

What is the new Consensome (beta) feature in Transcriptomine & how do I use it?

The previous "Any" option in Gene(s) of Interest was intended for users not familiar with a particular NR pathway to find out what genes it regulated. This was of limited value, however, since for the more frequently studied pathways it often resulted in a page saying that there were too many search results.

Our new feature, "Consensome" replaces the "Any" option with a more meaningful & user-friendly way of answering the questions: what genes are most frequently regulated by my pathway of interest in a given organ? What are the genes most frequently regulated across all NR pathways in my organ of interest? To do this. we surveyed across all experiments in a particular pathway category (e.g. ERs & estrogens) and biosample category (e.g. Female Reproductive, Mammary Gland) and ranked genes according to the frequency of their significant differential expression in these experiments and assigned them a Consensome Score, which is the negative log of the probability that the Discovery Rate (the frequency of significant differential expression in all the experiments in which that gene was assayed) is due to random chance.

To view a Consensome, at a minimum, you must make a selection from either the Pathway drop down or the Physiological System drop down. The Submit button will not be available if you select a pathway/biosample category combination that does not contain the minimum number of experiments (4) required for calculation of a Consensome. Say you're interested in the genes most frequently regulated by the ER & estrogens pathway in the human mammary gland. Here's how to do that in Transcriptomine using the Consensome feature. Numbers in parentheses refer to the figure on the next page.

Step A. To guide the user in a logical sequence through the query form, we re-arranged the key elements in the query form - Gene(s) of Interest, Pathway, Biosample Category, Species and Significance - in a single vertical column (1). When the form first loads, only the first of these is available, depending upon what selection you

make from "Genes of Interest" the other menus become ungrayed (i.e. available) in different ways.

Step B. Select "Consensome (beta)" from **Gene(s) of Interest** (2).

Step C. Select "ERs & Estrogens" from **Pathway** (3), "Female Reproductive" from **Physiological System** (4) and "Mammary Gland" from **Organ** (5). Leave **Species** at its default "Human" option, and click **Submit**.

Step D. You will see a list of genes ranked by descending Consensome Score (7). For reference, the C-Score for SIAH2 (~298) corresponds to a Consensome p-value of about 1 E-125. The list can be filtered by typing in the Search box (8). The top 1000 genes in a Consensome are shown by default; the full list can be downloaded by clicking on the Download Results button (9). The more experiments that contribute to a Consensome, the higher the overall scores in a Consensome will be - look at the top of the list for a summary (10) of the number of data points, experiments and datasets on which a Consensome is based. To look at the data points underlying a Consensome ranking for a gene of interest, click on the Query link.

Step E. You will be taken to a **Regulation Report** for that gene that shows all the data point that contributed to the Consensome. Because Consensomes are calculated across all significant (p < 0.05) data points in all relevant experiments, irrespective of fold change value, we've removed the lower fold change cut-off in the slider bar to display all the data points. For ease of visualization, any < 2-fold change values are in gray (12).

Although we've shown an example of a specific pathway below, any combination of pathway and biosample category (except All & All) is valid. For example, to view the highest regulated human hepatic genes over all NR pathways, leave NR Pathways = All and select Physiological System = Metabolic & Organ = Liver and leave Human = All.

