

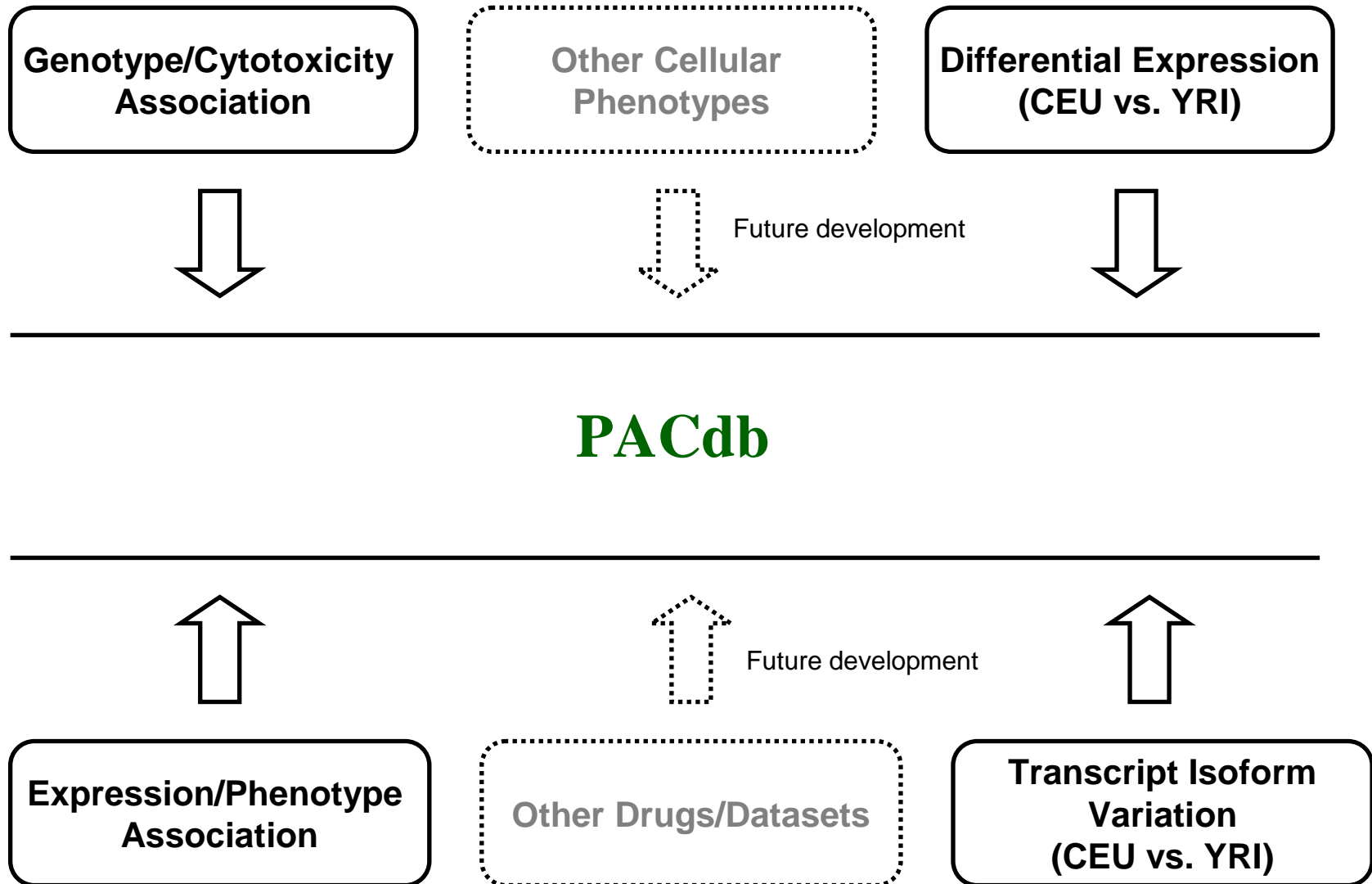
PACdb <http://www.PACdb.org/>

Tutorial Version 1.0 (Updated 12-01-2009)

What is PACdb?

PACdb is a **P**harmacogenetics **a**nd **C**ell line **datab**ase for use as a central repository of pharmacology-related phenotypes that integrates genotypic, gene expression, and pharmacological data obtained via lymphoblastoid cell lines (LCLs), particularly the HapMap CEU (Caucasians from Utah, USA) and YRI (Yoruba people from Ibadan, Nigeria) samples.

PACdb Architecture



Primary Data Served (PACdb v1.0, Dec. 2009)

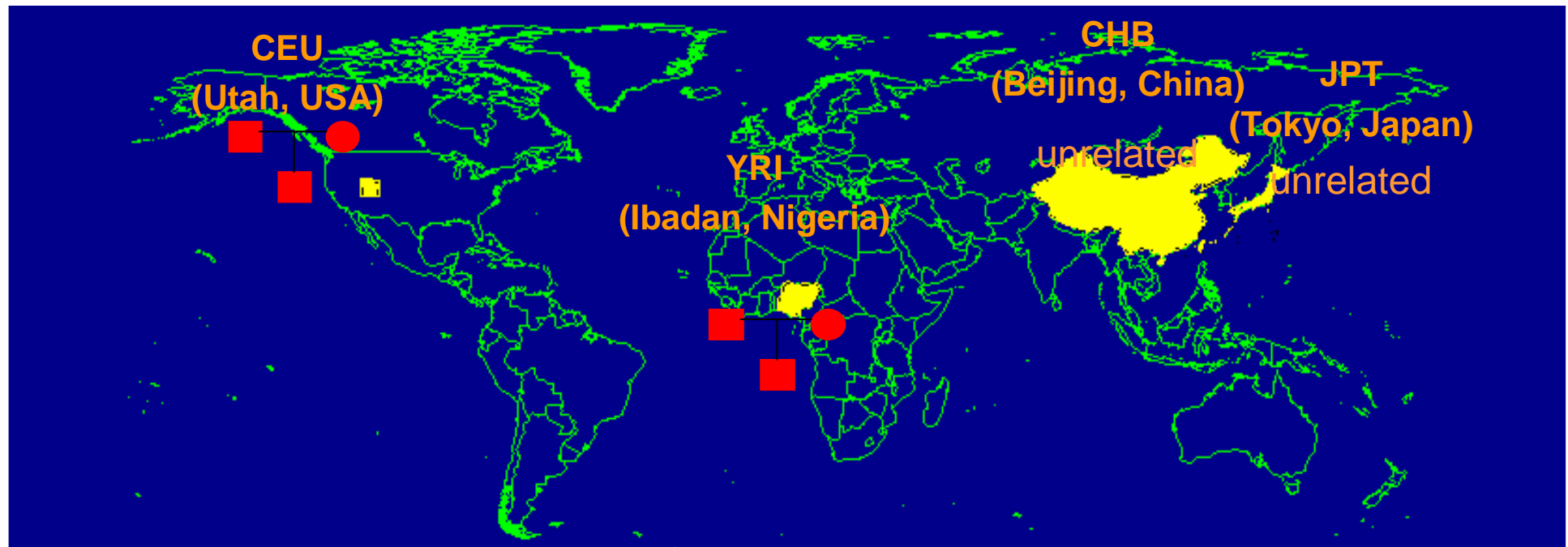
- Whole genome analysis of genotype and cytotoxicity association in the HapMap CEU and YRI samples, separately;
- Summary analysis which identifies differentially expressed transcript clusters between the CEU and YRI samples;
- Analysis of genotype and gene expression association;
- Summary information of correlations between gene expression and pharmacological phenotypes;
- Functional and physical annotations of single nucleotide polymorphisms (SNPs) and genes currently distributed across several public databases;
- Five anticancer drugs are included: carboplatin, cisplatin, etoposide, daunorubicin and cytarabine (Ara-C).



What are the HapMap LCL Samples?

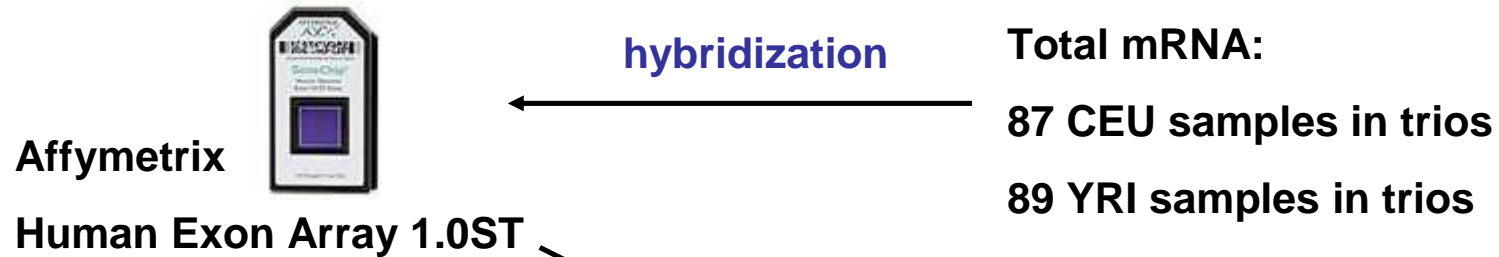
<http://www.hapmap.org/>

Epstein Barr Virus-transformed LCLs derived from apparently healthy individuals
Extensive genotypic data (>3.1 million SNPs) are publicly available

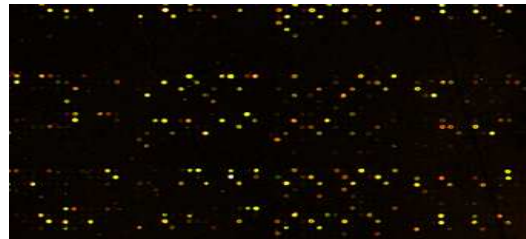


Primary Data I.

Exon Array mRNA Expression Data

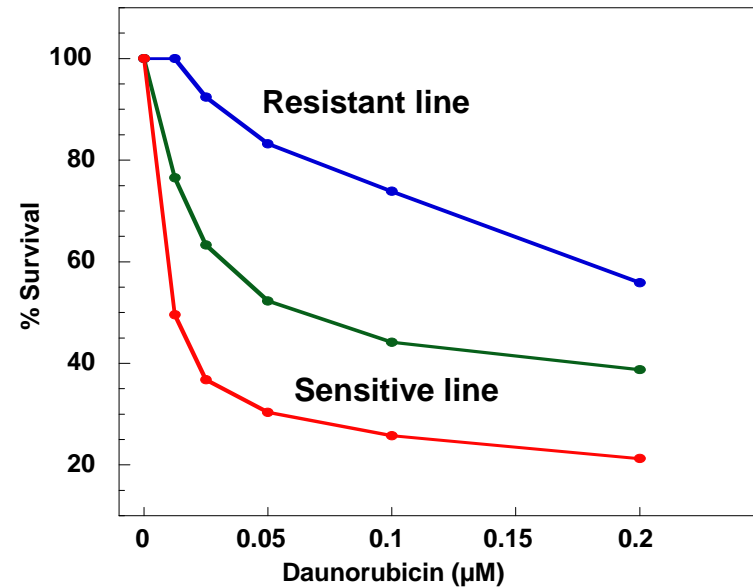


mRNA expression data (GSE9703)
~10,000 expressed gene-level transcripts
~110,000 expressed exon-level probesets



Primary Data II.

Drug Response/Cytotoxicity Data



- Cell growth inhibition experiments were conducted using a high-throughput alamarBlue™ assay
- IC_{50} --- concentration at which 50% of cell growth inhibition occur

Primary Data III.

HapMap Phase 2 Data

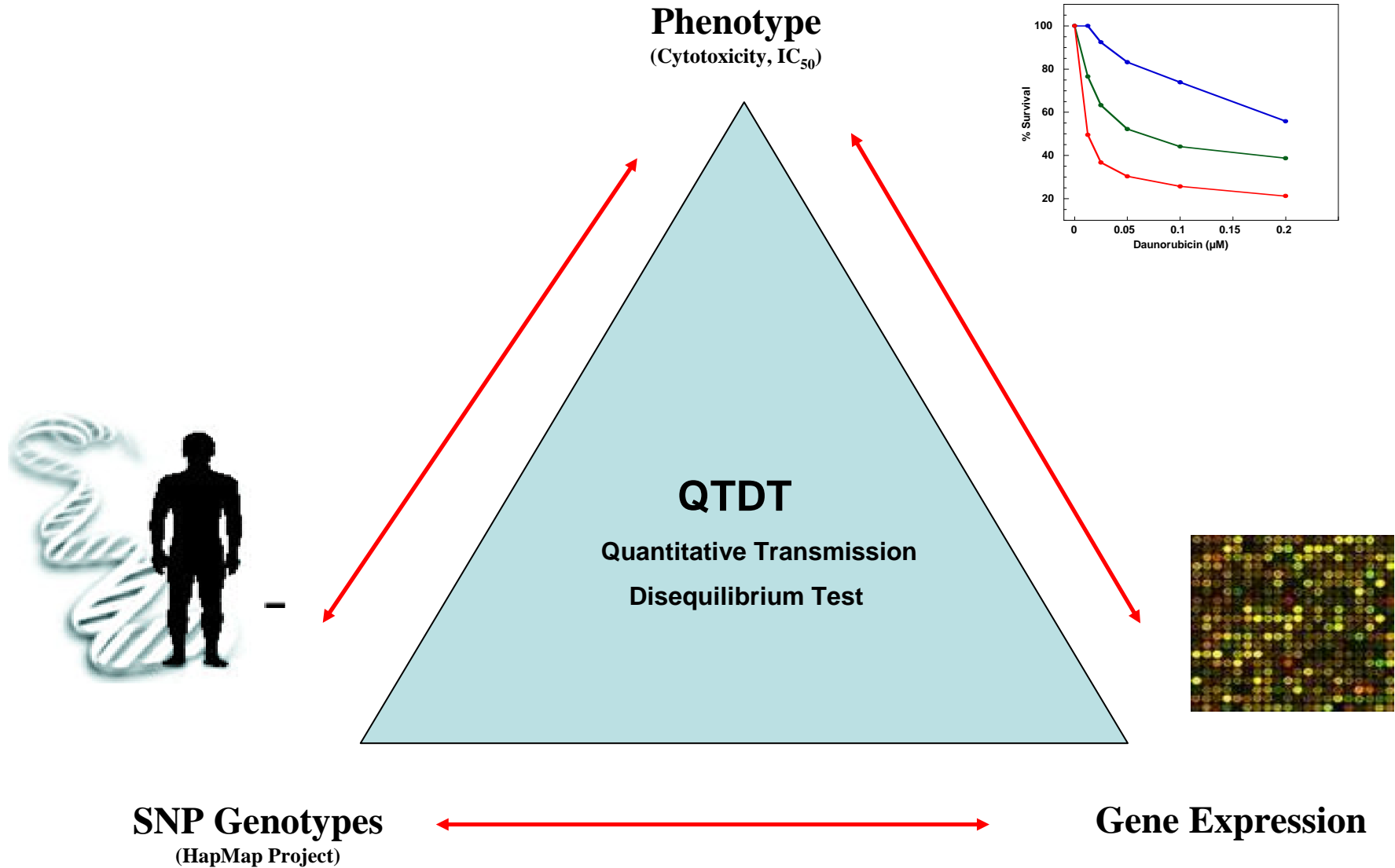


Chromosome 2 AACACGCCA.... TTCGAGGTC.... AGTCAACCG....
Chromosome 3 AACATGCCA.... TTCGGGGTC.... AGTCAACCG....
Chromosome 4 AACACGCCA.... TTCGGGGTC.... AGTCAACCG....

~2 million common HapMap SNPs (release 23a)

<http://www.hapmap.org/>

The "Triangle" Approach



Example 1: Search for Cytotoxicity/Genotype Association

PACTB

Home | Search | Resources | SCAN | Contact Us

Cytotoxicity / Genotype Association

Cytotoxicity / Genotype Association
Differential Expression
Gene Expression / Phenotype Association
Splicing Index

Select drug:

Select population:

Enter SNPs:

or

Upload SNP list:

Enter p-value threshold:

Enter q-value threshold:

Select a drug

Select a population

SNPs (optional)

Specify p-value or q-value

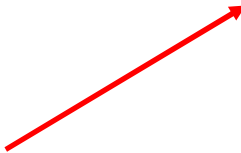
Example 2: Output Format for Cytotoxicity/Genotype Association

PACDB

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Population	Drug	Phenotype	SNP	Chrom	Position	Annotation (Host Gene, SNP Function)	P-value	Q-value	df	test stat
CEU	CEU	cisIC50	rs4385460	8	74600166	NA, NA	3e-07	0.134016	84	30.94
CEU	CEU	cisIC50	rs4237006	8	74600498	NA, NA	3e-07	0.134016	84	30.94
CEU	CEU	cisIC50	rs4237009	8	74600943	NA, NA	3e-07	0.134016	84	30.94
CEU	CEU	cisIC50	rs7002974	8	74604073	NA, NA	3e-07	0.134016	84	30.94
CEU	CEU	cisIC50	rs7012096	8	29033527	KIF13B , intron[NM_015254.3]	4e-07	0.142951	82	30.58



Link to more annotation
information

Example 3: Gene Annotation

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Link to SCAN

(SNP and Copy Number Annotation Database)

Search Gene:

Exon/Intron, RNA and protein products:	<p style="text-align: center;">NC_000008.10</p> <p>◀ 29120610] 5' ----- 3' ◀ 28924795]</p> <p>NM_015254.3 ----- NP_056069.2 ----- NP_056069.2</p> <p>■ - coding region ■ - untranslated region</p>
Gene Info:	<p>GeneID: 23303 Name: KIF13B Description: kinesin family member 13B Gene Type: protein-coding Chromosome: 8 Start: 28980713 End: 29176528 Strand: - Map Location: 8p21.1 Locus Tag: - Other Designations: guanylate kinase associated kinesin kinesin 13B Nomenclature: kinesin family member 13B Chr Accession Ver: NC_000008.9</p>

Example 4: Search for Genes Differentially Expressed (CEU vs. YRI)

PAEdb

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[Cytotoxicity / Genotype Association](#)

[Differential Expression](#)

[Gene Expression / Phenotype Association](#)

[Splicing Index](#)

Differential Expression

P-value of differential expression:

GLM p-value*

Permuted p-values of differential expression:

» Upper = one-sided p-value for CEU > YRI

» Lower = one-sided p-value for CEU < YRI

Upper:

Westfall-Young p-value*

Lower:

Enter transcript ID if interested in particular genes

» Enter Transcript Clusters:

*Specify a cutoff based on either the General Linear Model or Westfall-Young approach

Example 5: Output Format for Differential Expression

PACDB

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Transcript ID	Gene	P-value lower ¹	P-value upper ¹
3226340	PTGES2	1	0
3820727	QTRT1	1	0
3816611	THOP1	1	0
3181240	TMOD1	1	0
3937252	ZDHHC8	1	0
3261643	NFKB2	1	0
3225096	LOC253842	1	0
2865050	RPS23	1	0
2560141	MRPL53	1	0
3774635	FASN	1	0
3893642	LIME1	1	0
3299504	ACTA2	1	0
3230811	DPP7	1	0
2326993	SYTL1	1	0
3431892	SH2B3	1	0

Download results

Link to more annotation information

Example 6: Search for Cytotoxicity/Expression Association

PTCAS

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Expression / Phenotype Information

Cytotoxicity / Genotype Association
Differential Expression
Gene Expression / Phenotype Association
Splicing Index

Select drug:

Enter Transcript Clusters:

or

Upload Transcript Cluster list:

Enter Genes:

or

Upload Gene list:

Enter p-value threshold:

Enter q-value threshold:

Select a drug

Enter transcript IDs or gene symbols

Specify p-value or q-value

Example 7: Search for Splicing Index

PACTB

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Splicing Index

- Cytotoxicity / Genotype Association
- Differential Expression
- Gene Expression / Phenotype Association
- Splicing Index

Enter transcript IDs or gene symbols

Enter Transcript Clusters:

or

Upload Transcript Cluster list:

Enter Genes:

or

Upload Gene list:

Example 8: Output Format for Splicing Index Search

PACDB

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Transcript ID	Sample	Probeset ID	Splicing Index	Chrom	Gene
3432438	GM06985	3432440	1.025	12	OAS1
3432438	GM06991	3432440	0.9832	12	OAS1
3432438	GM06993	3432440	0.9866	12	OAS1
3432438	GM06994	3432440	0.984	12	OAS1
3432438	GM07000	3432440	0.9556	12	OAS1
3432438	GM07019	3432440	1.005	12	OAS1
3432438	GM07022	3432440	0.9962	12	OAS1
3432438	GM07029	3432440	1	12	OAS1
3432438	GM07034	3432440	0.9873	12	OAS1
3432438	GM07048	3432440	0.948	12	OAS1
3432438	GM07055	3432440	1.011	12	OAS1
3432438	GM07056	3432440	0.981	12	OAS1
3432438	GM07345	3432440	0.9692	12	OAS1
3432438	GM07348	3432440	0.9615	12	OAS1
3432438	GM07357	3432440	0.9938	12	OAS1
3432438	GM10830	3432440	0.9582	12	OAS1
3432438	GM10831	3432440	0.9873	12	OAS1
3432438	GM10835	3432440	0.9791	12	OAS1
3432438	GM10838	3432440	0.9828	12	OAS1
3432438	GM10839	3432440	0.9801	12	OAS1
3432438	GM10846	3432440	1.027	12	OAS1
3432438	GM10847	3432440	1.015	12	OAS1

Download results

Link to more annotation information

CITATION INFO

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Additional References: <http://www.pacdb.org/references.html>

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