Release of New Mammal ChemEffect® DiseaseFx® CellEffect™ database

January 2016

Elsevier is pleased to announce the release of the updated Mammal ChemEffect DiseaseFx CellEffect database. This new baseline was built using the latest release of our natural language processing technology and includes dictionary updates such as the latest Entrez Gene and Uniprot annotations.

In addition, the Mammal ChemEffect DiseaseFx database now includes a new dataset, CellEffect, a cell-centric database designed specifically to increase and enhance support of immunology and cancer immunology research. To read more about this new dataset please see: “Release of CellEffect™ in Pathway Studio Web.”

This new expanded database includes the following:

- Additional curated pathways (total over 1800 curated pathways and groups) including:
  - 42 new Cell Process pathways
  - 49 new Signaling pathways
  - 141 new Disease pathways and 19 new Disease groups in the Disease Collections
    (See Appendix for list of new pathways)

- Expanded Pathway Studio Ontology to include many more genes, more levels and additional branches. Genes assigned to Pathway Studio ontology: 54,016, whereas genes assigned to Gene Ontology: 23,843.
Over 6.1 million unique relations representing over 38 million individual facts (extracted from over 25 million PubMed abstracts and almost 4 million full-text papers)

Expanded shapes for protein classes:

a. All non-protein coding RNAs, including nucleolar, miRNA, ribosomal, etc. will display using the same shape at previously used for miRNAs

28S ribosomal 5  small nucleolar RNA  microRNA 21

RNA28S5  SNORD31  MIR21

b. Transporters are assigned a new shape:

ABCA13  MRS2

c. Non-transcribed genes, such as pseudogenes, chromosomal aberration genes, chromosomal fragile sites, DNA segment genes have an assigned shape:

fragile site, fra(16)(q23.2)  BRCA1 pseudogene 1

FRA16D  BRCA1P1

Chromosomal aberration gene DUPC1  Inversion In(17)4t

DUPC1  m_In(17)4t
d. A new property “Class” is assigned to appropriate genes/proteins/small molecules.

Class information can be seen in the Properties view under “Other Properties.”

Search the database to find proteins associated with a specific class by using the Advanced Search.

Using the Advanced search you can now easily create a group of proteins for a specific class, (ex. a group of all known transcription factors or all protein kinases.)
Naturally occurring small molecules are also annotated with the class “Endogenous compound.” This annotation differentiates the naturally occurring small molecules from other small molecules, such as drugs, found in the ChemEffect data set.

With the greatly expanded database (new relations, new entities, and new pathways) we recommend that customers rerun their enrichment analysis (Gene Set Enrichment analysis, Fisher’s Exact text and Sub-Network Enrichment analysis) to see if additional results are obtained when using this new dataset.


In addition, Elsevier’s Customer Care is available to assist you.

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Appendix: New Pathways in January 2016 release

Cell Process Pathways (42 pathways)

Cell Cycle Regulation
1. G0/G1 Cell Cycle Phase Transition
2. G1/S Cell Cycle Phase Transition
3. G1/S DNA Damage Checkpoint
4. G2/M Cell Cycle Phase Transition
5. G2/M DNA Damage Checkpoint
6. Metaphase/Anaphase Phase Transition
7. S/G2 Cell Cycle Phase Transition

Lipogenesis and Lipolysis
1. Adipokines Production by Adipocyte
2. Gastric and Pancreatic Lipase Function
3. Regulation of Lipogenesis in Adipocytes
4. Regulation of Lipolysis in Adipocyte

Mechanisms of Sex Determination
1. Female Sex Determination
2. Male Sex Determination
3. Regulation of Testicular AMH Production by FSH and Testosterone
4. Role of Retinoic Acid Signaling in Female Sex Determination and Meiosis Regulation
5. Role of Retinoic Acid Signaling Inhibition in Male Sex Determination and Pre-puberty Block of Meiosis

Renal Physiology
1. Collecting Duct Acid-Base Homeostasis
2. Proximal Tubule Acid-Base Homeostasis

Reproductive Biology
1. Activin, Inhibin and Follistatin Pituitary Action
2. Mechanism of Luteinizing Hormone-Dependent Oocyte Meiotic Resumption
3. Procoagulant Activity of Estrogens
4. Role of GPR3 in Oocyte Meiotic Arrest

Sleep Regulation
1. Antidepressant Action of Agomelatine
2. Circadian Clock Regulation by Melatonin
3. Melatonin Synthesis in Pinealocytes
4. Regulation of Circadian Clock Genes in Suprachiasmatic Nuclei Neurons
5. Role of Adenosine in Sleep Regulation
6. Role of Endocannabinoids in Sleep Regulation
7. Role of Histamine in Arousal Regulation
8. Role of HRH3 in Negative Regulation of Histamine Production and Release
9. Role of Hypocretin (Orexin) in Arousal Regulation
10. Role of Melatonin in Cell Survival and Antioxidant Response
11. Role of Prostaglandins in Sleep Regulation
12. Role of Retinal Ganglion and Suprachiasmatic Nucleus in Melatonin Synthesis Regulation

Visual Phototransduction
1. Rod Photoreceptor Signaling Step 1 (Dark)
2. Rod Photoreceptor Signaling Step 2 (Light)
3. Rod Photoreceptor Signaling Step 3 (Light Signal Termination and Photoreceptor Recovery)
4. Visual Cycle in Retinal Cones
5. Visual Cycle in Retinal Rods

**Vitamin D Biology**
1. Activation of Transcription by Vitamin D
2. Non-genomic Rapid Actions of Vitamin D
3. Repression of Transcription by Vitamin D

**Disease Collections** (141 pathways and 19 groups)

**Age-Related Macular Degeneration**
1. Dual Role of TLR3 in Retinal Pigment Epithelial Cell
2. Endoplasmic Reticulum Stress in Age-Related Macular Degeneration
3. IL10-Mediated STAT3 Signaling in M2 Macrophage Makes an Impact on Pathological Retinal Angiogenesis
4. Major Age-Related Macular Degeneration Susceptibility Genes (group)
5. Major Drusen Components in Age-Related Macular Degeneration (group)
6. Netrin-1 Signaling in Age-Related Macular Degeneration
7. Oxidative Stress, All-Trans-Retinal and Lipofuscin Toxicity in Age-Related Macular Degeneration
8. Proteins Involved in Pathogenesis of Age-Related Macular Degeneration
9. Role of Complement Activation in Age-Related Macular Degeneration

**Antiphospholipid Syndrome**
1. Events Triggered by Antiphospholipid Antibodies in Endothelial Cell
2. Events Triggered by Antiphospholipid Antibodies in Platelets and Coagulation Cascade
3. Proteins Involved in Pathogenesis of Antiphospholipid Syndrome

**Arterial Hypertension** (update)
1. Potential Role of TRPM4/6/7/8 in Arterial Hypertension

**Asthma**
1. ADAM33 Role in Asthma
2. Genes with Mutation in Linkage Studies and Positional Cloning Associated with Asthma (group)
3. Genes with Mutations in GWA Studies Associated with Asthma (group)
4. Top Genes with Mutations Associated with Asthma (group)
5. Eosinophil Activation and Degranulation in Asthma
6. Eosinophil Survival in Asthma
7. IL17 Signaling-Related Neutrophilia in Asthma
8. IL33 Signaling-Related Eosinophilia in Asthma
9. IL17F Signaling in Bronchial Epithelial Cell in Asthma
10. Periostin (POSTN) Production by Airway Epithelium in Asthma
11. TSLP Signaling in Bronchial Epithelial Cell in Asthma
12. Airway Smooth Muscle Cell Contraction in Asthma
13. Airway Smooth Muscle Cell High Rate Proliferation in Asthma
14. IgE Induces Airway Smooth Muscle Cell Proliferation in Asthma
15. Club Cell Role in Asthma Development
16. Goblet Cell Exocytosis in Asthma
17. Goblet Cell Related Mucus Secretion in Asthma
18. Basophil Activation in Asthma
19. Mast Cell Activation in Asthma
20. Mast Cell Chemokines Signaling in Asthma
21. Neutrophil Degranulation via FPR1/IL8 in Asthma
22. Antigen-Presenting Cell Role in Asthma
23. B-cell IgE Production in Asthma
24. Th17 Cell Differentiation in Asthma
25. Th2 Cell Response in Asthma

**Cholesteatoma**
1. Cholesteatoma Overview
2. IL-6/JAK/STAT3 Signaling Pathway in Middle Ear Cholesteatoma
3. Macrophage Migration Inhibitory Factor in Human Cholesteatoma
4. Proteins Involved in Pathogenesis of Cholesteatoma
5. Role of EGF/cyclinD1 Signaling Pathway in Acquired Middle Ear Cholesteatoma
6. Role of Subepithelial Fibroblasts in Middle Ear Cholesteatoma
7. Role of the HMGB1/RAGE Signaling in Middle Ear Cholesteatoma Pathogenesis

**Dilated Cardiomyopathy**
1. Alcoholic Dilated Cardiomyopathy (Mouse Model)
2. Desmosomes in Dilated Cardiomyopathy
3. Dilated Cardiomyopathy Overview
4. Genes with Mutations Associated with Dilated Cardiomyopathy (group)
5. Proteins Involved in Pathogenesis of Dilated Cardiomyopathy
6. Role of Intracellular Calcium in Dilated Cardiomyopathy
7. The Sarcomere in Cardiomyocyte in Dilated Cardiomyopathy

**Disorders of Phenylalanine and Tyrosine Metabolism**
1. Disorders of Phenylalanine and Tyrosine Metabolism
2. Genes with Mutations Associated with Tyrosinemia (group)
3. Proteins Involved in Pathogenesis of Tyrosinemas

**Endometriosis**
1. Enhanced Angiogenesis in Endometriosis
2. Genes with Polymorphism Associated with Endometriosis (group)
3. Local Estrogen Production in Endometriosis
4. Progesterone Resistance in Endometriosis
5. Proteins Involved in Adhesion, Migration and Invasion of Endometriotic Cells
6. Proteins Involved in Pathogenesis of Endometriosis
7. Role of Coagulation Factors and PAR1/2 Receptors (F2R/F2RL1) in Endometriosis
8. Role of Dioxin in Endometriosis Development
9. Role of Leptin in Endometriosis
10. Role of Retinoic Acid in Endometriosis

**Erectile Dysfunction**
1. Penile Detumescence Augmentation Mechanisms in Erectile Dysfunction
2. Penile Erection Impairment Mechanisms in Erectile Dysfunction
3. Proteins Involved in Pathogenesis of Erectile Dysfunction
4. Role of Advanced Glycation End-Products in Diabetes- and Age-Related Erectile Dysfunction

**Familial Hemiplegic Migraine** (update)
1. Glutamate Overdose and Aura Effect in Hemiplegic Migraine Caused by Mutations in PRRT2 Gene
2. Glutamate Overdose and Aura Effect in Hemiplegic Migraine Caused by Mutations in SLC1A3 Gene
3. Glutamate Overdose and Aura Effect in Hemiplegic Migraine Caused by Mutations in SLC4A4 Gene
Female Infertility
1. Proteins Involved in Pathogenesis of Female Infertility
2. Proteins Involved in Pathogenesis of Spontaneous Abortion

Glomerulonephritis
1. Complement Role in Glomerulonephritis
2. Endothelial Cell Dysfunction in Glomerulonephritis
3. Genes with Mutation Associated with Glomerulonephritis and Nephrotic Syndrome (group)
4. Mesangial Cell Dysfunction in Glomerulonephritis
5. Plasmin Role in Glomerulonephritis
6. Podocyte Dysfunction in Glomerulonephritis
7. Proteins Involved in Pathogenesis of Glomerulonephritis

Huntington Disease
1. Axonal Transport Impairment in Huntington Disease
2. Effect of Huntington Mutation in Striatal Neuron in Huntington Disease
3. Endoplasmic Reticulum Stress in Huntington Disease
4. Excitotoxicity Damage of Striatum Medium Spiny Neurons in Huntington Disease
5. IKBKB and NF-kB Activation in Huntington Disease
6. Modification of Huntingtin Toxicity in Huntington Disease
7. PPARC1A Repression in Huntington Disease
8. Proteins Involved in Pathogenesis of Huntington Disease

Hypogonadotropic Hypogonadism
1. Genes with Mutations Associated with Hypogonadotropic Hypogonadism (Including Kallmann Syndrome) (group)
2. Hypogonadotropic Hypogonadism due to Impairment of Development and Migration of GNRH Neurons
3. Hypogonadotropic Hypogonadism due to Impairment of GNRH Release
4. Hypogonadotropic Hypogonadism due to Impairment of GNRH Signaling and Gonadotropins Production
5. Hypogonadotropic Hypogonadism due to Impairment of KISS1 Production
6. Proteins Involved in Pathogenesis of Hypogonadotropic Hypogonadism

Lesch-Nyhan Syndrome
1. Deficiency of HPRT1 Leads to Lesch-Nyhan Syndrome
2. Proteins Involved in Pathogenesis of Lesch-Nyhan Syndrome

Myocarditis
1. Genes with Mutations Associated with Myocarditis (group)
2. Lymphocyte-Mediated Myocardial Injury
3. MAVS in Antiviral Innate Immune Responses of Myocarditis
4. SOCS Proteins in Regulation of Negative Feedback in Myocarditis
5. TLRs in Antiviral Innate Immune Responses in Myocarditis

Obesity
1. Adipocyte Hypertrophy and Hyperplasia in Obesity
2. Dysregulation of Adipokines Production by Adipocyte in Obesity
3. Obesity-Related Genes with Single Nucleotide Polymorphisms (group)
4. Proteins Involved in Pathogenesis of Obesity
5. Role of Androgen Deficiency in Male Obesity
6. Role of Estrogen Deficiency in Female Obesity
7. Role of Fatty Acids in Hypertension and Atherosclerosis Development
8. Role of SOCS3 and PTPN1 in Hypothalamic Neuron Insensitivity to Insulin and Leptin
Otitis Media
1. Cytokines-Induced Development of Otitis Media
2. Induction of MUC5AC Expression via AP1-Dependent Mechanism by NTHi and S. pneumoniae in Otitis Media
3. Innate Immune Signaling in Otitis Media
4. Proteins Involved in Pathogenesis of Otitis Media

Pregnancy Related Coagulation Disorders
1. Hereditary Thrombophilia and Pregnancy Complications
2. Pregnancy Complications Associated with MTHFR Mutations, Hyperhomocysteinemia and Folate Deficiency
3. Proposed Mechanism of Trophoblast Damage in Antiphospholipid Syndrome
4. Role of Antiphospholipid Antibodies and Endothelial Cell Interaction in Pregnancy Complications
5. Role of Platelet and Coagulation Cascade Activation by Antiphospholipid Antibodies in Pregnancy Complications

Primary Ovarian Insufficiency
1. Genes with Mutations Associated with Primary Ovarian Insufficiency (group)
2. Hyperproduction of FSH due to INHA Mutation in Primary Ovarian Insufficiency
3. Impairment of BMP Signaling in Granulosa Cell in Primary Ovarian Insufficiency
4. Impairment of LH and FSH Signaling and Steroidogenesis in Primary Ovarian Insufficiency
5. Oocyte-Specific Gene Mutations in Primary Ovarian Insufficiency
6. Proteins Involved in Pathogenesis of Primary Ovarian Insufficiency
7. Role of FOXL2 Mutation in Ovarian Dysgenesis and Dysfunction Leading to Primary Ovarian Insufficiency
8. Role of FOXO3 and PTEN Inactivation in Premature Ovarian Failure (Mouse Model)
9. The Impact of INHA Mutation on Granulosa Cell Proliferation

Pyelonephritis
1. Apoptosis of Renal Tubule Epithelial Cell in Pyelonephritis
2. Endothelial Cell Dysfunction in Pyelonephritis
3. Proteins Involved in Pathogenesis of Pyelonephritis
4. Proteins With Low Expression Level in Pyelonephritis (group)
5. Role of Interstitial Fibroblasts in Pyelonephritis
6. Role of Toll-like Receptors in Pyelonephritis

Sleep Dysregulation
1. Aralkylamine-N-Acetyltransferase-Associated Sleep Dysregulation
2. Cholinesterase Inhibitors-Induced Insomnia
3. Circadian Clock Genes Polymorphisms/Mutations That Cause Insomnia
4. Main Human Susceptibility Loci for Sleep Disorders (group)
5. Proposed Mechanism of Sleep Disturbance in Alzheimer's Disease (Mouse Model)
6. Proteins Involved in Pathogenesis of Sleep Disorders
7. Proteins Involved in Pathogenesis of Sleep Initiation and Maintenance Disorders
8. Role of GABRB3 Mutation and Adenosine Deaminase Polymorphism in Insomnia
9. Role of Hypocretin Elevation and Monoamine Oxidase Decrease/Inhibition in Insomnia
10. Role of Prostaglandin D2 Synthase Downregulation in Insomnia
11. Serotonin Reuptake Inhibitors-Induced Insomnia

Testicular Male Infertility
1. Genes with Mutations and Deletions Associated with Male Infertility (group)
2. Genes with Mutations Associated with Ambiguous Genitalia Development or Sex Reversal (group)
3. Genes with Mutations Associated with Gonadal Dysgenesis (group)
4. Infertility Due to Testicular Dysgenesis
5. Male Infertility Due to Dysfunction of Leydig Cells and Impairment of Testosterone Production
6. Male Infertility Due to Dysfunction of Sertoli Cells
7. Male Infertility Due to Impairment of Sperm Motility
8. Proposed Mechanisms of Cryptorchidism
9. Proteins Involved in Pathogenesis of Azoospermia
10. Proteins Involved in Pathogenesis of Cryptorchidism
11. Proteins Involved in Pathogenesis of Male Infertility

**Thrombophilia**
1. Genes with Mutations and Polymorphisms Associated with Hereditary Thrombophilia (group)
2. Hereditary Thrombophilia
3. Hyperhomocysteinemia-Induced Thrombophilia
4. Proteins Involved in Pathogenesis of Thrombophilia

**Signaling Pathways** (49 pathways)

**Receptor Signaling**
1. AGTR1 -> ARRB1/ARRB2 Signaling
2. Beta-Arrestin-Dependent Desensitization of GPCRs
3. Beta-Arrestin-Dependent Internalization of GPCRs
4. CXCR4 -> ARRB1 Signaling
5. GLP1R -> ARRB1 Signaling
6. IFNG -> ARRB1/STAT1 Signaling
7. IGF1R -> ARRB1/ERK1/3
8. INSR -> ARRB2/ AKT/SRC
9. TGFBR3 -> ARRB2 Signaling
10. TLR -> ARRB2/NF-kB Signaling
11. ARRB2 Mediated FZD Endocytosis
12. Frizzled Receptors -> ARRB1/ARRB2 Canonical Signaling
13. Frizzled Receptors -> ARRB1/ARRB2 Non-Canonical Signaling
14. SMO -> ARRB1/ARRB2 Canonical Hedgehog Signaling
15. SMO -> ARRB1/ARRB2 Non-Canonical Hedgehog Signaling
16. Hypothalamic GUCY2C Signaling
17. Role of GUCY2C in Intestinal Ion and Fluid Homeostasis

**Signal Transduction Pathways**
1. AMPK Signaling
2. Androgen Receptor Genomic Signaling
3. Androgen Receptor Non-Genomic Signaling
4. BMP Signaling
5. EGFR Signaling
6. ERK/MAPK Canonical Signaling
7. ERK5/MAPK7 Signaling
8. Estrogens/ESR1 Genomic Canonical Signaling
9. Estrogens/ESR1 Non-Genomic Signaling
10. FOXO1 Signaling
11. Hedgehog Signaling
12. HIF1 Signaling
13. Hippo/YAP1 Signaling
14. HRAS Signaling
15. Insulin Signaling
16. JNK/MAPK Signaling
17. KRAS Signaling
18. mTOR Signaling
19. NF-kB Canonical Signaling
20. NF-kB Non-Canonical Signaling
21. Notch Signaling
22. p38 MAPK/MAPK14 Signaling
23. Ras Signaling Overview
24. Ras-GAP Regulation Signaling
25. Ras-GRF Regulation Signaling
26. TGF-beta Signaling
27. TNF-alpha/TNFRSF1A Signaling
28. TNF-alpha/TNFRSF1B Signaling
29. VEGF Signaling
30. WNT Canonical Signaling
31. WNT Planar Cell Polarity (PCP) Non-Canonical Signaling
32. WNT/Calcium Non-Canonical Signaling