kinase". *FEBS J / EFT* (Netherlands) 271 (3): 35–40. doi:10.1016/j.febslet.2004.07.090. ISSN 0014-5793. PMID 15388330.
9. ^ Shan, X; Wang R L (Oct. 1999). "Itk/Emt/Tsk activation in response to CD3 cross-linking in Jurkat T cells requires ZAP-70 and Lat and is independent of membrane recruitment". *J. Biol. Chem.* (UNITED STATES) 274 (41): 29323–30. ISSN 0021-9258. PMID 10506192.
10. ^ Perez-Villar, Juan J, Whitehead-Pepin, Standaert

Protein structure

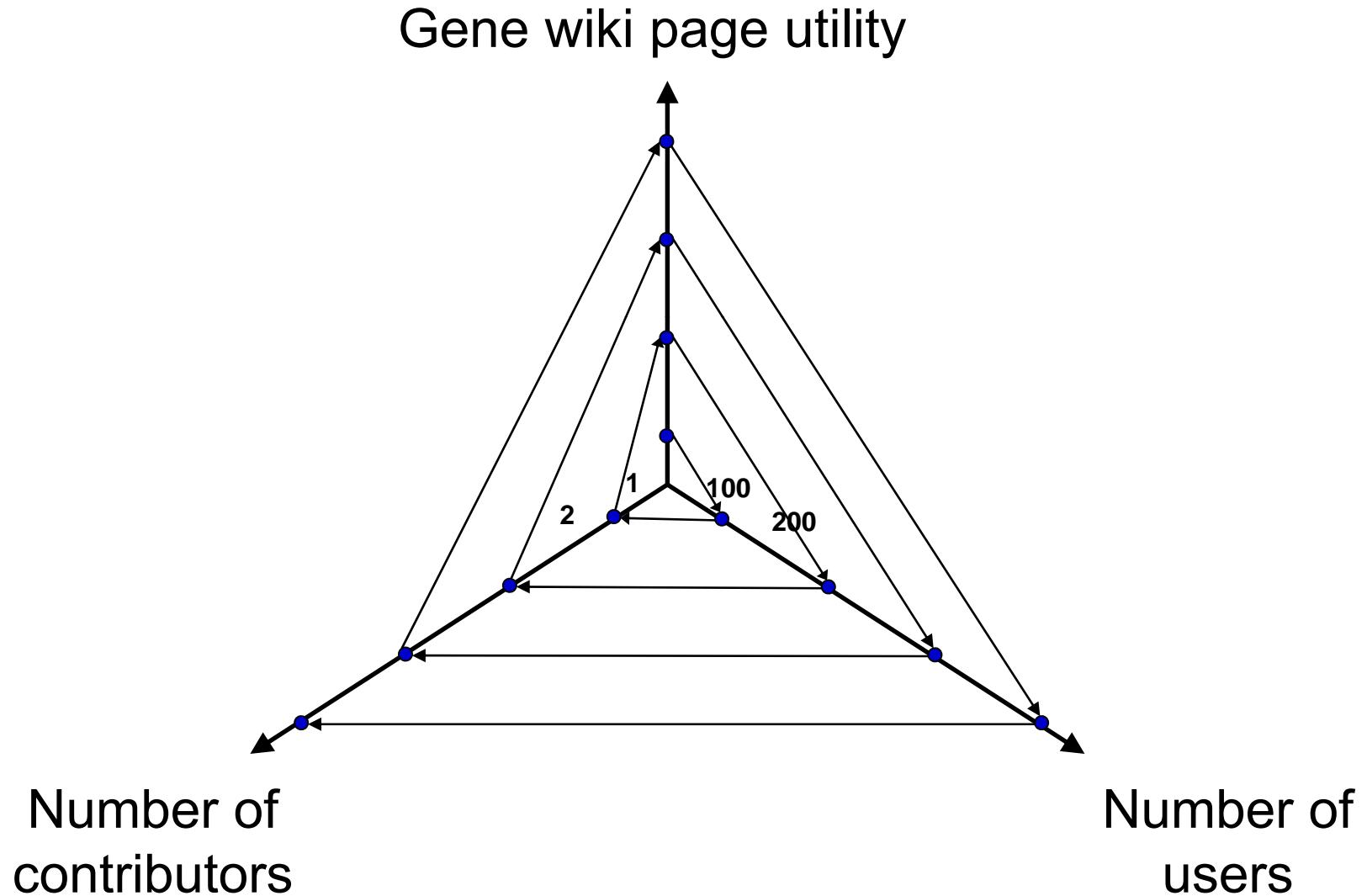
Symbols and identifiers

Gene Ontology annotations

Tissue expression pattern

Links to structured databases

Wiki success depends on a positive feedback



A review article for every gene is powerful

Role in brain pathology

Lissencephaly: Disruption of Reelin protein. The protein is involved in the sitting and walking of children.

Disruption of Reelin protein: Norman-Roberts syndrome. The protein is involved in the sitting and walking of children.

Schizophrenia: Reduced expression of Reelin mRNA in the prefrontal cortex of patients with schizophrenia. The reduction may be due to a genetic mutation or environmental factors. The reduction may reach 50% in some patients.

Reduced expression of Reelin mRNA: and independent of the genetic mutation, the reduction may reach 50% in some patients.

disorders, according to one study. ^[38] Reduced reelin mRNA prefrontal expression was found in the prefrontal cortex of patients with schizophrenia. The reduction was statistically relevant. ^[38] Disturbances found in the multicenter study conducted by the Neuropathology Consortium.

Hyperlinks to related concepts

Reelin: 68 editors, 543 edits since July 2002

Heparin: 175 editors, 320 edits since June 2003

AMPK: 44 editors, 84 edits since March 2004

RNAi: 232 editors, 708 edits since October 2002

References

1. ^ Weeber, E. J., U. Beffert, C. Jones, J. M. Christian, E. Forster, J. D. Sweatt, and J. Herz. 2002. *Reelin and ApoE receptors cooperate to enhance hippocampal synaptic plasticity and learning*. *J. Biol. Chem.* 277: 36331–36336. PMID: 12047222

34. ^ Fatemi, S. H., Earle, J. A. & McMenomy, T. (2000) *Reduction in Reelin immunoreactivity in hippocampus of subjects with schizophrenia, bipolar disorder and major depression*. *Mol. Psych.* 5, 654-663. PMID: 10875003

2003) *Interstitial white matter abnormally distributed in schizophrenia: a hypothesis of molecular and morphologic abnormalities*. *Mol. Psychiatry*, 8, 100-106.

Russo, A., Smith, C. L., Faraone, S., Nguyen, G., Ponte, J. F., et al. (2003) *Regulation of the RELN promoter in the brain of schizophrenia patients*. *Am J Med Genet Part B*, 43, 100-106.

References to the literature

External links

Articles, publications, webpages

- The real role of reelin publication in The Journal of Neuroscience
- Phenotypic Action of Reelin in Psychosis - Webinar
- Genetics of Reelin - the scientist who discovered it
- Neuronal Migration in Cortical Development - article
- Kazunori Nakajima MD, PhD (2003) *J Child Neurol* 18(10):753-759. PMID: 14603046
- A short biography of the scientist who discovered it (1933-2004) Heeddy. *BSQ* 119:21. PMID: 15241466

Figures and images

- Schematic representation of signaling through the receptor
- Proposed mechanism by which mouse RELN protein (MeCP2, HDAC1, and Coiled-coil) regulates reelin signaling
- Figure showing the effect of reelin on the brain
- The lack of reelin brings to the cerebral microvessels
- Reelin gene expression in mice - images from Blakely et al.
- Effects of human and naturally occurring mouse RERL
- Hong et al.

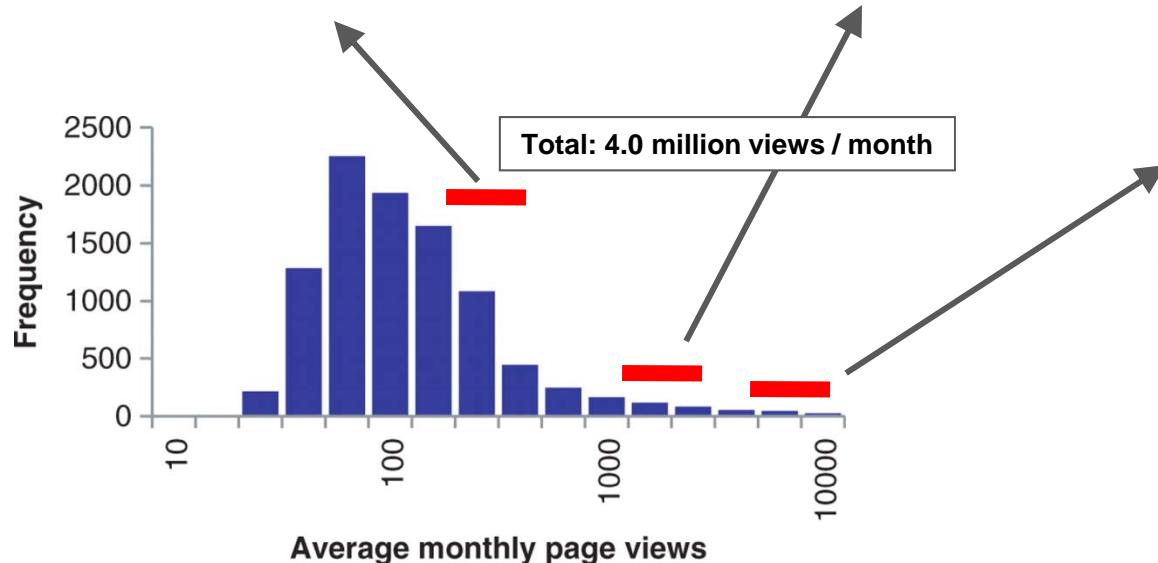
Filtering, extracting, and summarizing PubMed

The screenshot shows the PubMed search results for the query "Fibronectin". The search bar at the top contains "PubMed" and "Fibronectin". Below the search bar, the text "Display Settings: Summary, 20 per page, Sorted by Recently Added" and "Send to:" are visible. The main area displays "Results: 1 to 20 of 30174". A red box highlights the total result count "30174". Navigation links include "<< First", "< Prev", "Page 1", "Next >", and "Last >>". Below the results, a diagram shows several blue user icons with arrows pointing down towards a browser window. The browser window displays the Wikipedia page for "Fibronectin". The page title is "Fibronectin – Wikipedia, the free encyclopedia". The content includes a brief description of fibronectin as a high-molecular-weight glycoprotein that binds to integrins and extracellular matrix components like collagen, fibrin, and heparan sulfate proteoglycans. It also mentions its existence as a dimer and alternative splicing. A 3D molecular model of a three-module fragment of fibronectin 1 is shown on the right.

Gene Wiki has a diverse critical mass of readers

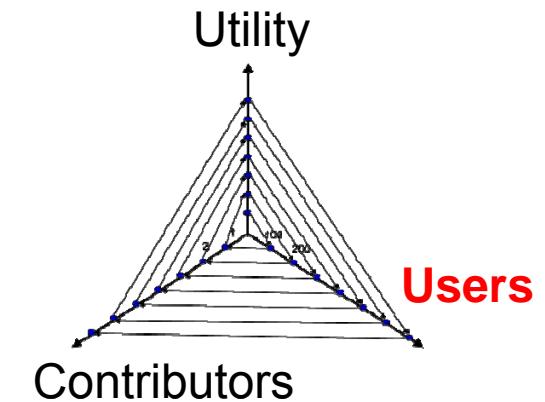
Rank 1001-1010: Specialists

CSDA
 CNTNAP2
 IGSF8
 Adenosine A3 receptor
 RYR1
 ETV6
 Small heterodimer partner
 5-HT1D receptor
 TRPC6
 Interleukin-6 receptor



Rank 101-110: Scientists

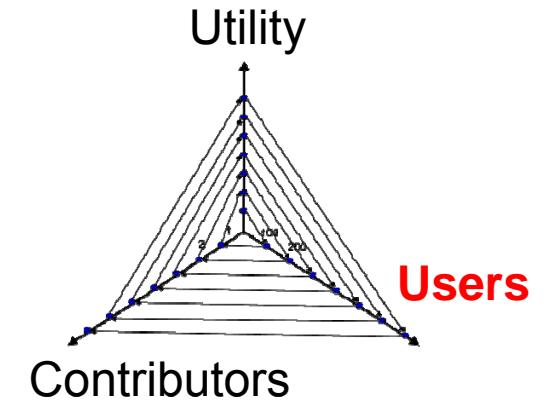
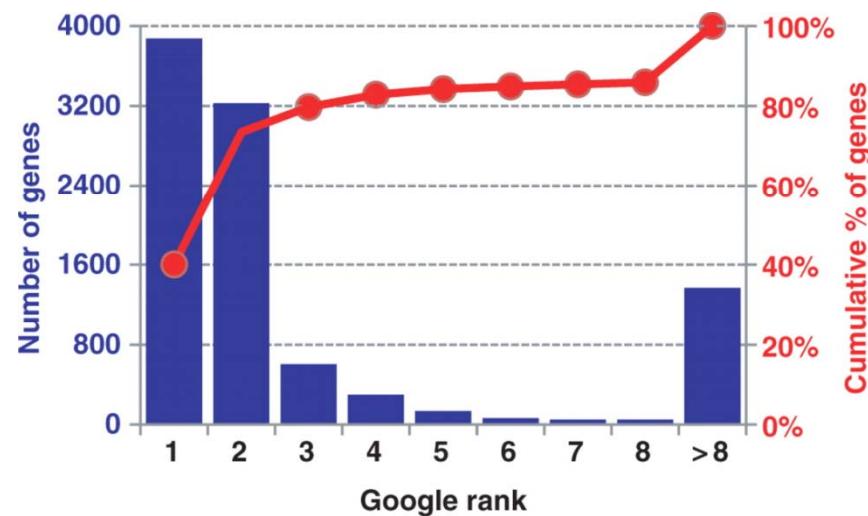
Tau protein
 Interleukin 10
 APC
 C-Met
 Factor V
 Interleukin 8
 CD44
 Histamine H1 receptor
 Kappa Opioid receptor
 Dihydrofolate reductase



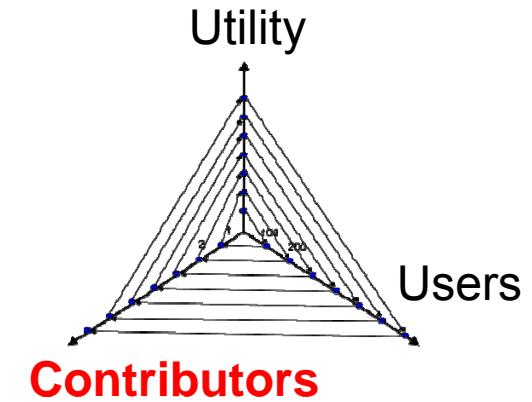
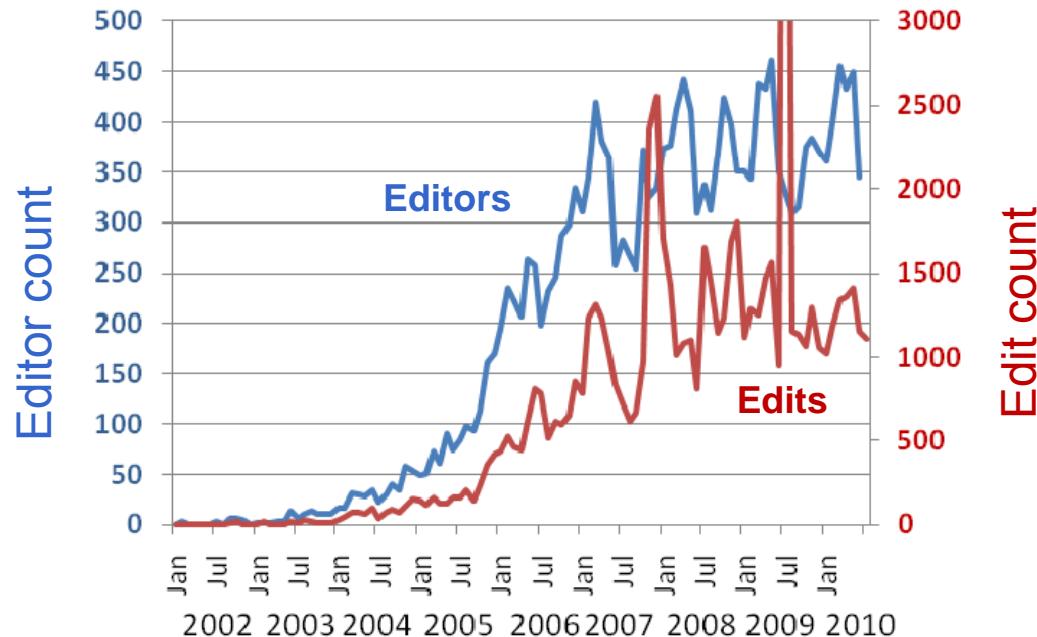
Rank 1-10: Laypeople

Insulin
 Titin
 Human chorionic gonadotropin
 Vasopressin
 ANKH
 CLOCK
 Catalase
 Erythropoietin
 Glucagon
 Parathyroid hormone

Readership is poised to grow



The Gene Wiki has a critical mass of editors



In Jan – Jun 2010 ...

... 7474 edits were made by 2109 unique users

... total increase in text \approx 20 *PLoS Biology* research articles

Making the Gene Wiki more reliable

WikiTrust principles:

- Authors who contribute long-lived content tend to be trustworthy
- Added content initially inherits the trust of its author
- Content persisting over time becomes more trusted
- Highlight untrusted text

11:10, 19 May 2008

Article Discussion Read Edit View history ☆ WikiTrust ▾

Novartis

Novartis International AG (NYSE: NVS) is a multinational pharmaceutical company based in Basel, Switzerland that manufactures drugs such as clozapine (Clozaril), diclofenac (Voltaren), carbamazepine (Tegretol), valsartan (Diovan), imatinib mesylate (Gleevec / Glivec), cyclosporin A (Neoral / Sandimmune), letrozole (Femara), methylphenidate hydrochloride (Ritalin), terbinafine (Lamisil), etc. The company name is derived from old Greek, and means "destroyer of birds". Novartis owns Sandoz, a large manufacturer of generic drugs. The company formerly owned the Gerber Products Company, a major infant and baby products producer, but announced in April 2007 it was selling Gerber to Nestlé. Legal responsibility for Gerber was transferred from Novartis to Nestlé on 1 September 2007.^[1]

Contents

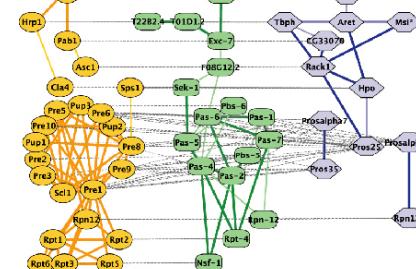
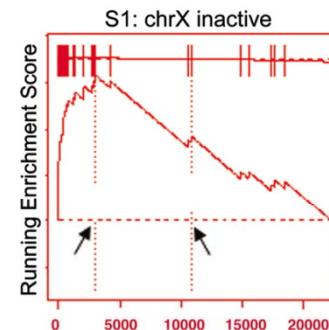
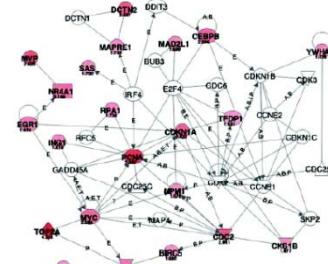
<http://www.wikitrust.net/>

Making the Gene Wiki more computable

Structured annotations

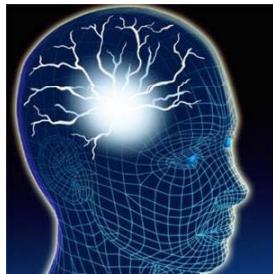
Function	Evidence
metal ion binding	IEA
peptidase activity	IEA
protein serine/threonine/tyrosine kinase activity	ISS
serine-type peptidase activity	IEA

Process	Evidence
axon guidance	ISS
brain development	ISS
cell adhesion	IEA
cell morphogenesis involved in differentiation	ISS
central nervous system development	ISS
cerebral cortex tangential migration	ISS
glial cell differentiation	ISS
multicellular organismal development	IEA
neuron migration	ISS
peptidyl-tyrosine phosphorylation	ISS
positive regulation of protein kinase activity	ISS
positive regulation of small GTPase mediated signal transduction	ISS
response to pain	ISS
spinal cord patterning	ISS

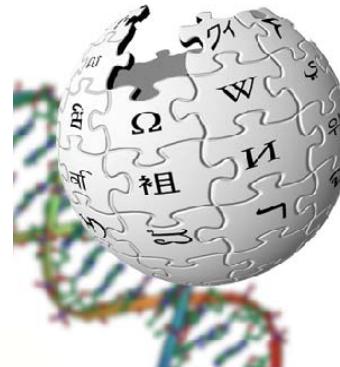


Making the Gene Wiki more computable (Part I)

Generation



Representation



Utilization



Unstructured

Structured

“Semantic Wiki Links”

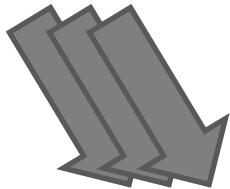


Data mining/
statistics

Semantic
Gene Wiki

See poster from
Salvatore Loguerchio

Making the Gene Wiki more computable (Part II)



Free text

The screenshot shows a Wikipedia article page for "Reelin". The page includes a sidebar with language and print options, a main content area with text about Reelin's function in neuronal migration and its role in Alzheimer's disease, and a detailed 3D ribbon model of the Reelin protein structure.



Structured annotations

Function	Evidence
metal ion binding	IEA
peptidase activity	IEA
protein serine/threonine/tyrosine kinase activity	ISS
serine-type peptidase activity	IEA

Process	Evidence
axon guidance	ISS
brain development	ISS
cell adhesion	IEA
cell morphogenesis involved in differentiation	ISS
central nervous system development	ISS
cerebral cortex tangential migration	ISS
glial cell differentiation	ISS
multicellular organismal development	IEA
neuron migration	ISS
peptidyl-tyrosine phosphorylation	ISS
positive regulation of protein kinase activity	ISS
positive regulation of small GTPase mediated signal transduction	ISS
response to pain	ISS
spinal cord patterning	ISS



Mining community-contributed content

Text, links, and citations

WIKIPEDIA
The Free Encyclopedia

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Article Discussion WikiTrust Read Edit View history Go Search

ITK (gene)

From Wikipedia, the free encyclopedia

Navigation

- Main page
- Contents
- Featured content
- Current events
- Random article

Interaction

- About Wikipedia
- Community portal
- Recent changes
- Contact Wikipedia
- Donate to Wikipedia
- Help

Toolbox

- What links here
- Related changes
- Upload file
- Special pages
- Permanent link
- Cite this page

Print/export

- Create a book
- Download as PDF
- Printable version

Contents [hide]

- 1 Function
- 2 Structure
- 3 Interactions
- 4 References
- 5 Further reading

Function

This gene encodes an intracellular tyrosine kinase expressed in T-cells. The protein is thought to play a role in T-cell proliferation and differentiation.^{[2][3]}

Structure

This protein contains the following domains, which are often found in intracellular kinases:^[4]

- N-terminus – PH (pleckstrin homology domain)
- BTK – Bruton's tyrosine kinase Cys-rich motif
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- C-terminus – tyrosine kinase, catalytic domain

Interactions

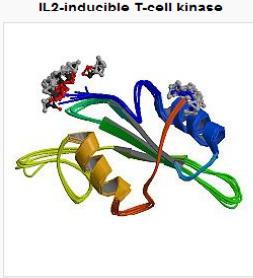
ITK (gene) has been shown to interact with FYN^{[5][6]} Wiskott-Aldrich syndrome protein^{[7][8]} KHDRBS1,^{[8][9][10]} PLCG1,^{[10][11]} Lymphocyte cytosolic protein 2,^{[11][12]} Linker of activated T cells,^{[12][13]} Karyopherin alpha 2,^[14] Grb2^{[5][9]} and Peptidylprolyl isomerase A.^[15]

References

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13. ^ a b c Perez-Villar, Juan J; Whitehead, Sean P; Sitkoff, Daniel; et al. (Oct. 1999). "Itk/Emt/Tsk activation in response to CD3 cross-linking in Jurkat T cells requires ZAP-70 and Lat and is independent of membrane recruitment". *J. Biol. Chem. (UNITED STATES)* 274 (41): 29323–30. ISSN 0021-9258. PMID 10506192.

edit

IL2-inducible T-cell kinase



1Lui

Available structures

1lui, 1luk, 1lum, 1lun, 1sm2, 1snu, 1snx, 2etz, 2eu0

Identifiers

Symbols ITK; PSCTK2; EMT; LYK; MGC126257; MGC126258

External OMM: 186973 MGI: 96621 HomoloGene: 4051

IDs GeneCards: ITK Gene

EC 2.7.10.2

number

Gene ontology [show]

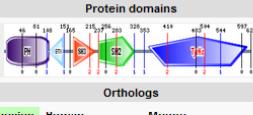
RNA expression pattern

211339_s_at

GeneAtlas Tissues

More reference expression data

Protein domains



Orthologs

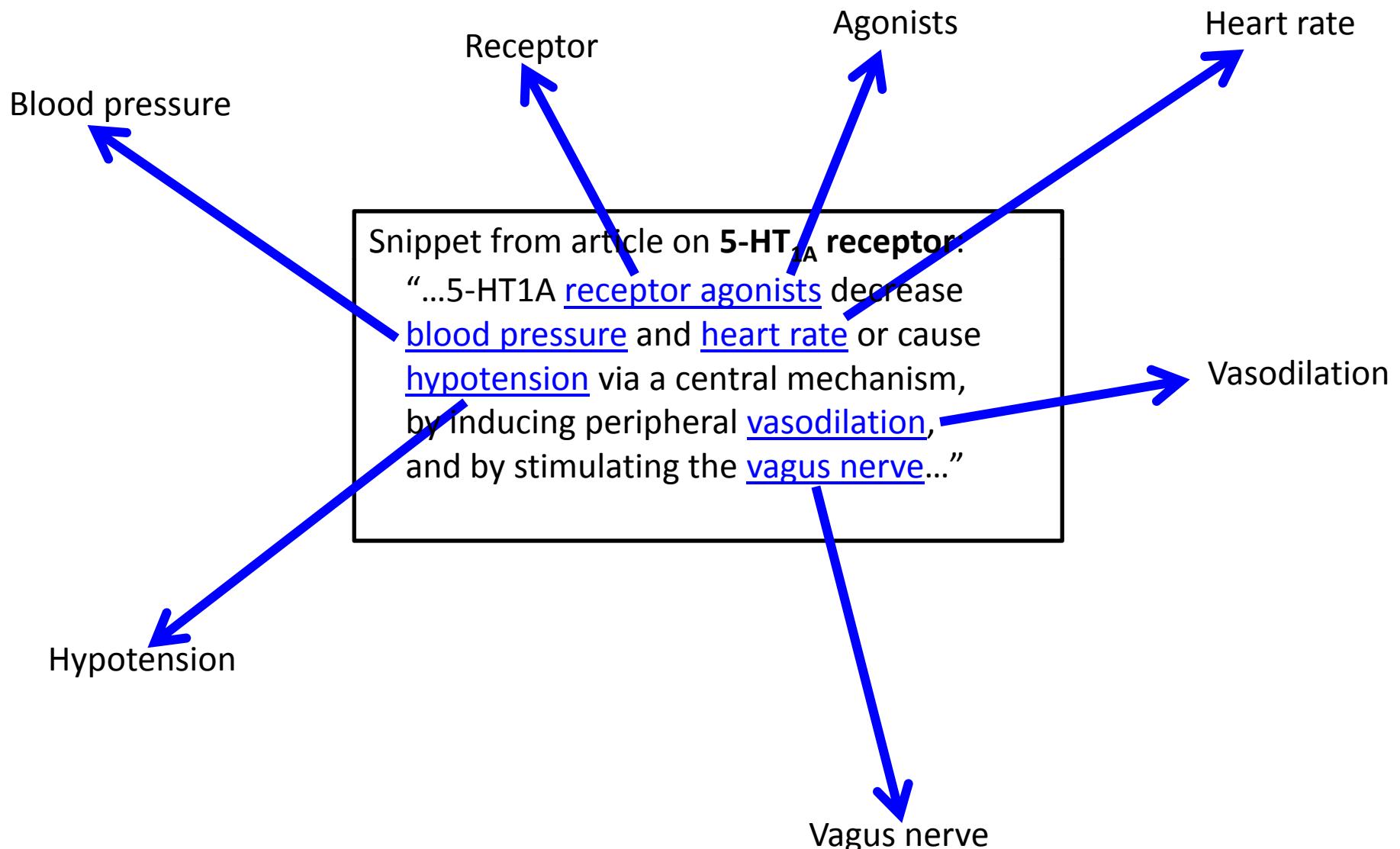
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Entrez	3702	16428
Ensembl	ENSG00000113263	ENSMUSG0000020395
UniProt	Q08881	A1A560
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RefSeq (protein)	NP_005537	NP_034713

Example text from **5-HT_{1A} receptor**

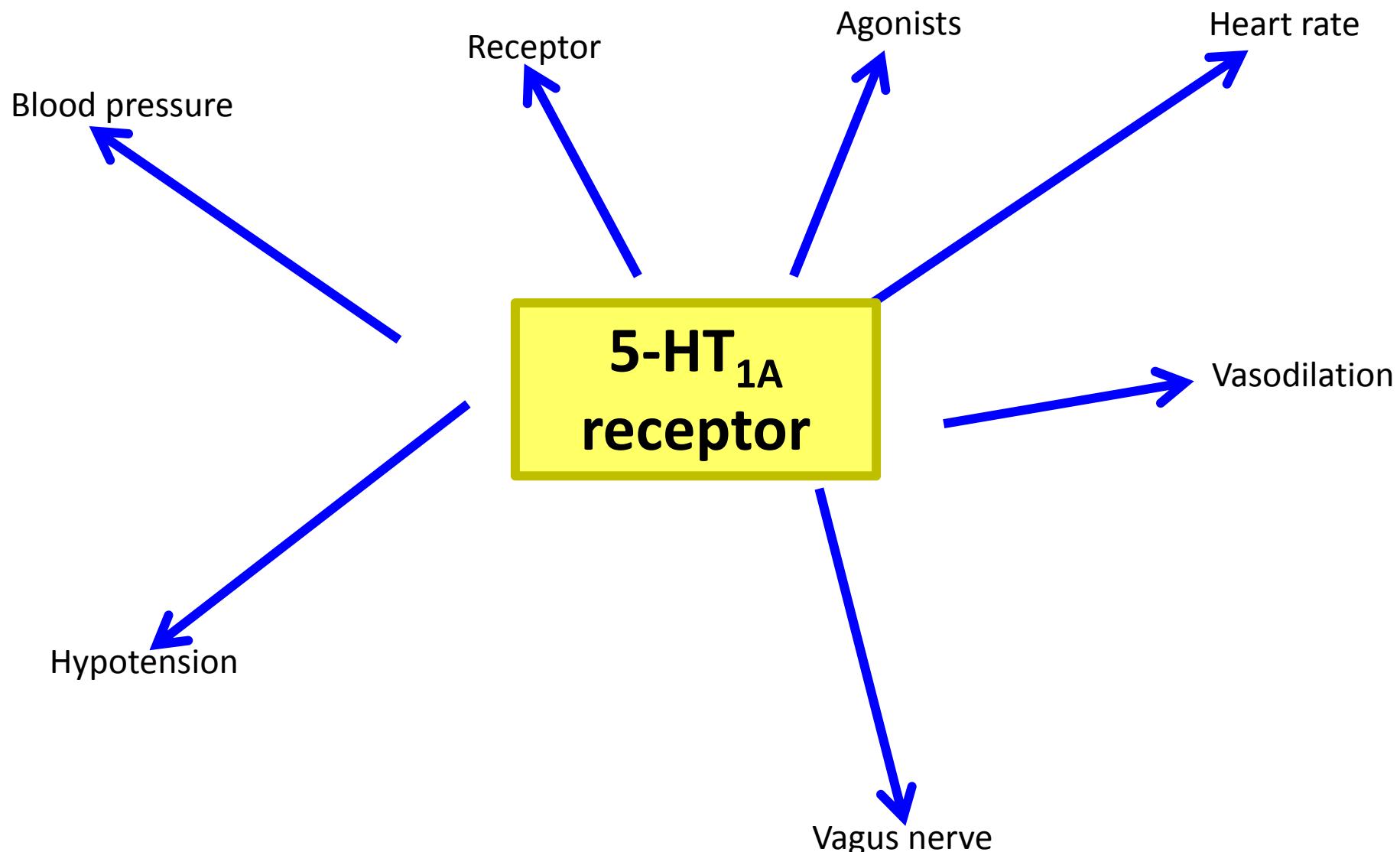
Snippet from article on **5-HT_{1A} receptor**:

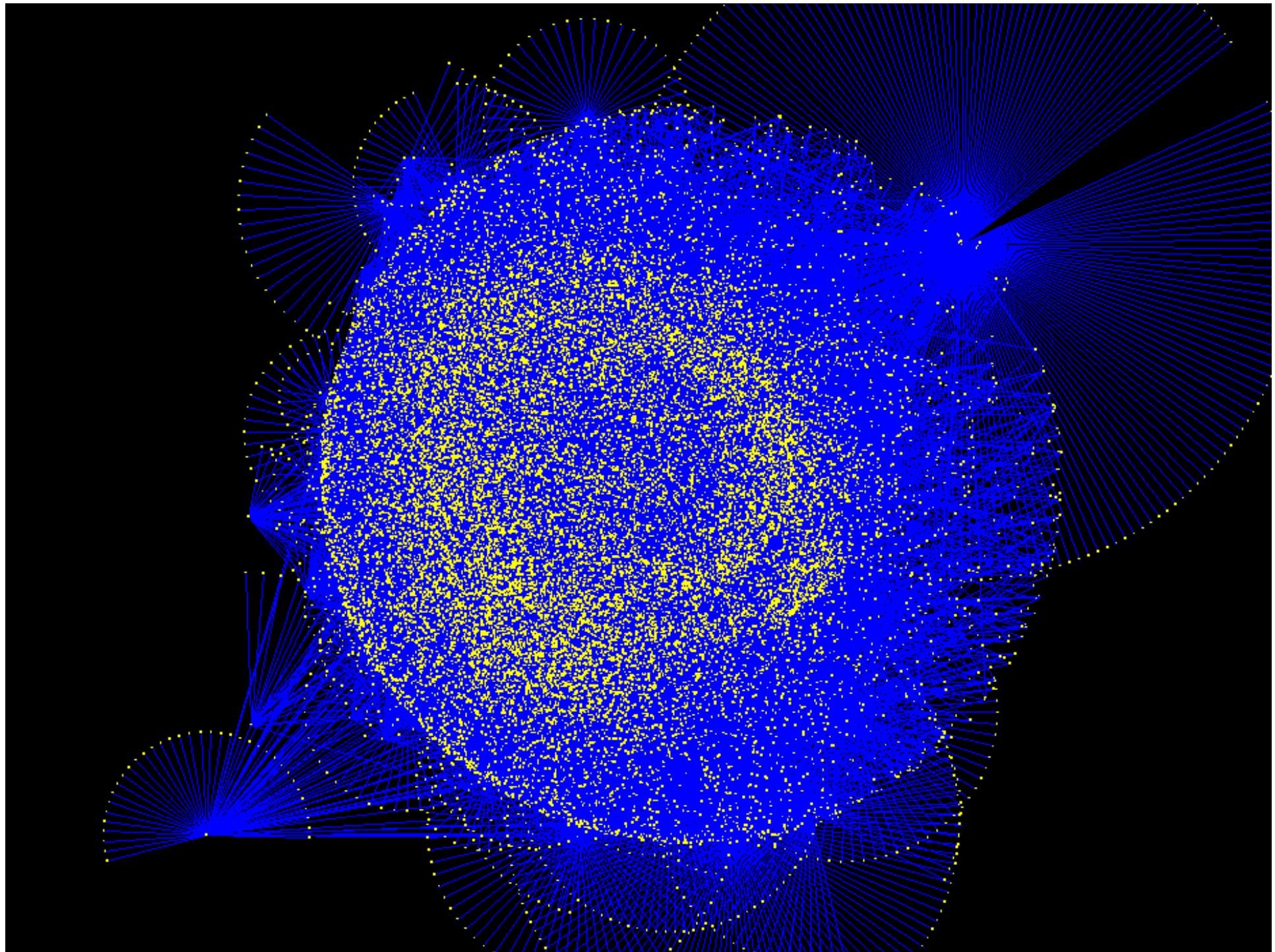
“...5-HT1A receptor agonists decrease blood pressure and heart rate or cause hypotension via a central mechanism, by inducing peripheral vasodilation, and by stimulating the vagus nerve...”

Example Hypertext from 5-HT_{1A} receptor



Example Hypertext from 5-HT_{1A} receptor





Re-discovering common knowledge

The screenshot shows a gene information page for the 5-HT₆ receptor (Gene ID: 3362). The top section displays the gene's name, its status as a pseudogene, and its chromosomal location (17q11.2). Below this are two tables: one for evidence codes (IEA, TAS) and one for publications (PubMed). A large yellow box highlights the publication "J Neurochem. 1996 Jan;66(1):47-56." The abstract for this paper describes the cloning, characterization, and chromosomal localization of the human 5-HT₆ serotonin receptor. The receptor is a G protein-coupled receptor (GPCR) located in the plasma membrane, coupled to G_s/G_o. The bottom section of the page includes a table for protein associations and a link to AmiGO for further analysis.

From Wikipedia, the free encyclopedia

The 5-HT₆ receptor is a subtype of 5-HT receptor that binds the endogenous neurotransmitter serotonin (5-HT).^[1] It is a G protein-coupled receptor coupled to G_s/G_o and mediates excitatory responses.

Evidence

Evidence Code	Pubs
IEA	
TAS	PubMed

J Neurochem. 1996 Jan;66(1):47-56.

J Neurochem. 1996 Jan;66(1):47-56.

Cloning, characterization, and chromosomal localization of a human 5-HT₆ serotonin receptor.

Kohen R, Metcalf MA, Khan N, Druck T, Huebner K, Lachowicz JE, Meltzer HY, Sibley DR, Roth BL, Hamblin MW.

Department of Psychiatry and Behavioral Sciences, University of Washington, USA.

Abstract

We describe the cloning and characterization of a human 5-HT₆ serotonin receptor. The open reading frame is interrupted by two introns in positions corresponding to the third cytoplasmic loop and the third extracellular loop. The human 5-HT₆ cDNA encodes a 440-amino-acid polypeptide whose sequence diverges significantly from that published for the rat 5-HT₆ receptor.

Integral to plasma membrane

Evidence Code	Pubs
TAS	PubMed
IEA	

AmiGO

More tools Help

terms genes or search Submit Query

ceptor activity

External references 60 genes

protein associations

Mining the most recent literature

NCBI Entrez Gene: 57620

J Biol Chem. 2010 Jul 16;285(29):22437-47. Epub 2010 May 1.

Human muscle economy myoblast differentiation and excitation-contraction coupling use the same molecular partners, STIM1 and STIM2.

Abstract

Our recent work identified store-operated Ca(2+) entry (SOCE) as the critical Ca(2+) source required for the induction of human myoblast differentiation (Darbellay, B., Arnaudeau, S., König, S., Jousset, H., Bader, C., Demaurex, N., and Bernheim, L. (2009) J. Biol. Chem. 284, 5370-5380). The present work indicates that STIM2 silencing, similar to STIM1 silencing, reduces myoblast SOCE amplitude and differentiation. Because myoblasts in culture can be induced to differentiate into myotubes, which spontaneously contract in culture, we used the same molecular tools to explore whether the Ca(2+) mechanisms of excitation-contraction coupling are shared by myoblasts and myotubes.

Cellular differentiation

From Wikipedia, the free encyclopedia

In developmental biology, cellular differentiation is the process by which a less specialized cell becomes a more specialized cell type. Differentiation occurs numerous times during the development of a multicellular organism as the organism changes from a simple zygote to a complex system of tissues and cell types.

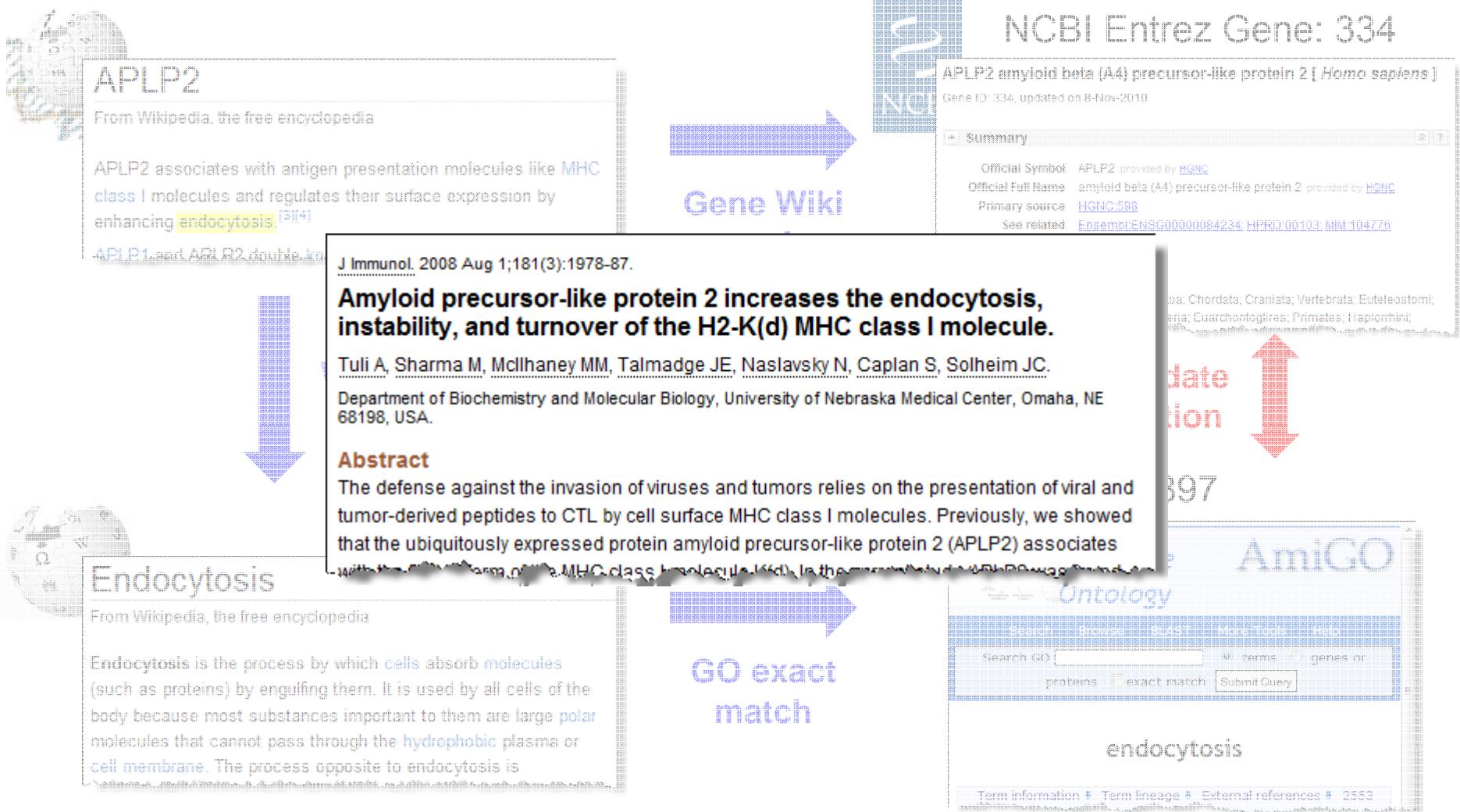
GO related concept

cell differentiation

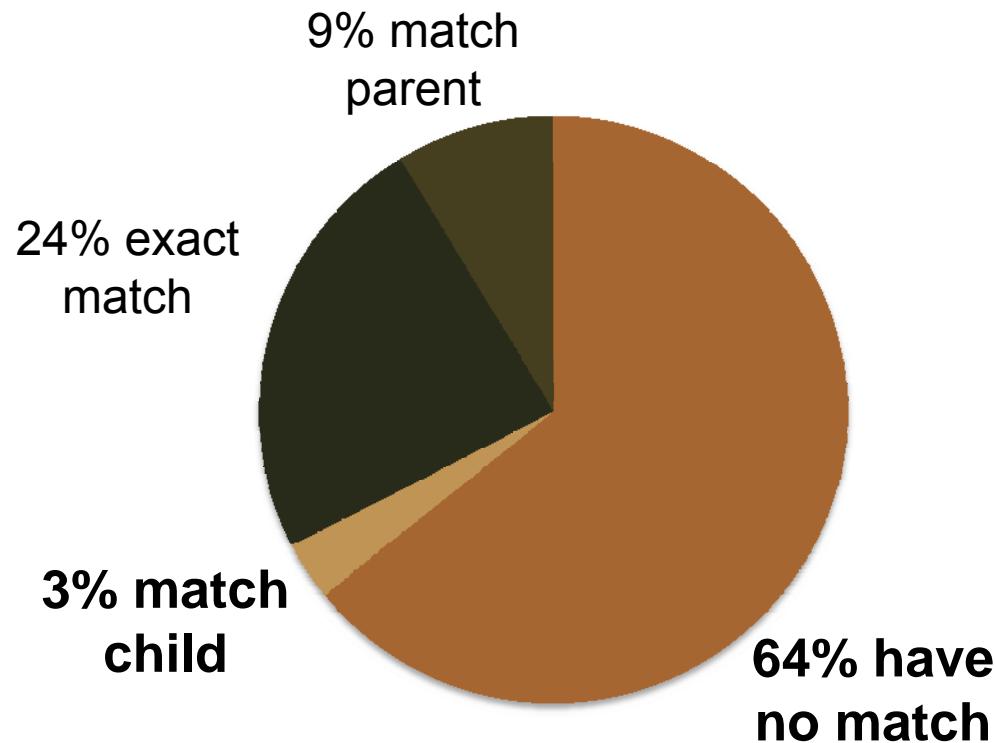
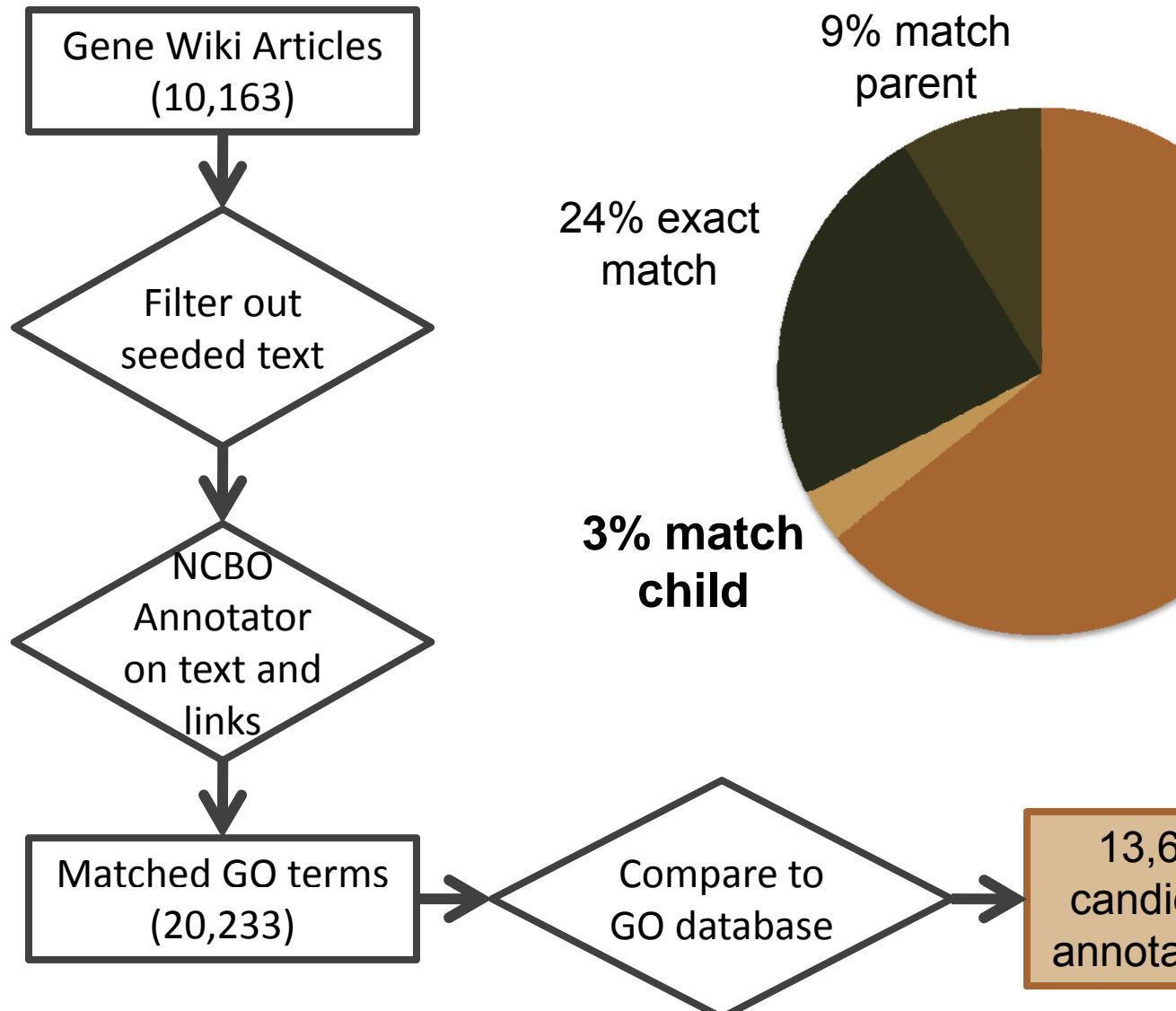
Search GO terms genes or proteins exact match Submit Query

Term information Term lineage External references 11685

Filling the gaps in gene annotation



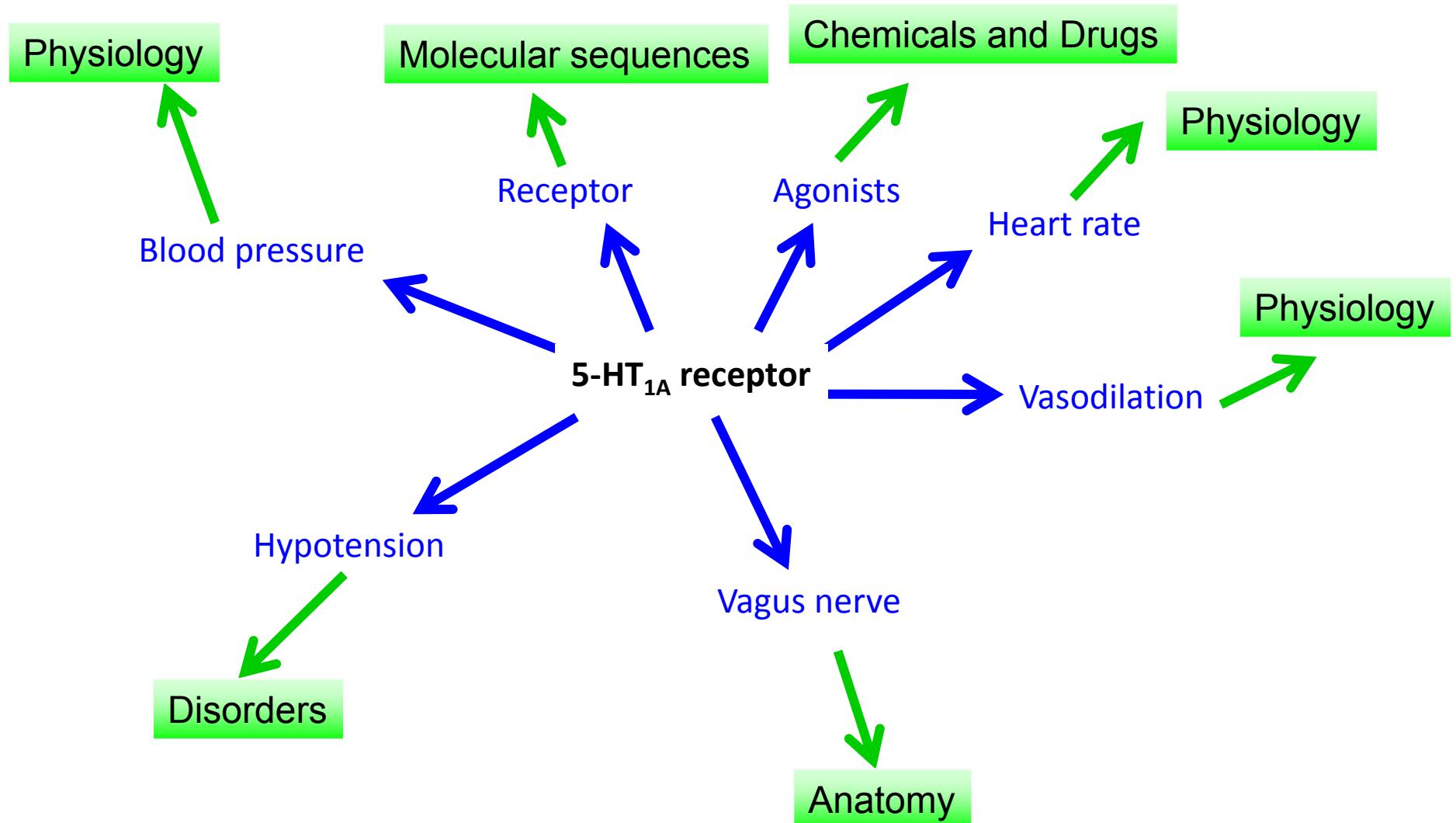
Associations mined from links and text



Prioritization

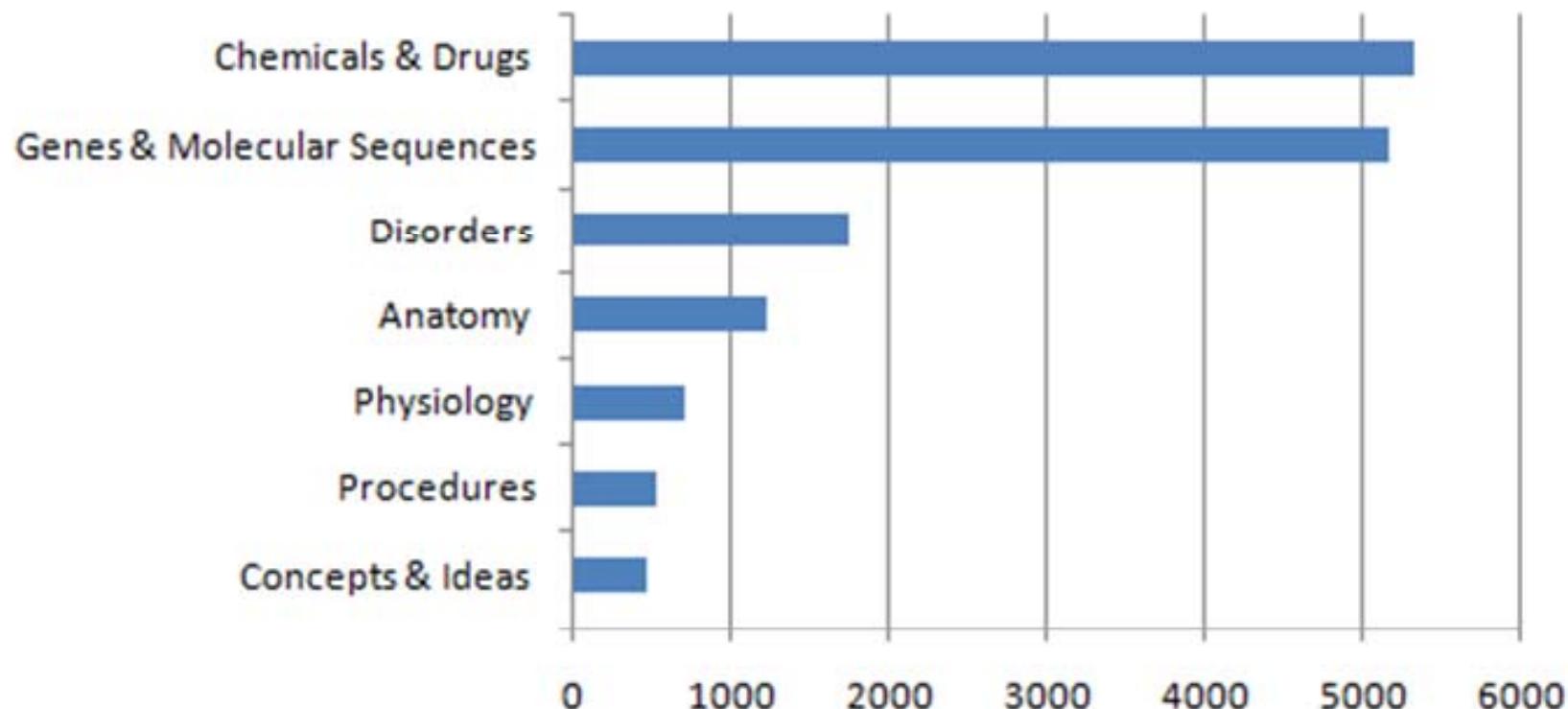
Orthology
Literature mining
Computational prediction

Not just Gene Ontology mappings



UMLS (Unified Medical Language System) Semantic Groups

Mapping to many biomedical semantic groups



For community-based science, data is king

Data without structure is valuable,
but structure without data is not.

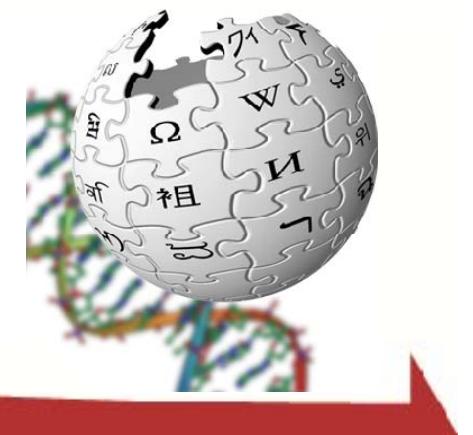
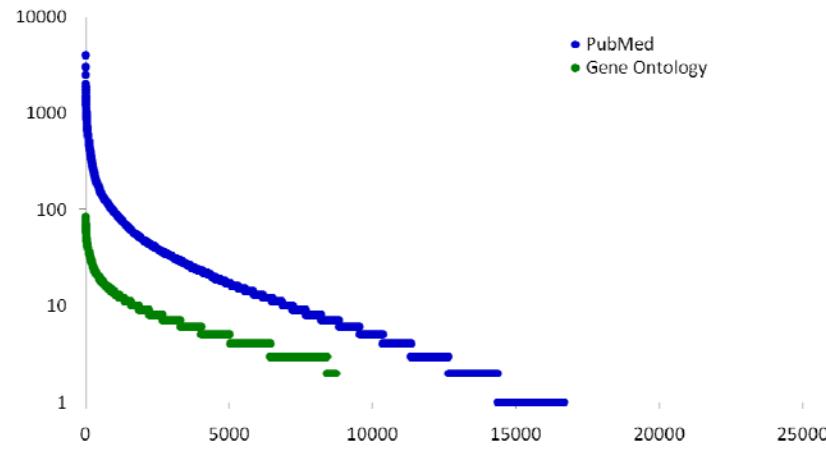
For community-based science, data is king

Data without X is valuable,
but X without data is not.

		<u>Wikipedia</u>
	Copy-editing	→ WP:MCB, Boghog
	Figures	→ Artists and illustrators
X	Structure	→ Wiki links, infoboxes
	Citations	→ DOI bot, CitationBot
	Provenance	→ WikiTrust



The Gene Wiki
successfully harnesses the
Long Tail of scientists
for community annotation of
gene function



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Thanks also to:

Christopher Roeder, U.Col.

Conrad Plake, GoGene

Funding and Support



Genomics Institute of the
Novartis Research
Foundation



NIGMS

(BioGPS: GM83924, Gene Wiki: GM089820)

