Pathway Studio ResNet Database Description and Workflow Examples

Jun 10, 2015

1. Entities: Definitions and Annotation

a. Entity Types and Definition

Entity Type	Definition
Cell Process	Basic processes occurring within and carried out by the cell. Cell processes may contain proteins as property = child concepts.
Clinical Parameter	Parameters measured in clinical
Complex	Several polypeptides that form a complex via physical interactions.
Disease	Health conditions and diseases
Functional Class	Classes of proteins, such as enzyme families. Functional classes contain proteins as property = child concepts.
Protein	Genes and gene products defined by Entrez Gene, including proteins, miRNAs, pseudogenes and non-coding RNAs
Small Molecule	ResNet Mammal: Naturally occurring metabolites and small molecules found in cells; ResNet Mammal + ChemEffect® adds drugs (including biologically active peptides and antibody drugs), environmental chemicals and non-naturally occurring small molecules.
Treatment	Non-chemical treatments and environmental conditions

b. Entity Annotations

Complex

Property Name	Property Type	Source	Description
Name	short string	GO Cellular Component with manual curation	The display name for a complex.
Alias	short string	manual curation from multiple sources	Other identifiers assigned to the complex.
MedScanID	short string	MedScan	Internal Elsevier's identifier
GO ID	short string	http://geneontology.org/	The Gene Ontology project provides a controlled vocabulary of terms for describing gene product characteristics.
KEGG ID	short string	http://www.genome.jp/kegg/	KEGG is a database resource for understanding high-level functions and utilities of the biological system, such as the cell, the organism and the ecosystem, from molecular-level information, especially large-scale molecular datasets generated by genome sequencing and other high-throughput experimental technologies.

Functional Class

Property Name	Property Type	Source	Description
Name	short string	http://www.expasy.org/	The display name for the functional class
Alias	short string	Manual curation from multiple sources	Other identifiers assigned to the functional class
MedScanID	short string	MedScan	Internal Elsevier's identifier
GO ID	short string	http://geneontology.org/	The Gene Ontology project provides a controlled vocabulary of terms for describing gene product characteristics.
Cell	dictionary	http://geneontology.org/	Gene Ontology – Cellular Component. Not all cellular

Localization			processes have localization assignment.
Mol Function	dictionary	http://geneontology.org/	Functional classes with associated activities: ligand, phosphatases, protein kinases, receptor and transcription factor are annotated as such in the Mol Function property.
Description	short string	manually curated from multiple sources	Full names of the functional class.
EC Number	short string	Enzyme Commission Number	The Enzyme Commission number (EC number) is a numerical classification scheme for enzymes, based on the chemical reactions they catalyze.

Protein

Property Name	Property Type	Source	Description
Name	short string	Entrez official gene symbol http://www.ncbi.nlm.nih.gov/gquery/	Display symbol for a gene
Alias	short string	Entrez with manual curation	Other identifiers assigned to the protein.
MedScanID	short string	MedScan dictionary – Elsevier	Internal Elsevier's identifier
GO ID	short string	http://geneontology.org/	The Gene Ontology project provides a controlled vocabulary of terms for describing gene product characteristics.
Cell Localization	dictionary	http://geneontology.org/	Gene Ontology – Cellular Component. The Gene Ontology project provides a controlled vocabulary of terms for describing gene product characteristics. Cellular Process entities are derived from Gene
Organism	dictionary	http://www.ncbi.nlm.nih.gov/taxonomy	The Entrez Taxonomy database displays the species names (and higher-level classification) of all of the organisms that are represented in the Entrez sequence databases (or any of the other Entrez databases that are indexed by taxonomy).
Primary Cell Localization	dictionary	http://geneontology.org	Gene Ontology – Cellular Component. The Gene Ontology project provides a controlled vocabulary of terms for describing gene product characteristics. Cellular Process entities are derived from Gene
Notes	long Text		Summary of gene/gene product function provided by RefSeq
Description	short string	Official full name from Entrez	Full name for the gene
EC Number	short string		The Enzyme Commission number (EC number) is a numerical classification scheme for enzymes, based on the chemical reactions they catalyze.
Ensembl ID	short string	http://www.ensembl.org/	
GenBank ID	short string	http://www.ncbi.nlm.nih.gov/	
Homologene ID	short string	http://www.ncbi.nlm.nih.gov/homologene	An automated system for constructing putative homology groups from the complete gene sets of a wide range of eukaryotic species.
Hugo ID	short string	http://www.genenames.org/	HUGO Gene Nomenclature Committee is a curated online repository of HGNC-approved gene nomenclature, gene families and associated resources including links to genomic, proteomic and phenotypic information.
Human chromosome position	short string	http://www.ncbi.nlm.nih.gov/gene	Gene cytoband location
KEGG ID	short string	http://www.genome.jp/kegg/	KEGG is a database resource for understanding high-level functions and utilities of the biological system,

			such as the cell, the organism and the ecosystem, from molecular-level information, especially large-scale molecular datasets generated by genome sequencing and other high-throughput experimental technologies.
LocusLink ID	short string	http://www.ncbi.nlm.nih.gov/LocusLink	Old NCBI identifier that has transitioned to Entrez IDs.
MGI ID	short string	http://www.informatics.jax.org/	Mouse Genome Informatics identifier for genes.
Mouse chromosome position	short string	http://www.ncbi.nlm.nih.gov/gene	Gene cytoband location
OMIM ID	short string	http://omim.org/	Online Mendelian Inheritance in Man® is an Online Catalog of Human Genes and Genetic Disorders. OMIM focuses on the relationship between phenotype and genotype.
PIR ID	short string	http://pir.georgetown.edu/pirwww/index.shtml	Integrated Protein Informatics Resources for Genomic, Proteomic and Systems Biology Research
RGD ID	short string	http://rgd.mcw.edu/wg/home	Rat Genome Database gene identifiers.
Rat chromosome position	short string	http://www.ncbi.nlm.nih.gov/gene	Gene cytoband location
Swiss-Prot Accession	short string	http://www.uniprot.org/	The Universal Protein Resource (UniProt) is a comprehensive resource for protein sequence and annotation data.
Swiss-Prot ID	short string		
Unigene ID	short string	http://www.ncbi.nlm.nih.gov/unigene	UniGene computationally identifies transcripts from the same locus; analyzes expression by tissue, age, and health status; and reports related proteins (protEST).and clone resources.
miRBase ID	short string	http://www.mirbase.org/	miRBase is a database of published miRNA sequences and annotation.

Small Molecule

Property Name	Property Type	Source	Description
Name	short string	PubChem compounds and manual curation from multiple sources	Display name for the small molecule
Alias	short string	PubChem compounds and manual curation from multiple sources	Other identifiers assigned to the small molecule.
MedScanID	short string	MedScan dictionary – Elsevier	Internal Elsevier's identifier
Molecular Weight	Numerical	https://pubchem.ncbi.nlm.nih.gov/	Molecular weight of a small molecule
Rotatable Bond Count	Numerical	https://pubchem.ncbi.nlm.nih.gov/	Number of rotatable bonds in the molecule. Rotatable bonds are defined as single bonds between heavy atoms. It doesn't include ring bonds, those connected to a heavy atom that is attached to only hydrogens or amide bonds.
CAS ID	short string	https://www.cas.org/content/chemical-substances/faqs	A CAS Registry Number, is a unique numerical identifier assigned by Chemical Abstracts Service (CAS) to every chemical substance described in the open scientific literature.
ChEBI ID	short string	http://www.ebi.ac.uk/chebi/init.do	ChEBI stands for 'Chemical Entities of Biological Interest'. It is a freely available database of 'small molecular entities', developed at the EBI. The term 'molecular entity' encompasses any constitutionally or isotopically distinct atom, molecule, ion, ion pair,

			radical, radical ion, complex, conformer, etc., identifiable as a separately distinguishable entity.
HMDB ID	short string	http://www.hmdb.ca/	The Human Metabolome Database (HMDB) is an electronic database containing detailed information about small molecule metabolites found in the human body.
IUPAC Name	short string	http://www.iupac.org/	Name assigned according to the IUPAC nomenclature of organic chemistry,
InChIKey	short string	http://www.iupac.org/	The IUPAC International Chemical Identifier (InChI™) is a non-proprietary identifier for chemical substances that can be used in printed and electronic data sources thus enabling easier linking of diverse data compilations.
KEGG ID	short string	http://www.genome.jp/kegg/	KEGG is a database resource for understanding high-level functions and utilities of the biological system, such as the cell, the organism and the ecosystem, from molecular-level information, especially large-scale molecular datasets generated by genome sequencing and other high-throughput experimental technologies.
Molecular Formula	short string	https://pubchem.ncbi.nlm.nih.gov/	Molecular formula of a small molecule
PharmaPendium Name	short string	https://www.pharmapendium.com /#/home	The name of the drug as it appears in Pharmapendium. Elsevier's PharmaPendium offers dedicated data modules that provide insights and information on the critical focused areas of drug development, drug safety, ADME and drug-drug interactions.
PubChem CID	short string	https://pubchem.ncbi.nlm.nih.gov/	The PubChem Compound Database contains validated chemical depiction information provided to describe substances in PubChem Substance. Structures stored within PubChem Compounds are pre-clustered and cross-referenced by identity and similarity groups. A compound identifier (CID) is the permanent identifer for a unique chemical structure. Each stereoisomer of a compound has its own CID. It is also possible for different tautomeric forms of the same compound to have different CID's.
PubChem SID	short string	http://pubchem.ncbi.nlm.nih.gov/	The PubChem Compound Database contains validated chemical depiction information provided to describe substances in PubChem Substance. Structures stored within PubChem Compounds are pre-clustered and cross-referenced by identity and similarity groups. A substance identifier (SID) is the permanent identifier for a depositor-supplied molecule. Each SID corresponds to a unique external registry ID provided by a PubChem data source.
Reaxys ID	short string	https://www.reaxys.com	Elsevier's Reaxys and Reaxys Medicinal Chemistry combine comprehensive databases of chemistry data and literature with powerful search interfaces. They return relevant extracted data and citations in optimal formats for chemistry research. Both can seamlessly integrate into an existing environment of tools and systems, saving time and reducing the risk of inconsistencies.
XLogP	Numerical	https://pubchem.ncbi.nlm.nih.gov/	A partition coefficient or distribution coefficient that is a measure of differential solubility of a compound in two solvents.
XLogP-AA	short string	https://pubchem.ncbi.nlm.nih.gov/	A partition coefficient or distribution coefficient that is a measure of differential solubility of a compound in two solvents.

Cell Process

Property Name	Property Type	Source	Description
Name	short string	Manual curation from GO http://geneontology.org/	Display name for the cell process
Alias	short string	Manual curation from multiple sources	Other identifiers assigned to the cell process.
MedScanID	short string	MedScan dictionary – Elsevier	Internal Elsevier's identifier
GO ID	short string	http://geneontology.org/	The Gene Ontology project provides a controlled vocabulary of terms for describing gene product characteristics. Cellular Process entities are derived from Gene Ontology with additional manual curation.
Cell localization	dictionary	http://geneontology.org/	Gene Ontology – Cellular Component. The Gene Ontology project provides a controlled vocabulary of terms for describing gene product characteristics. Cellular Process entities are derived from Gene Ontology with additional manual curation.
Description	short string	manually curated	Full name for the cell process

Treatment

Property Name	Property Type	Source	Description
Name	short string	Manually curated from multiple sources	Display name for the treatment
Alias	short string	Manually curated from multiple sources	Other identifiers assigned to the treatment.
MedScanID	short string	MedScan dictionary – Elsevier	Internal Elsevier's identifier

Clinical Parameters

Property Name	Property Type	Source	Description
Name	short string	Manually curated from multiple sources	Display name for the clinical parameter
Alias	short string	Manually curated from multiple sources	Other identifiers assigned to the clinical parameter
MedScan	short string	MedScan dictionary – Elsevier	ID assigned in the MedScan dictionary (text mining tool)

Disease

Property Name	Property Type	Source	Description
Name	short string	MeSH with manual curation, OphaNet with manual curation http://www.ncbi.nlm.nih.gov/mesh http://www.orpha.net/consor/cgi-bin/index.php	Display name for the disease
Alias	short string	MeSH with manual curation, OphaNet with manual curation http://www.ncbi.nlm.nih.gov/mesh http://www.orpha.net/conso	Other identifiers assigned to the disease.

		r/cgi-bin/index.php	
MedScanID	short string	MedScan dictionary – Elsevier	Internal Elsevier's identifier
MeSH heading	short string	https://www.nlm.nih.gov/mesh/	MeSH (Medical Subject Headings) is the National Library of Medicine controlled vocabulary thesaurus used for indexing articles for PubMed.

Additional Annotation for Entities

Property Name	Description
ObjectType	For entities, the object types are each entity type (protein, small molecule, etc.) For relations, the object types are each relation type (expression, binding, etc.)
ChildConcepts	Concepts (proteins) mapped to a concept. For example, functional classes include all the proteins associated with the functional class as "child concepts."
ParentConcepts	The ontological parent of a protein, which can be a functional class, or cellular process
URN	Elsevier internal identifier

2. Relations: Definitions and Annotations

The following relation types are included in the Mammal+ChemEffect+DiseaseFx Database.

a. Relation Types and Definitions

Type	Filtering Field Name	Sub-Categories	Definition
Binding	-	-	Direct physical interaction between two molecules. This relation type has no Direction and no Effect
Biomarker	BiomarkerType	diagnostic, prognostic	Molecule was reported as a biomarker for a disease (Disease → Protein/ Complex/Functional class/small molecule). This relation type has no Effect.
ChemicalReaction	-	-	Enzyme catalyzes reaction involving small molecule
ClinicalTrial	Phase	N/A, Phase 0, Phase 1, Phase1/Phase2, Phase2, Phase2/Phase3, Phase 3, Phase4	Disease/cell process relation representing clinical trials conducted for a drug against a disease (from clinicaltrials.gov) (Small molecule → Disease, CellProcess). This relation type has no Effect Food and Drug Administration (FDA) categories for describing the clinical trial of a drug based on the study's characteristics. There are five phases: Phase 0: Exploratory study involving very limited human exposure to the drug, with no therapeutic or diagnostic goals. Phase 1: Studies that are usually conducted with healthy volunteers and that emphasize safety. Phase 2: Studies that gather preliminary data on effectiveness (whether the drug works in people who have a certain disease or condition. Safety continues to be evaluated, and short-term adverse events are studied. Phase 3: Studies that gather more information about safety and effectiveness by studying different populations and different dosages and by using the drug in combination with other drugs. Phase 4: Studies occurring after FDA has approved a drug for marketing. These studies gather additional information about a drug's safety, efficacy, or optimal use.
DirectRegulation	-	-	Regulator influences target activity by direct physical interaction (excluding promoter binding interactions)
Expression	-	-	Regulator changes protein abundance by affecting levels of transcript or protein stability
FunctionalAssociation	-	-	Disease is associated to cell process, clinical parameter or another disease. This relation type has no Direction and no Effect.
GeneticChange	ChangeType	gene deletion, mutation, gene amplification, epigenic methylation	Genetic changes associated with a disease (Disease → Protein/ Complex/Functional class)
miRNAEffect	-	-	The inhibitory effect of a miRNA on its mRNA target. These relations have two sources: 1) literature, 2) Public databases: miRanda (human, mouse, rat), PicTar(human) and TargetScan (human, mouse, rat).

			This information is provided in the field “source.”
MolSynthesis	-	-	Regulator changes the concentrations of the target (usually a small molecule target)
MolTransport	-	-	Regulator changes the localization of the target (molecular translocation, export, import etc.)
PromoterBinding	-	-	Regulator binds to the promoter of a gene
ProtModification	Mechanism	acetylation, cleavage, deacetylation, demethylation, dephosphorylation, direct interaction, methylation, phosphorylation, posttrascriptional inhibition, proteolysis, ubiquitination	Regulator changes the modification of the target molecule, usually by a direct interaction
QuantitativeChange	Quantitative Type	expression, abundance, activity	Changes in abundance/activity/expression of a gene/protein/small molecule associated with a disease (Disease → Protein/ Complex/Functional class)
Regulation	-	-	Regulator changes the activity of the target by an unknown mechanism (direct or indirect). This is a less specific relation type than others provided
StateChange	Change Type	alternative splicing, phosphorylation	Changes in a protein’s posttranslational modification status or alternative splicing events associated with a disease (Disease → Protein/ Complex/Functional class)

b. Relation Annotations

Most of the annotations for relations share common annotations fields. Below is a list of shared annotations for all relation types except Clinical Trials. Relations are assigned effect (positive, negative, or unknown) and directionality except Binding and Functional Association. Biomarker is assigned directionality but has no assigned effect.

Property Name	Property Type	Source	Description
CellType	dictionary	Elsevier’s Natural Language Processing (NLP) tool	Contains cell name recognized by Elsevier NLP in the supporting sentence or in the text upstream from the sentence
Organ	dictionary	Elsevier’s Natural Language Processing (NLP) tool	Contains organ name recognized by Elsevier NLP in the supporting sentence or in the text upstream from the sentence
Organism	dictionary	Elsevier’s Natural Language Processing (NLP) tool	Contains organism name recognized by Elsevier NLP in the supporting sentence or in the text upstream from the sentence
Tissue	dictionary	Elsevier’s Natural Language Processing (NLP) tool	Contains tissue recognized by Elsevier NLP in the supporting sentence or in the text upstream from the sentence
CellLineName	short string	Elsevier’s Natural	Contains cell line name recognized by Elsevier NLP in the

		Language Processing (NLP) tool	supporting sentence or in the text upstream from the sentence
Effect	dictionary	Elsevier's Natural Language Processing (NLP) tool	Relations are assigned effect (positive, negative, or unknown) except binding, functional association and biomarker.
TextMods	long text	Elsevier's Natural Language Processing (NLP) tool	The "TextMods" property for a reference indicates a substitution has been made in the original text resulting in the display of the full entity name in place of the abbreviation appearing in the original text.
Title	long text	Elsevier's Natural Language Processing (NLP) tool	Article title
msrc	long text	Elsevier's Natural Language Processing (NLP) tool	Display name in UI: Sentence. Contains sentence recognized by Elsevier NLP supporting the relation
PubYear	numerical	Elsevier's Natural Language Processing (NLP) tool	Publication year of the article with the sentence
Authors	short string	Elsevier's Natural Language Processing (NLP) tool	Article author
DOI	short string	Elsevier's Natural Language Processing (NLP) tool	Document Object Identifier
EMBASE	short string	Elsevier's Natural Language Processing (NLP) tool	Embase article identifier
ESSN	short string	Elsevier's Natural Language Processing (NLP) tool	Electronic ISSN number
ISSN	short string	Elsevier's Natural Language Processing (NLP) tool	International Standard Serial Number
Journal	short string	Elsevier's Natural Language Processing (NLP) tool	Journal name for a journal not included in PubMed
MedlineTA	short string	Elsevier's Natural Language Processing (NLP) tool	Journal name for journals from Pubmed
PII	short string	Elsevier's Natural Language Processing (NLP) tool	Publisher Item Identifier
PMID	short string	Elsevier's Natural Language Processing (NLP) tool	Pubmed abstract identifier
PUI	short string	Elsevier's Natural Language	Publisher Item Identifier from Embase

		Processing (NLP) tool	
PubVersion	short string	Elsevier's Natural Language Processing (NLP) tool	Version number of article
TextRef	short string	Elsevier's Natural Language Processing (NLP) tool	Information in the TextRef field indicates if the relation was identified in an abstract, title, body of a paper or when no location can be identified. For example: #title:1 means the "first sentence of the article's title' #abs:9 meand the '9th sentence of the article's abstract' #body:21 means the '21st sentence of the article's body' #cont:21 means the '21st sentence of the article's extracted text with no identifiable parts
mref	short string	Elsevier's Natural Language Processing (NLP) tool	Display name in UI: MedLine reference. Contains Pubmed abstract identifier (PMID)

Clinical Trials

Clinical Trials data is obtained directly from ClinicalTrials.gov (it is not literature extracted using MedScan).

Property Name	Property Type	Source	Description
Phase	dictionary	clinicaltrials.gov	Food and Drug Administration (FDA) categories for describing the clinical trial of a drug based on the study's characteristics, such as the objective and number of participants. There are five phases: Phase 0: Exploratory study involving very limited human exposure to the drug, with no therapeutic or diagnostic goals (for example, screening studies, microdose studies) Phase 1: Studies that are usually conducted with healthy volunteers and that emphasize safety. The goal is to find out what the drug's most frequent and serious adverse events are and, often, how the drug is metabolized and excreted. Phase 2: Studies that gather preliminary data on effectiveness (whether the drug works in people who have a certain disease or condition). For example, participants receiving the drug may be compared with similar participants receiving a different treatment, usually an inactive substance (called a placebo) or a different drug. Safety continues to be evaluated, and short-term adverse events are studied. Phase 3: Studies that gather more information about safety and effectiveness by studying different populations and different dosages and by using the drug in combination with other drugs. Phase 4: Studies occurring after FDA has approved a drug for marketing. These including postmarket requirement and commitment studies that are required of or agreed to by the sponsor. These studies gather additional information about a drug's safety, efficacy, or

			optimal use.
msrc	long text	text extraction	Display name in UI: Sentence. Contains sentence recognized by Elsevier NLP supporting the relation
TrialStatus	dictionary	clinicaltrials.gov	The status of the trial: Active not recruiting, approved for marketing, available, completed, enrolling by invitation, no longer available, not yet recruiting, recruiting, suspended temporarily not available, terminated, withdrawn, withheld
Condition	long text	clinicaltrials.gov	A disease, disorder, syndrome, illness, or injury that is being studied. On ClinicalTrials.gov, conditions may also include other health-related issues such as lifespan, quality of life, and health risks.
Intervention	long text	clinicaltrials.gov	A process or action that is the focus of a clinical study. This can include giving participants drugs, medical devices, procedures, vaccines, and other products that are either investigational or already available. Interventions can also include noninvasive approaches such as surveys, education, and interviews.
Title	long text	clinicaltrials.gov	The title given to the specific study.
Collaborator	short string	clinicaltrials.gov	A collaborator is an organization other than the sponsor that provides support for a clinical study. This may include funding, design, implementation, data analysis, or reporting.
Company	short string	clinicaltrials.gov	The company sponsoring the trial.
NCT ID	short string	clinicaltrials.gov	ClinicalTrials.gov identifier
Start	short string	clinicaltrials.gov	The start date of the study.
TextRef	short string	MedScan Reader	TextRef for clinical trials includes the NCT identifier
mref	short string	Elsevier's Natural Language Processing (NLP) tool	Display name in UI: MedLine reference. Contains Pubmed abstract identifier (PMID)

Additional Annotation for Relations

Property Name	Description
Effect	The described effect of a relation (positive, negative, unknown) on a target.
In/Out	Indicator of the directionality of the relation (in or out from the entity). In the
RelationNumberOfReferences	The number of sentences from which the relation has been extracted.
URN	Elsevier internal identifier

3. Additional Database Information

a. Groups and Pathways

Groups in ResNet consist simply of a list of entities. Ontologies are presented as groups.

Pathways in ResNet include both entities and relations. The Elsevier curated pathway collection includes over 1300 pathways. A complete list of the pathways included in the ResNet database is provided at the end of this document (see Appendix).

b. Ontologies

Two ontologies are included in ResNet: Gene Ontology (cellular component, molecular function, and biological process) and Pathway Studio Ontology.

Gene Ontology:
The Gene Ontology IDs, from the Gene Ontology Consortium, for each protein and cellular process are listed in their annotation fields. Please visit http://geneontology.org/ for more information.

Pathway Studio Ontology:

Pathway Studio Ontology was designed from a different prospective than 'the Gene Ontology' (GO) provided by the Gene Ontology Consortium. Whereas GO is a multi-level hierarchy with multiple, often overlapping, functional descriptions of genes, Pathway Studio Ontology consists of a non-overlapping core set of cell-level molecular function groups. To complement the molecular function groups, Elsevier has defined the cellular process groups that represent the most basic and well-established cellular processes. Elsevier experts have manually assigned proteins to these groups based on protein primary function. The result is a well-designed organization of proteins that reflect the current knowledge of their primary function(s) in the cell. Organism-level biological processes can be represented by combination of basic cellular processes and molecular function groups.

ResNet Mammal, Pathway Studio Ontology includes 8,666 genes and 1006 miRNAs, organized in 519 groups, with 11,788 'assignments'.

Cellular Processes:

Biochemical Pathways:	41 groups	1573 proteins
Metabolite/Ion Transport:	42 groups	1053 proteins
Structural Processes: (DNA replication, translation, actin polymerization, endocytosis)	63 groups	3814 proteins

Molecular Functions:

Ligands:	42 groups	448 proteins
Receptors:	68 groups	930 proteins
Signaling Proteins:	155 groups	766proteins
miRNAs:	10 groups	2154 miRNAs
Transcription Factors:	94 groups	1,822 proteins

Disease Regulation:

Oncogenes:	1 group	271 proteins
Tumor Suppressors:	1 group	92 proteins

APPENDIX: WORKFLOW EXAMPLES

The examples below include the biological question, the relation types and the entity types selected, and considerations for each workflow.

	Question	Wizard Selections	Considerations
Gene/Protein Expression			
1	What proteins (transcription factors) bind to the promoter of a gene(s)?	**initial selection:** protein **directionality:** upstream **entity type:** protein **relation type:** promoterbinding	Finds transcription factors for genes (directly binding to promoters)
2	What known miRNAs regulate expression of a gene(s)?	**initial selection:** protein **directionality:** upstream **entity type:** protein **relation type:** miRNAEffect	Finds miRNA targets.
3	What proteins are involved in the expression of a gene(s), either directly or indirectly?	**initial selection:** protein **directionality:** upstream **entity type:** protein **relation type:** promoterbinding or expression	Finds both direct expression regulators (promoterbinding) and proteins with possibly an indirect effect on expression (expression)
Physical Interaction with Proteins			
4	What proteins bind to a protein?	**initial selection:** protein **directionality:** (all) **entity type:** protein **relation type:** binding or directregulation	Identifies protein binding partners (no additional regulatory event known) Binding relations have no directionality (DirectRegulation is regulation through a direct physical interaction and can also be considered here.)
5	What small molecules bind to a protein?	**initial selection:** protein ***directionality:*** (all) **entity type:** small molecules **relation type:** binding or directregulation	Identifies small molecules that bind to a protein (no additional regulatory event known) (DirectRegulation is regulation through a direct physical interaction and can also be considered here.)

	Question	Wizard Selections	Considerations
6	What proteins regulate a protein through a direct physical interaction?	**initial selection:** protein **directionality:** upstream **entity type:** protein **relation type:** directregulation	Finds proteins that regulate the activity of a target protein through a direct physical interaction Can also consider "protmodification" relations
7	What small molecules regulate a protein through direct physical interactions?	**initial selection:** protein **directionality:** upstream **entity type***:* small molecule **relation type:** directregulation	Finds small molecules that regulate the activity of a protein through a direct physical interaction (Drugs/non-naturally occurring small molecules included in ChemEffect data)
Protein Modification(s)			
8	What protein(s) acetylate/deacetylate a protein?	**initial selection:** protein **directionality:** upstream **entity type:** protein **relation type:** protmodification **mechanism:** acetylation or deacetylation	Identifies proteins involved in acetylation/deacetylation of target protein(s).
9	What protein(s) cleave a protein?	**initial selection:** protein **directionality:** upstream **entity type:** protein **relation type:** protmodification **mechanism**: cleavage	Identifies proteins involved in the proteolytic cleavage of target protein(s).
10	What proteins(s) methylate/demethylate a protein?	**initial selection:** protein **directionality:** upstream **entity type:** protein **relation type:** protmodification **mechanism**: methylation or demethylation	Identifies proteins involved in the methylation/demethylation of target protein(s).
11	What protein(s) phosphorylate/dephosphorylate a protein?	**initial selection:** protein **directionality:** upstream **entity type***:* protein **relation type:** protmodification **mechanism:** phosphorylation or dephosphorylation	Identifies protein(s) involved in the phosphorylation/ dephosphorylation of target protein(s).

	Question	Wizard Selections	Considerations
12	What protein(s) ubiquitinate a protein?	**initial selection:** protein **directionality:** upstream **entity type:** protein **relation type:** protmodification **mechanism:** ubiquitination	Identifies proteins involved in the ubiquitination of target protein(s).
Protein /Small Molecule Transport			
13	What protein mediates the translocation of a protein or small molecule?	**initial selection:** protein or small molecule **directionality:** upstream **entity type:** protein **relation type:** moltransport	Identifies proteins involved in the translocation of a protein or small molecule target.
14	What small molecule mediates the translocation of a protein	**initial selection:** protein *directionality:* upstream *entity type:* small molecule *relation type:* moltransport	Identifies small molecules involved in the translocation of a protein target.

	Question	Wizard Selections	Considerations
Proteins/Small molecules involved in chemical interactions			
15	What enzymes are involved in a chemical reaction with a small molecule?	**initial selection:** small molecule **directionality:** all **entity type(s):** proteins, functional classes **relation type:** chemical reaction	Identifies functional classes and proteins that catalyze chemical reactions of small molecules. Most metabolism enzymes in the metabolism pathways are represented by functional classes.
Protein/Small Molecule associations and changes in Diseases and Cell Processes			
16	What proteins are known to be associated with a disease or cellular process?	**initial selection:** disease or cell process **directionality:** upstream **entity type:** protein **relation type:** regulation	Identifies proteins known to be associated with a specific disease or cellular process. (More specific data relating proteins to diseases is available in DiseaseFx data including statechange, genetic change and quantitativechange.)
17	What small molecules are associated with a disease or cellular process?	**initial selection:** disease or cell process **directionality:** upstream **entity type:** small molecules **relation type:** regulation	Identifies small molecules that are associated with diseases or cellular processes. Small molecule association with diseases and cell processes through regulation relations are found in the ChemEffect® Database. In addition, more information about small molecules associated with diseases can be found in the DiseaseFx database through quantitivechange and biomarker relations.
18	What proteins are known to change in expression, activity or abundance in a disease?	**initial selection:** disease **directionality***:* downstream **entity type:** protein **relation type:** quantitativechange **quantitativeType:** expression or abundance or activity	Identifies proteins that are changed in activity abundance or expression in a disease. Quantitativechange relations are found only in DiseaseFx data
19	What small molecules are known to change in abundance in a disease?	**initial selection:** disease **directionality:** downstream **entity type:** small molecules **relation type:** quantitativechange **quantitativetype:** abundance	Identifies small molecules that are changed in abundance in a disease. Quantitativechange relations are found in DiseaseFx data

	Question	Wizard Selections	Considerations
20	What proteins with genetic mutations are associated with a disease?	**initial selection:** disease **directionality:** downstream **entity type:** protein **relation type:** geneticchange	Identifies proteins with genetic changes (gene deletions, amplifications, mutations, epigenic changes, or methylation) associated with a disease. Geneticchange relations are found in DiseaseFx data.
21	What proteins or small molecules are diagnostic for a disease?	**initial selection:** disease **directionality:** downstream **entity type:** protein **relation type:** biomarker **biomarkertype**: diagnostic	Identifies proteins/small molecules know to be diagnostic for a disease. Biomarker relations are found in DiseaseFx data.
22	What proteins or small molecules are prognostic for a disease?	**initial selection:** disease **directionality:** downstream **entity type:** protein **relation type:** biomarker **biomarkertype**: prognostic	Identifies proteins/small molecules known to be prognostic for a disease. Biomarker relations are found in DiseaseFx data.
23	What protein phosphorylation/dephosphorylation events are associated with a disease?	**initial selection:** disease **directionality:** downstream **entity type:** protein **relation type:** statechange **changetype**: phosphorylation or dephosphorylation	Identifies post translational protein phosphorylation/dephosphorylation events associated with a disease. Statechange relations are found in DiseaseFx data.
24	What protein/gene splice variants are associated with a disease?	**initial selection:** disease **directionality:** downstream **entity type:** protein **relation type:** statechange **changetype**: alternative splicing	Identifies alternate gene splicing events/splice variants associated with a disease. Statechange relations are found only in DiseaseFx data.

	Question	Wizard Selections	Considerations
Small Molecule concentrations			
25	What proteins regulate the synthesis or catabolism of a small molecule?	**initial selection:** small molecule **directionality:** upstream **entity type(s):** protein **relation type(s):** molsynthesis	Identifies proteins that regulat the concentrations of small molecules through metabolic events
Clinical Trials			
26	What small molecules/drugs have been tested in clinical trials for a disease?	**initial selection:** small molecules **directionality:** downstream **entity type(s):** disease or cell process **relation type:** clinicaltrials	Identifies small molecules/drugs that have been involved in clinical trials. Drugs are included in ChemEffect Data. Clinicaltrials relations are included in DiseaseFx data. Monoclonal antibodies are represented as small molecules on the ChemEffect database.
Functional Associations between Diseases and Cell Processes			
27	What cellular processes are associated with a disease?	**initial selection:** disease **directionality:** (all) **entity type:** cellular process **relation type:** functional class	Identifies associations between cellular processes and diseases (no directionality in the relations). Functionalassociation relations are found in DiseaseFx data.

APPENDIX: LIST OF CURATED PATHWAYS IN RESNET MAMMAL+CHEMEFFCT+DISEASEFX

Cell Process Pathways

Apoptosis

- Apoptosis
- Cleavage of Lamina in Apoptosis

Cell Division

- Centriole Duplication and Separation
- Chromosome Condensation
- Kinetochore Assembly
- Nuclear Envelope
- Sister Chromatid Cohesion
- Spindle Assembly

Cellular Contacts

- Adherens Junction Assembly (Cadherins)
- Adherens Junction Assembly (Nectin)
- Desmosome Assembly
- Extracellular Matrix Turnover
- Focal Junction Assembly
- Gap Junction Assembly
- Hemidesmosome Assembly
- Tight Junction Assembly (Claudins)
- Tight Junction Assembly (JAMs)
- Tight Junction Assembly (Occludin)

Chromatin Remodeling

- CHRAC Chromatin Remodeling
- INO80 Chromatin Remodeling
- NURD Chromatin Remodeling
- NURF Chromatin Remodeling
- SRCAP Chromatin Remodeling
- SWI/SNF BRG1/BAF Chromatin Remodeling
- SWI/SNF BRG1/PBAF Chromatin Remodeling
- SWI/SNF BRM/BAF Chromatin Remodeling
- TRRAP/TIP60 Chromatin Remodeling

Complement Activation

- Alternative Complement Pathway
- Classical Complement Pathway
- Lectin-Induced Complement Pathway

Cytoskeleton Assembly

- Actin Cytoskeleton Assembly
- Actomyosin-Based Movement

- Intermediate Filament Polymerization
- Microtubule Cytoskeleton Assembly

DNA Repair

- Direct DNA Repair
- Double Strand DNA Homologous Repair
- Double Strand DNA Non-Homologous Repair
- Single-Strand Base Excision DNA Repair
- Single-Strand Mismatch DNA Repair
- Single-Strand Nucleotide Excision DNA Repair

Histone Modification

- Histone Acetylation
- Histone and DNA Methylation
- Histone Phosphorylation
- Histone Sumoylation
- Histone Ubiquitylation

Mitochondrial

- Mitochondrial DNA Replication and Transcription
- Mitochondrial Fusion and Fission
- Mitochondrial Protein Transport

Transcription

- mRNA Transcription and Processing
- rRNA Transcription and Processing
- tRNA Transcription and Processing

Vesicular Transport

- Co-Translational ER Protein Import
- Endosomal Recycling
- ER-Associated Degradation
- Exocytosis
- Golgi to Endosome Transport
- Peroxisome Protein Import and Peroxisome Division
- Secretory Pathway: Golgi Transport
- Transcytosis

Cell Cycle
Circadian Clock
Coagulation Cascade
DNA Replication
mRNA Degradation
Presentation of Endogenous Peptide Antigen
Protein Folding
Protein Nuclear Import and Export
RNA Gene Silencing
Telomere Maintenance
Translation

Ubiquitin-Dependent Protein Degradation

Cell Signaling

Actin Cytoskeleton Regulation
Adherens Junction Regulation
Adipocytokine Signaling
Apoptosis Regulation
Axon Guidance
B Cell Activation
Cell Cycle Regulation
Focal Adhesion Regulation
Gap Junction Regulation
Gonadotrope Cell Activation
Guanylate Cyclase Pathway
Hedgehog Pathway
Insulin Action
Mast Cell Activation
Melanogenesis
NK Cell Activation
Notch Pathway
Skeletal Myogenesis Control
T Cell Activation
Tight Junction Regulation
Translation Control

Disease Collections

Acute Myeloid Leukemia

Acute Myeloid Leukemia Overview
Block of Apoptosis in Acute Myeloid Leukemia
Block of Differentiation in Acute Myeloid Leukemia
FLT3 and KIT Signaling to MLL Pathway in Acute Myeloid Leukemia (M5)
Proteins Involved in Pathogenesis of Acute Myeloid Leukemia
RARA Signaling Pathway in Acute Myeloid Leukemia (M3)

Alzheimer's Disease

Alzheimer's Disease Overview
Amyloid beta and APP Intracellular Transport in Alzheimer's Disease
Amyloid beta Formation
APP and Glutamate Signaling-Related Neuronal Dysfunction in Alzheimer's Disease
APP Processing
Ca2+ Toxicity in Alzheimer's Disease
Complement Activation in Alzheimer's Disease
Mechanism of Amyloid beta Clearance
Metals and Amyloid beta Toxicity
Microglia Activation in Alzheimer's Disease
Mitochondria Enlargement and Apoptosis in Alzheimer's Disease

Mitochondrial Respiratory Chain Dysfunction in Alzheimer's Disease
Multiple Functions of Estrogen in Mitochondria in Alzheimer's Disease
Neurofibrillary Tangle Formation in Alzheimer's Disease
Overview of Mitochondrial Dysfunction in Alzheimer's Disease
Proteins Involved in Pathogenesis of Alzheimer's Disease
Traffic and Degradation of Extracellular Amyloid beta in Alzheimer's Disease
Tricarboxylic Acid Cycle Involvement in Alzheimer's Disease

Amyotrophic Lateral Sclerosis

Dysregulation of Endosomal Trafficking in Amyotrophic Lateral Sclerosis
Dysregulation of RNA and DNA Metabolism in Amyotrophic Lateral Sclerosis
Glutamate-Mediated Excitotoxicity in Amyotrophic Lateral Sclerosis
Impairment of Microglia Inhibition by Motor Neuron in Amyotrophic Lateral Sclerosis
Neuroinflammation in Amyotrophic Lateral Sclerosis
Oxidative Stress in Amyotrophic Lateral Sclerosis
Proteins Involved in Pathogenesis of Amyotrophic Lateral Sclerosis
SOD1 Mutation in Amyotrophic Lateral Sclerosis

Atherosclerosis

Activation and Proliferation of Th1 Cells in Atherosclerosis
Arterial Calcification in Atherosclerosis
Chemokines and their Receptors in Atherogenic Cell Recruitment
Proteins Involved in Pathogenesis of Atherosclerosis
RAGE/AGER and S100 Proteins in Cardiovascular Injury in Atherosclerosis
Role of Dendritic Cells in Atherosclerosis
Role of Low-density Lipoproteins and Chemokines in Atherogenesis
Role of Scavenger Receptor OLR1 in Inflammation-Related Endothelial Dysfunction in Atherosclerosis

Atopic Dermatitis

Acute Phase of Atopic Dermatitis
Atopic Dermatitis Overview
Corneodesmosomes in Atopic Dermatitis
Epidermal Barrier Dysfunction in Atopic Dermatitis
Mast Cells in Atopic Dermatitis
Onset of Atopic Dermatitis
Proteins Involved in Pathogenesis of Atopic Dermatitis

B-cell Acute Lymphoblastic Leukemia

B-cell Acute Lymphoblastic Leukemia Overview

B-cell Chronic Lymphocytic Leukemia

B-cell Chronic Lymphocytic Leukemia Overview
Proteins Involved in Pathogenesis of B-cell Chronic Lymphocytic Leukemia

Breast Cancer

Basal Breast Cancer
Breast Cancer Related to ERBB/VEGFR/Akt Signaling Pathway
Breast Cancer Related to ESR1 Signaling Pathway

Breast Cancer Related to IGF1R/Akt Signaling Pathway
Breast Cancer Related to NOTCH1 Signaling Pathway
Breast Cancer Related to WNT Signaling Pathway
ESR1/ERBB-positive Luminal Breast Cancer
Proteins Involved in Pathogenesis of Breast Cancer Related to ERBB2/VEGFR/Akt Signaling Pathway
Proteins Involved in Pathogenesis of Breast Cancer Related to ESR1 Signaling Pathway
Proteins Involved in Pathogenesis of Breast Cancer Related to IGF1R/Akt Signaling Pathway
Proteins Involved in Pathogenesis of Breast Cancer Related to NOTCH Signaling Pathway
Proteins Involved in Pathogenesis of Breast Cancer Related to WNT Signaling Pathway

Cataract

Age-Related Cataract
Ca2+ Toxicity in Lens Cells
Cancer Overview
Congenital Cataract
Diabetes-Induced Cataract
Mutations in EPHA2 Cause Cataract
Steroid-Induced Cataract

Chronic Myeloid Leukemia

Proteins Involved in Pathogenesis of Cataract
Proteins Involved in Pathogenesis of Chronic Myeloid Leukemia

Colorectal Cancer

Chronic Myeloid Leukemia Overview
Mechanism of Cetuximab Resistance in Colorectal Cancer
Metastatic Colorectal Cancer Overview

Congenital Hypothyroidism

Congenital Secondary (Central) Hypothyroidism
FOXE1 Targets Possibly Involved in Thyroid Dysgenesis
GLIS3 Targets Possibly Involved in Thyroid Dysgenesis
Iodine Metabolism Related Thyroid Dyshormonogenesis
NKX2-1 Targets Possibly Involved in Thyroid Dysgenesis
Nuclear EGFR
PAX8 Targets Possibly Involved in Thyroid Dysgenesis
Proteins Involved in Pathogenesis of Congenital Hypothyroidism
Proteins Involved in Thyroid Dysgenesis
Thyroglobulin Related Thyroid Dyshormonogenesis

Crohn's Disease

B-cell Activation in Crohn's Disease
Congenital Hypothyroidism Due to Thyroid-Stimulating Hormone Resistance
Crohn's Disease Overview
Dendritic Cell Function in Crohn's Disease
Macrophage Function in Crohn's Disease

Paneth Cell Function in Crohn's Disease
Susceptibility Genes for Crohn's Disease and Ulcerative Colitis
Th1 Cell Activation in Crohn's Disease
Th17 Cell Activation in Crohn's Disease

Cystic Fibrosis

CFTR Expression in Epithelial Cells (Class I Mutations)
CFTR Up-regulates the Oxidative Stress in Airway Epithelium in Cystic Fibrosis
CFTR-Related Ion-Channel Dysfunction in Cystic Fibrosis Airway Epithelium (Class III Mutations)
Class II Mutations Cause CFTR Misfolding and Degradation in Cystic Fibrosis
Mucin Production in Goblet Airway Epithelial Cells in Cystic Fibrosis
Proteins Involved in Pathogenesis of Cystic Fibrosis
Proteins Involved in Pathogenesis of Inflammatory Bowel Diseases
The Role of CFTR in Sperm Capacitation and Acrosome Reaction

Diffuse Large-B-cell Lymphoma

Diffuse Large-B-cell Lymphoma Overview
Diffuse Large-B-cell Lymphoma, ABC Subtype
Diffuse Large-B-cell Lymphoma, GCB Subtype
Diffuse Large-B-cell Lymphoma, PMBL Subtype
Pancreatic Beta-cell Death in Diabetes Mellitus Type 2

Endometrial Cancer

Proteins Involved in Pathogenesis of Diffuse Large-B-cell Lymphoma
Proteins Involved in Pathogenesis of Endometrial Cancer
Type I Endometrial Cancer (Endometrioid Endometrial Cancer)
Type II Endometrial Cancer (Clear-cell Endometrial Cancer and Papillary Serous Endometrial Cancer)

Epileptiform Disorders

ADK Downregulation after Acute Seizures in Epilepsy
ADK Upregulation in Chronic Epilepsy
Astrocyte Dysfunction and GABA Signaling Deficiency in Epilepsy
Effects of BDNF Upregulation Induced by Seizures
Endometrial Cancer Overview
Epilepsies Associated with Blood-Brain Barrier Disruption
Glutamate, D-serine, and ATP Release from Astrocytes
Induction of Apoptosis and Immediate Early Gene Activation in Hippocampal Neurons Following Seizures
Inherited Channelopathies Associated with Epilepsy
mTOR Hyperactivation after Status Epilepticus
Proposed Mechanisms of Antiepileptic Effects of a Ketogenic Diet
Proteins Involved in Pathogenesis of Epilepsy
Role of HMGB1 and IL1B in Neuronal Hyperexcitation in Epilepsy

Familial Hemiplegic Migraine

Activation of eNOS (NOS3) via Prostaglandin E2 and Histamine in Familial Hemiplegic Migraine

Activation of nNOS (NOS1) and iNOS (NOS2) via Glutamate in Familial Hemiplegic Migraine
Activation of Prostaglandin E2 Synthesis via Glutamate in Familial Hemiplegic Migraine
Effect of NO on Vasodilation and Triptans on Vasoconstriction in Familial Hemiplegic Migraine
Glutamate Overdose and Aura Effect in Familial Hemiplegic Migraine Type 1
Glutamate Overdose and Aura Effect in Familial Hemiplegic Migraine Type 2
Role of HMGB1 and IL1B in Neuroinflammation in Epilepsy

Follicular Lymphoma

Follicular Lymphoma Overview
Glutamate Overdose and Aura Effect in Familial Hemiplegic Migraine Type 3
Proteins Involved in Pathogenesis of Follicular Lymphoma

Glioblastoma

Classical Subtype of Glioblastoma
Mesenchymal Subtype of Glioblastoma
Neural Subtype of Glioblastoma
Primary Glioblastoma
Proneural Subtype of Glioblastoma
Proteins Involved in Pathogenesis of Glioblastoma
Secondary Glioblastoma

Glioma

Activation of Glioma Stem Cell Program
Astrocytoma
Ependymoma
Glioma Invasion Signaling
Proteins Involved in Pathogenesis of Astrocytoma
Proteins Involved in Pathogenesis of Ependymoma
Proteins Involved in Pathogenesis of Glioma
Proteins Involved in Pathogenesis of Oligodendroglioma

Gout

Impaired Osteoblast Function in Gout
Impaired Renal Uric Acid Excretion in Gout
Increased Uric Acid Synthesis in Gout
Neutrophil Recruitment in Sinovium in Gout
Osteoclast Activation in Gout
Proteins Involved in Pathogenesis of Gout
The Action of Monocytes in Gout

Hashimoto's Thyroiditis

Apoptosis in Hashimoto's Thyroiditis
Hashimoto's Thyroiditis Overview
Immune Response Activation in Hashimoto's Thyroiditis
Proteins Involved in Pathogenesis of Hashimoto's Thyroiditis
Triggers of Hashimoto's Thyroiditis

Hepatocellular Carcinoma

- Growth Factor Signaling in Hepatocellular Carcinoma
- Hepatocellular Carcinoma Overview
- NOTCH Signaling in Hepatocellular Carcinoma
- Proteins Involved in Pathogenesis of Hepatocellular Carcinoma
- TP53 Signaling in Hepatocellular Carcinoma
- Vascularization in Hepatocellular Carcinoma
- WNT/beta-Catenin Signaling in Hepatocellular Carcinoma

Hereditary Syndromes Associated with Breast and/or Ovarian Cancer

- Cowden Syndrome
- Hereditary Breast and Ovarian Cancer Syndrome
- Li-Fraumeni Syndrome

Hirschsprung Disease

- Impairment of EDN, NRG, NRTN, and GDNF/RET Signaling in Hirschsprung Disease
- Mutation in KIF1-Binding Protein (KIAA1279) Gene in Hirschsprung Disease
- Mutations in Neurogenic Transcription Factor Genes in Hirschsprung Disease
- Proteins Involved in Pathogenesis of Hirschsprung Disease
- Syndromic Forms of Hirschsprung Disease

HIV Type 1 Infection

- Block of Apoptosis in Infected Cells in HIV Type 1 Infection
- Block of CD4+ T-cell Signaling in HIV Type 1 Infection
- CCR5 Signaling in Macrophages in HIV Type 1 Infection
- CD4+ T-cell Death in HIV Type 1 Infection
- Impairment of CD8+ T-cell Action in HIV Type 1 Infection
- Macrophage Survival through CCR5 and CXCR4 Mediated Signaling in HIV Type 1 Infection
- Proteins Involved in Pathogenesis of HIV Type 1 Infection
- Reduction of Th17 cell Numbers in HIV Type 1 Infection

Hodgkin Lymphoma

- Effects of Hodgkin and Reed-Sternberg Cells on Microenvironment Cells
- Hodgkin Lymphoma Overview
- Proteins Involved in Pathogenesis of Hodgkin Lymphoma
- Reprogramming of Hodgkin and Reed-Sternberg Cells

Hyper IgM Syndrome

- Hyper IgM Syndrome Overview

Hyperthyroidism

- Cardiovascular Effects of Hyperthyroidism
- Common Genomic Effects of Thyroid Hormones
- Common Non-genomic Effects of Thyroid Hormones
- Effects of Hyperthyroidism on Bone Remodeling
- Graves Ophthalmopathy
- Immune System Activation in Graves Disease Overview
- Proteins Involved in Pathogenesis of Graves Disease

Thyroid Dysfunction in Graves Disease
Thyroid Hormones in Adipose Tissue Metabolism

Hypertrophic Cardiomyopathy

Hypertrophic Cardiomyopathy Overview
Mechanisms of Cardiomyocyte Hypertrophy in Hypertrophic Cardiomyopathy
Proteins Involved in Pathogenesis of Hypertrophic Cardiomyopathy
Sarcomere Disorganization and Intracellular Calcium Overload in Hypertrophic Cardiomyopathy

Insulin Related Pathology

Diabetes Complications

Airway Epithelial Cell Dysfunction in Cystic Fibrosis (Overview)
Proliferative Diabetic Retinopathy
Role of Advanced Glycation End Products Pathway in Diabetic Microangiopathy
Role of Hexosamine Pathway in Diabetic Microangiopathy
Role of Polyol Pathway in Diabetic Microangiopathy
Role of Protein Kinase C in Diabetic Microangiopathy

Diabetes Mellitus Type 1

CD8+ T-cell Response to Self-Determinants in Diabetes Mellitus Type 1
Pancreatic Beta-cell Destruction in Diabetes Mellitus Type 1
Peripheral Tissue Microangiopathy in Insulin Resistance
Proteins Involved in Pathogenesis of Diabetes Mellitus Type 1

Diabetes Mellitus Type 2

Impaired Peripheral Tolerance to Autoantigens in Diabetes Mellitus Type 1
Proteins Involved in Pathogenesis of Diabetes Mellitus Type 2

Insulin Receptor Signaling

Glycolysis
Insulin Influence on Glycogenesis
Insulin Influence on Lipogenesis
Insulin Influence on Protein Synthesis
Insulin Secretion

Insulin Resistance

Adipose Tissue Inflammation Provokes Insulin Resistance
Impaired Adiponectin Synthesis in Insulin Resistance
Insulin Resistance in Hepatocytes
Obesity Induced Insulin Resistance in Myocytes
Proteins Involved in Pathogenesis of Insulin Resistance
Role of Adiponectin in Insulin Resistance Prevention

Mantle Cell Lymphoma

Canonical WNT Signaling in Mantle Cell Lymphoma
Deregulation of Apoptosis in Mantle Cell Lymphoma
Deregulation of Cell Cycle and DNA Repair in Mantle Cell Lymphoma
Hedgehog Signaling in Mantle Cell Lymphoma
Mantle Cell Lymphoma Overview

Medulloblastoma Overview
Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma Overview
PI3K/AKT/MTOR, NF-kB and BCR Signaling Deregulation in Mantle Cell Lymphoma
Proteins Involved in Pathogenesis of Mantle Cell Lymphoma
Proteins Involved in Pathogenesis of Marginal Zone Lymphoma
Proteins Involved in Pathogenesis of Medulloblastoma
Splenic Marginal Zone Lymphoma Overview

Melanoma

Block of Apoptosis in Melanoma
Dedifferentiation and Metastatic Progression of Melanoma
Deregulation of Cell Cycle in Melanoma
Melanoma Overview
MicroRNAs in Melanoma
MITF as a Regulator of Melanoma Cell Development
Proteins Involved in Pathogenesis of Melanoma
WNT Signaling in Melanoma

Multiple Myeloma

IL-6/IGF-1/VEGFA in Multiple Myeloma
Multiple Myeloma Overview
Notch Pathway in Multiple Myeloma Plasma Cells
Osteoclast Activation in Multiple Myeloma
Proteins Involved in Pathogenesis of Multiple Myeloma
TNFR to NF-kB Alternative Pathway in Multiple Myeloma Plasma Cells
TNFR to NF-kB Classical Pathway in Multiple Myeloma Plasma Cells
WNT Inhibition by DKK1 in Osteoblast in Multiple Myeloma

Muscular Dystrophies

Ca2+ Overload in Duchenne Muscular Dystrophy
Contraction-Induced IL6 Up-regulation in Skeletal Muscles
Duchenne Muscular Dystrophy Overview
Dystrophin Glycoprotein Complex Signaling in Duchenne Muscular Dystrophy
IGF1 in Muscle Hypertrophy
IL6 in Insulin Resistance
IL6 Promotes Inflammation
Myostatin-IGF1 Crosstalk in Skeletal Muscles
Role of Myostatin in Skeletal Muscles

Myocardial Ischemia

Changes of Homeostasis in Myocardial Ischemia
Myocardial Infarction
Myocardial Ischemia/Reperfusion Injury
Myocardial Remodeling in Myocardial Ischemia
Preconditioning Ischemia
Proteins Involved in Pathogenesis of Myocardial Ischemia
Renin-Angiotensin-Aldosterone System in Myocardial Ischemia

Neuroblastoma

- ALK-Associated Neuroblastoma
- Growth Factor Signaling in Neuroblastoma
- Neuroblastoma Overview
- Non-Hereditary Genetic Rearrangements in Neuroblastoma
- PHOX2B-Associated Neuroblastoma
- Proteins Involved in Pathogenesis of Neuroblastoma
- Sonic Hedgehog Signaling in Neuroblastoma

Non-autoimmune Hypothyroidism

- Central Hypothyroidism Overview
- Hypothyroidism Influence on Hypothalamic Release of Thyrotropin-Releasing Hormone
- Overt Hypothyroidism Influence on Thyroid-Stimulating Hormone Secretion
- Primary Overt Hypothyroidism Overview
- Proteins Involved in Pathogenesis of Hypothyroidism
- Proteins Involved in Pathogenesis of Thyroid Hormone Resistance
- Tertiary Hypothyroidism Overview

Osteoarthritis

- Chondrocyte Apoptosis in Osteoarthritis
- IL1B-Induced Arthralgia in Osteoarthritis
- Impaired TGFB2 Signaling in Osteoarthritis
- Osteoarthritis Overview
- Proteins Involved in Pathogenesis of Osteoarthritis
- TNF and IL1B Induce Metalloproteinase Synthesis

Ovarian Cancer

- Clear Cell Ovarian Carcinoma
- Endometrioid Ovarian Carcinoma
- High-grade Serous Ovarian Carcinoma
- Low-grade Serous Ovarian Carcinoma
- Mucinous Ovarian Carcinoma
- Ovarian Cancer Overview
- Proteins Involved in Pathogenesis of Clear Cell Ovarian Carcinoma
- Proteins Involved in Pathogenesis of Endometrioid Ovarian Carcinoma
- Proteins Involved in Pathogenesis of High-grade Serous Ovarian Carcinoma
- Proteins Involved in Pathogenesis of Low-grade Serous Ovarian Carcinoma
- Proteins Involved in Pathogenesis of Mucinous Ovarian Carcinoma
- Proteins Overexpressed in Ovarian Cancer

Pancreatic Neoplasms

- Block of DNA Repair and Chromatin Remodeling in Pancreatic Cancer
- Growth Factor Signaling in Pancreatic Cancer
- Pancreatic Ductal Carcinoma
- Pancreatic Neuroendocrine Tumors
- Proteins Involved in Pathogenesis of Pancreatic Cancer
- STK11 Signaling in Pancreatic Cancer

TGFBR Signaling in Pancreatic Cancer
TP53 Signaling in Pancreatic Cancer

Parkinson's Disease

Dopamine Metabolism in Parkinson's Disease
Glutamate in Parkinson's Disease
Microglia Activation in Parkinson's Disease
Neurotoxin-Induced Parkinson's Disease
Proteins Involved in Pathogenesis of Parkinson's Disease
Young Onset PARK2, PINK1, and UCHL1 Induced Parkinson's Disease
Young Onset PARK7 and LRRK2 Induced Parkinson's Disease
Young Onset SNCA Induced Parkinson's Disease

Peutz-Jeghers Syndrome

Peutz-Jeghers Syndrome Overview
Proteins Involved in Pathogenesis of Peutz-Jeghers Syndrome

Polycystic Ovary Syndrome

Block of Ovulation in Polycystic Ovary Syndrome
FSH Action in Polycystic Ovary Syndrome
Impaired SHBG and IGFBP1 Synthesis in Polycystic Ovary Syndrome
Impaired Steroidogenesis in Polycystic Ovary Syndrome
Polycystic Ovary Syndrome Overview
Proteins Involved in Pathogenesis of Polycystic Ovary Syndrome

Prostate Cancer

Androgen Receptor and Cell Cycle
Androgen Receptor Coregulator ARA55 (TGFB1I1) in Prostate Cancer
Androgen Receptor to Akt Signaling in Prostate Cancer
Androgen Receptor to Beta-2-Microglobulin Signaling in Prostate Cancer
Androgen Receptor to c-Met Signaling in Prostate Cancer
Androgen Receptor to FKBP5 Signaling in Prostate Cancer
Androgen Receptor to GJB1 Signaling in Prostate Cancer
Androgen Receptor to NKX-3.1 Signaling in Prostate Cancer
Androgen Receptor to Prostate Specific Antigen Signaling in Prostate Cancer
Androgen Receptor to Protein Kinase C-delta Signaling in Prostate Cancer
Androgen Receptor to SGK1 Signaling in Prostate Cancer
Beta-Catenin to Androgen Receptor Signaling in Prostate Cancer
Dihydrotestosterone Biosynthesis
Fatty Acid Synthase Signaling in Prostate Cancer
FOXA2 Signaling in Prostate Cancer
FOXM1 Signaling in Prostate Cancer
Kruppel-like Factor 6 Signaling in Prostate Cancer
Prostate Cancer Overview
Proteins Involved in Pathogenesis of Prostate Cancer
RNase L Signaling in Prostate Cancer

Psoriasis

Dendritic Cells in Psoriasis
Differentiation of Psoriatic T-cells
IFN-gamma/TNF-alpha Mediated anti-Apoptotic Effect in Psoriatic Keratinocytes
Interleukin-17 Signaling in Psoriatic Keratinocytes
Interleukin-22 Induced Keratinocyte Proliferation in Psoriasis
Proteins Involved in Pathogenesis of Psoriasis

Pulmonary Hypertension

BMP2 Activates Canonical WNT Signaling in Pulmonary Artery Endothelial Cells
BMP2 Activates Non-Canonical WNT Signaling in Pulmonary Artery Endothelial Cells
BMP2 Activates WNT Signaling in Pulmonary Artery Smooth Muscle Cells
Endothelial Cell Dysfunction in Pulmonary Arterial Hypertension
Hemolysis-Associated Arterial Pulmonary Hypertension
Impairment of BMP and TGF-beta Signaling in Familial and Idiopathic Pulmonary Arterial Hypertension
Proteins Involved in Pathogenesis of Hypoxia-Induced Pulmonary Hypertension
Proteins Involved in Pathogenesis of Pulmonary Hypertension
Smooth Muscle Cell Dysfunction in Pulmonary Arterial Hypertension

Raynaud Disease

Cold Stress and Adrenoceptor Alpha 2C Signaling in Raynaud Disease
NO and ADMA Signaling in Raynaud Disease
Proteins Involved in Pathogenesis of Raynaud Disease
Regulation of Vascular Reactivity in Raynaud Disease

Rheumatoid Arthritis

Block of Synovial Fibroblast Apoptosis in Rheumatoid Arthritis
Cytokine-Dependent Synovial Fibroblast Activation in Rheumatoid Arthritis
Osteoclast Activation in Rheumatoid Arthritis
Proteins Involved in Pathogenesis of Rheumatoid Arthritis
PTPN22 Involvement in Rheumatoid Arthritis
Synovial Fibroblast Proliferation in Rheumatoid Arthritis
TLR2-Induced Synovial Fibroblast Activation in Rheumatoid Arthritis

Systemic Lupus Erythematosus

B-cell Activation in Systemic Lupus Erythematosus
Defective Clearance of Apoptotic Keratinocytes in Systemic Lupus Erythematosus
Dendritic Cell Activation in Systemic Lupus Erythematosus
Neutrophil and Macrophage Function in Systemic Lupus Erythematosus
Proteins Involved in Pathogenesis of Systemic Lupus Erythematosus
Th0 Cell Aberrant Activation in Systemic Lupus Erythematosus
Th1 Cell Function in Systemic Lupus Erythematosus
Th17 Cell Function in Systemic Lupus Erythematosus
Th2 Cell Function in Systemic Lupus Erythematosus
The Complement System Defects in Systemic Lupus Erythematosus

Systemic Scleroderma

B-cells Function in Systemic Scleroderma

- FAS Mediated Apoptosis in Systemic Scleroderma
- Mechanism of Skin Fibrosis in Systemic Scleroderma
- Model Autocrine Cytokine/Chemokine Loops in Systemic Scleroderma Fibroblasts 1
- Proteins Involved in Pathogenesis of Systemic Scleroderma
- Role of Th2 cells in Systemic Scleroderma

T-cell Acute Lymphoblastic Leukemia

- Genetic Rearrangements Involved in T-cell Acute Lymphoblastic Leukemia Development
- Proteins Involved in Pathogenesis of T-cell Acute Lymphoblastic Leukemia
- T-cell Acute Lymphoblastic Leukemia Overview

Vasospasm

- Contraction due Vasospasm
- Hemoglobin Reduction and Leukocyte Adhesion Initiate Vasospasm
- Necrosis of Neurons Caused by Energy Deficiency in Late Vasospasm
- NO Synthesis in Early Vasospasm
- Proteins Involved in Pathogenesis of Vasospasm

WHIM Syndrome

- WHIM Syndrom Overview

Expression Targets Pathways

B-cell Receptors Expression Targets

- CD19 Expression Targets
- CD21 Expression Targets
- CD81 Expression Targets
- Gamma Globulins Expression Targets

Cell Adhesion Molecules Expression Targets

- CTGF/AP-1/CREB/MYC Expression Targets
- CTGF/FOXO3A Expression Target
- CTGF/NCOR2 Expression Target
- Fibrinogen Expression Targets
- Fibronectin Expression Targets
- ICAM1 Expression Targets
- NCAM1 Expression Targets
- PECAM1 Expression Targets

Cytokines Expression Targets

Chemokines Expression Targets

- CCL11 Expression Targets
- CCL15 Expression Targets
- CCL16 Expression Targets
- CCL2 Expression Targets
- CCL3 Expression Targets
- CCL3L1 Expression Target
- CCL4 Expression Targets
- CCL5 Expression Targets
- CCL7 Expression Target

- CCL8 Expression Targets
- CXCL12 Expression Targets
- IL8 Expression Targets

Colony Stimulating Factors Expression Targets

- CSF2/NF-kB Expression Targets
- CSF2/STAT Expression Targets
- CSF3 Expression Targets

Erythropoietin Expression Targets

- Erythropoietin/AP-1/MYC/CREB Expression Targets
- Erythropoietin/ELK-SRF Expression Targets
- Erythropoietin/FOXO3A Expression Targets
- Erythropoietin/NF-kB Expression Targets
- Erythropoietin/STAT Expression Targets

Growth Hormones Expression Targets

- CSH1-GHR Expression Targets
- CSH1-PRLR Expression Targets
- FLT3LG/AP-1/CREB/CREBBP Expression Targets
- GAS6/AP-1/CREB Expression Targets
- GH1-GHR/NF-kB/ELK-SRF/MYC Expression Targets
- GH1-GHR/STAT Expression Targets
- GH1-PRLR Expression Targets
- GH2-GHR Expression Target
- PGF/AP-1/CREB/CREBBP/MYC Expression Targets

Interferons Expression Targets

- IFNA1-IFNR Expression Targets
- IFNB1-IFNR Expression Targets
- IFNG-IFNR Expression Targets
- IFNW1-IFNR Expression Target

Interleukins Expression Targets

- IL10 Expression Targets
- IL11 Expression Targets
- IL12B Expression Targets
- IL13 Expression Targets
- IL15 Expression Targets
- IL2 Expression Targets
- IL21 Expression Targets
- IL22 Expression Targets
- IL3 Expression Targets
- IL31 Expression Targets
- IL4 Expression Targets
- IL5 Expression Targets
- IL6 Expression Targets
- IL7 Expression Targets

- IL9 Expression Targets
- **Leptin Expression Targets**
  - Leptin/ELK-SRF Expression Targets
  - Leptin/STAT Expression Targets
- **Oncostatin M Expression Targets**
  - OSM-IL6ST/LIFR Expression Targets
  - OSM-OSMR Expression Targets
- **Prolactin Expression Targets**
  - PRL-GHR/NF-kB/ELK-SRF/MYC Expression Targets
  - PRL-GHR/STAT Expression Targets
  - PRL-PRLR Expression Targets
- **Thrombopoietin Expression Targets**
  - Thrombopoietin/AP-1/CREB/CREBBP/MYC Expression Targets
  - Thrombopoietin/FOXO3A Expression Target
  - Thrombopoietin/SP1 Expression Targets
  - Thrombopoietin/SPI1 Expression Targets
  - Thrombopoietin/STAT Expression Targets
- CLCF1 Expression Targets
- CNTF Expression Targets
- CTF1 Expression Targets
- LIF Expression Targets

Delta/Notch Expression Targets

- ADAM17 Expression Targets
- DLL1 Expression Targets
- DLL3 Expression Targets
- DLL4 Expression Targets
- JAG1 Expression Targets
- NOTCH Expression Targets

GPCR Ligands Expression Targets

- Signaling via Gi
  - Acetylcholine Expression Targets
  - Dopamine/Gi Expression Targets
  - Dronabinol/Anandamide Expression Targets
  - LPA Expression Targets
  - NPY Expression Targets
  - SST Expression Targets
- Signaling via Gq
  - Adenosine Expression Targets
  - AVP/Gq -> CREB/ELK-SRF/AP-1/EGR Expression Targets
  - AVP/Gq -> MEF/MYOD/NFATC/MYOG Expression Targets
  - AVP/Gq -> STAT Expression Targets
  - CCK Expression Targets
  - EDN1 Expression Targets

- EDN3 Expression Targets
- Epinephrine/Gq Expression Targets
- F2 -> AP-1/CREB/ELK-SRF/SP1 Expression Targets
- F2 -> STAT1/NF-kB Expression Targets
- GAST Expression Targets
- Glutamate/Gq Expression Targets
- GNRH1 Expression Targets
- GNRH2 Expression Targets
- IFNA1/Gq Expression Targets
- Morphine Expression Targets
- Noreadrenaline/Gq Expression Targets
- NTS Expression Targets
- OXT Expression Targets
- PAF/Gq -> AP-1/ATF1/CREB/ERK-SRF Expression Targets
- PAF/Gq -> NF-kB Expression Targets
- PLG -> AP-1/CREB/ELK-SRF/SP1 Expression Targets
- PLG -> STAT1/NF-kB Expression Targets
- POMC Expression Targets
- Prostaglandin F Expression Targets
- Serotonin/Gq Expression Targets
- Thromboxane A2 Expression Targets

Signaling via Gq/i

- CXCL1 Expression Targets
- CXCL2 Expression Targets
- CXCL3 Expression Targets
- CXCL5 Expression Targets
- CXCL6 Expression Targets
- S1P Expression Targets

Signaling via Gq/s

- ADCYAP1 Expression Targets
- AGT/CREB Expression Targets
- AGT/ELK-SRF Expression Targets
- AGT/STAT Expression Targets
- AGT/TP53 Expression Targets
- Epinephrine/Gs Expression Targets
- Noradrenaline/Gs Expression Targets
- PGE1 Expression Targets
- TAC1 Expression Targets
- VIP Expression Targets

Signaling via Gs

- AVP/Gs -> CREB/ELK-SRF/AP-1/EGR Expression Targets
- AVP/Gs -> MEF/MYOD/NFATC/MYOG Expression Targets
- AVP/Gs -> STAT Expression Targets

- Dopamine/Gs Expression Targets
- FSHR Expression Targets
- GCG Expression Targets
- Serotonin/Gs Expression Targets

Neurotrophins Expression Targets

- BDNF Expression Targets
- NGF/AP-1/TP53/MYC Expression Targets
- NGF/CREB/CEBPB/MEF2A Expression Targets
- NGF/FOXO/MYCN/ELK-SRF Expression Targets
- NGF/SMAD3/NF-kB Expression Targets
- NTF3 Expression Targets
- NTF4 Expression Targets

NK-cell Receptors Expression Targets

- CD247 Expression Targets
- FCGR3A Expression Targets

RAGE Ligands Expression Targets

- HMGB1 Expression Targets
- S100A Expression Targets
- S100B Expression Targets
- S100P Expression Target
- TTR Expression Targets

Receptor Tyrosine Kinases Expression Targets

- Growth Factors Expression Targets
  - EGFR Ligands Expression Targets
    - AREG Expression Targets
      - AREG/AP-1 Expression Targets
      - AREG/CREB/CREBBP Expression Targets
      - AREG/CTNN Expression Targets
      - AREG/FOXO3A Expression Target
      - AREG/HIF1A Expression Targets
      - AREG/NCOR2 Expression Targets
      - AREG/NFATC Expression Target
      - AREG/SMAD1 Expression Target
      - AREG/STAT Expression Targets
    - BTC Expression Targets
      - BTC/AP-1/ATF/CREB Expression Targets
      - BTC/CTNN Expression Targets
      - BTC/EP300/ETS/ETV/SP1 Expression Targets
      - BTC/NFATC Expression Targets
      - BTC/STAT Expression Targets
    - EGF Expression Targets
      - EGF/AP-1/ATF Expression Targets
      - EGF/CREB/CREBBP/ELK-SRF/MYC Expression Targets

- EGF/CTNN Expression Targets
- EGF/FOXO3A Expression Targets
- EGF/HIF1A Expression Targets
- EGF/MEF/MYOD/NFATC Expression Targets
- EGF/NCOR2 Expression Target
- EGF/STAT Expression Targets
- EGF/TP53 Expression Targets

- EREG Expression Targets
  - EREG/AP-1/ATF Expression Targets
  - EREG/CREB Expression Target
  - EREG/CTNNB/CTNND Expression Target
  - EREG/EP300/SP1 Expression Targets
  - EREG/FOXO3A Expression Target
  - EREG/HIF1A Expression Target
  - EREG/STAT Expression Targets
- HBEGF Expression Targets
  - HBEGF/AP-1/ATF Expression Targets
  - HBEGF/CREB/MYC Expression Targets
  - HBEGF/EP300/ETS/ETV/SP1 Expression Targets
  - HBEGF/FOXO3A Expression Target
  - HBEGF/HIF1A Expression Targets
  - HBEGF/MEF/MYOD Expression Target
  - HBEGF/STAT Expression Targets
  - HBEGF/TP53 Expression Targets
- TGFA Expression Targets
  - TGFA/AP-1/ATF Expression Targets
  - TGFA/CREB/CREBBP/ELK-SRF/MYC Expression Targets
  - TGFA/CTNNB/CTNND Expression Targets
  - TGFA/FOXO3A Expression Targets
  - TGFA/HIF1A Expression Targets
  - TGFA/MEF/MYOD/NFATC Expression Targets
  - TGFA/STAT Expression Targets
  - TGFA/TP53 Expression Targets

FGF Expression Targets

- FGF1 Expression Targets
  - FGF1/AP-1/CREB/ELK-SRF/MYC Expression Targets
  - FGF1/NCOR2 Expression Target
  - FGF1/RUNX Expression Targets
  - FGF1/STAT Expression Targets
- FGF10 Expression Targets
  - FGF10/AP-1/CREB/CREBBP/MYC Expression Targets
  - FGF10/FOXO3A Expression Target
  - FGF10/STAT Expression Targets

- FGF18 Expression Targets
  - FGF18/AP-1/CREB Expression Targets
  - FGF18/STAT Expression Targets
- FGF2 Expression Targets
  - FGF2/AP-1/CREB/CREBBP/ELK-SRF/MYC Expression Targets
  - FGF2/FOXO3A Expression Targets
  - FGF2/NCOR2 Expression Targets
  - FGF2/RUNX Expression Targets
  - FGF2/STAT Expression Targets
- FGF23 Expression Targets
  - FGF23/NCOR2 Expression Targets
- FGF4 Expression Targets
  - FGF4/AP-1/MYC Expression Targets
- FGF7 Expression Targets
  - FGF7/AP-1/CREB/CREBBP/MYC Expression Targets
  - FGF7/FOXO3A Expression Target
  - FGF7/RUNX Expression Targets
- FGF8 Expression Targets
  - FGF8/AP-1/CREB/MYC Expression Targets
  - FGF8/RUNX Expression Targets
  - FGF8/STAT Expression Targets
- FGF9 Expression Targets
  - FGF9/AP-1/CREB/MYC Expression Targets
  - FGF9/RUNX Expression Targets
  - FGF9/STAT Expression Targets

HGF Expression Targets

- HGF/AP-1/CREB/ELK-SRF/MYC Expression Targets
- HGF/FOXO3A Expression Targets
- HGF/STAT Expression Targets

Insulin/IGF Expression Targets

- IGF1 Expression Targets
  - IGF1/CEBPA/FOXO1A Expression Targets
  - IGF1/ELK-SRF/HIF1A/MYC/SREBF Expression Targets
  - IGF1/MEF/MYOD/MYOG Expression Targets
  - IGF1/STAT Expression Targets
- IGF2 Expression Targets
  - IGF2/CEBPA/FOXO1A Expression Targets
  - IGF2/HIF1A/MYC Expression Targets
  - IGF2/MEF/MYOD Expression Targets
  - IGF2/STAT Expression Targets
- Insulin Expression Targets
  - Insulin/CEBPA/CTNNB/FOXA/FOXO Expression Targets
  - Insulin/ELK-SRF/HIF1A/MYC/SREBF Expression Targets

- Insulin/MEF/MYOD Expression Targets
- Insulin/STAT Expression Targets

PDGFR Ligands Expression Targets

- CSF1 Expression Targets
  - CSF1/AP-1/CREB/CREBBP/MYC Expression Targets
  - CSF1/FOXO3A Expression Targets
  - CSF1/STAT Expression Targets
- KITLG Expression Targets
  - KITLG/AP-1/CREB/CREBBP/MYC Expression Targets
  - KITLG/STAT Expression Targets
- PDGFB Expression Targets
  - PDGFB/AP-1/CREB/MYC Expression Target
  - PDGFB/FOXO3A Expression Target
  - PDGFB/STAT Expression Target
- PDGFC Expression Targets
  - PDGFC/CREB Expression Target
  - PDGFC/STAT Expression Target
- PDGFD Expression Targets
  - PDGFD/AP-1 Expression Targets
  - PDGFD/STAT Expression Targets
- PDGF/AP-1/CREB/CREBBP/MYC Expression Targets
- PDGF/FOXO3A Expression Targets
- PDGF/STAT Expression Targets

VEGF Expression Targets

- FIGF Expression Targets
  - FIGF/AP-1 Expression Target
  - FIGF/NCOR2 Expression Target
- VEGFA Expression Targets
  - VEGFA/AP-1/CREBBP/MYC Expression Targets
  - VEGFA/ATF/CREB/ELK-SRF Expression Targets
  - VEGFA/CTNNB/CTNND Expression Targets
  - VEGFA/FOXO3A Expression Targets
  - VEGFA/NCOR2 Expression Target
  - VEGFA/NFATC Expression Targets
  - VEGFA/STAT Expression Targets
- VEGFC Expression Targets
  - VEGFC/ATF Expression Target
  - VEGFC/CTNNB Expression Target

EGFR Ligands Expression Targets

- Growth Factors Expression Targets
  - NRG1/AP-1/ATF Expression Targets
  - NRG1/Catenin Expression Targets
  - NRG1/CREB/CREBBP/ELK-SRF/MYC Expression Targets

NRG1/EP300/ETS/ETV/SP1 Expression Targets
NRG1/FOXO3A Expression Targets
NRG1/HIF1A Expression Target
NRG1/MEF/MYOD Expression Targets
NRG1/STAT Expression Targets
NRG1/TP53 Expression Target
ANGPT1/CREB/CREBBP Expression Targets
ANGPT1/STAT Expression Targets
ANGPT2/AP-1/CREBBP/MYC Expression Targets
ANGPT2/STAT Expression Targets
Collagen/NF-kB Expression Targets
EFNA1/STAT Expression Target
EphrinR Expression Targets
GDNF/HSF1 Expression Targets
MDK/PTN Expression Targets
PAF Expression Targets
RPTP Expression Targets
PTPRC/BCL6 Expression Targets
PTPRC/STAT6 Expression Targets
PTPRJ Expression Targets
T-cell Receptors Expression Targets
CD22/72/279 Expression Targets
CD22/NF-kB Expression Targets
CD22/STAT Expression Targets
CD72/AP-1 Expression Targets
CD72/CREB/CREBBP Expression Targets
CD72/NFATC Expression Targets
CD72/NF-kB Expression Targets
CD72/STAT Expression Target
PDCD1/AP-1 Expression Targets
PDCD1/ATF/CREB/CREBBP Expression Targets
PDCD1/NFATC Expression Targets
PDCD1/NF-kB Expression Targets
PDCD1/STAT Expression Targets
CD8 Expression Targets
CD8/AP-1 Expression Targets
CD8/ATF/CREB/CREBBP Expression Targets
CD8/NFATC Expression Targets
CD8/NF-kB Expression Targets
CD8/STAT Expression Targets
CD80 Expression Targets
CD80/AP-1 Expression Targets
CD80/ATF/CREB/CREBBP Expression Targets

- CD80/NFATC Expression Targets
- CD80/NF-kB Expression Targets
- CD80/STAT Expression Targets
- CD86 Expression Targets
  - CD86/AP-1 Expression Targets
  - CD86/ATF/CREB/CREBBP Expression Targets
  - CD86/NFATC Expression Targets
  - CD86/NF-kB Expression Targets
  - CD86/STAT Expression Targets
- IL16 Expression Targets
  - IL16/AP-1 Expression Targets
  - IL16/ATF/CREB/CREBBP Expression Target
  - IL16/NF-kB Expression Targets
  - IL16/STAT Expression Targets
- CD2 Expression Targets
- TCR/AP-1 Expression Targets
- TCR/CREB/CREBBP/ATF Expression Targets
- TCR/NFAT Expression Targets
- TCR/NF-kB Expression Targets
- TCR/STAT Expression Targets

TGFB Superfamily Expression Targets

- BMP Expression Targets
  - BMP15-BMPR2 Expression Targets
  - BMP2-BMPR2 Expression Targets
  - BMP4-BMPR2 Expression Targets
  - BMP6-ACVR2A Expression Targets
  - BMP7-ACVR2 Expression Targets
  - BMP7-BMPR2/ACVR2 Expression Targets
- INHB Expression Targets
  - INHBA-ACVR2/ACVR1 Expression Targets
  - INHBA-ACVR2/BMPR Expression Targets
  - INHBB-ACVR2 Expression Target
- Other ACVR/BMPR Ligands Expression Targets
  - AMH-AMHR2 Expression Targets
  - GDF5-BMPR2/ACVR2 Expression Targets
  - MSTN-ACVR2/ACVR1 Expression Targets
  - MSTN-ACVR2/BMPR Expression Targets
  - NODAL-ACVR2B Expression Targets
  - TDGF1-ACVR2B Expression Targets
- TGFB Expression Targets
  - TGFB1-ACVRL1 Expression Targets
  - TGFB1-TGFBR1 Expression Targets
  - TGFB1-TGFBR1/AP-1 Expression Targets

TGFB1-TGFBR2 Expression Targets
TGFB2-TGFBR1 Expression Targets
TGFB2-TGFBR2 Expression Targets
TGFB3-TGFBR1 Expression Targets
TGFB3-TGFBR2 Expression Targets

TNF Family Expression Targets

CD40LG/ATF2/AP-1/TP53/E2F Expression Targets
CD40LG/NF-kB/ELK-SRF/CREB/NFATC Expression Targets
CD40LG/STAT Expression Targets
EDA Expression Targets
FASLG Expression Targets
LTA Expression Targets
TNF/AP-1 Expression Targets
TNF/CREB Expression Targets
TNF/ELK-SRF Expression Targets
TNF/NF-kB Expression Targets
TNF/STAT Expression Targets
TNF/TP53/ATF Expression Targets
TNFSF10 Expression Targets
TNFSF13 Expression Targets
TNFSF13B Expression Targets
TNFSF14 Expression Targets

Toll-like Receptors Expression Targets

IL1A Expression Targets
IL1B Expression Targets
IL1B/NO Expression Targets
IL1B/PGE2 Expression Targets
TLR1/2/6 Expression Targets
TLR3 Expression Targets
TLR4/AP-1 Expression Targets
TLR4/AP-1/EGR1/HIF1A Expression Targets
TLR4/NF-kB/IRF Expression Targets
TLR5 Expression Targets
TLR7 Expression Targets
TLR9 Expression Targets

Urokinase Expression Targets

PLAU/ELK-SRF/AP-1 Expression Targets
PLAU/STAT1 Expression Targets

WNT Expression Targets

Canonical WNT Signaling Expression Targets
WNT1 Expression Targets
WNT2 Expression Targets
WNT3A Expression Targets

WNT4 Expression Targets
WNT5A Expression Targets
WNT7A Expression Targets
WNT7B Expression Targets
WNT9A Expression Targets
WNT9B Expression Targets

Immunological Pathways

Antigen Processing

MHC1-Mediated Antigen Presentation
MHC2-Mediated Antigen Presentation

B-cell Activation

T-cell-Dependent B-cell Activation
T-cell-Independent B-cell Activation

Natural Killer Cell Receptors Signaling

Leukocyte Adhesion to Endothelial Cell
Natural Killer Cell Activation through C-type Lectin-like Receptors
Natural Killer Cell Activation through ITAM-Containing Receptors
Natural Killer Cell Activation through ITSM-Containing Receptors
Natural Killer Cell Inhibitory Receptor Signaling

Production of Immunoglobulins

Activation of Immunoglobulin Class-Switch Recombination
Immunoglobulin Class-Switch Recombination via Alternative End-Joining
Immunoglobulin Class-Switch Recombination via Classical Non-Homologous End-Joining
Natural Killer Cell Activation through Integrins and non-ITAM-Containing Receptors
V(D)J Recombination
V(D)J Recombination Activation

Receptors of Antigen Recognition in Innate Immune System

Antiviral Signaling through Pattern Recognition Receptors
DCIR1 (CLEC4A) Signaling
Dectin-1 (CLEC7A) Signaling
Dectin-2 (CLEC6A), Mincle (CLEC4E), and BDCA2 (CLEC4C) Signaling
Mannose Receptor Signaling
NOD-like Receptors in Pathogen Recognition
TLR4 Signaling in Leukocytes
Toll-like Receptors Act through MYD88 Signaling
Toll-like Receptors Act through MYD88-TIRAP Signaling
Transcriptional Activation of Immunoglobulin Genes

Self Tolerance

CD8+ T-cell Activation
Central T-cell Tolerance
DC-SIGN (CD209) Signaling
Model of T-cell Maturation
Natural Killer Cell Activation

Peripheral T-cell Tolerance Overview
T-cell Positive Selection and Neglect-Induced Death

T-cell Activation and Differentiation

Cell Death Mediated by Cytotoxic Cells
Regulatory T-cell Differentiation
T-cell Receptor Signaling
Th1 Cell Differentiation
Th17 Cell Differentiation
Th2 Cell Differentiation

Metabolic Pathways

Alanine metabolism
Alpha oxidation of phytanic acid
Amino sugars synthesis
Arachidonic acid metabolism
Ascorbate biosyntesis
Aspartate metabolism
Bile acid metabolism (alternative pathway)
Bile acids metabolism
Biosynthesis of cholesterol
Biotin metabolism
Branched chain amino acids metabolism
Caffeine metabolism
Capecitabine and Fluorafur metabolism
Cholesterol catabolism
D-amino acid metabolism
Ethanol metabolism
Fatty acid biosynthesis
Fatty acid oxidation
Folate biosynthesis
Galactose metabolism
Ganglioside-type glycosphingolipid biosynthesis
Globoside-type glycosphingolipid biosynthesis
Glu/Gln/Pro metabolsm
Glucose metabolism
Glutathione metabolism
Glycogen metabolism
Glycosylphosphatidylinositol(GPI)-anchor biosynthesis
Glyoxylate and glycerate metabolism
Heme biosynthesis
Heme oxidation
Histidine metabolism
Inositol phosphate metabolism
Irinotecan metabolism

Ketonogenesis
Lacto- and neolacto-type glycosphingolipid biosynthesis
Lipoyl-protein complex biosynthesis I
Lipoyl-protein complex biosynthesis II
L-sugars oxidation
Lysine metabolsm
Malonate, propanoate and beta-alanine metabolism
Mannose metabolism
Metabolism of estrogens and androgens
Metabolism of glucocorticoids and mineralcorticoids
Metabolism of glycerophospholipids and ether lipids
Metabolism of triacylglycerols
Methionine metabolism
Mevalonate pathway
N-Glycan biosynthesis
Nicotinate and nicotinamide metabolism
Omega-3-fatty acid metabolism
Omega-6-fatty acid metabolism
Organophosphorus compounds degradation
Pentose-phosphate shunt
Phenylalanine and Tyrosine metabolism
Polysaccharide degradation
Pterine biosynthesis
Purine metabolism
Pyrimidine metabolism
Pyruvate metabolism
Respiratory chain and oxidative phosphorylation
Riboflavin metabolism
ROS metabolism
Selencompound biosynthesis
Ser/Gly/Thr/Cys metabolism
Serine and Glycine metabolism
Sphingolipid metabolism
Sulfur metabolism
Tricarboxylic acid cycle
Tryptophan metabolism
Ubiquinoine biosynthesis
Ubiquinoine biosynthesis in humans
Ubiquinoine biosynthesis in rats
Urea cycle and arginine metabolism
Vitamin A (retinol) metabolism and visual cycle
Vitamin B1(thiamine) metabolism
Vitamin B5 (pantothenate) metabolism and biosynthesis of CoA and holo-ACP

Vitamin B6 (pyridoxine) metabolism
Vitamin K metabolism

Nociception Pathways

Neuronal Signaling

Adrenergic receptors

ADRA1 -> ion channels
ADRA2A -> hyperpolarization
ADRA2A -> neurotransmitter release
ADRA2C/ADRB2 -> synaptic endocytosis
ADRB1 -> ion channels

ATP receptors

P2RXs -> synaptic transmission
P2RY1/2/4/6 -> potassium channels
P2RY11/13/14 -> IL8/10 production
P2RY2/12/13/14 -> N-type calcium channel

Bradykinin receptors

BDKRB1/2 -> ion channels

Cannabinoid receptors

CNR1/2 -> membrane transport

Cholecystokinin B receptor

CCKBR -> neurotransmitter uptake

Dopamine receptors

DRD1/3 -> potassium uptake
DRD2 -> TRPC1 transcription
DRD2/4 -> membrane transport
DRD3 -> dopamine uptake

Ephrin receptors

EPHB -> NMDA receptor activation

GABA receptors

GABA(A)R -> membrane hyperpolarization
GABA(B)R -> postsynaptic inhibition

Galanin receptors

GALR1/2/3 -> neurotransmitter metabolism

GFs signaling

GFs/TNF -> ion channels

Glutamate receptors

AMPA receptors -> calcium influx
GRM1/5 (postsynaptic) -> ion channels
GRM2-4/6-8 (presynaptic) -> glutamate release attenuation
NMDA receptor -> synaptic excitation
NMDA receptors -> Ca2+/CREB activation/PGE2 synthesis

Glycine receptor

GlyR -> synaptic inhibition

- **Histamine receptor**
  - HRH1/2 -> membrane polarization
  - HRH1/3 -> synaptic transmission
- **Muscarinic receptors**
  - CHRM1/2/3/5 -> ion channels
- **Neuropeptide Y receptor**
  - NPY1R -> CRH/POMC production
- **Neurotrophin receptors**
  - NTRK1/2/3 -> acetylcholine production
- **Nicotinic receptors**
  - CHRNA3-B4/A4-B2/A7 -> ion transport
  - CHRNA7 -> NOS1 production
- **Opioid receptors**
  - OPRD/OPRM -> ion channels
  - OPRK -> pain perception
  - OPRL1 -> ion channels
- **Serotonin receptors**
  - HTR1 -> membrane transport
  - HTR2 -> membrane transport
  - HTR3A -> cation transport
  - HTR4/6/7 -> cation channels
- **Substance P receptor**
  - TACR1 -> membrane transport
- **Trace amine receptor**
  - TAAR1 -> neurotransmitter uptake

Neurotransmitter Release Cycles

- Acetylcholine release cycle
- Dopamine release cycle
- Epinephrine/Norepinephrine release cycle
- GABA release cycle
- Glutamate release cycle
- Serotonin release cycle

Reference Nociception Pathways

- Regulation of calcium flux
- Regulation of potassium flux
- Regulation of sodium flux
- Summarized nociception-related expression targets
- Summarized vascular motility pathway

Tissue Signaling

- **Non-transcriptionally Regulated Processes**
  - **Adenosine receptors**
    - ADORA1/2A -> exocytosis
    - ADORA2A/B -> vasodilation

ADORA3 -> mast cell degranulation

Adrenergic receptors

ADRA1 -> prostaglandin generation

ADRA1 -> vasoconstriction

ADRA2C/ADRB2 -> vasoconstriction

ADRB1 -> prostaglandin generation

ADRB1/3 -> vasodilation

Bradykinin receptors

BDKRB1/2 -> prostaglandin generation

BDKRB1/2 -> vasodilation

Calcitonin receptor-like receptor

CGRP -> calcium influx

Cannabinoid receptors

CNR1/2 -> vascular motility

Endothelin receptors

EDNRA/B -> vascular motility

Histamine receptors

HRH1/2 -> vascular motility

Leptin signaling

Leptin -> NO production/vasodilation

Muscarinic receptors

CHRM1/2/3 -> vascular motility

Prostaglandin receptors

PTGER2/3 -> inflammation-related expression targets

PTGIR -> IL6 production

Serotonin receptors

HTR1 -> vascular motility

HTR4/6/7 -> vasodilation

Transcriptionally Regulated Processes

Adrenergic receptors

ADRA1A -> IL6 production

Bradykinin receptors

BDKRB1/2 -> interleukins production

Cannabinoid receptors

CNR1/2 -> IL1B/2/4/6/10 production

Chemokine receptor 1

Nociception-related CCR1 expression targets

Corticotropin releasing hormone receptor

CRH -> synthesis of corticosteroids

Dopamine receptors

Nociception-related DRD1/5 expression targets

Nociception-related DRD2 expression targets

Galanin receptors

GALR1/2/3 -> POMC/NPY production

Histamine receptor

HRH2/4 -> IL6/10 production

Interleukin signaling

Nociception-related IL1B expression targets

Nociception-related IL6 expression targets

Leptin signaling

Leptin -> CD25/IL6/IL10 production

Muscarinic receptors

CHRM1 -> IL2 production

Neurotensin receptor

Nociception-related NTSR1 expression targets

Nicotinic receptors

CHRNA7 -> IL8 production

Prostaglandin receptors

PTGDR -> vasodilation

PTGER1/4 -> vascular motility

PTGER2/3 -> vascular motility

PTGFR -> vasoconstriction

PTGIR -> vasodilation

Serotonin receptors

HTR1 -> IL6 production

HTR5 -> TNF production

HTR7 -> IL6 production

Substance P receptor

TACR1 -> TNF/IL6/IL8 production

Signaling Pathways

Receptor Signaling

Advanced Glycosylation End Product-specific Receptor

AGER -> CREB/SP1 signaling

AGER -> NF-kB signaling

B-cell Receptors

B-cell receptor -> AP-1 signaling

B-cell receptor -> NFATC signaling

B-cell receptor -> NF-kB signaling

CD19 -> AP-1/ELK-SRF signaling

CD19 -> NF-kB signaling

Cytokine Receptors

CNTFR -> STAT3 signaling

CSF2R -> NF-kB signaling

CSF2R -> STAT signaling

CSF3R -> STAT signaling

ErythropoietinR -> AP-1/CREB/MYC signaling

ErythropoietinR -> ELK-SRF/FOS signaling
ErythropoietinR -> FOXO3A signaling
ErythropoietinR -> NF-kB signaling
ErythropoietinR -> STAT signaling
GHR -> ELK-SRF/MYC signaling
GHR -> NF-kB signaling
GHR -> STAT signaling
IFNAR -> STAT signaling
IFNGR -> STAT signaling
LeptinR -> ELK-SRF signaling
LeptinR -> STAT signaling
LIFR -> STAT5A signaling
OncostatinR -> STAT3 signaling
ProlactinR -> STAT signaling
ThrombopoietinR -> AP-1/CREB/ELK-SRF/MYC signaling
ThrombopoietinR -> SP1 signaling
ThrombopoietinR -> SPI1 signaling
ThrombopoietinR -> STAT signaling

Frizzled Receptor family

FrizzledR -> CTNNB signaling
FrizzledR -> JUN/PAX2 signaling

G-protein-coupled Receptors

Gi-coupled Receptors

CannabinoidR -> AP-1/EGR signaling
CCR1 -> STAT signaling
CCR2/5 -> STAT signaling
CCR5 -> TP53 signaling
CholinergicRm -> CREB/ELK-SRF signaling
CXCR4 -> STAT signaling
DopamineR2 -> AP-1/CREB/ELK-SRF signaling
DopamineR2 -> NF-kB signaling
EDG2 -> ELK-SRF signaling
NeuropeptideYR -> ATF/CREB signaling
SerotoninR1 -> FOS signaling
SomatostatinR -> ATF1/TP53 signaling

G-protein-coupled Receptors

ThrombinR -> AP-1/CREB/ELK-SRF/SP1 signaling
ThrombinR -> NF-kB signaling
ThrombinR -> STAT1 signaling
ThromboxaneR -> CREB signaling

Gq/i-coupled Receptors

EDG3/5 -> AP-1/ELK-SRF signaling
EndothelinRb -> AP-1/CREB/ELK-SRF signaling

IL8R -> CREB/EGR signaling

Gq/s-coupled Receptors

AdrenergicRb -> CREB signaling
AdrenergicRb -> STAT3 signaling
AngiotensinR -> CREB/ELK-SRF/TP53 signaling
AngiotensinR -> STAT signaling
EndothelinRa -> AP-1/CREB signaling
ProstaglandinIR -> ATF1/ELK-SRF/CREB signaling
TachykininR -> ELK-SRF signaling
VIPR -> CREB/CEBP signaling

Gq-coupled Receptors

AdenosineR -> AP-1 signaling
AdenosineR -> NF-kB signaling
AdrenergicRa -> ELK-SRF signaling
AdrenergicRa -> STAT1 signaling
AdrenergicRa -> STAT3 signaling
BradykininR -> STAT3 signaling
CholecystokininR -> ELK-SRF signaling
CholecystokininR -> STAT signaling
GNRHR -> ELK-SRF signaling
GRM1/5 -> CREB signaling
NeurotensinR -> ELK-SRF/AP-1/EGR signaling
OpioidR -> CREB/ELK-SRF/STAT3 signaling
OxytocinR -> ELK-SRF/GATA/AP-1 signaling
ProstaglandinFR -> ATF1/ELK-SRF/CREB signaling
PTAFR -> AP-1/ATF1/CREB/ERK-SRF signaling
PTAFR -> NF-kB signaling
PTAFR -> STAT3 signaling
SerotoninR2 -> ELK-SRF/GATA4 signaling
SerotoninR2 -> STAT3 signaling
VasopressinR1 -> CREB/ELK-SRF/AP-1/EGR signaling
VasopressinR1 -> MEF/MYOD/NFATC/MYOG signaling
VasopressinR1 -> STAT signaling

Gs-coupled Receptors

DopamineR1 -> CREB/ELK-SRF signaling
FSHR -> CREB/ELK-SRF/GATA4 signaling
FSHR -> FOXO1A signaling
GlucagonR -> CREB/ELK-SRF/SP1 signaling
SerotoninR4/6/7 -> NR3C signaling
VasopressinR2 -> CREB/ELK-SRF/AP-1/EGR signaling
VasopressinR2 -> MEF/MYOD/NFATC/MYOG signaling
VasopressinR2 -> STAT signaling

Integrins and Cell Adhesion Receptors

FibronectinR -> AP-1/ELK-SRF/SREBF signaling
FibronectinR -> CTNNB signaling
FibronectinR -> ICAP-1A/MYC signaling
FibronectinR -> NF-kB signaling
ICAM1 -> AP-1/CREB/ELK-SRF signaling
ICAM2 -> CTNNB/FOXO/STAT3 signaling
MacrophageR -> CEBPB/NF-kB signaling
NCAM1 -> CREB/ELK-SRF/MYC signaling
PECAM -> CTNNB1 signaling
PECAM -> SP1 signaling
PECAM -> STAT signaling
SELE -> ELK-SRF signaling
Sialophorin -> CTNNB/MYC/TP53 signaling

Interleukin Receptors

IL10R -> STAT signaling
IL11R -> STAT3 signaling
IL12R -> NF-kB/NFATC signaling
IL12R -> STAT signaling
IL13R -> STAT signaling
IL13R -> STAT6 signaling
IL15R -> NF-kB/NFATC signaling
IL15R -> STAT signaling
IL21R -> STAT signaling
IL22R -> STAT3 signaling
IL2R -> ELK-SRF/MYC signaling
IL2R -> STAT signaling
IL31R -> STAT signaling
IL3R -> STAT signaling
IL4R -> ELK-SRF/HMGY signaling
IL4R -> STAT signaling
IL5R -> SOX4 signaling
IL5R -> STAT signaling
IL6R -> CEBP/ELK-SRF signaling
IL6R -> STAT signaling
IL6ST -> STAT5B signaling
IL7R -> FOXO/NF-kB signaling
IL7R -> STAT signaling
IL9R -> STAT signaling

NK-cell Receptors

FcIgER -> ELK-SRF signaling
FcIgER -> NFATC1 signaling

Notch Receptors

Notch -> EP300/ASCL signaling

Notch -> LEF1 signaling
Notch -> MEF/MYOD signaling
Notch -> NF-kB signaling
Notch -> RBPJ/HES/HEY signaling
Notch -> SMAD3 signaling
Notch -> TCF3 signaling

Protein Tyrosine Phosphatase Receptors

PTPRC -> BCL6 signaling
PTPRC -> STAT6 signaling
PTPRF -> CTNNB signaling
PTPRJ -> CTNND signaling
PTPRU -> CTNNB signaling

Receptor Tyrosine Kinases

Growth Factor Receptors

HGFR

HGFR -> AP-1/CREB/MYC signaling
HGFR -> FOXO3A signaling
HGFR -> STAT signaling

EGFR family

EGFR -> AP-1/ATF2 signaling
EGFR -> AP-1/CREB/ELK-SRF/MYC signaling
EGFR -> CTNND signaling
EGFR -> NCOR2 signaling
EGFR -> SMAD1 signaling
EGFR -> ZNF259 signaling
EGFR/ERBB -> STAT signaling
EGFR/ERBB2 -> CTNNB signaling
EGFR/ERBB2 -> HIF1A signaling
EGFR/ERBB2 -> TP53 signaling
EGFR/ERBB3 -> MEF/MYOD/NFATC/MYOG signaling
ERBB2/3 -> EP300/ETS/ETV/SP1 signaling

FGFR family

FGFR -> AP-1/CREB/CREBBP/ELK-SRF/MYC signaling
FGFR -> RUNX2 signaling
FGFR1 -> STAT signaling
FGFR3 -> STAT signaling

PDGFR family

CSF1R -> STAT signaling
KIT -> MITF signaling
KIT -> STAT signaling
PDGFR -> AP-1/MYC signaling
PDGFR -> FOXO3A signaling
PDGFR -> STAT signaling

VEGFR family

VEGFR -> AP-1/CREB/MYC signaling
VEGFR -> ATF/CREB/ELK-SRF signaling
VEGFR -> CTNNB signaling
VEGFR -> CTNND signaling
VEGFR -> FOXO3A signaling
VEGFR -> NFATC signaling
VEGFR -> STAT signaling

Insulin Receptors

IGF1R -> CEBPA/FOXO1A signaling
IGF1R -> ELK-SRF/HIF1A/MYC/SREBF signaling
IGF1R -> MEF/MYOD/MYOG signaling
IGF1R -> STAT signaling
InsulinR -> CTNNB/FOXA/FOXO signaling
InsulinR -> ELK-SRF/SREBF signaling
InsulinR -> STAT signaling

ALK -> STAT signaling
AngiopoietinR -> AP-1 signaling
AngiopoietinR -> FOXO signaling
AngiopoietinR -> STAT signaling
DDR1 -> NF-kB signaling
EphrinR -> actin signaling
EphrinR -> STAT signaling
GDNF -> HSF1 signaling
NTRK -> AP-1/CREB/ELK-SRF/MYC/SMAD3/TP53 signaling
NTRK -> FOXO/MYCN signaling

T-cell Receptors

CD2 -> NFATC1 signaling
CD2 -> STAT signaling
T-cell receptor -> AP-1 signaling
T-cell receptor -> ATF/CREB signaling
T-cell receptor -> CREBBP signaling
T-cell receptor -> NFATC signaling
T-cell receptor -> NF-kB signaling
T-cell receptor -> STAT signaling

TGFBR family

ActivinR -> SMAD2/3 signaling
ActivinR/BMPR -> SMAD1/5/9 signaling
TGFBR -> AP-1 signaling
TGFBR -> ATF/GADD/MAX/TP53 signaling
TGFBR -> CREB/ELK-SRF signaling
TGFBR -> MEF/MYOD/MYOG signaling
TGFBR -> SMAD1/5/9 signaling

TGFBR/BMPR -> SMAD2/3 signaling

TNFR family

EctodysplasinR -> AP-1 signaling
EctodysplasinR -> LEF1 signaling
EctodysplasinR -> NF-kB signaling
NGFR -> AP-1/CEBPB/CREB/ELK-SRF/TP53 signaling
NGFR -> MEF signaling
NGFR -> NF-kB signaling
TNFR -> AP-1/ATF/TP53 signaling
TNFR -> CREB/ELK-SRF signaling
TNFR -> NF-kB signaling
TNFRSF1A -> AP-1/ATF/TP53 signaling
TNFRSF1A -> CREB/ELK-SRF signaling
TNFRSF1A -> STAT signaling
TNFRSF5 -> STAT signaling
TNFRSF5/13B -> NFATC1 signaling
TNFRSF5/6 -> RB1/E2F signaling
TNFRSF6 -> DDIT3 signaling
TNFRSF6 -> FOXO3A signaling
TNFRSF6 -> HSF1 signaling

Toll-like Receptors

IL1R -> NF-kB signaling
IL1R -> STAT3 signaling
TLR -> AP-1 signaling
TLR1/2/6 -> NF-kB signaling
TLR3 -> IRF signaling
TLR3 -> NF-kB signaling
TLR4 -> IRF signaling
TLR4/5/7/9 -> NF-kB signaling

Urokinase Receptor

UrokinaseR -> ELK-SRF signaling
UrokinaseR -> STAT signaling

CD38 -> NF-kB signaling
CholinergicRn -> CREB signaling
EphrinB -> JUN signaling

Atlas of Signaling

Toxicity Pathways

Drug Toxicity Pathways

Acetaminophen-Induced Hepatotoxicity
Clozapine-Induced Granulocytopenia
Cocaine-Induced Hepatotoxicity
Cyclosporine-Induced Nephrotoxicity
Dexamethasone-Induced Diabetes

Dexamethasone-Induced Neurotoxicity
Dexamethasone-Induced Osteoporosis
Doxorubicin-Induced Cardiotoxicity
Ethanol-Induced Hepatotoxicity
Ritonavir-Induced Cardiovascular Dysfunction
Ritonavir-Induced Diabetes
Tamoxifen-Induced Endometrial Cancer
Valdecoxib-Induced Ischemic Disease

General Mechanisms of Toxicity

Cytosolic Calcium Overload
ER Stress (Unfolded Protein Response)
Glutamate-Mediated Excitotoxicity
Hypoxia-Induced Mitochondrial Damage
Protein Oxidation and Nitration Products as Disease Biomarkers
ROS and RNS in the Regulation of Vasoconstriction and Vasodilation
ROS in Angiotensin-Mediated Cardiovascular Remodeling and Hypertrophy
ROS in Neutrophil-Mediated Cell Damage
ROS in Triggering Vascular Inflammation