

IPAD: the Integrated Pathway Analysis Database for Systematic Enrichment Analysis

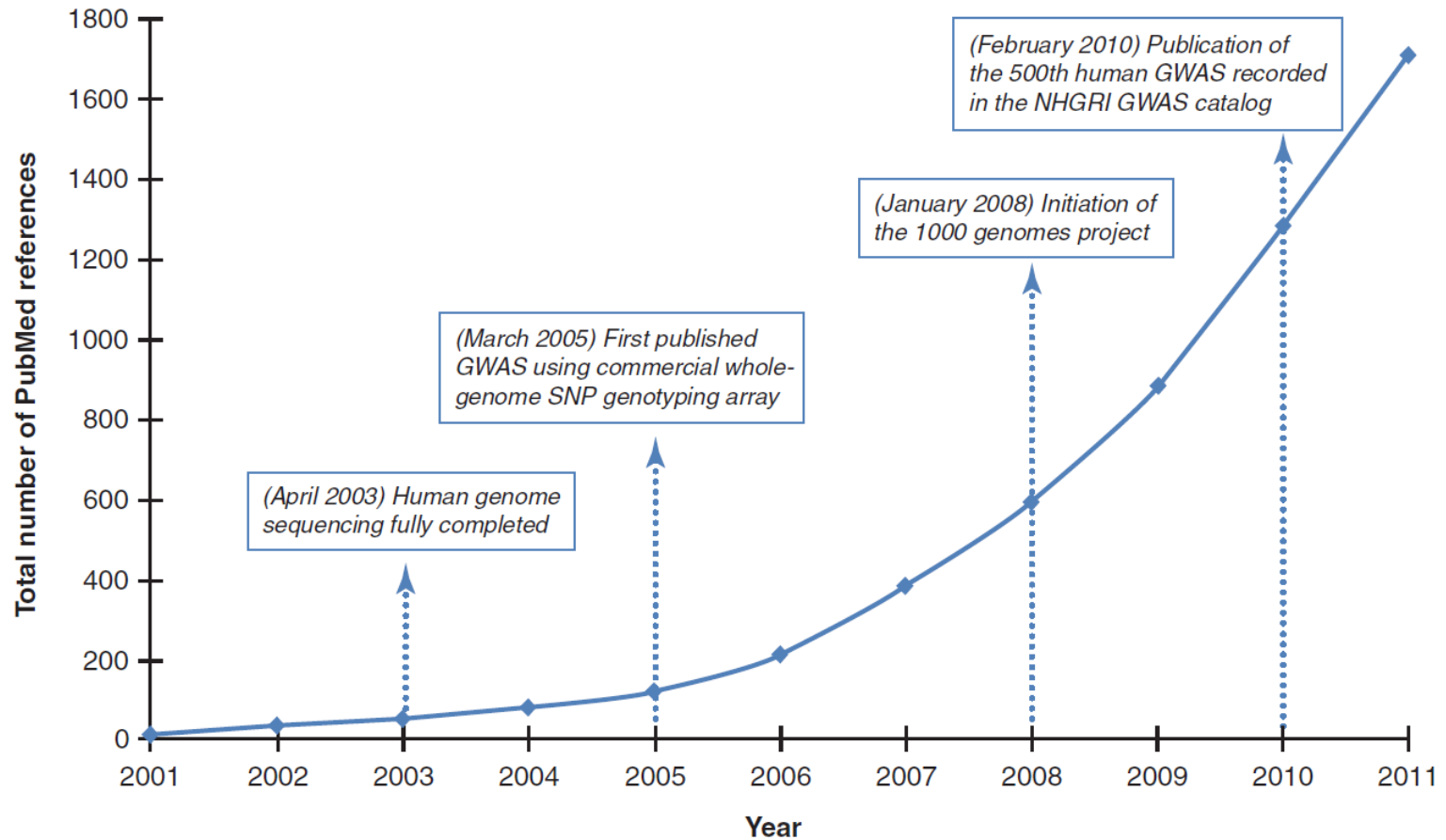
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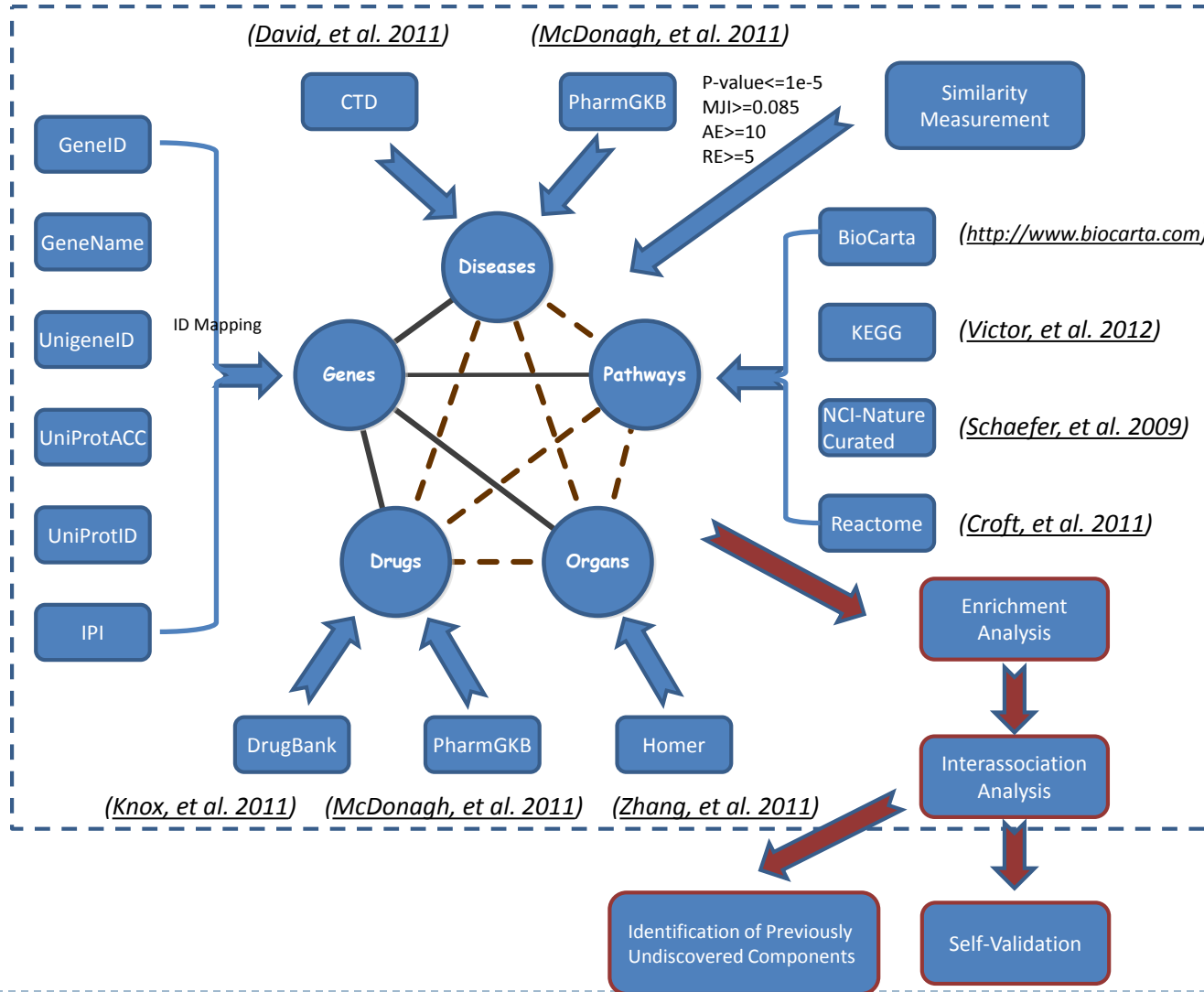
Introduction



TRENDS in Genetics

Vijay K. Ramanan et al. 2012

What is IPAD



Five criteria for designing the IPAD

- ▶ 1) comprehensive pathway coverage;
- ▶ 2) gene/protein to pathway/disease/drug/organ association;
- ▶ 3) interassociation between pathway, disease, drug, and organ;
- ▶ 4) multiple and quantitative measurement of enrichment and interassociation;
- ▶ and 5) cross-linking of multiple available data sources.



Current Statistics of IPAD

Pathways and Molecules	Count
Total Number of Pathways	1956 (BioCarta:310,KEGG:247, NCI-Nature curated:222, Reactome:1177)
Total Number of Molecules	11663
Diseases and Molecules	Count
Total Number of Diseases	6704 (CTD:5892, PharmGKB:812)
Total Number of Molecules	17925
Drugs and Molecules	Count
Total Number of Drugs	5615 (DrugBank:4604, PharmGKB:1011)
Total Number of Molecules	3735
Organs and Molecules	Count
Total Number of Organs	52
Total Number of Molecules	5599

Three Innovative Functions

- ▶) The most interesting and novel aspect is "inter-association analysis", which predicts relationships between components (pathways, diseases, drugs, and organs) on the basis of intermediating gene sets,
- ▶ 2) ability to identify previously undiscovered components (pathways, diseases, drugs, and organs) by the traditional pathway enrichment analysis.
- ▶ 3) ability to self-validate by enrichment analysis and inter-association analysis,



IPAD Search Interface

Search by Genes or Proteins

Enter a Unigene ID such as Hs.523852, a Entrez Gene ID such as 4916, a Gene Name BRCA2 of a gene, a Uniprot ID such as P53_HUMAN, or a IPI ID such as IPI01010829 of a protein. **a**

To enter multiple values delimit them by comma, semi-colon, line, or space.
 Examples: 1) AKT1, Hs.523852;BRCA2 2) IPI01010829, Hs.517517 ERBB2 3) 5925;Hs.514681,P53_HUMAN BAP1;PBRM1 4) **Example**

Home > Enrichment Analysis

Pathway Disease Drug Organ

Enrichment Thresholds Pvalue less than: 1.0

Show 10 entries Search:

PathwayID	PathwayName	Molecule	AE	RE	N	MJI	Pvalue
hsa05212	Pancreatic cancer	PKCA_HUMAN; AKT1; ERBB2; Hs.523852; 5925; P53_HUMAN; BRCA2	7	75.59	72	-2819	7.42e-11

b

Home > Enrichment Analysis

Pathway Disease Drug Organ

Enrichment Thresholds Pvalue less than: 1.0

Show 10 entries Search:

DiseaseID	DiseaseName	Molecule	AE	RE	N	MJI	Pvalue
MESH:D002528	Cerebellar Neoplasms	5925; ERBB2; Hs.523852; Hs.514681; IPI01010829; AKT1; Hs.517517; P23771; P53_HUMAN	9	32.39	332	.3136	2.51e-10
MESH:D042883	Cholelithiasis	Hs.514681; BRCA2; Hs.523852; AKT1; ERBB2; P53_HUMAN	6	45.67	157	.2191	2.36e-8

c

Home > Enrichment Analysis

Pathway Disease Drug Organ

Enrichment Thresholds Pvalue less than: 1.0

Show 10 entries Search:

DrugID	DrugName	Molecule	AE	RE	N	MJI	Pvalue
PA451581	tamoxifen	ERBB2; BRCA2; AKT1; P53_HUMAN; 5925	5	18.03	74	.2124	3.06e-5
PA13101952	gefitinib	Hs.523852; ERBB2; BAP1	4	27.36	39	.1941	3.91e-5

d

Home > Enrichment Analysis

Pathway Disease Drug Organ

Enrichment Thresholds Pvalue less than: 1.0

Show 10 entries Search:

OrganID	OrganName	Molecule	AE	RE	N	MJI	Pvalue
larynx	larynx	Hs.523852; Hs.517517	2	25.45	88	-.2114	4.93e-3
salivary gland	salivary gland	Hs.523852	1	10.00	112	.1045	1.13e-1
mouth	mouth	P53_HUMAN	1	7.00	160	-.1031	1.56e-1
lymph node	lymph node	BRCA2	1	5.23	214	-.1023	2.02e-1

Showing 1 to 4 of 4 entries

e

Browse > Molecule P53_HUMAN

Pathway Disease Drug Organ

Show 10 entries Search:

Molecule	GeneName	PathwayID	PathwayName
P53_HUMAN	TP53	109581	Apoptosis
P53_HUMAN	TP53	109582	Hemostasis

f

Browse > Component hsa05212

Pathway Disease Drug Organ

Show 10 entries Search:

Component	PathwayID	PathwayName	AE	RE	MJI	Pvalue
hsa05212	hsa05200	Pathways in cancer	71	33.05	-.5951	3.04e-66
hsa05212	hsa05220	Chronic myeloid leukemia	42	91.94	.5755	1.67e-57

g

Pathway-Pathway, Disease-Pathway, Drug-Pathway, Organ-Pathway

Browse > Component hsa05212

Pathway Disease Drug Organ

Show 10 entries Search:

Component	DiseaseID	DiseaseName	AE	RE	MJI	Pvalue
hsa05212	MESH:D046152	Gastrointestinal Stromal Tumors	27	30.40	-.2841	1.28e-27
hsa05212	MESH:D008209	Lymphedema	25	15.37	-.2247	2.58e-19

h

Pathway-Disease, Disease-Disease, Drug-Disease, Organ-Disease

Browse > Component hsa05212

Pathway Disease Drug Organ

Show 10 entries Search:

Component	DrugID	DrugName	AE	RE	MJI	Pvalue
hsa05212	PA450191	lecithin	14	45.37	-.2334	1.35e-17
hsa05212	PA450635	nitric oxide	19	16.74	-.1995	7.83e-16
hsa05212	PA7000	sorafenib	10	83.13	-.2994	2.77e-15

i

Pathway-Drug, Disease-Drug, Drug-Drug, Organ-Drug

Browse > Component 1643685

Pathway Disease Drug Organ

Show 10 entries Search:

Component	OrganID	OrganName	AE	RE	MJI	Pvalue
1643685	tonsil	tonsil	23	12.83	-.1694	1.19e-16

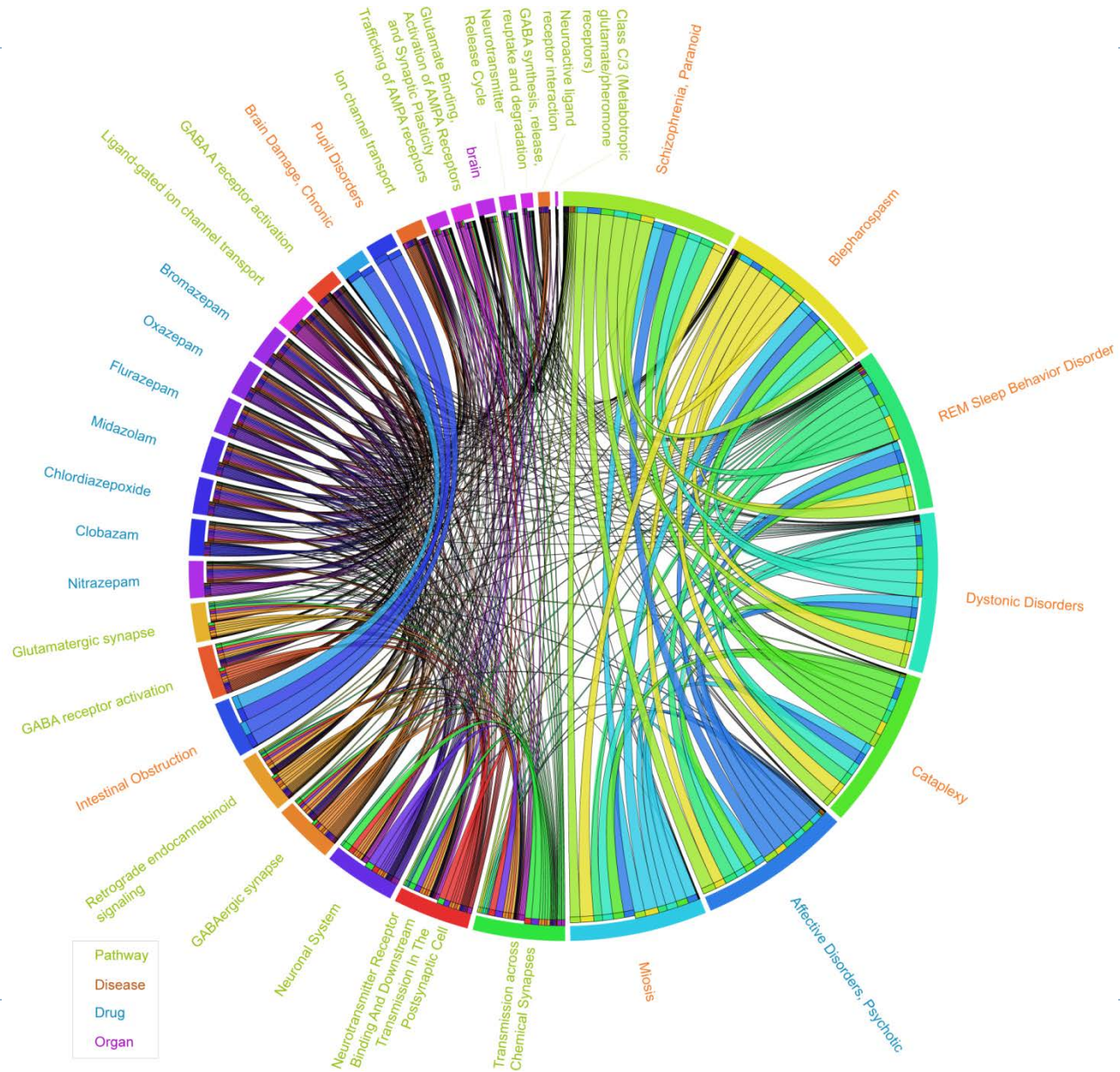
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Pathway-Organ, Disease-Organ, Drug-Organ, Organ-Organ

Identification of Previously Undiscovered Components

Novel	pathwayid	pathwayname	p-value	C	AE	RE	MJI
yes	381150	Diabetes pathways	1.76E-96	2	108.00	52.19	0.701
yes	109582	Hemostasis	4.33E-64	1	78.00	24.87	0.583
yes	913709	O-linked glycosylation of mucins	1.61E-57	1	63.00	30.85	0.583
yes	76005	Response to elevated platelet cytosolic Ca2+	1.06E-110	1	78.00	140.52	0.970
yes	597592	Post-translational protein modification	1.68E-154	1	183.00	30.85	0.742
yes	391251	Protein folding	9.19E-50	1	54.00	30.85	0.571
yes	446203	Asparagine N-linked glycosylation	3.60E-76	1	85.00	30.85	0.612
Novel	Diseaseid	DiseaseName	p-value	C	AE	RE	MJI
yes	MESH:D058729	Peripheral Arterial Disease	2.58E-19	1	29.00	11.82	0.211
yes	MESH:D056006	Leprosy, Multibacillary	3.92E-19	1	26.00	13.83	0.201
yes	MESH:C537153	Hypomagnesemia primary	9.35E-21	1	31.00	12.15	0.223
yes	MESH:D001025	Aortitis	2.09E-19	1	31.00	10.79	0.218
yes	MESH:D001661	Biliary Tract Neoplasms	4.82E-20	1	31.00	11.42	0.221
yes	MESH:D002754	Choanal Atresia	7.89E-19	1	26.00	13.41	0.199
yes	MESH:D002528	Cerebellar Neoplasms	6.22E-28	1	38.00	15.34	0.276
yes	MESH:D008850	Microphthalmos	4.81E-19	1	30.00	10.96	0.213
yes	MESH:D009175	Mycoplasma Infections	2.55E-20	1	30.00	12.30	0.218
yes	MESH:D008947	Mixed Connective Tissue Disease	3.62E-21	1	29.00	14.03	0.219
yes	MESH:D012555	Schistosomiasis mansoni	1.72E-22	1	37.00	10.78	0.253
yes	MESH:D008179	\Lupus Erythematosus, Discoid\	6.06E-22	1	26.00	18.44	0.218
yes	MESH:D011665	Pulmonary Valve Insufficiency	2.76E-22	1	27.00	17.74	0.221
yes	MESH:D018188	Cardiovirus Infections	1.22E-22	1	37.00	10.90	0.253
yes	MESH:D008010	Lichen Planus	4.45E-22	1	28.00	16.25	0.222
yes	MESH:D007918	Leprosy	1.05E-20	1	32.00	11.53	0.227
Novel	DrugID	DrugName	p-value	C	AE	RE	MJI
yes	PA131301952	gefitinib	8.52E-17	8	29.88	10.84	0.395
yes	PA451283	rosiglitazone	7.73E-22	5	41.40	10.58	0.386
yes	PA448803	carboplatin	2.57E-15	5	27.00	11.36	0.397
yes	PA449552	etoposide	2.32E-18	4	33.25	11.28	0.400
yes	PA450198	leucovorin	9.91E-16	4	31.25	10.94	0.423
yes	PA450947	phenytoin	2.13E-15	3	27.67	10.62	0.366
yes	PA448771	capecitabine	7.75E-16	2	26.50	11.68	0.412
yes	PA449165	cyclophosphamide	2.35E-23	2	40.50	10.94	0.385
yes	PA449015	citalopram	8.78E-17	1	31.00	10.02	0.465
yes	DB00143	Glutathione	3.34E-18	1	32.00	10.65	0.432
Novel	OrganID	OrganName	p-value	C	AE	RE	MJI
yes	tonsil	tonsil	5.26E-18	23	20.52	37.17	0.263

Self-Validation



Thank you for your attention!

