



# Feature Highlight –

- Upstream Regulator
- Mechanistic Networks
- Downstream Effects Analysis

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## The Upstream Regulator Analytic in QIAGEN's Ingenuity Pathway Analysis (IPA) allows you to:

- Identify the cascade of upstream transcriptional regulators that explain the observed gene expression changes in a dataset and bring clarity to the biological activities occurring in the tissues or cells being studied.
- Further study WHAT biological processes, pathways, and diseases the transcriptional regulators and their targets may control, and HOW these upstream molecules may regulate one another's activities.
- Visualize this network of regulators and targets to explain how the regulators interact with one another and their targets to provide testable hypothesis for gene regulatory networks.

IPA will predict which transcriptional regulators are involved and whether they are likely activated or inhibited.

### Step 1

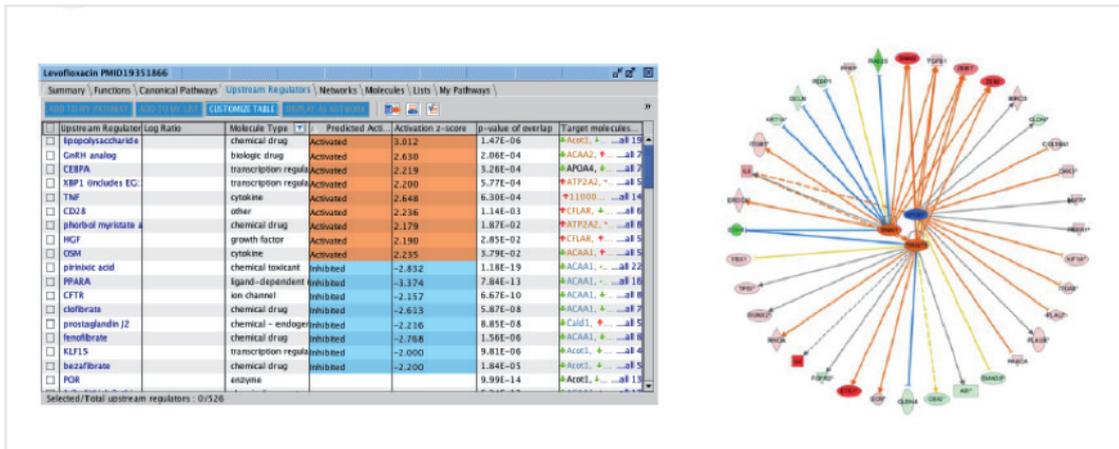
- Run an analysis on your dataset: Select File > New, and select either Core Analysis or Tox Analysis.

### Step 2

- Once the analysis is complete, double-click the analysis name to open the Summary tab (Default view).

### Step 3

- Click the 'Upstream Regulators' tab to see the upstream regulator prediction results in the table view.



From here you can display the results as a network and optionally configure the table view or export the 'Upstream Regulator' data.

## Mechanistic Networks in QIAGEN's Ingenuity Pathway Analysis (IPA) generates:

Signaling cascades that connect upstream regulators to visualize how they may work together to elicit gene expression changes observed in your experimental data.

### Step 1

- Open an analysis in IPA and click on the 'Upstream Regulators' tab.
- Look for the 'Mechanistic Network' column at the far right of the table.

### Step 2

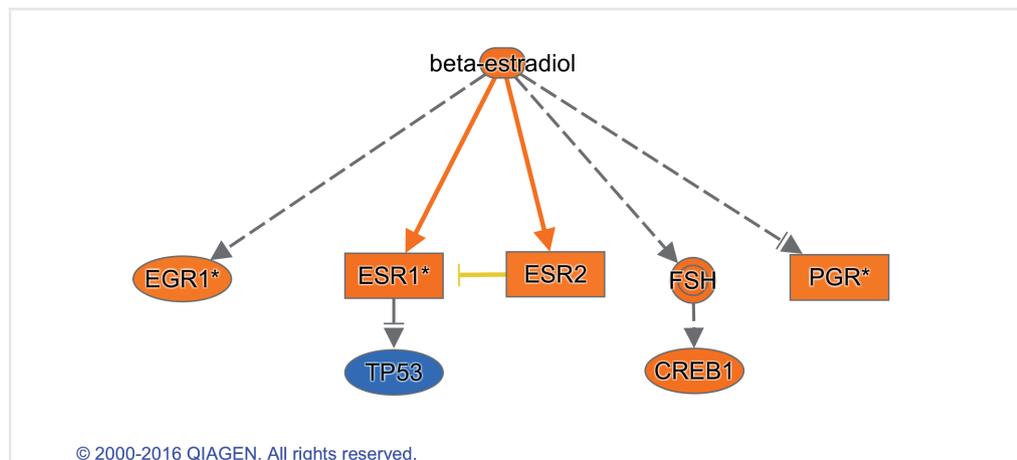
- Click on the link within the column to display the 'Mechanistic Network'. The color of the lines indicates the expected directional effect between the two molecules based on the literature. The color of the molecule reflects the z-score calculated from the analysis of the dataset, indicating predicted activation (orange) or inhibition (blue) of that molecule.

## Step 3

- Click on the 'Mechanistic Networks' button to change the algorithm's parameters to increase or decrease the stringency of the criteria used to create the network.
- The 'Mechanistic Network' column in the 'Upstream Regulator Analysis' table will contain the links to the re-calculated networks.

Upstream Reg...	Exp Fold C...	Molecule T...	Predicted Activ...	Activation z-sc...	p-value of ...	Target mol...	Mechanisti...
beta-estradiol		chemical - endogen...	Activated	6.921	9.78E-34	↓ABCA1, ↓...all 196	380 (9)
ESR1	↓-1.708	ligand-dependent n...	Activated	2.966	2.61E-23	↓ABCC5, ↑...all 141	384 (11)
trans-hydroxytamoxif		chemical drug	Activated	2.000	1.22E-20	↓ABCC5, ↑...all 36	247 (4)
TCFB1		growth factor		-0.233	4.43E-20	↓ABCA1, ↑...all 157	
raloxifene		chemical drug		-0.141	2.11E-16	↑AREG, ↑A...all 38	
ESR2		ligand-dependent n...		1.781	1.12E-13	↓ABCA1, ↑...all 57	364 (10)
tretinoin		chemical - endogen...	Inhibited	-3.756	1.34E-13	↓ABCA1, ↑...all 126	268 (9)
progesterone		chemical - endogen...		0.768	1.48E-13	↓ACPP, ↓ADM...all 69	
PGR	↑5.528	ligand-dependent n...		1.811	3.10E-13	↑AREG, ↓B...all 43	105 (3)
RAF1		kinase		0.000	1.28E-12	↑ANKRD2, ↑...all 37	
IL2		cytokine		1.057	1.79E-12	↑BCL2, ↓B...all 61	
trichostatin A		chemical drug		0.219	2.06E-12	↓ABCA1, ↑...all 66	
TP53		transcription regulator	Inhibited	-2.235	2.35E-12	↓ACSL3, ↑...all 121	244 (8)
dexamethasone		chemical drug		-1.256	2.82E-12	↑ABHD2, ↑...all 133	
ZNF217	↓-1.315	transcription regulator		1.554	4.14E-12	↓ADM, ↓ANK3...all 21	
IFNG		cytokine		-1.213	5.05E-12	↓ABCA1, ↑...all 112	

Selected/Total molecules: 1 / 1458



The Downstream Effect Analysis in IPA allows you to:

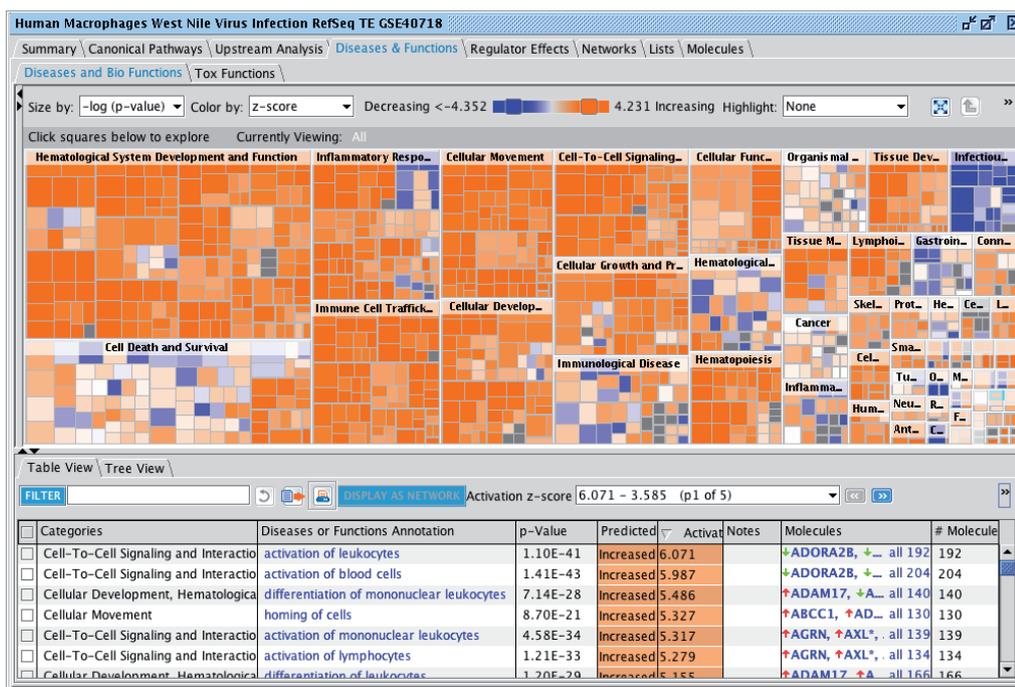
- Predict and visualize biological trends and activities occurring in the tissues or cells being studied.
- Compute the likely effect on diseases and cell biological processes such as cancer, apoptosis, and cell migration using the direction of change of the genes.

## Step 1

- Click the 'Diseases & Functions' tab to see the Downstream Effects Analysis results in the hierarchical heat map and table view.

## Step 2

- Examine the heat map. The large labeled boxes are major biological functional categories. The smaller colored squares within are predicted impacts on specific diseases & functions, where orange is a predicted increase and blue a predicted decrease. For example many immune cell trafficking functions are predicted to be increasing in the pictured dataset.



Learn about how IPA can help you understand your data at:

[www.qiagenbioinformatics.com](http://www.qiagenbioinformatics.com)

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