

H-InvDB: a Comprehensive Annotation Resource for Human Transcriptome

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1: Biomedical Information Research Center, National Institute of Advanced Industrial Science and Technology, 2: Japan Biological Informatics Consortium, 3: DYNACOM Co., Ltd., 4: National Institute of Genetics

Outline of my talk



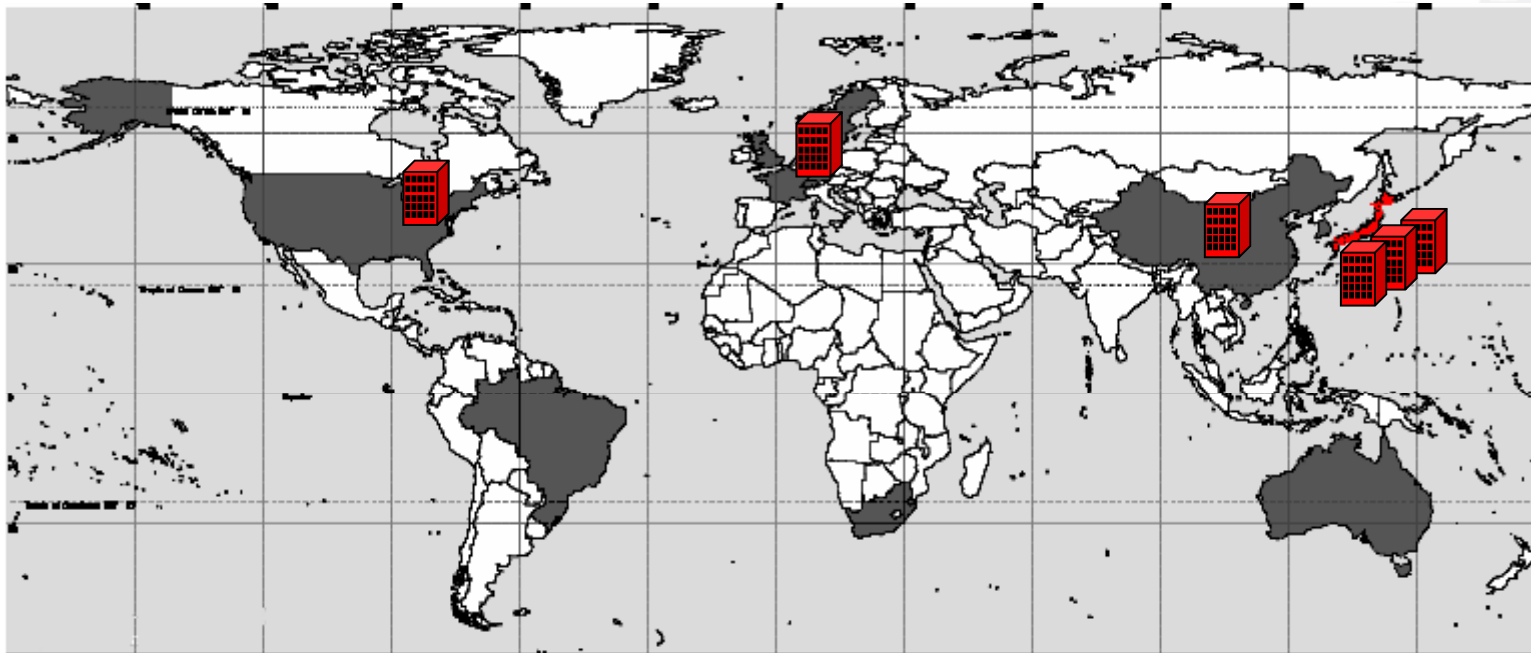
- **H-Invitational project**
- **H-InvDB**
 - Annotation
 - Main views and sub-databases
 - Search Navigation
- **HEAT: data-mining tool for enrichment analysis**
- **H-InvDB Web service**
 - Database integration by web service

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International Collaborative Project “H-Invitational”



Human full-length cDNAs were collected from

6 FLcDNA projects

World's 44 institutes, 118 scientists participated



International Collaborative Project "H-Invitational"

Manually curated by scientists



At H-Inv annotation jamboree,
Annotated by unified pipeline

Construct database



Free public human gene database

H-InvDB_1.0 was released 2004/04/20

Provided by BIRC/AIST and DDBJ, Japan.

Current release of H-InvDB release 7.5

Released on 10th Sep., 2010.

*Re-definition of human gene clusters
based on NCBI b37.1*

NEW !!

◆ The features of this release include:

- Re-difinition of human gene clusters on NCBI b37.1 (UCSC hg19) by re-filtering the predicted gene models
- 242,813 human transcripts in 44,806 human gene clusters (loci).
- Improvement on alternative splicing annotation pipeline and update of [H-DBAS](#)
- Update in human protein-protein interaction (PPI) and update of [PPI view](#)
- Updates of subdatabases; G-integra, DiseaseInfo Viewer, H-ANGEL, Gene family/groups

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H-InvDB annotation overview



**Transcripts
(242,813 HITs)**

**Proteins
(137,607 HIPs)**

Mapping transcript nucleotide sequence
onto human genome

Predict CDS
≡ CDS

**Similarity search
(against Protein DBs)
Functional motif
(InterPro)**

**Genome
NCBI b37.1**

Determine gene locus for transcript with
>=1bp overlap in genome location

**Protein functional
annotation**

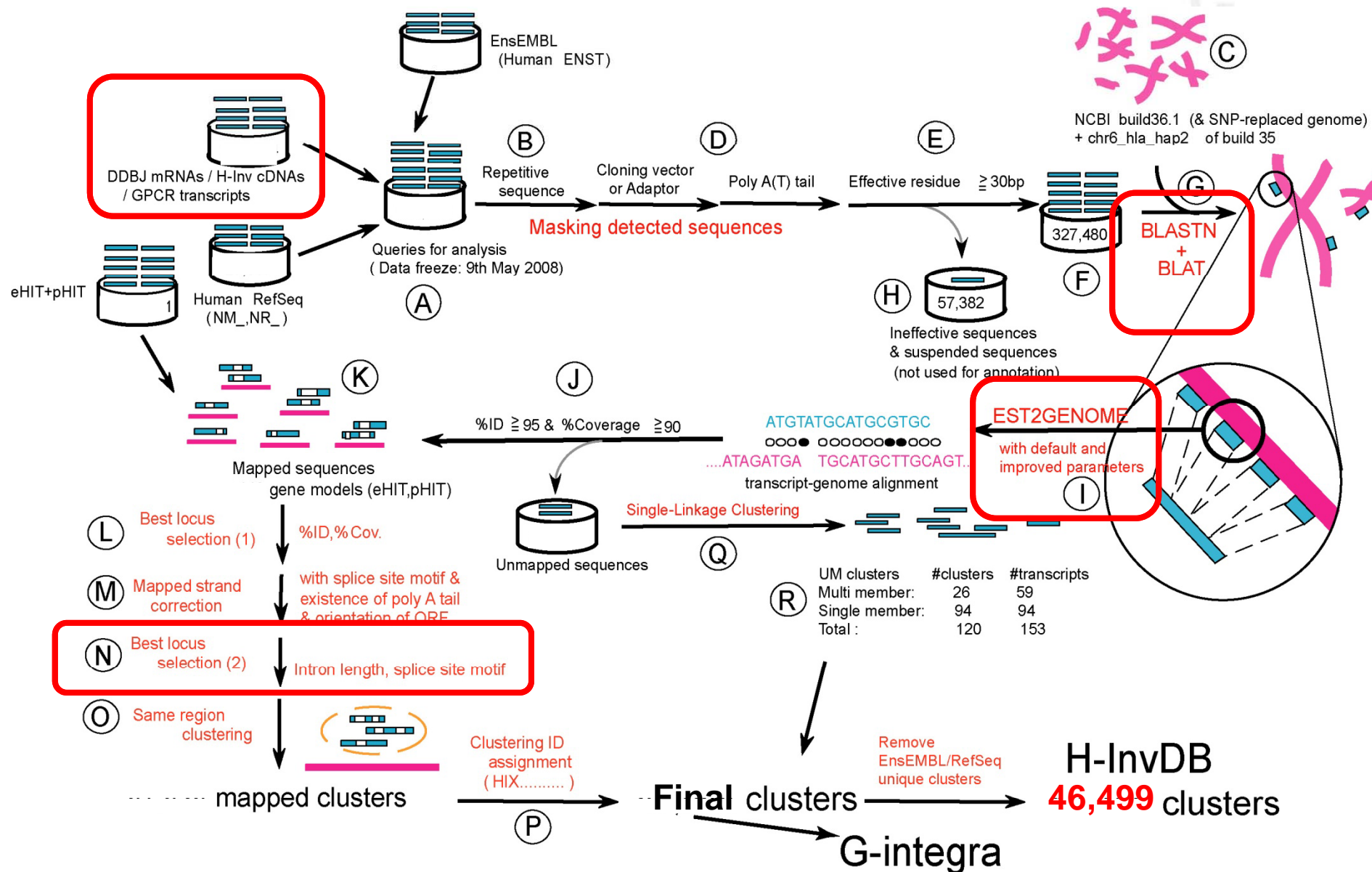
**Clusters
(44,806 HIXs)
671 UM clusters**

Locus 1

Locus 2

**Further analysis:
structure, localization,
etc**

H-InvDB human gene annotation pipeline



Classification of H-InvDB protein coding genes



Annotation flow

Similarity search against protein databases (FASTY, BLASTX)



Curate papers if there is evidence of protein experiments (I, II)



Predict protein function by InterPro domain (III)

Category	Definition	No. of genes
I	Identical to known human proteins	14,175
II	Similar to known proteins	5,004
III	InterPro domain containing proteins	1,786
IV	Conserved hypothetical proteins	5,057
V	Hypothetical proteins	4,059
VI	Hypothetical short protein. (protein length of 20-79aa)	6,274
VII	Pseudogene candidates	759
total		34,511

Non-protein coding genes : 7,692

20,965 protein coding genes of Category I, II, III are human gene set with high confidence

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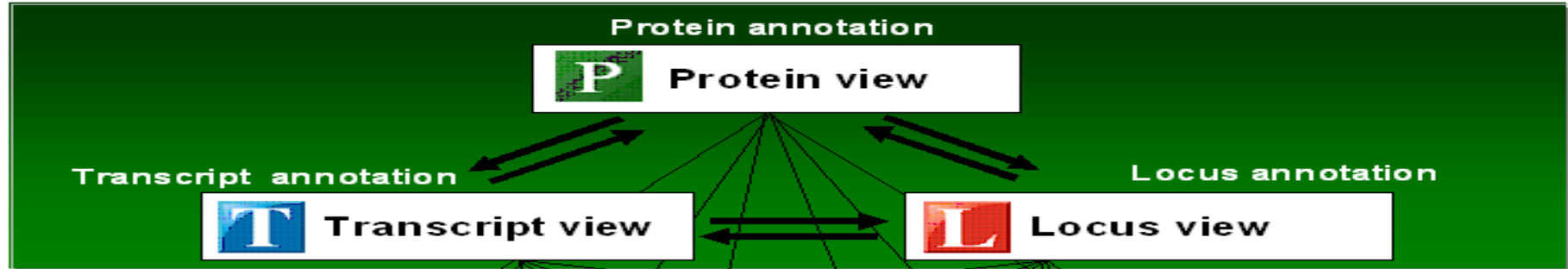


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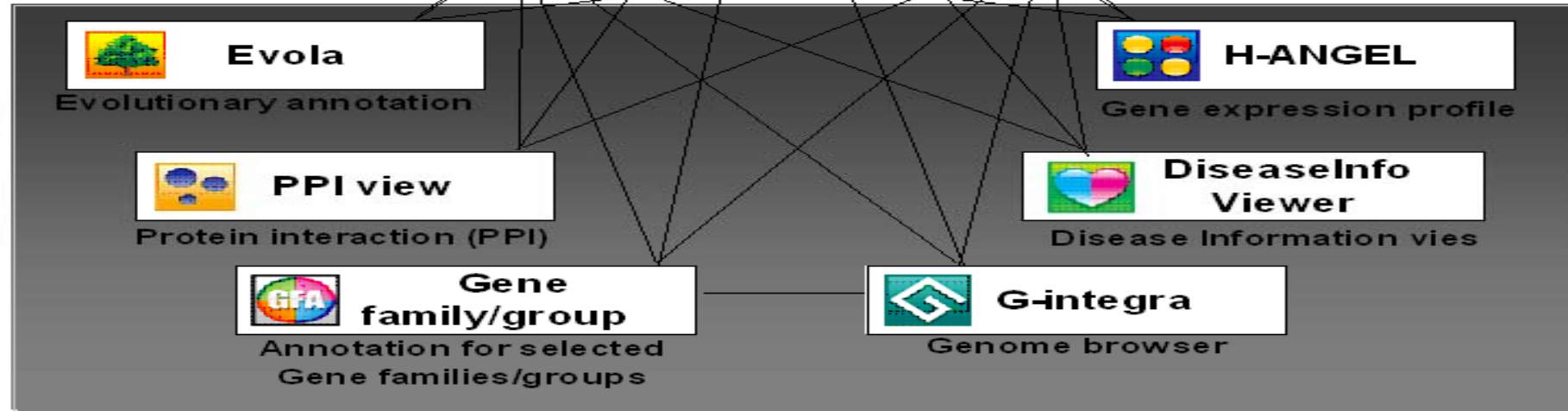
H-InvDB interfaces

3 main veivs and 6 sub-databases

Main views in H-InvDB



Subdatabases in H-InvDB



Links to relateed databases

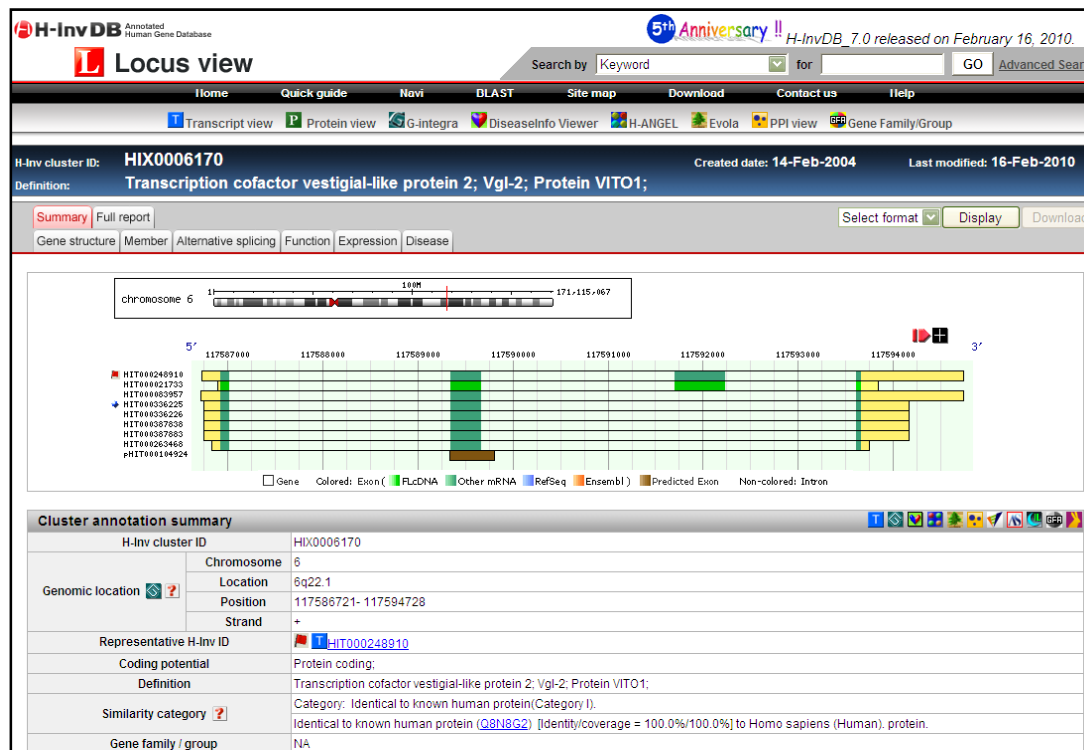
*CHGC	BIND	DIP	Gene ontology (GO)	HPRD	LIFEdb	PubMed	NC-IUBMB (EC)
*DKFZ/MIPS	BodyMap	DNA Probe Locator	GeneCards	IntAct	LSBM	RefSeq	OMIM
*IMSUT	CCDS	Ensembl	GTOP	InterPro	MGI	UCSC	fRNAdb
*KDRI	dbSNP	EntrezGene	HGNC	KEGG	MINT	UniGene	GGDB
*MGC/NCI	DDBJ/EMBL/GenBank	GenAtlas	H-GOLD (GDBS)	LEGENDA	Mutation view	UniProt	GlycoProtDB

*Human FLcDNA sequence data providers

Main view in H-InvDB(1) *Locus view*



Provide annotation of human gene cluster



- ◆ Location on genome
- ◆ Gene structure
- ◆ Gene name, definition
- ◆ Gene family/group
- ◆ Alternative splicing
- ◆ Gene expression profile
- ◆ Probe mapping
- ◆ Disease relation
- ◆ Locus member transcripts
- ◆ Links to related DBs

Man view in H-InvDB (2) *Transcript view*



Providing the annotation of each transcript (mRNA, cDNA)

Transcript original information

Accession number	BC053657.1
CAGE tag ID	NA
EST ID	NA
Clone Number	MGC:61459 IMAGE:5752337
Experimental resources	NBRRC HGPD Antibody (ST8SIA4)
Sequence data provider	Provider: MGC(INC)
Annotation project	H-Invitational FLCDNA
Length of cDNA	3680[bp] (No. of exon:5[A:1213 T:1088 G:728 C:651])
Devison	HUM
Molecular type	mRNA
Cell type	NA
Library origin	Tissue type: Brain, Lung, Testis, adult, pooled whole
	Developmental stage: NA

Sequence quality information

CDS feature	Complete CDS
Kozak sequence	NA
PolyA	Site: 3586(+); Signal: 3558-3582(+)
Vector/adaptor sequence	NA
Frame shift	NA
Remaining intron	NA
Splice site acceptor (NAGNAG)	NA

Nucleotide sequence:

```
GCTGCAGAGCTGCCGCCACCTCCAAATGCACAAGTGTCTCATCTGSA  
GAAACCTGAGCCCGCAGGAGGCGCGCGCGAGCCCTGGCAGGCTGSC  
GCAAACGCGCGAGGAGGCTGCTGGCAGCCTTCAGAGCCAGAGGAGCT  
CGCCACAGAGAGCCCGAGTGTCTGATCCCGGATCCGCGCTCCAGCT  
CTCCTGCAATTTACAGATTTTCAACCCCGCGCAGTATCTCCGCAAA  
GCGCTTATATCAAGAGAGGTTCCGCGAGCTGGGCAACCGAGACTTTC  
GCGCACCCCAAGATGCGCTCCATAGAGAGAGGTTGAGCAGTCTGCACAA  
AGTCTGCTCCTGATCTTTTAAAGACAAAAGAAATAGCAAGACTGAGGA  
GCACCGAGAGAGCGCACTCATCGAGATGGTGAATTTCTTTGAGTCGGT  
CACTTGTCAATAGCTCTGATAAAATCAATCGAAAGGCTGGCTCTTCAATC  
TTCCAGCAATGTAGAGGTTGGAAATCAATTCCTCTTTTGGTCTTAGA
```

- ◆ Nucleotide sequence
- ◆ Clone ID, library origin
- ◆ Location on the genome
- ◆ Translation (ORF)
- ◆ Amino acid sequence
- ◆ Protein function
- ◆ Gene ontology (GO)
- ◆ Functional RNA
- ◆ Enzyme
- ◆ Pathway (KEGG)
- ◆ Evolutionary analysis (orthplogs)
- ◆ Polymorphism (SNP, STR)
- ◆ Links to related DBs

Main view in H-InvDB (3) *Protein view*



NEW !!
In H-InvDB_7.0

Provide annotation for each human protein

Protein information

HIP ID	HIP000031798
Length	484
Codon Adaptation Index (CAI)	0.827
Database links	RefSeq: NM_003793 ; UniProt: Q9UBX1 ; CCDS: NA

Original transcript information

Representative H-Inv transcript ID	HIT000035371
H-Inv cluster ID	HX0009840
Predicted CDS	85..1539; 484[aa]; Orientation:+1;
Genomic location	Chromosome: 11 Location: 11q13.2 CDS position: 66330934-66336041 Strand: -
Accession number	BC011682.2
CAGE tag ID	NA
EST ID	NA
Clone Number	MGC:19716 IMAGE:3535532
Experimental resources	NBRC HGPD Antibody (CTSF)

Protein structure (GTOP)

HIP000031798 (GLP-00028e, *Caenorhabditis elegans*)

Annotations: Glycosylation site (red dot at 371), Signal peptide (green bar), Transmembrane (SOSUI) (green bar), Single amino acid repeat (SAR) (blue bar), Synonymous SNP (purple bar), Nonsynonymous SNP (red bar).

Sequence: MAPWLQLLSLLGLLPGAVAAPQPRASFOAWGPPPELLAPTRFALEMFNRRGRAGTRAVLGLVGRVRRAGQGSLSLEATLEPPCNDMPVCRLPVSKKTLCSFQVLDLELGRHLLRKDCGFPVDTKVPAGEPKSAFTQSSAMISLSQNHDPNRNETFSSVISLLNEDPLSQDLPVKMASIFKNFVITYNRTYESKEEARWLSVFNMMVRAQKIQALDRGTAQYGVTRKFSDLTEEFRTIYLNLLRKEFGNKKQAKSVGDLAPPEWDWRSGAVTKVKDQMGSCWAFSVTGNVEGQWFLNQSTLLSLSEQELLDCKMDKACMGGLPSNAYSIAIKNLGSELEDDYSYQGHMQSCNFSAEKAKVYINDSVLSQNEQKLAAWLAKRGPISVAINAFGMQFYRHGISRFLRPLCSFWLIDHAVLLVGYGNRSDVPFWAIKNSWGTDWGEKGYVYLHRSGAGCVNTMASSAVVD*

- ◆ Amino acid sequence
- ◆ Protein function
- ◆ Post translational modification (PTM)
- ◆ Functional motif (InterPro)
- ◆ Protein-protein interaction (PPI)
- ◆ Protein structure (GTOP)
- ◆ Subcellular localization (SOSUI, wPSORT)
- ◆ Polymorphism (SAR:)
- ◆ Links to related DBs

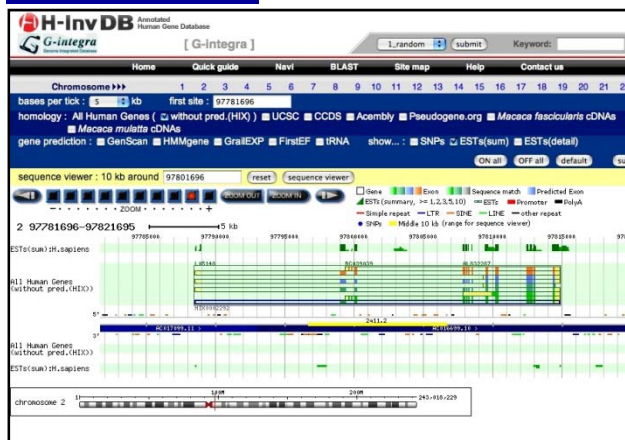
H-InvDB subdatabases



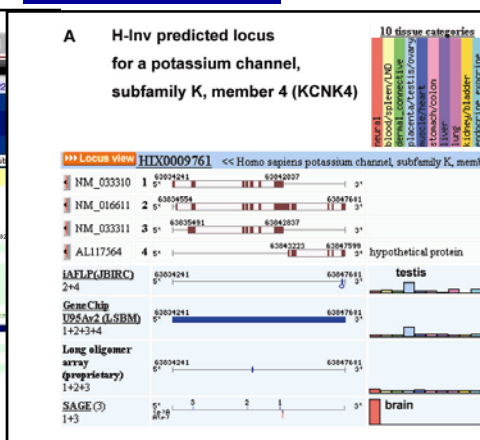
6 sub-databases for specific annotation topics

- ◆ **G-integra:** Original genome browser
- ◆ **H-ANGEL:** Gene expression profile database
- ◆ **Evola:** Database of molecular evolution
- ◆ **DiseaseInfo Viewer:** Database for disease relation
- ◆ **PPI view:** Database of Protein-protein interaction (PPI)
- ◆ **Gene family/group:** Annotation database of gene families/groups

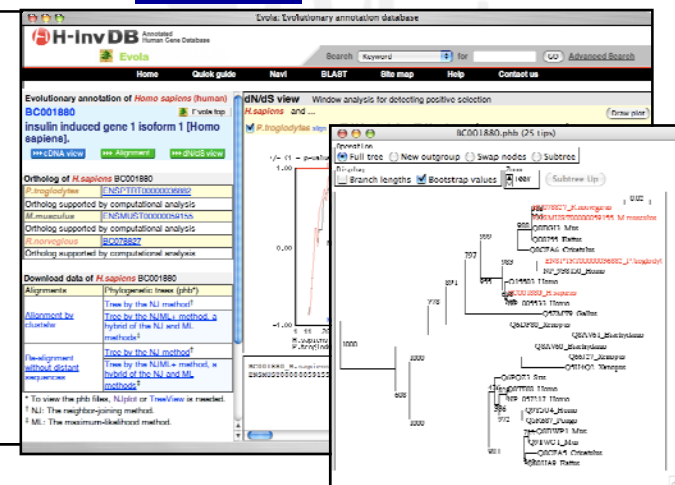
G-integra



H-ANGEL



Evola



H-InvDB satellite DBs and tools



H-DBAS: database of splicing variants



VarySysDB: database of annotated polymorphisms



LEGENDA: text-mining database



H-Exp: Human gene expression profile database



DNAProbeLocator: microarray probe database



G-compass: comparative genome browser



TACT: Transcriptome auto-annotation conducting tool

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H-InvDB searches



The screenshot shows the H-InvDB website interface. At the top, there is a search bar with a dropdown menu set to 'Keyword' and a 'GO' button. Below the search bar is a navigation menu with links: Home, Quick guide, Navi, BLAS, Site map, Download, Contact us, and Help. On the left side, there is a sidebar with a '[Japanese]' link and a list of navigation links: About Projects, Publications, Presentation, Release Information, Web Service, Topic Annotation, Gene Families/Groups, News, Statistics, Mail magazine, Maintenance, and FAQ. The main content area features a 'What is H-InvDB' section with a 'Sample view' link, followed by a detailed description of the database. To the right of the main content is a 'Human Chromosome Map' showing chromosomes 1 through 22 and X. At the bottom, there is a 'News' section with several entries. Red circles highlight the search bar, the 'Navi' and 'BLAS' menu items, the 'GO' button, the 'Human Chromosome Map' section, the 'Site Search' button, and the 'FAQ' link. Red arrows point from these circles to callout boxes on the right side of the page.

#1 Simple search
search by IID/keyword

#2 Advanced search
16 search contents
Detailed search by contents

#3 Chromosome map
Jump to genome location

#4 blast search
Search by sequence

#5 Search navi
Search navigation menu

#6 Site search
Search documents

Data availability



HTTP, FTP, web APIs

HTTP

FTP

H-InvDB
Annotated Human Gene Database

6th Anniversary H-InvDB_7.0 released on February 16, 2010.

Home Quick guide Navi BLJ Help

Download

[Japanese] What is H-InvDB [Sample]

What is H-InvDB
[About Projects](#)
[Publications](#)
[Presentation](#)
[Release Information](#)
[Web Service](#)
[Topic Annotation](#)
[Gene Families/Groups](#)
[News](#)
[Statistics](#)
[Mail magazine](#)
[Maintenance](#)
[FAQ](#)

An Integrated Database of Annotated Human Genes

H-Invitational Database (H-InvDB) is an integrated database of human genes and transcripts. By extensive analyses of all human transcripts, we provide curated annotations of human genes and transcripts that include [gene structures](#), [alternative splicing isoforms](#), [non-coding functional RNAs](#), [protein functions](#), [functional domains](#), [sub-cellular localizations](#), [metabolic pathways](#), [protein 3D structure](#), [genetic polymorphisms](#) (SNPs, indels and microsatellite repeats), [relation with diseases](#), [gene expression profiling](#), and [molecular evolutionary features](#), [protein-protein interactions \(PPIs\)](#) and [gene families/groups](#). This database is produced by the "Genome Information Integration Project" (2005-) based upon the annotation technology established in the H-Invitational Project for annotation of human full-length cDNAs.

0 annotation ([details](#))

- 14-Jan-10 Update of H-InvDB Enrichment Analysis Tool ([HEAT](#))
- 14-Jan-10 Renewal of FTP site ([new FTP](#))

Web Service

Current dataset

[Japanese] [ReadMe](#) [Previous dataset](#)

H-InvDB_7.0 released on February 16, 2010.

- List of H-Invitational IDs
- List of new, deleted and updated H-Invitational IDs
- Annotation data sets
- Section data of annotation
- Sequence data sets
- Results of computational analysis

FTP Download

FTP site for downloading data files in H-Invitational Database (DNA Data Bank of Japan).
ftp://ftp.ddbj.nig.ac.jp/mirror_database/hinv/

H-InvDB Web service REST API list

H-InvDB Web service provides the following APIs.

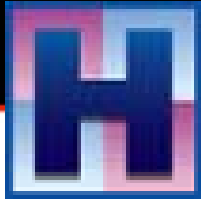
No.	API	Description	Document	Sample
1	acc2hit.php	query = Accession No. output = HIT ID	document	http://h-invitational.jp/hinv/hws/entry/BC053657/acc2hit.xml
2	band_list.php	query = genomic location output = chromosome band	document	http://h-invitational.jp/hinv/hws/get_band_list/chr1:10000-10000000
3	hit2acc.php	query = HIT ID output = Accession No	document	http://h-invitational.jp/hinv/hws/entry/HIT000022181/hit2acc.xml
4	hit_cnt.php	output = total number of HIT ID	document	http://h-invitational.jp/hinv/hws/get_hit_list/count
5	hit_definition.php	query = HIT ID output = HIT definition	document	http://h-invitational.jp/hinv/hws/entry/HIT000000001/definition.xml
6	hit_domain.php	query = HIT ID output = InterPro domain information	document	http://h-invitational.jp/hinv/hws/entry/HIT000000001/domain.xml
7	hit_evolution.php	query = HIT ID output = evolutionary information	document	http://h-invitational.jp/hinv/hws/entry/HIT000000001/evolution.xml
8	hit_expression.php	query = HIT ID output = gene expression information	document	http://h-invitational.jp/hinv/hws/entry/HIT000000001/expression.xml
9	hit_genename.php			

Web service APIs (SOAP, REST)

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-InvDB Enrichment Analysis Tool (HEAT)

Data-mining tool
Against integrated database, H-InvDB.

A data-mining tool for automatically identifying features specific to a given human gene set

Available annotation items:

- InterPro
- Gene Ontology (GO)
- KEGG pathway
- Chromosomal band
- Gene family
- Protein structure (SCOP)
- Subcellular localization (Wolf PSORT)
- Tissue-specific expression (H-ANGEL)
- Promoter sequence motif (JASPAR)

Execute



URL; <http://hinv.jp/heat/>

Example of HEAT execution

Submitted dataset: six gene names related to diabetes
(ADIPOQ, CAPN10, PPARG, TCF7L2, HNF4A, HHEX)

H-InvDB Enrichment Analysis Tool
H-InvDB Enrichment Analysis Tool (HEAT)

STEP 1 Gene-Set Submission | STEP 2 Converted Gene List | **STEP 3 Results**

Results
Enriched features

Resubmit Download

No.	Feature	Name	Submitted Gene-Set	Occurrences / Genes		P-value *
					All Representative Transcripts	
1	GO: 0003677	DNA binding		4 / 6	838 / 34511	0.00000498
2	GO: 0006355	regulation of transcription, DNA-dependent		4 / 6	1066 / 34511	0.0000129
3	Gene family: HIF0000022	Steroid hormone receptor (IPR001723).		2 / 6	46 / 34511	0.0000260
4	GO: 0004879	ligand-dependent nuclear receptor activity		2 / 6	48 / 34511	0.0000283
5	InterPro: IPR001723	Steroid hormone receptor		2 / 6	48 / 34511	0.0000283
6	InterPro: IPR001628	Zinc finger, nuclear hormone receptor-type		2 / 6	49 / 34511	0.0000295
7	SCOP: g.39.1.2	Nuclear receptor		2 / 6	49 / 34511	0.0000295
8	InterPro: IPR000536	Nuclear hormone receptor, ligand-binding, core		2 / 6	50 / 34511	0.0000307
9	GO: 0003707	steroid hormone receptor activity		2 / 6	51 / 34511	0.0000320
10	InterPro: IPR008946	Nuclear hormone receptor, ligand-binding		2 / 6	51 / 34511	0.0000320
11	SCOP: a.123.1.1	Nuclear receptor ligand-binding domain		2 / 6	51 / 34511	0.0000320
12	InterPro: IPR013088	Zinc finger, NHR/GATA-type		2 / 6	51 / 34511	0.0000320

Download

Annotation items

Frequency Scores

* Fisher's exact test

Publications related H-InvDB

The latest publication of H-InvDB in Nucleic Acids Research 2010 Database issue

D626–D632 Nucleic Acids Research, 2010, Vol. 38, Database issue
doi:10.1093/nar/gkp1020

Published online 23 November 2009

H-InvDB in 2009: extended database and data mining resources for human genes and transcripts

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Akiko Noda¹, Ryuichi Sakate¹, Takuya Habara¹, Hajime Nakaoka^{2,3}, Fusano Todokoro^{2,4},
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¹BIRC, AIST, ²JBIC, ³C's Lab Co. Ltd, ⁴DYNACOM Co. Ltd, ⁵Hitachi Ltd, ⁶CIB-DDBJ, NIG Waterfront Bio-IT
Research Building, 4-7 Aomi, Koto-ku, Tokyo 135-0064, Japan

Received September 16, 2009; Revised and Accepted October 19, 2009

Other publications:

http://h-invitational.jp/index_jp.html

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H-InvDB web service



- # H-InvDB web service provide SOAP and REST APIs.
- # System designed on the standard web-service guideline proposed in “Odaiba Manifesto”.



“Odaiba Manifesto”

Proposed at W4 of Biocuration2010 on 13th Oct., 2010.

Web service standard guideline @ Biohackathon

Tokyo Manifesto for semantic web

BIO HACKATHON '09
15-21 Mar. 2009
DBCLS Tokyo / OIST Okinawa
Japan

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Guideline for Web Services (Manifesto ver.2.0)


This document is a guideline to design web services toward integration.

- REST
 - For a database service, REST services to call entries and search by a keyword should be provided.
 - To unify query formats, the query languages should conform to Common Query Language.
 - A method to get the number of hits for a keyword should be provided.
 - A method to get the list of hit entries for a keyword should be provided.
 - A method to get the entry from an ID should be provided.
 - If the entry does not exist, the method should return code 404 and an empty entry.
 - Path parameters (/foo/bar/baz) should be used for a REST URL and query parameters (param1=value1¶m2=value2) should not be used.
 - Lower-case letters should be used for path parameters in principle.
 - If a URL ends "/", a list of possible strings after the URL should be returned in principle.
 - When a method returns a list, each line should correspond to an entry and each line should be divided by tab into fields.
 - As REST web services can be called from AJAX, an alternative could be ⇨JSON.
 - ⇨HTTP codes should be used for error signaling. It is allowed to also send in the answer some text.
- SOAP

<http://hackathon2.dbcls.jp/wiki/GuidelineForWebService>



METI Life science integrated database Project, Japan



MEDALS
METI database portal for life science

HOME Database Tool Download Integrated DB MEDALS Tool

Japanese Search

METI Life science integrated database portal site

This portal site provides information about the database, analysis tool, and the relevant projects, that conducted with financial support from Ministry of Economy, Trade and Industry, JAPAN. NOW PRODUCTS:107 (Database:62, Analysis tool:45) NOW PROJECTS:19 To make these outcomes access-friendly and utilized more effectively, we are still surveying all the projects and increasing the number of the outcomes to the list. MEDALS stands for METI DAatabase portal for Life Science; and METI stands for Ministry of Economy, Trade and Industry. [READ MORE](#)

Database catalog All list (62)

- Various information of databases.
- DNA/Genome (23) RNA (18)
- Protein (23) The others (41)

Tool catalog All list (45)

- Information about useful tools of data analysis.
- DNA/Genome (13) RNA (16)
- Protein (16) The others (16)

Project catalog All list (19)

- [Links between projects and products](#)
- [Genome Information Integration Project \(GIIP\)](#)
- [Life science database integration project](#)

Integrated DB

- Various integrated databases.
- All human gene database (H-InvDB)
- MEXT Integrated Database Project (collaborator) [UBCLIS](#)

Advanced search

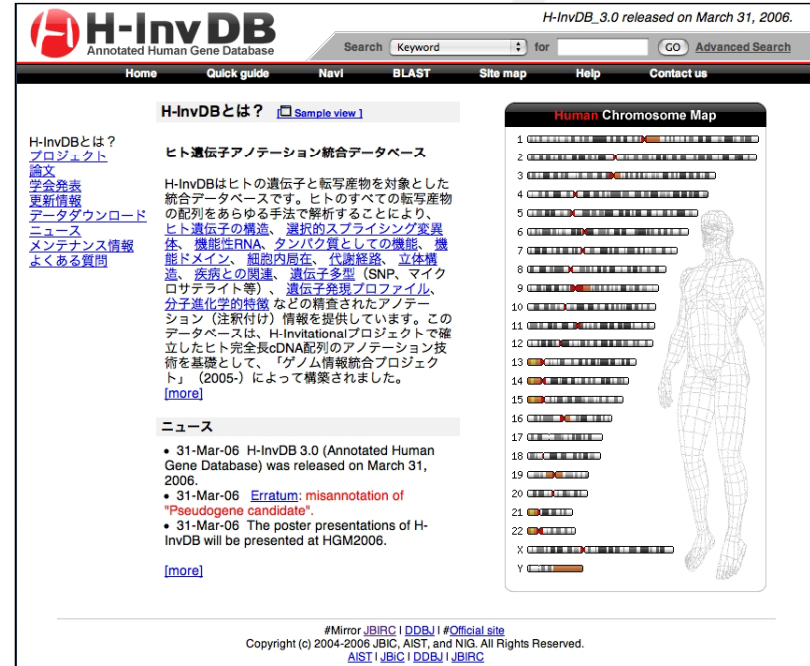
- Keyword search in MEDALS site.
- Advanced search

MEDALS Tool All list (4)

- Tools developed in this project.
- [Hyperlink Management System](#)
- [ID Converter System](#)
- [Paper recommendation tool \(PubMedScan\)](#)
- [PMID-Extractor](#)

MEDALS

Life science integrated database
portal site



H-InvDB
Annotated Human Gene Database

Search Keyword for GO Advanced Search

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ヒト遺伝子アノテーション統合データベース

H-InvDBはヒトの遺伝子と転写産物を対象とした統合データベースです。ヒトのすべての転写産物の配列をあらゆる手法で解析することにより、**ヒト遺伝子の構造、選択的スプライシング変異体、機能性RNA、タンパク質としての機能、機能ドメイン、細胞内局在、代謝経路、立体構造、疾病との関連、遺伝子多型 (SNP、マイクロサテライト等)、遺伝子発現プロファイル、分子進化的特徴**などの精査されたアノテーション (注釈付け) 情報を提供しています。このデータベースは、H-Invitationalプロジェクトで確立したヒト完全長cDNA配列のアノテーション技術を基礎として、「ゲノム情報統合プロジェクト」(2005-)によって構築されました。
[\[more\]](#)

ニュース

- 31-Mar-06 H-InvDB 3.0 (Annotated Human Gene Database) was released on March 31, 2006.
- 31-Mar-06 [Erratum: misannotation of "Pseudogene candidate"](#).
- 31-Mar-06 The poster presentations of H-InvDB will be presented at HGM2006.

[\[more\]](#)

Human Chromosome Map

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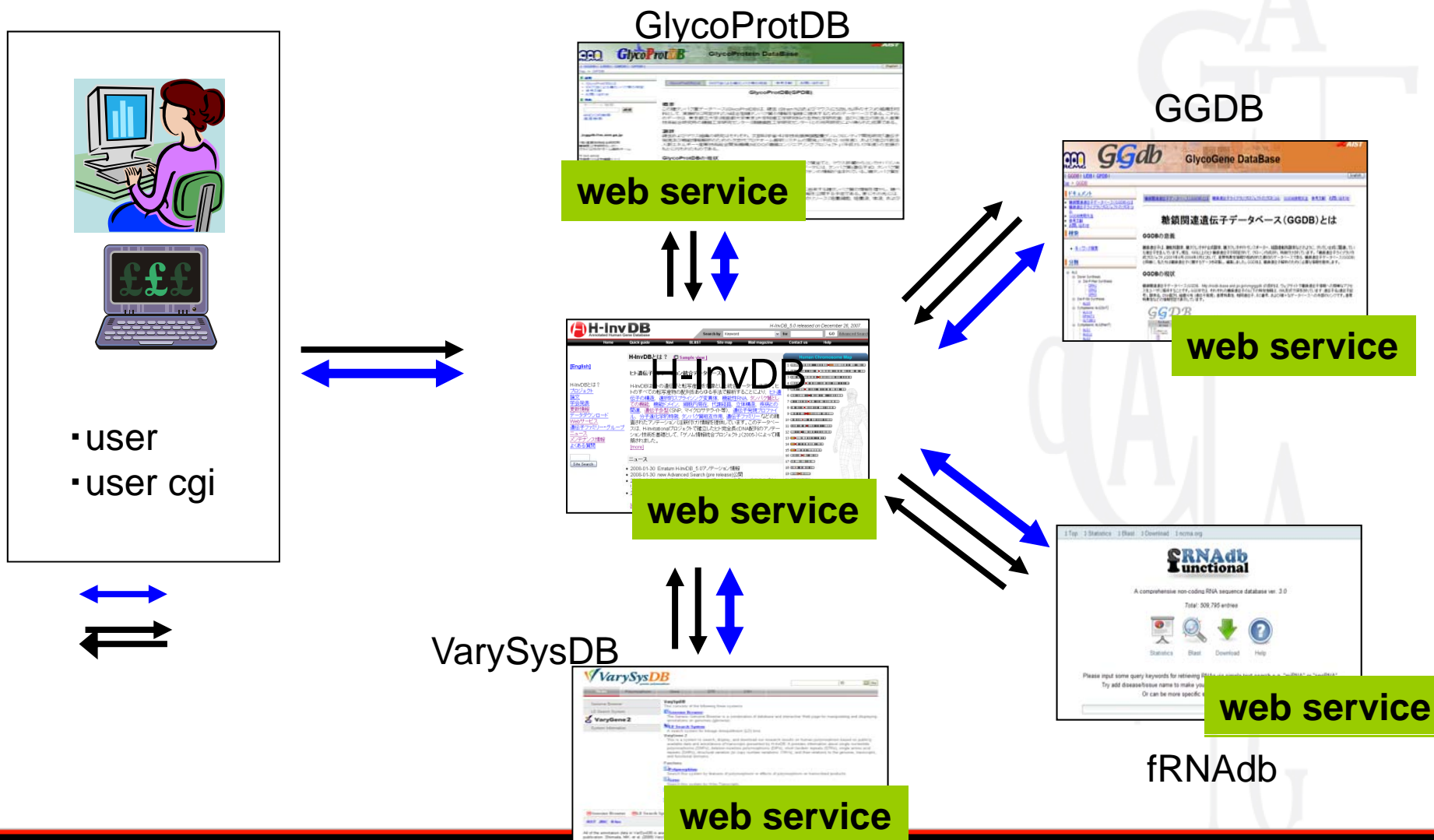
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H-InvDB

Integrated database of human genes
Database integration by web service

Database integration by web services

We integrated H-InvDB and five databases by web services
All six services were designed on the standard web-service guideline proposed in "Odaiba Manifesto".





H-InvDB is freely available at

hinv.jp

