

# BPA Grantee Research Update and Coordination Meeting



# Web-based Portal for Sharing BPA-related Genomics Data And Gene Lists

(<http://BPAGenomics.org>)

## Goals:

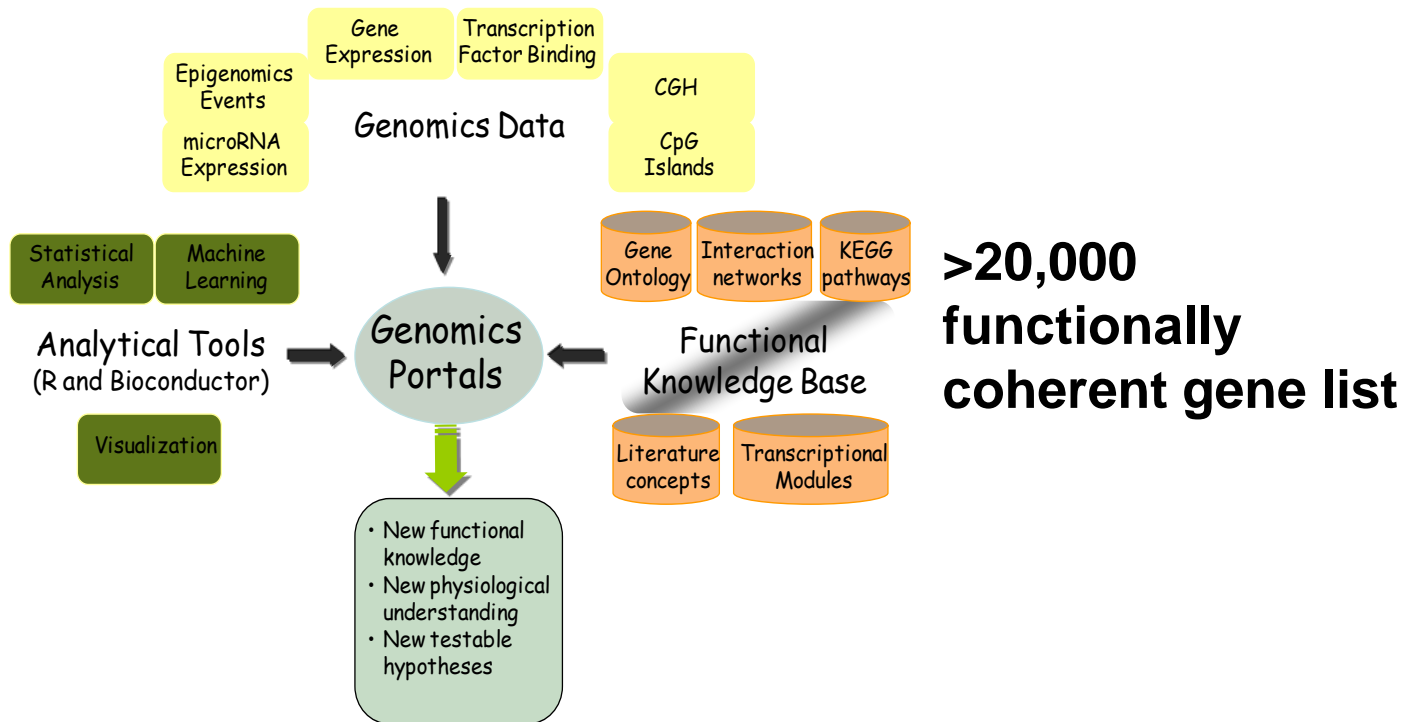
- Facilitate exchange and mining of genomics data between different projects
- Facilitate access and mining of relevant public genomics data
- Leveraging existing knowledge base in mining own data
- Building BPA-related “knowledge base”
- Facilitate integrative analyses

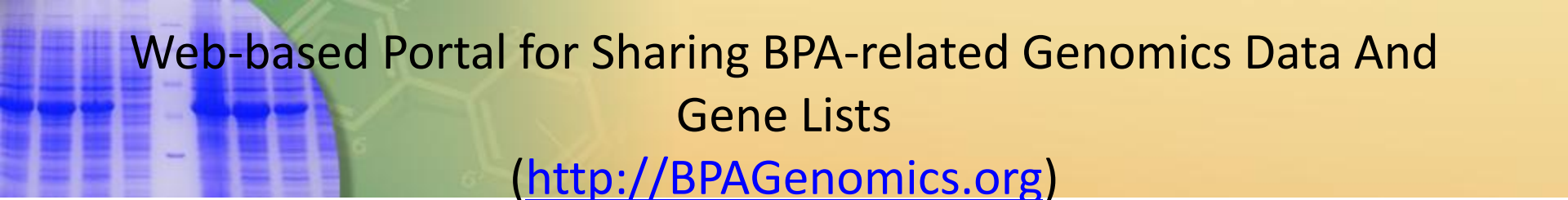
# Genomics Portals

(<http://GenomicsPortals.org>)

Web-based integrative computational platform for the analysis and mining of genomics data  
(data + knowledge base + analytical tools)

**~2 billion data points** (100k  
genome-scale vectors)





# Web-based Portal for Sharing BPA-related Genomics Data And Gene Lists

(<http://BPAGenomics.org>)

## **Progress (first two months):**

- Uploaded several datasets from provided by BPA researchers – one public domain and two private
- Uploaded some public domain data we found in GEO
- Uploaded CTD gene lists
- Expanded the functionality of the portals:
  - Associating gene lists to the portal – beginning so the BPA “knowledge base”
  - Global differential gene expression analysis
  - Global comparisons of differentially expressed genes between datasets
  - Numerous “behind the scene tweaks” (additional servers etc)

# Genomics Portals – Data and Gene Lists

(<http://BPAgenomics.org>)

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**My Data**

Local users only

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**BPA Genomics Data Portal**

This is a **web-portal** for accessing our (soon to be) comprehensive database of **genomics datasets** related to **health effects of BPA exposure**. Genomics data types in this portal range from simple **gene expression** datasets to **comparative genomics hybridization** and **epigenomics** datasets. Please see the slides for the **objectives** of this portal and the example of how to **analyze** the data in the portal.

Gene lists relevant to this portal

	Name	Description	Reference
<input type="checkbox"/>	<a href="#">G006780</a> <a href="#">view genes</a>	bisphenol A	Davis AP, et al. Nucleic Acids Res. 2009 Jan;37(Database issue):D786-92.
<input type="checkbox"/>	<a href="#">G006780_expression</a> <a href="#">view genes</a>	bisphenol A	Davis AP, et al. Nucleic Acids Res. 2009 Jan;37(Database issue):D786-92.

**Filter experiments** [help](#)

organism:  sample type:

data type:  portal:

keyword:

**Public datasets**

Description	Reference	
8 [MOE430A] Affymetrix Mouse Expression 430A Array arrays. Bisphenol A effect on testicular Sertoli cells, time course. Analysis of testicular Sertoli cells (TSCs) treated with bisphenol A (BPA) for up to 12 hours. BPA, an industrial chemical that acts as an environmental estrogen, induces TSC death. Results provide insight into the mechanisms underlying TSC injury, which is accompanied by ER stress, induced by BPA. internal id =gdsGDS2043, source = <a href="#">GDS2043</a>	Y Tabuchi, I Takasaki, T Kondo. Identification of genetic networks involved in the cell injury accompanying endoplasmic reticulum stress induced by bisphenol A in testicular Sertoli cells. Biochem Biophys Res Commun. Jul 2006 <a href="#">Pub Med</a>	<input type="button" value="Analyze"/>
24 [HG-U133_Plus_2] Affymetrix Human Genome U133 Plus 2.0 Arrays. Bisphenol A effect on nonmalignant breast epithelial cell aspirates from breast cancer patients. Analysis of random periareolar fine-needle aspirates collected from unafflicted, contralateral breast tissue of breast cancer patients and treated with bisphenol A (BPA). Results provide insight into early molecular events induced by BPA in susceptible breast tissue internal id =GDS3368, source = <a href="#">GDS3368</a>	Dairkee SH, Seok J, Champion S, Sayeed A et al. Bisphenol A induces a profile of tumor aggressiveness in high-risk cells from breast cancer patients. Cancer Res 2008 Apr 1;68(7):2076-60. <a href="#">Pub Med</a>	<input type="button" value="Analyze"/>
36 Agilent-014868 Whole Mouse Genome Microarray 4x44K. Uterine gene profiles from Ovariectomized WT, KIKO (DNA-binding deficient ERα) or αERKO female mice were injected (ip) with saline (vehicle), estradiol (E2; 250 ng), bisphenol A (BPA; 750 μg) or 2,2-bis(p-hydroxyphenyl)-1,1-trichloroethane (HPTE; 750 μg) and uteri were collected after 2 or 24 hours. Uterine profiles were compared and indicated the early (2 hour) responses to E2 were highly correlated to the BPA and HPTE profiles. Note: Sample values are log2 of ratio of treatment/control. internal id =GSE18168, source = <a href="#">GSE18168</a>	Hewitt SC et al. Selective disruption of ER[alpha] DNA-binding activity alters uterine responsiveness to estradiol. Mol Endocrinol. 2009 Dec;23(12):2111-6. Epub 2009 Oct 7. <a href="#">Pub Med</a>	<input type="button" value="Analyze"/>

Done

# Genomics Portals – Private Data

(<http://BPAGenomics.org>)

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*Local users only*  
User menu  
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## BPA Genomics Data Portal

This is a **web-portal** for accessing our (soon to be) comprehensive database of **genomics datasets** related to **health effects of BPA exposure**. Genomics data types in this portal range from simple **gene expression** datasets to **comparative genomics hybridization** and **epigenomics** datasets. Please see the slides for the **objectives** of this portal and the example of how to **analyze** the data in the portal.

Gene lists relevant to this portal

Filter experiments [help](#)

organism	all <input type="button" value="v"/>	sample type	all <input type="button" value="v"/>
data type	all <input type="button" value="v"/>	portal	all <input type="button" value="v"/>
keyword	<input type="text"/>	<input type="button" value="Submit"/>	

### Private datasets

Description	Reference	
18 Nimblegen Rat 385K Promoter Arrays profiling promoter DNA methylation status in High EB, Low EB, BPA and Control treated rats. Values are the log ratios of IP/input with loess-like normalization. internal id=BPA_MeDIP_WinnieXiangHo, source = <a href="#">BPA_MeDIP_WinnieXiangHo</a>	<a href="#">Pub Med</a>	<input type="button" value="Analyze"/>
4 Illumina HumanHT-12 V3.0 expression beadchip. Analysis of the genome-wide response of the ER:PRL-HeLa cell line to treatment with estrogen receptor ligands estradiol, 4H-tamoxifen and bisphenol-A. internal id=GSE22941, source = <a href="#">GSE22941</a>	Ashcroft F. et al. To be Published <a href="#">Pub Med</a>	<input type="button" value="Analyze"/>

### Public datasets

Description	Reference	
8 [MOE430A] Affymetrix Mouse Expression 430A Array arrays. Bisphenol A effect on testicular Sertoli cells, time course. Analysis of testicular Sertoli cells (TSCs) treated with bisphenol A (BPA) for up to 12 hours. BPA, an industrial chemical that acts	Y Tabuchi, I Takasaki, T Kondo. Identification of genetic networks involved in the cell injury accompanying endoplasmic reticulum	<input type="button" value="Analyze"/>

Done

# BPA Genomics Knowledge Base – Gene Lists

(<http://BPAGenomics.org>)

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## BPA Genomics Data Portal

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☐ Gene lists relevant to this portal

Check All    UnCheck All    Submit

	Name	Description	Reference
<input type="checkbox"/>	<a href="#">C006780</a> <a href="#">view genes</a>	bisphenol A	Davis AP. et al. Nucleic Acids Res. 2009 Jan;37(Database issue):D786-92.
<input checked="" type="checkbox"/>	<a href="#">C006780_expression</a> <a href="#">view genes</a>	bisphenol A	Davis AP. et al. Nucleic Acids Res. 2009 Jan;37(Database issue):D786-92.

Check All    UnCheck All    Submit

Information Click on the corresponding ☐ sign next to the gene description to access the full Entrez gene description.

Go Back   Download   Export

GeneID	Symbol	Description
59	ACTA2	<input type="checkbox"/> actin, alpha 2, smooth muscle, aorta
196	AHR	<input type="checkbox"/> aryl hydrocarbon receptor
205	AK3L1	<input type="checkbox"/> adenylate kinase 3-like 1
211	ALAS1	<input type="checkbox"/> aminolevulinic acid, delta-, synthase 1
327	APEH	<input type="checkbox"/> N-acylaminoacyl-peptide hydrolase
332	BIRC5	<input type="checkbox"/> baculoviral IAP repeat-containing 5
336	APOA1	<input type="checkbox"/> apolipoprotein A-I
338	APOB	<input type="checkbox"/> apolipoprotein B (including AgV antigen)
341	APOC1	<input type="checkbox"/> apolipoprotein C-I
367	AR	<input type="checkbox"/> androgen receptor
374	AREG	<input type="checkbox"/> amphiregulin
403	ARL3	<input type="checkbox"/> ADP-ribosylation factor-like 3
405	ARNT	<input type="checkbox"/> aryl hydrocarbon receptor nuclear translocator
467	ATF3	<input type="checkbox"/> activating transcription factor 3
481	ATP1B1	<input type="checkbox"/> ATPase, Na <sup>+</sup> /K <sup>+</sup> transporting, beta 1 polypeptide
483	ATP1B3	<input type="checkbox"/> ATPase, Na <sup>+</sup> /K <sup>+</sup> transporting, beta 3 polypeptide
537	ATP6AP1	<input type="checkbox"/> ATPase, H <sup>+</sup> transporting, lysosomal accessory protein 1
539	ATP5O	<input type="checkbox"/> ATP synthase, H <sup>+</sup> transporting, mitochondrial F1 complex, O subunit
596	BCL2	<input type="checkbox"/> B-cell CLL/lymphoma 2
632	BGLAP	<input type="checkbox"/> bone gamma-carboxyglutamate (gla) protein
634	CEACAM1	<input type="checkbox"/> carcinoembryonic antigen-related cell adhesion molecule 1 (biliary glycoprotein)
641	BLM	<input type="checkbox"/> Bloom syndrome, RecQ helicase-like
672	BRCA1	<input type="checkbox"/> breast cancer 1, early onset
677	ZFP36L1	<input type="checkbox"/> zinc finger protein 36, C3H type-like 1
694	BTG1	<input type="checkbox"/> B-cell translocation gene 1, anti-proliferative
701	BUB1B	<input type="checkbox"/> budding uninhibited by benzimidazoles 1 homolog beta (yeast)
719	C3	<input type="checkbox"/> complement component 3
759	CA1	<input type="checkbox"/> carbonic anhydrase I
771	CA12	<input type="checkbox"/> carbonic anhydrase XII
794	CALB2	<input type="checkbox"/> calbindin 2
795	S100G	<input type="checkbox"/> S100 calcium binding protein G
827	CAPN6	<input type="checkbox"/> calpain 6
836	CASP3	<input type="checkbox"/> caspase 3, apoptosis-related cysteine peptidase
842	CASP9	<input type="checkbox"/> caspase 9, apoptosis-related cysteine peptidase
847	CAT	<input type="checkbox"/> catalase
890	CCNA2	<input type="checkbox"/> cyclin A2
900	CCNG1	<input type="checkbox"/> cyclin G1
949	SCARB1	<input type="checkbox"/> scavenger receptor class B, member 1

Local users only  
User:   
Password:   
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hpaggenomics.org - Mozilla Firefox

http://BPAgenomics.org/

Comparative Toxicogenomics Database

Search Chemicals for Name, CAS RN, ID

Home Search Tools Downloads Resources Query History Contact Us Help

Chemical: bisphenol A

Basics Interactions Genes ChemComps GO Diseases Pathways References Links

Name: bisphenol A  
CAS Type 1 Name: 4,4'-isopropylidenediphenol  
Equivalent Terms: 2,2-bis(4-hydroxyphenyl)propane; bisphenol A, disodium salt; bisphenol A, sodium salt; diphenylolopropane  
CAS Registry Number: 80-05-7  
Chemical Drawing

MeSH ID: C006780

Top Interacting Genes

Gene	Interactions
ESR1	55
AR	15
PGR	10
S100G	10
ESR2	10
STAT3	10
CYP19A1	10
LIF	10
THRA	10
THRB	10

Hierarchies

Path 1: Chemicals > Organic Chemicals > Phenols > bisphenol A

Legend: = Related chemicals, = Related genes, = Related diseases, = References, = Is curated.

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Data updated: September 6, 2010  
Revision: 2772

# Using (nascent) BPA Knowledge Base

(<http://BPAGenomics.org>)

Information

## BPA Genomics Data Portal

health effects of BPA exposure. Gen  
ation and epigenomics datasets. Pleas

Information

## Combine selected gene lists into the final query list

Information

## BPA Genomics Data Portal

comprehensive database of **genomics datasets** related to **health effects of BPA exposure**. Genomics  
pression datasets to **comparative genomics hybridization** and **epigenomics** datasets. Please see  
sample of how to **analyze** the data in the portal.

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My Data

Local users only

User

Password

Log in

GeneList	Human genes
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Description	Reference
36 Agilent-014868 Whole Mouse Genome Microarray 4x44K.Uterine gene profiles from Ovariectomized WT, KIKO (DNA-binding deficient ER $\alpha$ ) or $\alpha$ ERKO female mice were injected (ip) with saline (vehicle), estradiol (E2; 250 ng), bisphenol A (BPA; 750 $\mu$ g) or 2,2-bis(p-hydroxyphenyl)-1,1,1-trichloroethane (HPTE; 750 $\mu$ g) and uteri were collected after 2 or 24 hours. Uterine profiles were compared and indicated the early (2 hour) responses to E2 were highly correlated to the BPA and HPTE profiles. Note: Sample values are log2 of ratio of treatment/control. internal id = GSE18168 , source = <a href="#">GSE18168</a>	Hewitt SC et al. Selective disruption of ER( $\alpha$ ) DNA-binding activity alters uterine responsiveness to estradiol. Mol Endocrinol. 2009 Dec;23(12):2111-6. Epub 2009 Oct 7. <a href="#">Pub Med</a>

View genes found in the platform

#Samples	#Probes	#Genes	Data download
24	921	391	<a href="#">Tabular format (xls)</a> <a href="#">RData (eset)</a>

Step 1 (optional) Select samples for analysis. [demo](#)

include  exclude

- sample
- genotype
- treatment
- time
- genotype.treatment.time
- description

Step 2) Select sample grouping for analysis [help](#)

- none
- sample
- genotype
- treatment
- time
- genotype.treatment.time
- description

Step 3) Specify analysis to perform [help](#)

Cluster **Genes and samples**

Logistic Regression Enrichment Analysis

Analyze!

sample type

all

portal

all

Submit

	Reference
430A Array arrays. time course. Analysis of bisphenol A (BPA) for up to 24 hours. BPA acts as an environmental stressor and provides insight into the mechanisms of BPA accompanied by ER S2043. source =	Y Tabuchi, I Takasaki, T Kondo. Identification of genetic networks involved in the cell injury accompanying endoplasmic reticulum stress induced by bisphenol A in testicular Sertoli cells. Biochem Biophys Res Commun. Jul 2006 <a href="#">Pub Med</a>
genome U133 Plus 2.0 breast epithelial cell analysis of random periaureolar, contralateral breast with bisphenol A. Molecular events induced by BPA. source = GDS3388.	Dairkee SH, Seok J, Champion S, Sayeed A et al. Bisphenol A induces a profile of tumor aggressiveness in high-risk cells from breast cancer patients. Cancer Res 2008 Apr 1;68(7):2076-80. <a href="#">Pub Med</a>
microarray 4x44K.Uterine gene profiles from Ovariectomized WT, KIKO (DNA-binding deficient ER $\alpha$ ) (ip) with saline (vehicle), estradiol (E2; 250 ng), bisphenol A (BPA; 750 $\mu$ g) or 2,2-bis(p-hydroxyphenyl)-1,1,1-trichloroethane (HPTE; 750 $\mu$ g) and uteri were collected after 2 or 24 hours. Uterine profiles were compared and indicated the early (2 hour) responses to E2 were highly correlated to the BPA and HPTE profiles. Note: Sample values are log2 of ratio of treatment/control. internal id = GSE18168	Hewitt SC et al. Selective disruption of ER( $\alpha$ ) DNA-binding activity alters uterine responsiveness to estradiol. Mol Endocrinol. 2009 Dec;23(12):2111-6. Epub 2009 Oct 7. <a href="#">Pub Med</a>



# Data Analysis Using Pre-Defined Gene Lists

(<http://BPAGenomics.org>)

**Information**

Accession	Description	Reference
GSE18168	36 Agilent-G14868 Whole Mouse Genome Microarray 4x44k gene profiles from Ovarian-carcinoma WT, KIKO (DNA-binding deficient ERα) or aERKO female mice were injected (i.p) with saline (vehicle), estradiol (E2; 250 ng), bisphenol A (BPA; 750 µg or 2,2-bis[4-hydroxyphenyl]-1,1-tetrachloroethane (HPTe; 750 µg) and uteri were collected after 2 or 24 hours. Uterine profiles were compared and indicated the early (2 hour) responses to E2 were highly correlated to the BPA and HPTe profiles. Note: Sample values are log2 of ratio of treatment/control. <a href="#">GSE18168</a>	Hewitt SC et al. Selective disruption of ERα/β DNA-binding activity alters uterine responsiveness to estradiol Mf. <i>Endocrinology</i> . 2009 Dec;150(12):3111-6. Epub 2009 Oct 7. <a href="#">PubMed</a>

**Query**

Click on a Pathway (D) to view graphical representation of the pathway. Significantly expressed genes are painted yellow and other genes that were found in the pathway but were not significantly expressed are painted blue.

**Analysis**

Pathway ID	Description	# genes in pathway	# significant genes in pathway
mmu04350	Metabolism of xenobiotics by cytochrome P450	8	8
mmu04115	p53 signaling pathway	14	8
mmu04300	Tight junction	10	7
mmu04211	Renal cell carcinoma	8	7
mmu05222	Small cell lung cancer	12	7
mmu04081	Glycolysis/gluconeogenesis	6	6
mmu04320	Drug metabolism - cytochrome P450	6	6
mmu04212	Prostate cancer	11	6
mmu04216	Prostate cancer	14	6

**My Data**

**Description**

36 Agilent-G14868 Whole Mouse Genome Microarray 4x44k gene profiles from Ovarian-carcinoma WT, KIKO (DNA-binding deficient ERα) or aERKO female mice were injected (i.p) with saline (vehicle) (E2; 250 ng), bisphenol A (BPA; 750 µg) or 2,2-bis[4-hydroxyphenyl]-1,1-tetrachloroethane (HPTe; 750 µg) and uteri were collected after 2 or 24 hours. Uterine profiles were compared and indicated the early (2 hour) responses to E2 were highly correlated to the BPA and HPTe profiles. Note: Sample values are log2 of ratio of treatment/control. internal id = GSE18168, source = GSE18168

#Samples	#Probes	#Genes
24	921	39

**Interactive Treeview Browsing**

Legend for all HT: Original Data, Centered Data, Statistical Analysis, Original Data, Centered Data

\* Please note that unless the original data is in the form of log-transformed values represented by heatmaps correspond to average expression levels

Kegg Pathways for submitted genes

**Functional TreeView: [http://eh3.uc.edu/tmp/TreeViewTue\\_Sep\\_21\\_09:10:10\\_2010\\_1487928.cdf](http://eh3.uc.edu/tmp/TreeViewTue_Sep_21_09:10:10_2010_1487928.cdf)**

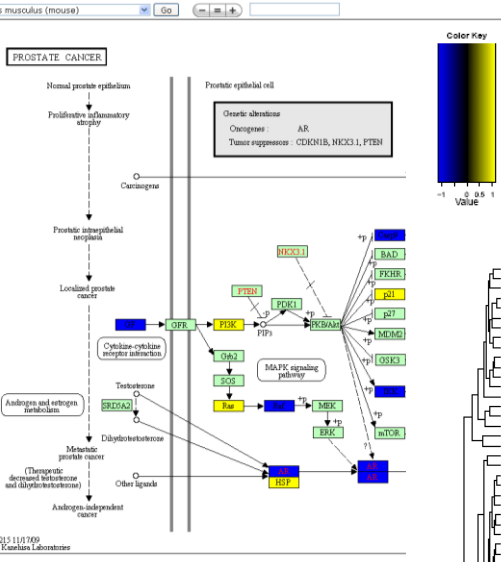
File Settings Analysis Export Window Help

View Status: No status info for T

**Usage Hints**

Click and drag to scroll

16584 : Fos : 14281 : FBJ osteosarcoma oncog  
14532 : Egr3 : 13655 : early growth response  
4540 : Fos : 14281 : FBJ osteosarcoma oncog  
7317 : Fos : 14281 : FBJ osteosarcoma oncog  
7493 : Fos : 14281 : FBJ osteosarcoma oncog  
19229 : Fos : 14281 : FBJ osteosarcoma oncog  
15772 : Fos : 14281 : FBJ osteosarcoma oncog  
36398 : Fos : 14281 : FBJ osteosarcoma oncog  
29995 : Fos : 14281 : FBJ osteosarcoma oncog  
11530 : Fos : 14281 : FBJ osteosarcoma oncog  
14160 : Fos : 14281 : FBJ osteosarcoma oncog  
4667 : Cebp2 : 12609 : CCAAT/enhancer bindin  
19243 : Ctpa : 51797 : cytidine 5'-triphospha  
16401 : Nppc : 18159 : natriuretic peptide p  
13568 : Klf4 : 16600 : Kruppel-like factor 4  
21126 : Slc16a1 : 20501 : solute carrier fam  
45138 : Slc16a1 : 20501 : solute carrier fam  
28073 : Gadd45a : 13197 : growth arrest and  
43639 : Nr1p : 268903 : nuclear receptor in  
14541 : Nr1p : 268903 : nuclear receptor in  
29072 : Nr1p : 268903 : nuclear receptor in  
12331 : Paepl : 65112 : prostate transmembr  
29943 : Kpna2 : 16647 : karyopherin (importi  
30453 : Kpna2 : 16647 : karyopherin (importi  
29430 : Egr3 : 13655 : early growth response  
9853 : Egr1 : 13655 : early growth response  
5187 : Irf1 : 16000 : interferon-γ-inducible  
36509 : Junb : 16477 : Jun-B oncogene  
16074 : Junb : 16477 : Jun-B oncogene  
14552 : Crisp1d2 : 78892 : cysteine-rich sec  
19355 : Arid1b : 11910 : activating transcrip  
22011 : Prkcdp : 109042 : protein kinase C,  
34168 : Myh6 : 17888 : myosin, heavy polypep



# Genotype Effect In Response To BPA

(<http://BPAGenomics.org>)

» GRS Enrichment

**My Data**

*Local users only*

User

Password

#Samples	#Probes	#Genes	Data download
24	921	391	<a href="#">Tabular format (xls)</a> <a href="#">RData (eset)</a>

Step 1 (optional) ) Select samples for analysis. [demo](#)

include  exclude

- sample
- genotype
  - WT
  - KIKO
  - aERKO
- treatment
  - HPTE
  - BPA
- time
  - 2h
  - 24h
- genotype.treatment.time
- description

Step 2) Select sample group

none

sample

genotype

treatment

time

genotype.treatment.time

description

Step 3) Specify analysis

Cluster

Logistic Regression

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**Query**

» [GRS Enrichment](#)

**Analysis**

» [GRS Enrichment](#)

**My Data**

*Local users only*

User

Password

Information	Description	Reference
<p>» <a href="#">About</a></p> <p>» <a href="#">Help</a></p> <p>» <a href="#">Gene list</a></p> <p>» <a href="#">Experiment</a></p>	<p>36 Agilent-014868 Whole Mouse Genome Microarray 4x44K.Uterine gene profiles from Ovariectomized WT, KIKO (DNA-binding deficient ER<math>\alpha</math>) or <math>\alpha</math>ERKO female mice were injected (ip) with saline (vehicle), estradiol (E2; 250 ng), bisphenol A (BPA; 750 <math>\mu</math>g) or 2,2-bis(p-hydroxyphenyl)-1,1,1-trichloroethane (HPTE; 750 <math>\mu</math>g) and uteri were collected after 2 or 24 hours. Uterine profiles were compared and indicated the early (2 hour) responses to E2 were highly correlated to the BPA and HPTE profiles. Note: Sample values are log2 of ratio of treatment/control. internal id = GSE18168 , source = <a href="#">GSE18168</a></p>	<p>Hewitt SC et al. Selective disruption of ER{alpha} DNA-binding activity alters uterine responsiveness to estradiol. Mol Endocrinol. 2009 Dec;23(12):2111-6. Epub 2009 Oct 7. <a href="#">Pub Med</a></p>

#Samples	#Probes	#Genes	Data download
24	921	391	<a href="#">Tabular format (xls)</a> <a href="#">RData (eset)</a>

4 samples found for your search

Interactive Treeview Browsing	Static Heatmaps(pdf)	Gene list Statistics	Data Download
<p>* <a href="#">Original Data</a></p> <p><a href="#">Centered Data</a></p>	<p><a href="#">Legend for all the heatmaps</a></p> <p><a href="#">Statistical Analysis</a> †</p> <p><a href="#">Original Data</a></p> <p><a href="#">Centered data</a></p>	<p>LR Enrichments p-value 0.0062</p>	<p><a href="#">Tabular format (xls)</a></p> <p><a href="#">RData (eset)</a></p>

\* Please note that unless the original data is in the form of log-transformed ratios, Non-centered treeview might not be very informative  
 † Values represented by heatmaps correspond to average expression levels for the same sample type. Red box in the left color box indicates pvalue less than 0.05

# Finding Differentially Expressed Genes

(<http://BPAGenomics.org>)

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**Description**

36 Agilent-014868 Whole Mouse Genome Microarray 4x44K. Uterine gene profiles from Ovariectomized WT, KIKO (DNA-binding deficient ER $\alpha$ ) or  $\alpha$ ERKO female mice were injected (ip) with saline (vehicle), estradiol (E2; 250 ng), bisphenol A (BPA; 750  $\mu$ g) or 2,2-bis(p-hydroxyphenyl)-1,1,1-trichloroethane (HPTE; 750  $\mu$ g) and uteri were collected after 2 or 24 hours. Uterine profiles were compared and indicated the early (2 hour) responses to E2 were highly correlated to the BPA and HPTE profiles. Note: Sample values are log2 of ratio of treatment/control. internal id = GSE18168 , source = [GSE18168](#)

**Reference**

Hewitt SC et al. Selective disruption of ER( $\alpha$ ) DNA-binding activity alters uterine responsiveness to estradiol. Mol Endocrinol. 2009 Dec;23(12):2111-6. Epub 2009 Oct 7. [Pub Med](#)

**Query**

» [Gene list](#)

» [Experiment](#)

**Analysis**

**Properties stored for the experiment:**

sample  
genotype  
treatment

**Information**

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» [Help](#)

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» [Gene list](#)

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**My Data**

Local users only

User:

Password:

**Genomics portals - Mozilla Firefox**

File Edit View History Bookmarks Tools Help

http://www.eh3.uc.edu/GenomicsPortals/diffGenesResults\_tl.jsp?exp=GSE18168&db=GPL4134&prop=time

**Genomics portals**

**Information**

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» [Help](#)

Description	Reference
36 Agilent-014868 Whole Mouse Genome Microarray 4x44K. Uterine gene profiles from Ovariectomized WT, KIKO (DNA-binding deficient ER $\alpha$ ) or $\alpha$ ERKO female mice were injected (ip) with saline (vehicle), estradiol (E2; 250 ng), bisphenol A (BPA; 750 $\mu$ g) or 2,2-bis(p-hydroxyphenyl)-1,1,1-trichloroethane (HPTE; 750 $\mu$ g) and uteri were collected after 2 or 24 hours. Uterine profiles were compared and indicated the early (2 hour) responses to E2 were highly correlated to the BPA and HPTE profiles. Note: Sample values are log2 of ratio of treatment/control. internal id = GSE18168 , source = <a href="#">GSE18168</a>	Hewitt SC et al. Selective disruption of ER( $\alpha$ ) DNA-binding activity alters uterine responsiveness to estradiol. Mol Endocrinol. 2009 Dec;23(12):2111-6. Epub 2009 Oct 7. <a href="#">Pub Med</a>

4 samples found for your search  
No of genes matching the criteria 3

Interactive Treeview Browsing	Static Heatmaps(pdf)	Data Download
<a href="#">* Original Data</a> <a href="#">Centered Data</a>	<a href="#">Legend for all the heatmaps</a> <a href="#">Statistical Analysis †</a> <a href="#">Original Data</a> <a href="#">Centered data</a>	<a href="#">Tabular format (.xls)</a>

**Query**

» [Gene list](#)

» [Experiment](#)

**Analysis**

» [GRS Enrichment](#)

**Step 1 (optional)** Select samples for analysis

include  exclude

- sample
- genotype
  - WT
  - KIKO
  - $\alpha$ ERKO
- treatment
  - HPTE
  - BPA
- time
- genotype.treatment.time
- description

**Step 2** Select sample grouping for analysis

sample

genotype

treatment

time

genotype.treatment.time

description

**Step 3** Statistical significance parameters

Statistical significance measure

Differentially expressed genes filter:

Statistical significance cut-off:

Ratio cut-off:

**Step 3** Specify analysis to perform [help](#)

Cluster:

# Using Genomics Portals Knowledge Base

(<http://BPAGenomics.org>)

**Information** Use one of the methods below to construct a gene list or click help links for tutorials

- Predefined gene lists [help](#)
- Transcription factor binding and epigenomics gene lists

**Information**

» [About](#)

» [Help](#)

**Query**

» [Gene list](#)

» [Experiment](#)

**Analysis**

» [GRS Enrichment](#)

**My Data**

Local users only

User

Password

Description	Reference
<p>8 [MOE430A] Affymetrix Mouse Expression 430A Array arrays. Bisphenol A effect on testicular Sertoli cells, time course. Analysis of testicular Sertoli cells (TSCs) treated with bisphenol A (BPA) for up to 12 hours. BPA, an industrial chemical that acts as an environmental estrogen, induces TSC death. Results provide insight into the mechanisms underlying TSC injury, which is accompanied by ER stress, induced by BPA. internal id = gdsGDS2043 , source = <a href="#">GDS2043</a></p>	<p>Y Tabuchi, I Takasaki, T Kondo. Identification of genetic networks involved in the cell injury accompanying endoplasmic reticulum stress induced by bisphenol A in testicular Sertoli cells. <i>Biochem Biophys Res Commun.</i> Jul 2006 <a href="#">Pub Med</a></p>

#Samples	#Probes	#Genes	Data download
8	195	103	<a href="#">Tabular format (xls)</a> <a href="#">RData (eset)</a>

Interactive Treeview Browsing	Static Heatmaps(pdf)	Gene list Statistics	Data Download
<p>* <a href="#">Original Data</a></p> <p><a href="#">Centered Data</a></p>	<p><a href="#">Legend for all the heatmaps</a></p> <p><a href="#">Statistical Analysis</a> †</p> <p><a href="#">Original Data</a></p> <p><a href="#">Centered data</a></p>	<p>LR Enrichments p-value 3.3e-05</p>	<p><a href="#">Tabular format (xls)</a></p> <p><a href="#">RData (eset)</a></p>

\* Please note that unless the original data is in the form of log-transformed ratios, Non-centered treeview might not be very informative  
 † Values represented by heatmaps correspond to average expression levels for the same sample type. Red box in the left color box indicates pvalue less than 0.05

# Comparing Global Genomics Profiles – GRS Enrichment

(<http://BPAGenomics.org>)

Information
Step 1: Select query dataset
Step 2: Select reference dataset
Step 3: Calculating GRS
Step 4: Results

» About

» Help

**Query**

» Gene list

» Experiment

**Query Dataset**

Description	Reference
12 [MG_U74Av2] Affymetrix Murine Genome U74 Version 2 Array arrays. Uterine response to physiologic, plant-derived, and synthetic estrogen. Analysis of immature Alpk,APICD-1 uterus 72 hours after 3 daily injections of physiologic estrogen 17beta-estradiol (E2), phytoestrogen genistein (GEN), or synthetic estrogen diethylstilbestrol (DES). Similarity in gene expression indicates synthetic estrogen may not pose unique threat to health. internal id = gdsGDS982 , source = <a href="#">GDS982</a>	JG Moggs, J Ashby, H Tinwell, FL Lim, DJ Moore, I Kimber, G Orphanides. The need to decide if all estrogens are intrinsically similar. Environ Health Perspect. Aug 2004 <a href="#">Pub Med</a>

**Reference Dataset**

Description	Reference
36 Agilent-014868 Whole Mouse Genome Microarray 4x44K. Uterine gene profiles from Ovariectomized WT, KIKO (DNA-binding deficient ERα) or αERKO female mice were injected (ip) with saline (vehicle), estradiol (E2; 250 ng), bisphenol A (BPA; 750 µg) or 2,2-bis(p-hydroxyphenyl)-1,1,1-trichloroethane (HPTE; 750 µg) and uteri were collected after 2 or 24 hours. Uterine profiles were compared and indicated the early (2 hour) responses to E2 were highly correlated to the BPA and HPTE profiles. Note: Sample values are log2 of ratio of treatment/control. internal id = GSE18168 , source = <a href="#">GSE18168</a>	Hewitt SC et al. Selective disruption of ER{alpha} DNA-binding activity alters uterine responsiveness to estradiol. Mol Endocrinol. 2009 Dec;23(12):2111-6. Epub 2009 Oct 7. <a href="#">Pub Med</a>

**Results:**

	Reference	Reference up	Reference down
<b>Query</b>	Pvalue: 0.016 Z score: 2.4	Pvalue: NA Z score: NA	Pvalue: NA Z score: NA
<b>Query up</b>	Pvalue: NA Z score: NA	Pvalue: NA Z score: NA	Pvalue: NA Z score: NA
<b>Query down</b>	Pvalue: NA Z score: NA	Pvalue: NA Z score: NA	Pvalue: NA Z score: NA

	Query Dataset	Reference Dataset
<b>Sample property used in analysis</b>	agent	genotype.treatment.time
<b>Sample groups compared</b>	More than two levels.. vehicle,genistein,17beta-estradiol,diethylstilbestrol	More than two levels.. WT V vs HPTE 2hr,WT V vs HPTE 24hr,WT V vs BPA 2hr,WT V vs BPA 24hr,KIKO V vs HPTE 2hr,KIKO V vs HPTE 24hr,KIKO V vs BPA 2hr,KIKO V vs BPA 24hr,aERKO V vs HPTE 2hr,aERKO V vs HPTE 24hr,aERKO V vs BPA 2hr,aERKO V vs BPA 24hr

[Concordant Gene Table](#)

Query ▼ and Reference ▼ Kegg Pathways for concordant genes

# Web-based Portal for Sharing BPA-related Genomics Data And Gene Lists

(<http://BPAGenomics.org>)

## **Future (will be based in part on the feedback):**

- Adding data and gene lists
- Creating reference meta-datasets by analyzing by analyzing individual datasets
- Integration with additional external resources (CTD, DAVID,...)
- Expand Functionality:
  - Analysis of multiple datasets at a time
  - Queries against reference meta-datasets
  - Adding different types of structured “knowledge” (ie pre-computed pathways with meaningful topology instead of gene lists)

# Web-based Portal for Sharing BPA-related Genomics Data And Gene Lists

(<http://BPAGenomics.org>)

## Future (will be based largely on the feedback):

### ➤ INTEGRATIVE ANALYSIS

- The objective of the current effort is to provide the infrastructure (process and upload data, create combined datasets, user interfaces for data analysis, etc)
- These efforts will make meaningful integrative analysis technically possible, but challenging
- Significant effort by data analysts
- Input, interpretation and feedback from numerous researchers