

# NCATS BioPlanet of Pathways

Ruili Huang

*DPI/NCATS*

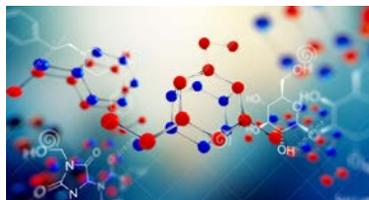
*October 24, 2019*



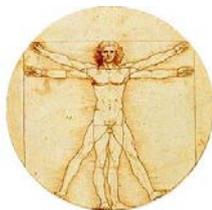
# Background – Toxicity Prediction



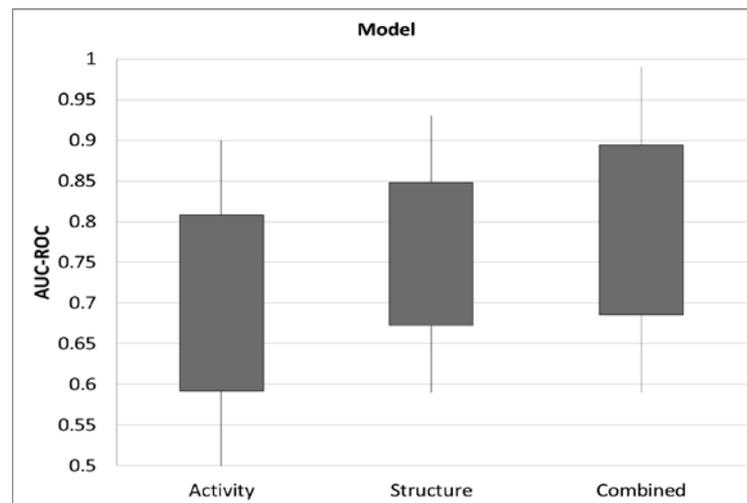
*In vitro* assays



*Chemical Structure*



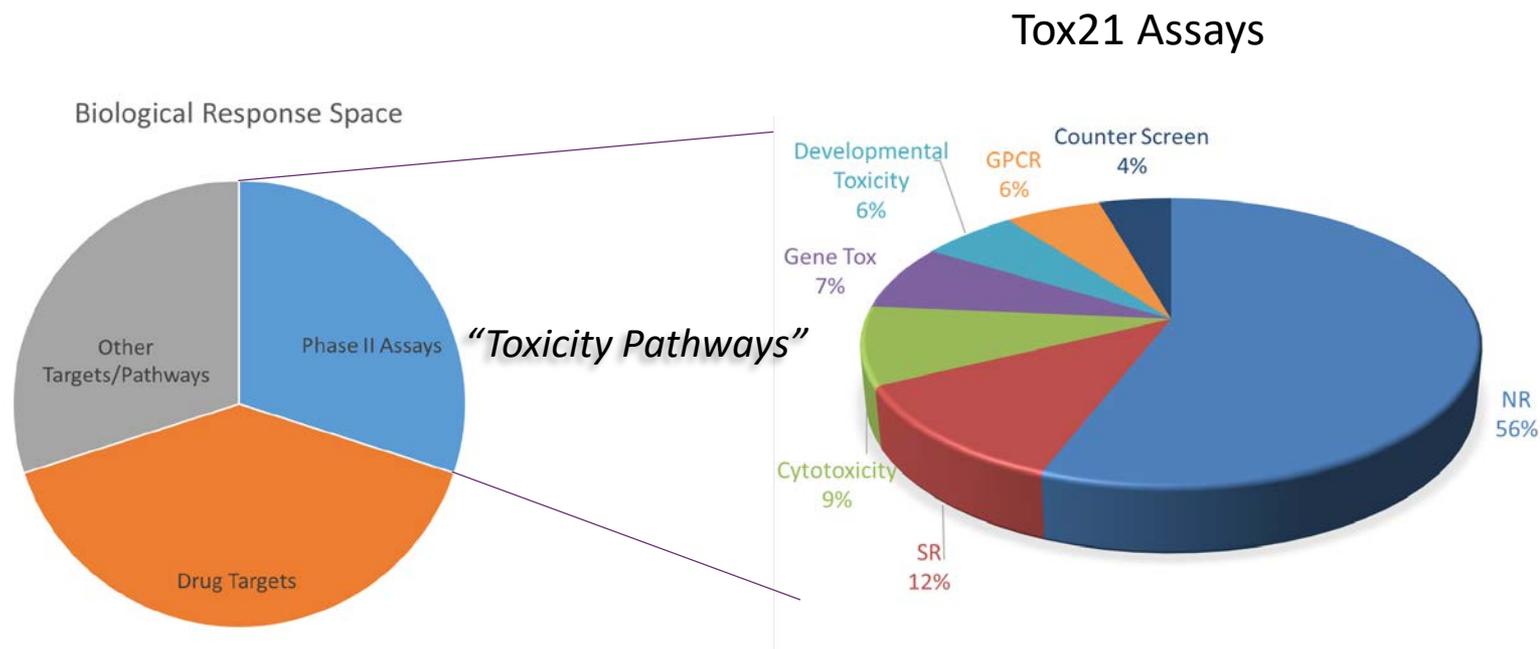
*In vivo* toxicity



Tox21 Assays



# Biological Response Space Coverage



- **Problem** – Disruption of any pathway could potentially result in toxicity
- **Question** – How many assays and what types of assays should be screened to cover enough toxicity mechanisms to effectively predict *in vivo* toxicity?
- **Solution** – A comprehensive pathway resource that represents the entire biological response space

# A Comprehensive Pathway Resource

- Issues with existing pathway databases
  - Focus on particular areas of biology, e.g., metabolism vs. signaling
  - Data are computationally generated without direct experimental evidence
  - Simple data integration of individual resources without further curation or validation
  - Different types of data mixed together with no distinctions made between, e.g., pathways and protein–protein interactions
  - No additional annotations provided beyond gene-pathway memberships
  - Restricted access – commercial databases with high cost
- Need a complete, non-redundant, open-source solution for integrated data analysis



# NCATS BioPlanet of Pathways

- A comprehensive resource for
  - Assay selection/prioritization for toxicity prediction
  - Gene expression data analysis
  - Integrated data analysis
- Data from all public sources
- Manual curation to ensure data quality
- Detailed annotations on source, species, biological function/process, disease/toxicity relevance, assay availability
- Currently: 1658 curated human pathways (~10,000 genes)
- Public web browser for easy data visualization and analysis
  - <http://tripod.nih.gov/bioplanet/>



# Constructing the BioPlanet

Source Databases

- BioCarta
- KEGG
- NCI-Nature PID
- NetPath
- Reactome
- Science Signaling
- WikiPathways

Auto merge by gene component

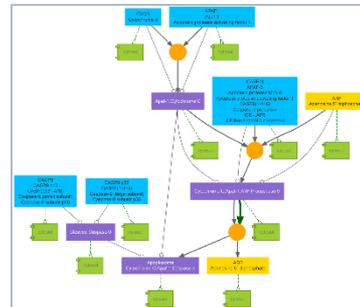
Manual curation

- Standardize names
- Edit gene list
- Merge by gene function

Add annotations

- Literature support
- Category/function tags
- Disease relevance
- Assay availability

Generate interactive diagrams



NIH National Center for Advancing Translational Sciences BioPlanet

Home Pathway Category Assay Availability- Enrichment Resource

Total 105 pathways

1 AP-1 transcription factor network

2 ATM-dependent DNA damage response

3 Activation of mRNA upon binding of the cap-binding complex and eIF

4 Adaptive immune system

5 Androgen receptor signaling, proteolysis, and transcription regulation

6 Antigen-activated B-cell receptor generation of second messengers

NCATS BioPlanet Browser



NIH National Center for Advancing Translational Sciences

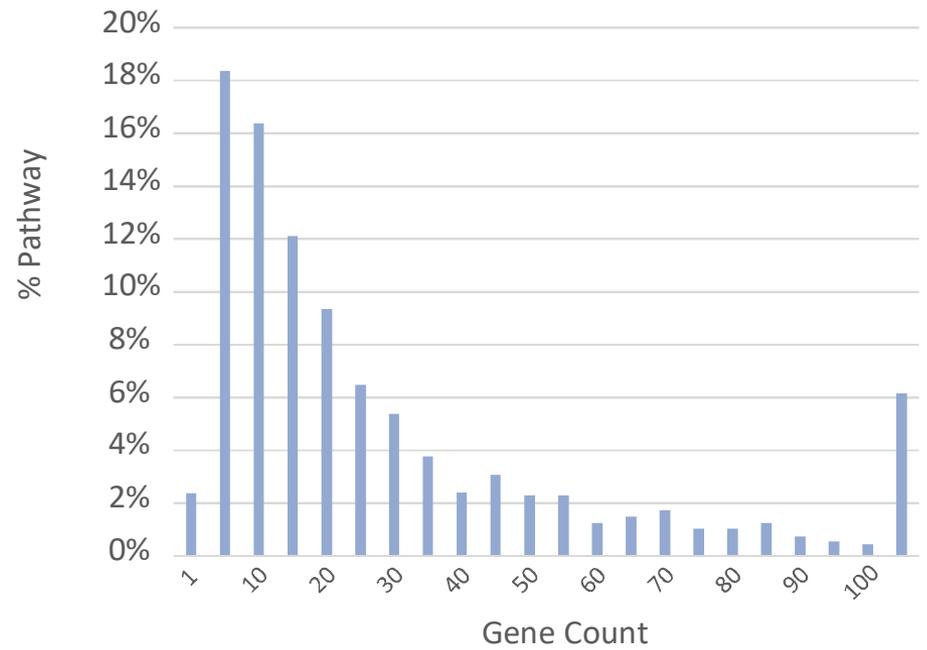
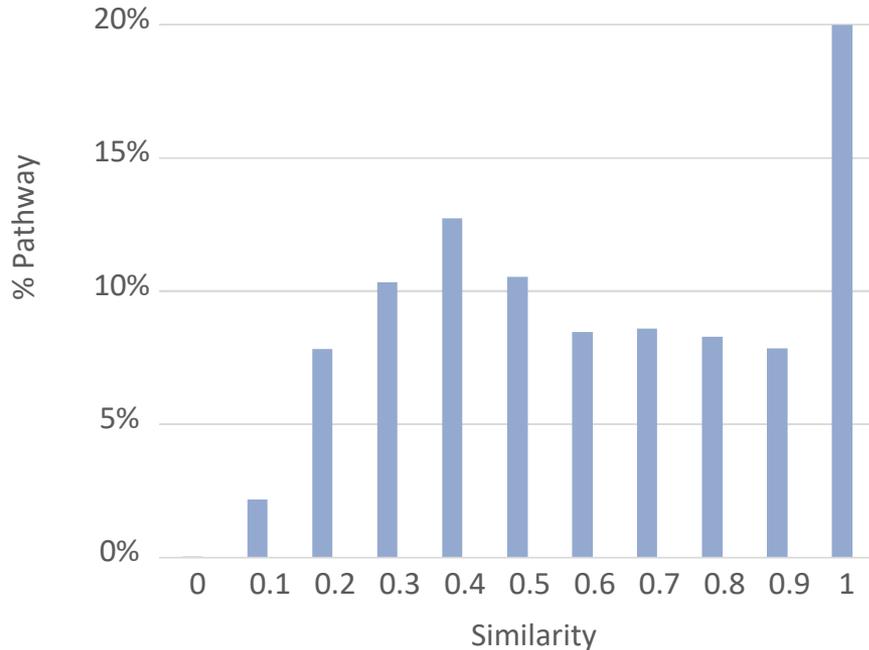
# Pathway data sources

Database	Number of human pathways	Number of genes	URL
KEGG	214	5520	<a href="http://www.genome.jp/kegg/pathway.html">http://www.genome.jp/kegg/pathway.html</a>
BioCarta*	314	1494	<a href="https://cgap.nci.nih.gov/Pathways/BioCarta_Pathways">https://cgap.nci.nih.gov/Pathways/BioCarta_Pathways</a>
Reactome	1283	6125	<a href="http://www.reactome.org/">http://www.reactome.org/</a>
WikiPathways	204	4064	<a href="http://www.wikipathways.org/">http://www.wikipathways.org/</a>
NCI-Nature - Pathway Interaction Database*	722	3725	<a href="http://pid.nci.nih.gov/">http://pid.nci.nih.gov/</a>
Science Signaling*	58	1234	<a href="http://stke.sciencemag.org/about/help/cm">http://stke.sciencemag.org/about/help/cm</a>
NetPath	35	2877	<a href="http://www.netpath.org/">http://www.netpath.org/</a>

\*Original database site is no longer supported.



# Overview of source pathways – Data redundancy



## Manual curation

- Remove redundancy - merge pathways by gene function
- Pathways with too few genes – remove or merge into larger pathways

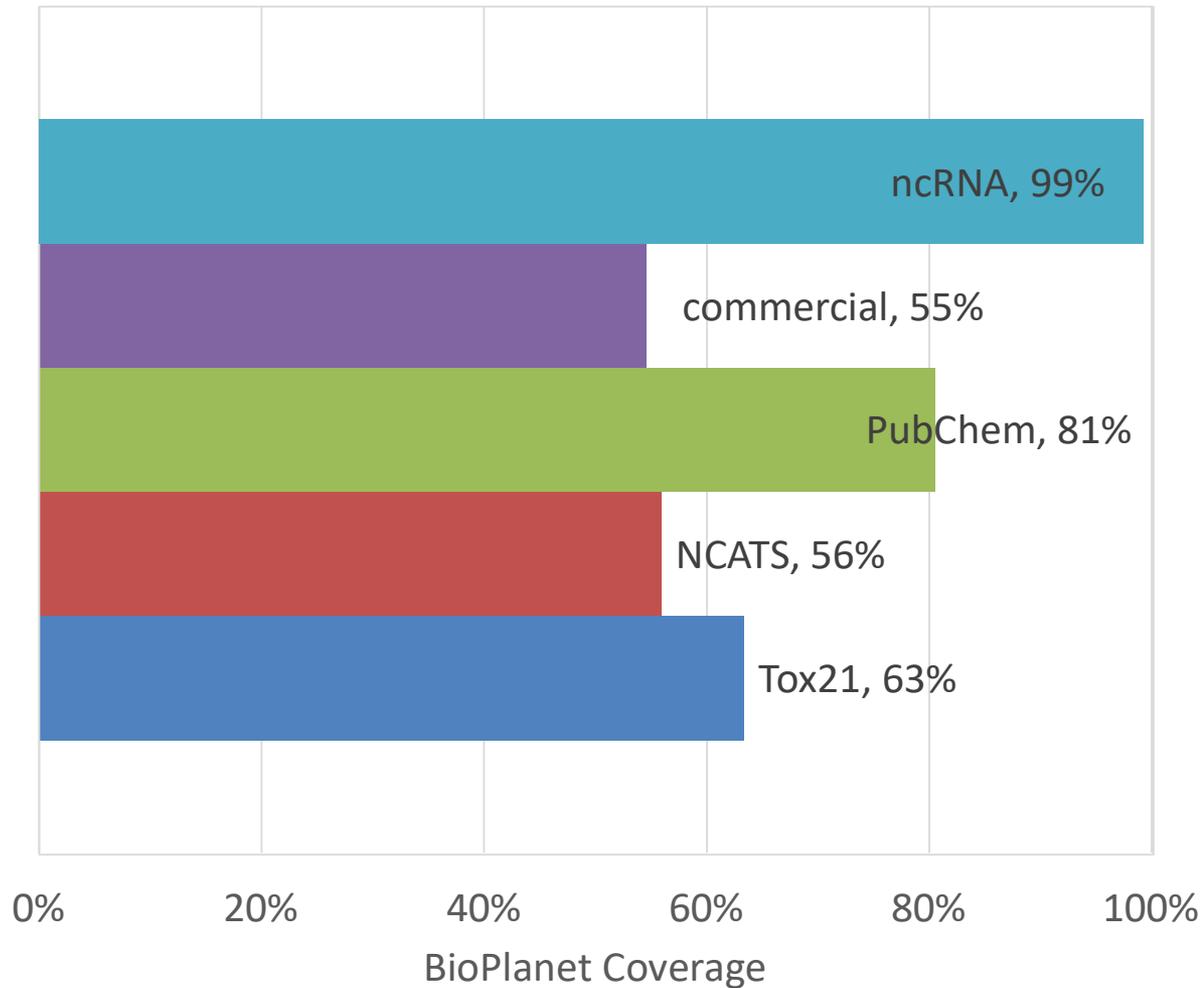


# Pathway tags

<b>Major Systems</b>	<b>Metabolism</b>	<b>Signalling</b>
Circulatory system	Nucleic acid metabolism	Cell signalling
Digestive system	Carbohydrate metabolism	G-protein coupled receptor
Endocrine system	Protein metabolism	Nuclear receptor
Excretory system	Lipid metabolism	Transcriptional regulation
Immune system	Vitamin and cofactor metabolism	Stress response
Musculoskeletal system	Small molecule metabolism	Environmental adaptation
Nervous system	Xenobiotic metabolism	Chronology
Sensory system	Energy metabolism	Transport
<b>Genetic Information Processing</b>	Protein folding, sorting and degradation	
DNA replication	Protein modification	<b>Disease</b>
DNA repair		Cancer
Transcription		Cardiovascular disease
RNA processing	<b>Cell Cycle</b>	Genetic disease
Translation	Cell cycle	Immune disease
	Cell growth	Infectious disease
<b>Development</b>	Cell death	Neurological disease
Development	Cell division	Physical disorder
Adhesion	Cell proliferation	Endocrine and metabolic disease
Cell differentiation	Reproduction	Sepsis
Cell motility		Substance dependence

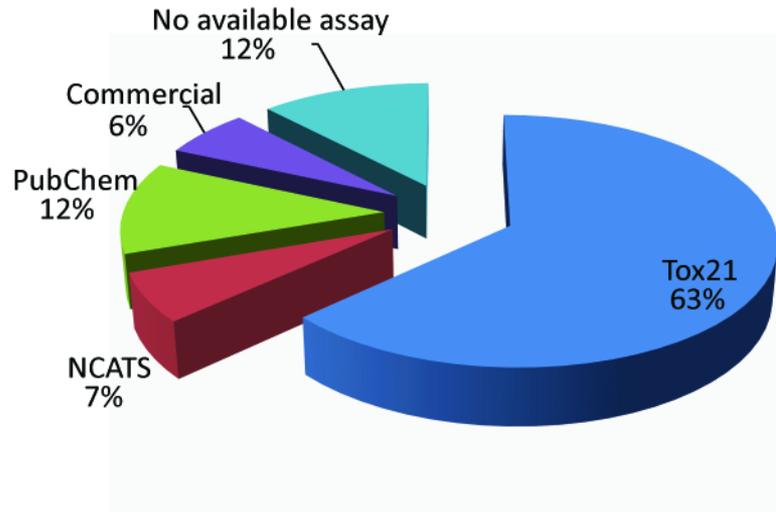


# Assay Coverage of BioPlanet

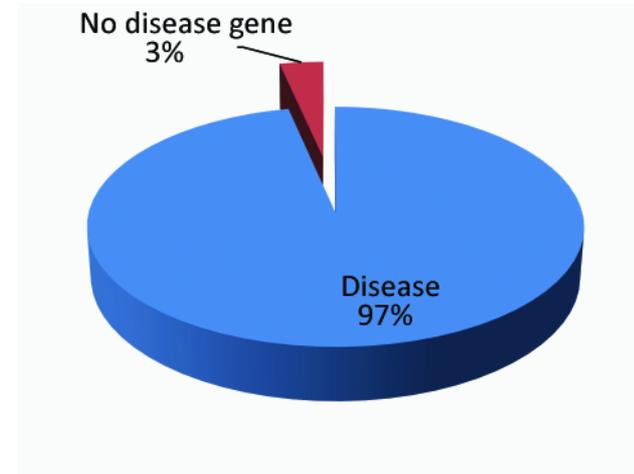


# Assay Coverage of BioPlanet: Disease

A

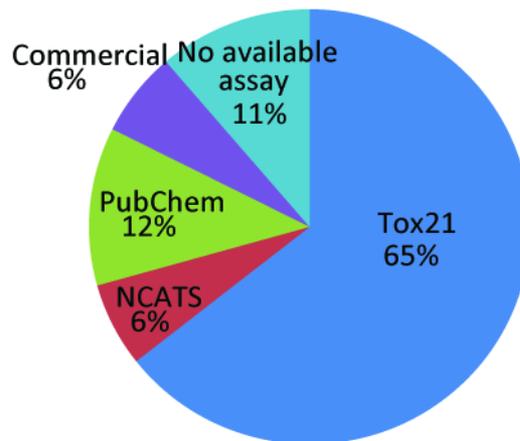


B



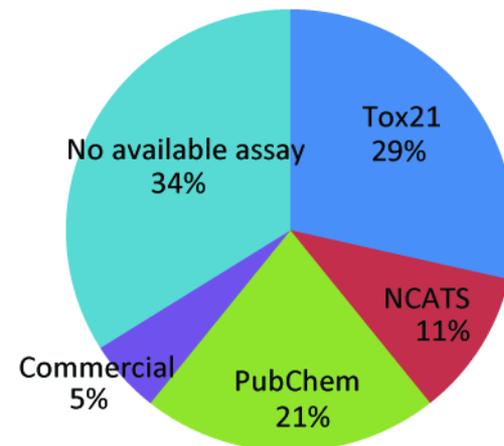
## Disease Pathways

C

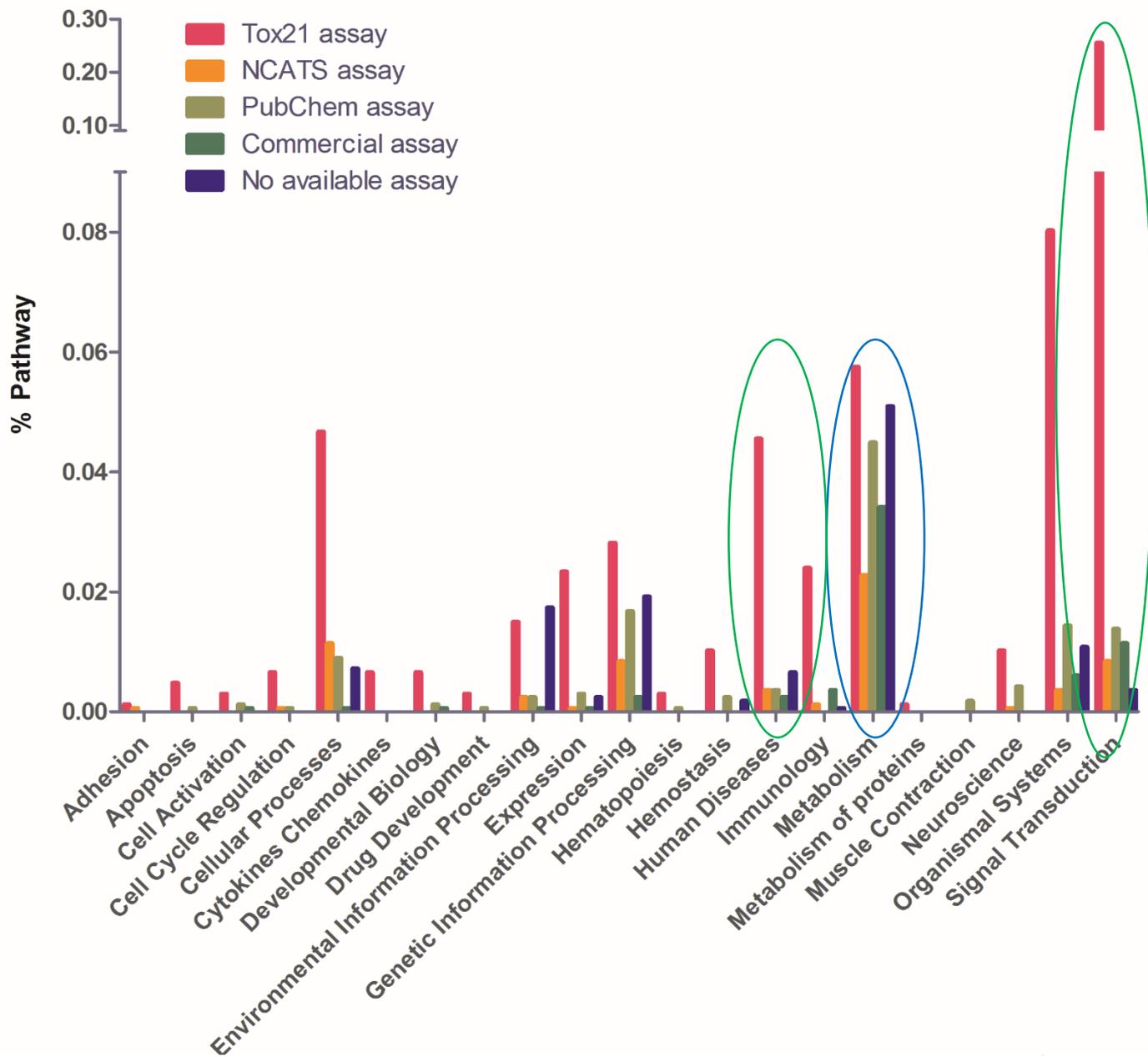


## Other Pathways

D



# Assay Coverage of BioPlanet: Pathway Category



# The BioPlanet Browser

U.S. Department of Health & Human Services | National Institutes of Health | National Center for Advancing Translational Sciences

NIH National Center for Advancing Translational Sciences **BioPlanet** Keywords or gene IDs

Home Pathway **Category** Assay Availability- Enrichment Resource

1-5 of 1658  Collapse All

Page size: 5

## 1 ▼ 2-LTR circle formation

- Pathway Map [↗](#)
- Genes [↗](#)
- Diseases [↗](#)
- Category [↗](#)
  - DNA repair
  - Human Diseases
    - Infectious diseases
      - Viral
  - Infectious disease
- Assay Availability [↗](#)
  - Tox21

## 2 ▼ 4-1BB-dependent immune response

- Pathway Map [↗](#)
- Genes [↗](#)
- Diseases [↗](#)
- Category [↗](#)
  - Cancer
  - CellActivation
  - CellSignaling
  - Immune system
  - Immunology
  - Infectious disease
  - Stress response
  - Transcription
- Assay Availability [↗](#)
  - Commercial
  - NCATS
  - PubChem
  - Tox21
  - ToxCast

## 3 ▼ ABC transporters

- Pathway Map [↗](#)
- Genes [↗](#)
- Diseases [↗](#)
- Category [↗](#)
  - Digestive system
  - Environmental Information Processing
    - Membrane transport
  - Lipid metabolism
  - Small molecule metabolism
  - Transport
- Assay Availability [↗](#)
  - Commercial
  - PubChem
  - ToxCast

## 4 ▼ ABCA transporters in lipid homeostasis

- Pathway Map [↗](#)
- Genes [↗](#)
- Diseases [↗](#)
- Category [↗](#)
  - Digestive system
  - Environmental Information Processing
    - Membrane transport
  - Lipid metabolism
  - Small molecule metabolism
  - Transport
- Assay Availability [↗](#)
  - N/A

NIH National Center for Advancing Translational Sciences **BioPlanet** Keywords or gene IDs

Home Pathway **Category** Assay Availability- Enrichment Resource

Comprehensive Collection of Human Pathways for Systems Toxicology and Chemical Genomics

BioPlanet offers interactive browsing and analysis of pathways, and exploration of pathway connections.

### About BioPlanet (Version 1.0)

The NCATS BioPlanet is a comprehensive, publicly accessible informatics resource that catalogues all pathways, their healthy and disease state annotations, and targets within and relationships among them. The BioPlanet integrates pathway annotations from publicly available, manually curated sources that have been subjected to thorough redundancy and consistency cross-evaluation via extensive manual curation. The browser supports interactive browsing, retrieval, and analysis of pathways, exploration of pathway connections, and pathway search by gene targets, category, and availability of bioactivity assays. We intend for such a platform to enable the rational construction of probing assays that could be used to query all of pathway space experimentally. The current version of the BioPlanet (v1.0) incorporates 1,658 distinct human pathways encompassing 9,818 human genes. In future releases, pathways for other species will be added as well as links to data from small molecule, gene expression and siRNA screens performed at NCATS and data from other researchers.

Since the BioPlanet is built on a foundation of current understanding of pathways and their interconnections, it is certainly prone to errors despite our best curation efforts. We therefore view the ongoing curation and growth of the BioPlanet as a community effort, and encourage comments, corrections, contributions, and suggestions for additional features through our feedback mechanism. All contributions will be acknowledged and attributed on this page.

If you make use of the BioPlanet in your research, please cite the BioPlanet paper to acknowledge the BioPlanet resource.

<http://tripod.nih.gov/bioplanet/>



National Center for Advancing Translational Sciences

Hepatotoxicity [10]

toxicity|

Cardiotoxicity [1]

Developmental toxicity [1]

Hepatotoxicity [10]

Liver toxicity [2]

Nephrotoxicity [1]

Neurotoxicity [2]

- Immunology
- Stress response
- Transcription

2 ▼ Cytochrome P450

Pathway Map

Genes

Diseases

Category

- Hepatotoxicity
- Metabolism
- Small molecule
- Xenobiotic metabolism

3 ▼ Cytochrome P450

Pathway Map

Genes

Diseases

Category

- Genetic disease
- Hepatotoxicity
- Lipid metabolism
- Metabolism
- Xenobiotic metabolism
- Small molecule
- Xenobiotic metabolism

4 ▼ Glutathione conjugation

Pathway Map

Genes

Diseases

Category

- Hepatotoxicity
- Metabolism
- Small molecule
- Xenobiotic metabolism

3 ▼ Adhesion

Pathway Map

Genes

Diseases

4 ▼ Adhesion

Pathway Map

Genes

Category

- Adhesion

Assay Availability

- Commercial

Cardiovascular disease [196]

disease

Cardiovascular disease [196]

Cardiovascular diseases [1]

Endocrine and metabolic disease [176]

Genetic disease [230]

Human Diseases [14]

Human Diseases:Cancer [5]

Human Diseases:Cancers: Overview [1]

Human Diseases:Cancers: Specific types [14]

Human Diseases:Cardiovascular diseases [6]

Human Diseases:Endocrine and metabolic diseases [5]

Human Diseases:Immune diseases [6]

Human Diseases:Infectious diseases [11]

Human Diseases:Infectious diseases: Bacterial [7]

Human Diseases:Infectious diseases: Parasitic [4]

Human Diseases:Infectious diseases: Viral [20]

Human Diseases:Neurodegenerative diseases [5]

Human Diseases:Substance dependence [3]

Immune disease [156]

Infectious disease [387]

Infectious diseases: Bacterial [1]

Infectious diseases: Viral [2]

Neurological disease [171]

Diseases

- ↳ Energy metabolism
- Physical disorder
- Transcription
- Transcriptional regulation

4 ▼ ATF2 transcription factor network

Pathway Map

Genes

Diseases

Category

- Cancer
- Cardiovascular disease

Assay Availability

- Commercial
- NCATS

Collapse All

Assay Availability  
Commercial  
PubChem  
PodCast



Availability  
Commercial  
PodCast



Transcriptional activation activity

Assay Availability



Assay Availability  
Commercial  
NCATS



[Home](#)
[Pathway](#)
1-5 of 911  Collapse All

## 1 ▼ 4-1BB-dependent imm

- [Pathway Map](#) [Category](#)  
[Genes](#)  
[Diseases](#)
- Cancer
  - CellActivation
  - CellSignaling
  - Immune system
  - Immunology
  - Infectious disease
  - Stress response
  - Transcription

## 2 ▼ ADP signalling through

- [Pathway Map](#) [Category](#)  
[Genes](#)  
[Diseases](#)
- G-protein coupled rec
  - Immune system

## 3 ▼ AHR signal transduction

- [Pathway Map](#) [Category](#)  
[Genes](#)  
[Diseases](#)
- Cancer
  - CellSignaling
  - CytokinesChemokines
  - Hepatotoxicity
  - Immunology
  - Stress response
  - Transcription

## 4 ▼ AIM2 inflammasome

- [Pathway Map](#) [Category](#)  
[Genes](#)  
[Diseases](#)
- Cell proliferation
  - Genetic disease
  - Immune system
  - Infectious disease
  - Organismal Systems
    - Immune system
  - Stress response

# ADP signalling through P2Y purinoceptor 12

Source: *Reactome*
[Pathway Map](#)
[Genes](#)
[Diseases](#)
[Category](#)
[Assay Availability](#)

#	Disease Name
1	ACTH-independent macronodular adrenal hyperplasia, 219080 (3)
2	Acromegaly, somatic, 102200 (3)
3	Auriculocondylar syndrome 1, 602483 (3)
4	Bleeding disorder, platelet-type, 8, 609821 (3)
5	Charcot-Marie-Tooth disease, dominant intermediate F, 615185 (3)
6	Epileptic encephalopathy, early infantile, 12, 613722 (3)
7	McCune-Albright syndrome, somatic, mosaic 174800 (3)
8	Osseous heteroplasia, progressive, 166350 (3)
9	Pituitary ACTH-secreting adenoma (3)
10	Platelet PLC beta-2 deficiency (1)
11	Pseudohypoparathyroidism Ia, 103580 (3)
12	Pseudohypoparathyroidism Ib, 603233 (3)
13	Pseudohypoparathyroidism Ic, 612462 (3)
14	Pseudopseudohypoparathyroidism, 612463 (3)
15	Ventricular tachycardia, idiopathic, 192605 (3)
16	Hypertension, essential, susceptibility to, 145500 (3)

Home Pathway Category

1-5 of 527 Collapse All

1 2-LTR circle formation

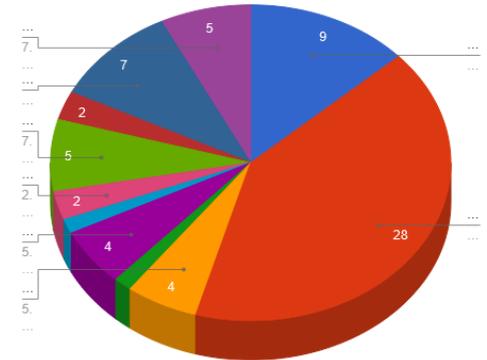
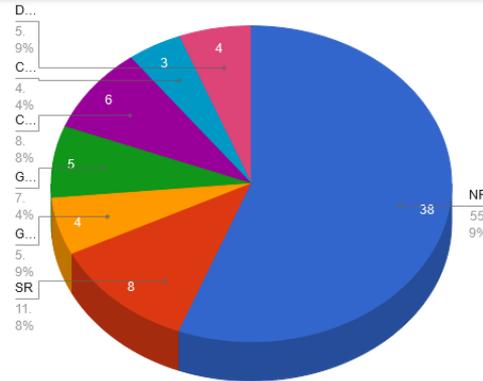
- Pathway Map
- Genes
- Diseases
- LncRNA
- Category
  - DNA repair
  - Human Diseases
  - Infect

2 4-1BB-depend

- Pathway Map
- Genes
- Diseases
- LncRNA
- Cate
  - Canc
  - CellAr
  - CellSi
  - Immu
  - Immu
  - Infect
  - Stres
  - Trans

3 AHR signal tra

- Pathway Map
- Genes
- Diseases
- LncRNA
- Cate
  - Canc
  - CellSi
  - Cytok
  - Hepat
  - Immu
  - Stres
  - Trans



☆ Used in Tox21 Challenge

Protocol Name	Assay Target	Target Category	Cell Line	Cell Type
tox21-ahr-p1 ☆	AhR	NR	HepG2	Liver
tox21-ap1-agonist-p1	AP-1 agonist	SR	ME-180	Cervical Cancer
tox21-ar-bla-agonist-p1 ☆	AR-BLA agonist	NR	HEK293	Kidney
tox21-ar-bla-antagonist-p1	AR-BLA antagonist	NR	HEK293	Kidney
tox21-are-bla-p1 ☆	ARE	SR	HepG2	Liver
tox21-ar-mda-kb2-luc-agonist-p1 ☆	AR-MDA agonist	NR	MDA-MB-453	Breast Cancer
tox21-ar-mda-kb2-luc-agonist-p3	AR-MDA agonist (with antagonist)	NR	MDA-MB-453	Breast Cancer

Source	Name	Assay Name
Tox21	tox21-ahr-p1	qHTS assay to identify small molecule that activate the aryl hydrocarbon receptor (AhR) signaling pathway
Tox21	tox21-ahr-p1	qHTS assay to identify small molecule that activate the aryl hydrocarbon receptor (AhR) signaling pathway: Summary

autism

- Autism
- autism

Total 103 pathways [Export](#)  Collapse All

1 ▼ AP-1 transcription factor network autism

<a href="#">Pathway Map</a>	<a href="#">Category</a>	<a href="#">Assay Availability</a>	
<a href="#">Genes</a>	<ul style="list-style-type: none"> <li>Cancer</li> <li>Immune system</li> <li>Infectious disease</li> <li>Signal transduction</li> <li>Stress response</li> <li>Transcription</li> <li>Transcriptional regulation</li> </ul>	<ul style="list-style-type: none"> <li>Commercial</li> <li>NCATS</li> <li>PubChem</li> <li>Tox21</li> <li>ToxCast</li> </ul>	

2 ▼ ATM-dependent DNA damage response

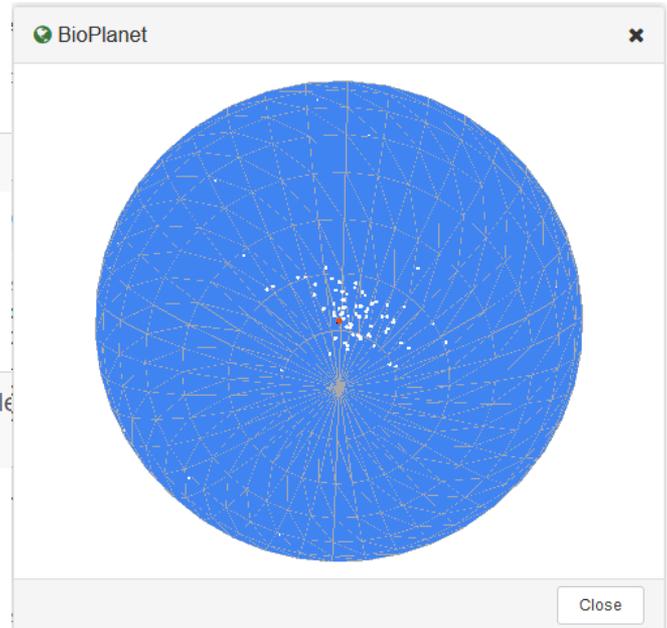
<a href="#">Pathway Map</a>	<a href="#">Category</a>	<a href="#">Assay Availability</a>	
<a href="#">Genes</a>	<ul style="list-style-type: none"> <li>Cancer</li> <li>DNA repair</li> <li>Genetic Information Processing                             <ul style="list-style-type: none"> <li>Replication and repair</li> </ul> </li> <li>Stress response</li> </ul>	<ul style="list-style-type: none"> <li>Commercial</li> <li>NCATS</li> <li>PubChem</li> <li>Tox21</li> <li>ToxCast</li> </ul>	

3 ▼ Activation of mRNA upon binding of the cap-binding complex and subsequent binding to 43S

<a href="#">Pathway Map</a>	<a href="#">Category</a>	<a href="#">Assay Availability</a>	
<a href="#">Genes</a>	<ul style="list-style-type: none"> <li>Cancer</li> <li>Genetic Information Processing                             <ul style="list-style-type: none"> <li>Translation</li> </ul> </li> <li>Genetic disease</li> <li>Transcription</li> <li>Transcriptional regulation</li> <li>Translation</li> </ul>	<ul style="list-style-type: none"> <li>Commercial</li> <li>PubChem</li> </ul>	

4 ▼ Adaptive immune system autism

<a href="#">Pathway Map</a>	<a href="#">Category</a>	<a href="#">Assay Availability</a>	
-----------------------------	--------------------------	------------------------------------	---

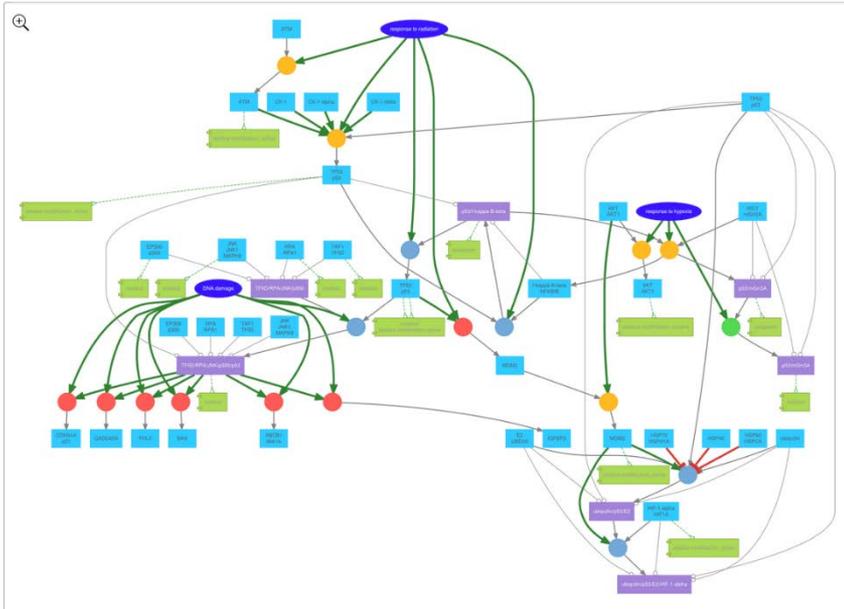


# Hypoxia and p53 in the cardiovascular system

Source: BioCarta

[Pathway Map](#)
[Genes](#)
[Diseases](#)
[Category](#)
[Assay Availability](#)

[Show Legend](#)
[Download](#)



### 3 Gene expression regulation by

- [Pathway Map](#)
- [Genes](#)
- [Diseases](#)
- [Category](#)
- Circulatory system
- Signal transduction
- Stress Response
- Stress response
- Transcription
- Translation

### 4 HIF-1 transcriptional activity in

- [Pathway Map](#)
- [Genes](#)
- [Diseases](#)
- [Category](#)
- Carbohydrate metabolism
- Chronology
- Circulatory system
- Energy metabolism
- Genetic disease
- Signal transduction
- Small molecule metabolism
- Stress response

3090	HIC1	hypermethylated in cancer 1
3091	HIF1A	hypoxia inducible factor 1, alpha subunit (basic helix-loop-helix transcription factor)
3303	HSPA1A	heat shock 70kDa protein 1A
3320	HSP90AA1	heat shock protein 90kDa alpha (cytosolic), class A member 1
3337	DNAJB1	DnaJ (Hsp40) homolog, subfamily B, member 1
3486	IGFBP3	insulin-like growth factor binding protein 3
4193	MDM2	MDM2 oncogene, E3 ubiquitin protein ligase
4793	NFKBIB	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, beta
5243	ABCB1	ATP-binding cassette, sub-family B (MDR/TAP), member 1
5599	MAPK8	mitogen-activated protein kinase 8
6117	RPA1	replication protein A1, 70kDa
6872	TAF1	TAF1 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 250kDa
7157	TP53	tumor protein p53
7319	UBE2A	ubiquitin-conjugating enzyme E2A
171221	DNAJB1P1	DnaJ (Hsp40) homolog, subfamily B, member 1 pseudogene 1

[ToxCast](#)

Genomics

[Burnham Center for Chemical Genomics](#)

Dose Response confirmation of Inhibitors of Mdm2/MdmX interaction in luminescent format

HYPOC1

HYPOC2

Hypoadosteronism

Hypoalphalipoproteinemia

Hypobetalipoproteinemia

Hypocalcemia

Hypocalciuric

Hypoceruloplasminemia

Hypochoondroplasia

Hypochromic

Hypodysfibrinogenemia

Hypofibrinogenemia

Assay Availability

hypoxia p53

Availability

### Cardiovascular system

[Category](#)
[Assay Availability](#)

trial oncogene homolog 1	
rated	
tein	
inhibitor 1A (p21, Cip1)	ivator Interactions Inhibitor Probe Project
damage-inducible, alpha	late Reader - 2121-02_Inhibitor_Dose_DryPowder_Activity
in, quinone 1	reactions Measured in Biochemical System Using Plate Reader -
10	Using Plate Reader - 2158-02_Inhibitor_Dose_CherryPick_Activity
ains 2	reactions Measured in Biochemical System Using Plate Reader -
	late Reader - 2121-02_Inhibitor_Dose_CherryPick_Activity
	icroArray - 2077-01_Other_SinglePoint_HTS_Activity
	stem Using Plate Reader -
	ystem Using Plate Reader -
	reactions Measured in Biochemical System Using Plate Reader -
	Using Plate Reader - 2158-02_Inhibitor_Dose_DryPowder_Activity
	ystem Using Plate Reader -
	nX interaction in luminescent format.

Hide Legend

Entities		Hubs		Edges	
	Protein		Complex Assembly		Activation
	Complex		Biochemical Reaction		Inhibition
	Small Molecule		Transport		Control (Unknown Type)
	Physical Entity		Transport with Biochemical Reaction		Complex Component
	RNA		Template Reaction		Reactant / Product
	DNA		Degradation		Component Property: • Cellular Location • Sequence Modification • Evidence • Interaction Type • Relationship Type
	Pathway				
	Component Property: • Cellular Location • Sequence Modification • Evidence • Interaction Type • Relationship Type				



2,3,7,8-tetrachlorodibenzo-p-dioxin  
7,8-tetrachlorodibenzodioxin  
tcdd  
tetrachlorodibenzodioxin

**External Resources**

Entrez Gene : [196](#)

AHR  
AhR

HSP90/HSP90/XAP2

2,3,7,8-tetrachlorodibenzo-  
2,3,7,8-tetrachlorodibenzo  
tcdd  
tetrachlorodibenzodio

ARNT

nucleus

nucleus

nucleus

AhR/Amt/TCDD



# Gene Enrichment Analysis

The image displays a screenshot of the NIH Pathway Commons website. The main interface shows a list of pathways, including "Amyotrophic lateral sclerosis", "Huntington's disease", "Alzheimer's disease", and "Parkinson's disease". Each pathway entry includes links for "Pathway Map", "Genes", "Diseases", and "Assay Availability".

An "Enrichment Analysis" dialog box is open in the foreground. It contains the following fields and options:

- 1. Cutoff Value:** A text input field containing the value "0.05".
- 2. Gene Id or Symbol:** A list box containing the following gene IDs: 102, 317, 322, 348, 351, 355, 487, 488, and 489.
- Buttons: "Cancel" and "Analyze".

In the background, the "BioPlanet" network visualization is visible. It features a blue globe with a network of nodes and edges. A red callout box points to a specific cluster of nodes, labeled "Phase I of biological oxidations: functionalization of compounds". The word "toxicity" is also visible on the right side of the interface.

# A Tool to Guide Assay Development

Home	Pathway	Category	Assay Availability -	Enrichment	Resource
<p>✓ Total 190 pathways <a href="#">Export</a></p>			<ul style="list-style-type: none"> <li>Commercial</li> <li>NCATS</li> <li>PubChem</li> <li>Tox21</li> <li>ToxCast</li> <li><b>No Assay</b></li> </ul>		<input type="checkbox"/> Collapse All
<p><b>1 ABCA transporters in lipid homeostasis</b></p> <p> <a href="#">Pathway Map</a> <a href="#">Genes</a> <a href="#">Diseases</a> </p> <p> <a href="#">Category</a> <ul style="list-style-type: none"> <li>Digestive system</li> <li>Environmental Information Processing                             <ul style="list-style-type: none"> <li>Membrane transport</li> </ul> </li> <li>Lipid metabolism</li> <li>Small molecule metabolism</li> <li>Transport</li> </ul> </p> <p> <a href="#">Assay Availability</a> N/A                 </p>					
<p><b>2 AMPA receptor activation</b></p> <p> <a href="#">Pathway Map</a> <a href="#">Genes</a> <a href="#">Diseases</a> </p> <p> <a href="#">Category</a> <ul style="list-style-type: none"> <li>Nervous system</li> <li>Neurological disease</li> <li>Organismal Systems                             <ul style="list-style-type: none"> <li>Nervous system</li> </ul> </li> <li>Substance dependence</li> <li>Transport</li> </ul> </p> <p> <a href="#">Assay Availability</a> N/A                 </p>					
<p><b>3 AMPK inhibition of chREBP transcriptional activation activity</b></p> <p> <a href="#">Pathway Map</a> <a href="#">Genes</a> <a href="#">Diseases</a> </p> <p> <a href="#">Category</a> <ul style="list-style-type: none"> <li>Cardiovascular disease</li> <li>Metabolism                             <ul style="list-style-type: none"> <li>Energy metabolism</li> </ul> </li> <li>Physical disorder</li> <li>Transcription</li> <li>Transcriptional regulation</li> </ul> </p> <p> <a href="#">Assay Availability</a> N/A                 </p>					
<p><b>4 ATP-sensitive potassium channels</b></p> <p> <a href="#">Pathway Map</a> <a href="#">Genes</a> <a href="#">Diseases</a> </p> <p> <a href="#">Category</a> <ul style="list-style-type: none"> <li>Endocrine and metabolic disease</li> <li>Nervous system</li> <li>Organismal Systems                             <ul style="list-style-type: none"> <li>Nervous system</li> </ul> </li> <li>Transport</li> </ul> </p> <p> <a href="#">Assay Availability</a> N/A                 </p>					
<p><b>5 Activation of C3 and C5</b></p>					
<p><b>6 Activation of calcium-permeable kainate receptor</b></p>					
<p><b>7 Adenylate cyclase inhibitory pathway</b></p>					

BioPlanet

Close



## Comprehensive Collection for Systems Toxicology and

BioPlanet offers interactive browsing  
and exploration of pathway connect

### About BioPlanet (Version 1.0)

The NCATS BioPlanet is a comprehensive, publicly accessible interactive platform for exploring pathway annotations, and targets within and relationships among them. The platform provides access to data sources that have been subjected to thorough redundancy and orthology reduction. It offers interactive browsing, retrieval, and analysis of pathways, exploration of pathway connectivity, and availability of bioactivity assays. We intend for such a platform to enable the rational construction of probing assays that could be used to query all of pathway space experimentally. The current version of the BioPlanet (v1.0) incorporates 1,658 distinct human pathways encompassing 9,818 human genes. In future releases, pathways for other species will be added as well as links to data from small molecule, gene expression and siRNA screens performed at NCATS and data from other researchers.

[BioPlanet Tutorial](#) provides a thorough, yet succinct description of all aspects of the BioPlanet resource, including navigation, key controls, and data structure.

Since the BioPlanet is built on a foundation of current understanding of pathways and their interconnections, it is certainly prone to errors despite our best curation efforts. We therefore view the ongoing curation and growth of the BioPlanet as a community effort, and encourage comments, corrections, contributions, and suggestions for additional features through our feedback mechanism. All contributions will be acknowledged and attributed on this page.

If you make use of the BioPlanet in your research, please cite the [BioPlanet paper](#) to acknowledge the BioPlanet resource.

### BioPlanet Files Download

1. Gene sets:

[pathway.csv](#)

2. Category annotations:

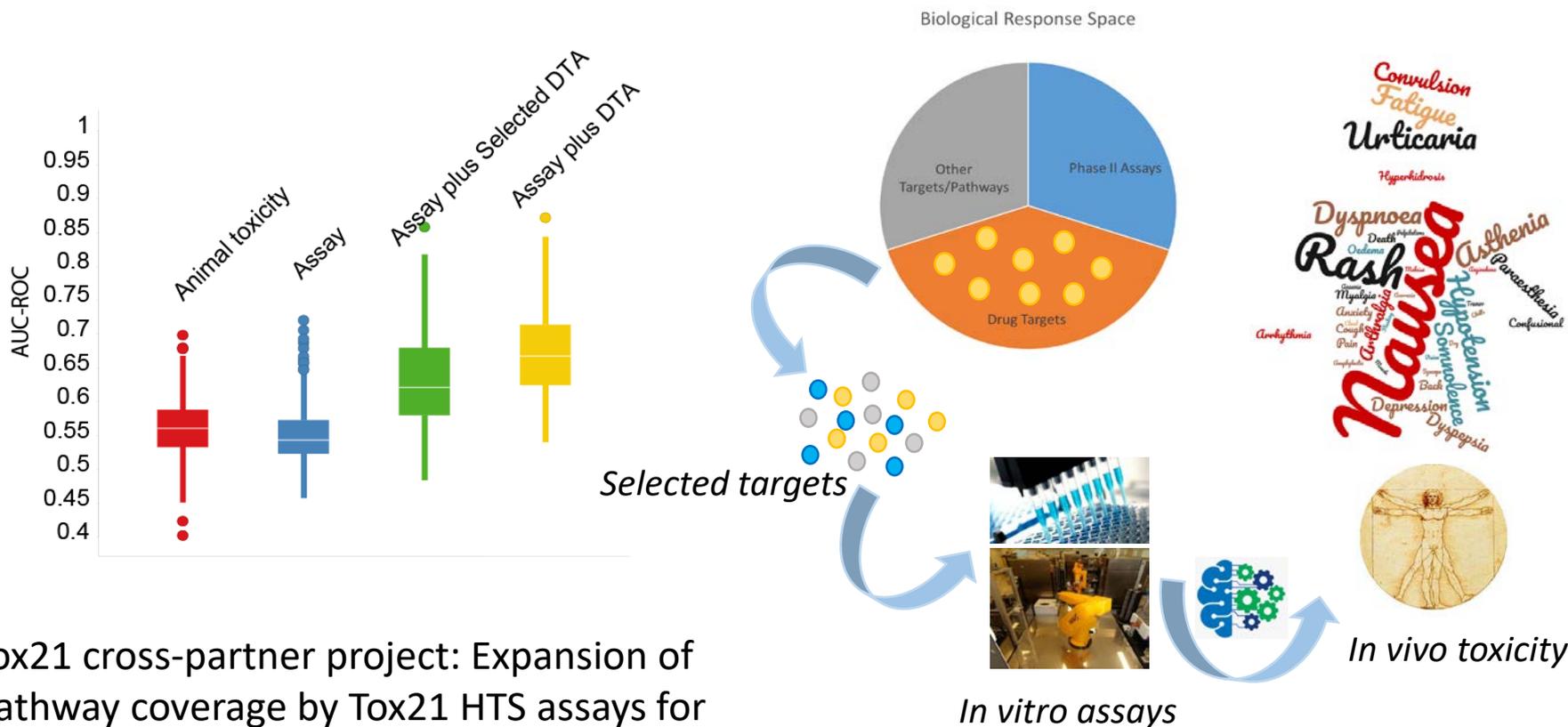
[pathway-category.csv](#)

3. BioPax file:

[pathway-biopax.tar.gz](#)

Close

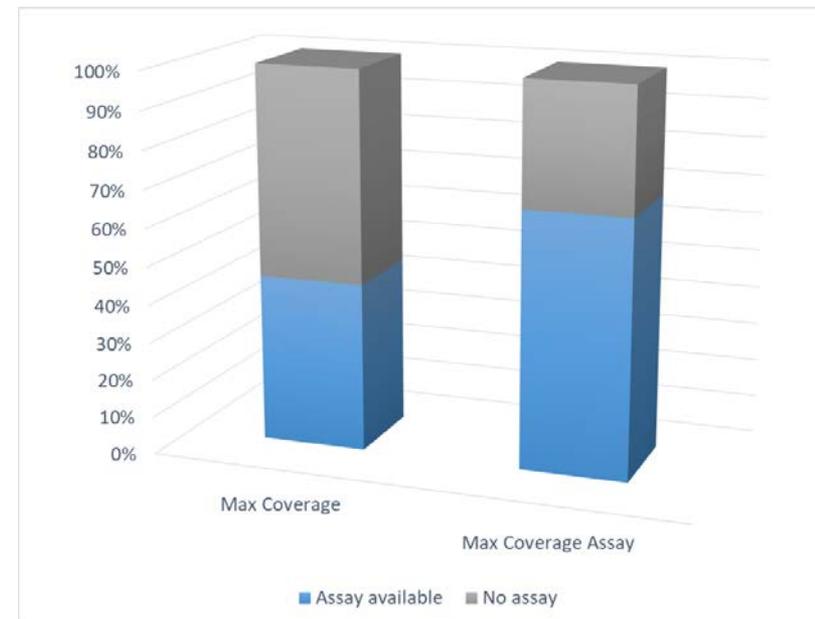
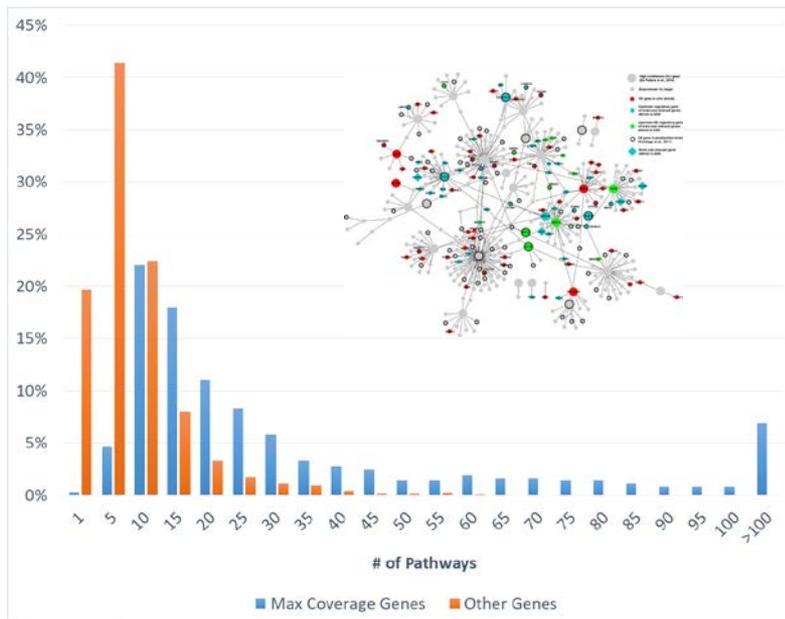
# Application – Design an optimal set of assays for human in vivo toxicity prediction



Tox21 cross-partner project: Expansion of pathway coverage by Tox21 HTS assays for better prediction of adverse drug effects

# Max Coverage Genes (Hub Genes)

- Minimum set of genes (362) that covers all pathways
  - 411 with preference given to targets with existing assays
- The figure shows that genes in this set each on average covers more pathways than other genes – right shift of “blue” distribution compared to “yellow” distribution
- Genes that each covers >100 pathways: AKT1, MAPK3, MAPK1, HRAS, MAP2K1, MAPK8, GRB2, MAPK14, JUN



ORIGINAL RESEARCH ARTICLE

Front. Pharmacol., 26 April 2019 | <https://doi.org/10.3389/fphar.2019.00445>



# The NCATS BioPlanet – An Integrated Platform for Exploring the Universe of Cellular Signaling Pathways for Toxicology, Systems Biology, and Chemical Genomics

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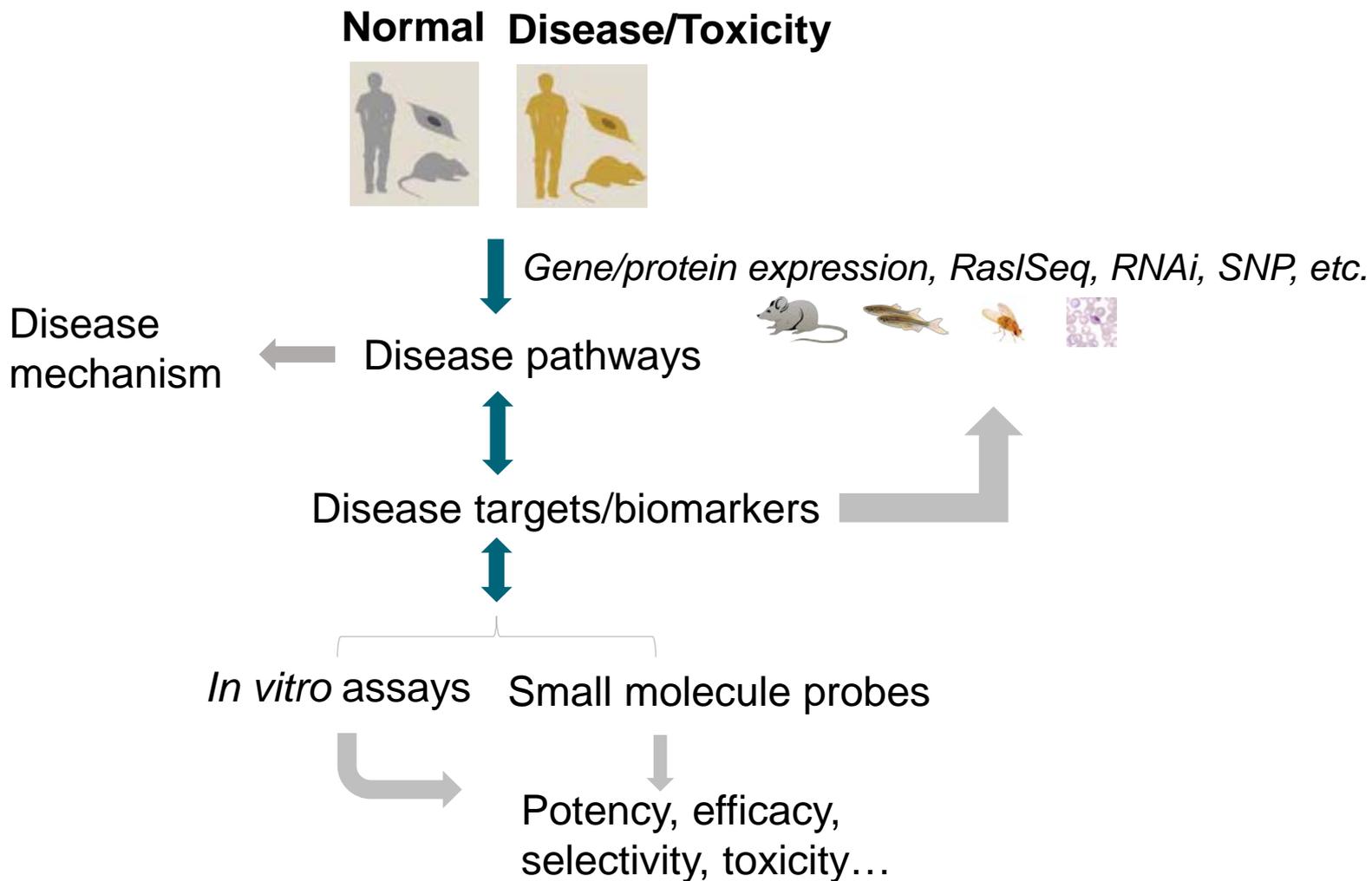
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Chemical genomics aims to comprehensively define, and ultimately predict, the effects of small molecule compounds on biological systems. Chemical activity profiling approaches must consider chemical effects on all pathways operative in mammalian cells. To enable a strategic

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# Moving Forward – A tool for chemical genomics



# An Ongoing Project

- Periodical update of pathway content
- Additional annotations
  - Toxicity: liver, kidney, heart, skin, etc.
  - Drug-target
- Linking small molecule and gene/protein expression data
  - qHTS, raslSeq, RNAi, SNP, proteomics, etc.
- Adding pathways for other species
  - Rat, mouse, zebra fish, drosophila, c. elegans, etc.



# BioPlanet Team

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- Yuhong Wang
- Dac-Trung Nguyen
- Rajarshi Guha
- Ajit Jadhav
- Noel Southall
- Anton Simeonov
- Christopher P. Austin

- Rancho BioSciences

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