

## TGx Benchmark Dose Response Guided Search Help

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### Function

The TGx Benchmark Dose Response Guided Search allows users to browse toxicogenomics studies to see the benchmark dose (BMD) values, Gene Ontology (GO) biological processes and accumulation plots for different DTT test articles. Where multiple organs are assayed per test article, data are displayed on separate pages.

### Search

From the CEBS Homepage (<https://cebs.niehs.nih.gov/cebs>), select the 'TGx Benchmark Dose Response' link under Guided Searches to open the '5-day TGx Models' home page. From this page, the options to Select Test Article and Show Results are available. From the home page:

- 1) Select a test article of interest
  - a. Test articles are displayed as a drop-down list
  - b. Organ of study shown in parentheses after test article name
- 2) Click the green 'Show Results' button

### Results

The Results page is comprised of 3 elements.

- Two accumulation plots
  - Most affected genes
  - Most affected GO biological processes

**Note: The most affected genes plot can be displayed using median BMD, maximum fold change or maximum fold change (absolute) values on the abscissa. To switch between these options, click the green buttons at the top of the page**

- Two tables of BMD values
  - Best BMD model
  - Best BMD
  - Best BMDL
  - BMD Mean
  - BMD Median

- Maximum Fold Change
- Links to
  - DTT report for the selected test article
  - Download coordinate data for median BMD plots
  - Download Input Data tables

## Most Affected Genes

The Most Affected Genes results shows the genes most changed by the selected exposure. Results are displayed as:

- Interactive accumulation plot
- Data table

### *Interactive Accumulation Plot*

After selecting a test article of interest, the plot defaults to showing the most affected genes ranked by median BMD values. Three options are available:

- BMD Median
- Maximum Fold Change
  - Plots the most affected genes based on the maximum fold change values

**Note: A negative fold change values shows decreased expression and positive fold change values show increased expression**
- Maximum Fold Change (Absolute)
  - Plots the most affected genes based on the absolute value of the maximum fold change

Above the Accumulation Plot the page reports a Point of Departure (POD).

The Accumulation Plot has several interactive features:

- Click the plot and use the mouse wheel to zoom in and out
- Hover over a single data point to display a pop-up window containing the BMD Median (or Maximum Fold Change or Absolute Value of the Maximum Fold Change depending on what value was selected to use on the abscissa), rank of the Gene(s), the Affymetrix probe number(s), and the gene symbols(s). Spike Lines connecting to the cartesian axes can also be displayed depending on settings (see below)

A series of buttons on the top right corner of the plot allows to save the graph and control its interactive features settings. Hover over each button to display a message explaining the function of the button. Click on the button to activate the function:

- Download
  - Download plot as a high-quality image file (.png)
- Zoom
  - Click and drag on the plot area to activate the zoom function
- Pan
  - Click and drag on the plot area to activate the pan function

- Box Select
  - Click and drag on the plot area to select a rectangular shaped area
- Lasso Select
  - Click and drag on the plot area to activate the hand-drawn section function

**Note: The Zoom, Pan, Box Select and Lasso Select functions are mutually exclusive, only one of them can be active at a time**

- Zoom in
  - Zooms into the current center of the plot
- Zoom out
  - Zooms out of the current center of the plot
- Autoscale
  - Resets the zoom of the plot to include all the available data
- Toggle Spike Lines
  - Display lines connecting to the axes by hovering over one of the data points
  - Click once to turn on, click again to turn off

### Data Table

The data table contains more detailed information on the most affected genes.

- The table contains 5 fields:
  - *Genes Symbol*: the official name of the gene
  - *Best Model*: the dose-response model function that best fit the data distribution. Best fitting is defined as lowest Akaike Information Criteria (AIC)
  - *Best BMD*: the BMD calculated for the curve generated by the best fitting model
  - *Best BMDL*: the Lowest Confidence Limit of the BMD confidence interval (or BMDL) for the best fitting model
  - *Max Fold Change*: The largest gene expression fold change between the changes at different doses
- The table can be sorted by any of the 5 columns by clicking on the column header
- The table defaults to displaying 10 entries; to change the display number use the drop-down menu on the top left corner on the table to 25, 50, 100, or 500 entries
- Use the page numbers in the bottom right corner to scroll through the table pages

### Most Affected Biological Processes

The Most Affected Biological Process section biological processes most changed by the selected exposure. Results are displayed as:

- Interactive accumulation plot
- Data table

The Biological Processes analyzed are defined in the biological processes branch of Gene Ontology (GO).

### *Interactive Accumulation Plot*

The Biological Processes are plotted by Median Benchmark Dose. All graph functions and features are described in the Most Affected Genes section above.

### *Data Table*

The data table has the same format as the Most Affected Genes data table. Some columns differ from the previous section:

- The table contains 5 fields:
  - *GO Gene Set ID*: the official Gene Ontology ID of the Biological Process
  - *GO Level*: the number of separation levels between the specific Biological Process and the beginning of the ontology tree
  - *GO Gene Set Name*: the name of the Biological Process
  - *BMD Mean*: the mean BMD for the genes in this Process
  - *BMD Median*: the median BMD for the genes in this Process
  - *Max Fold Change*: The largest gene expression fold change between the genes in the Process

### *Download Data*

The last section of the page contains links to useful pages with more information on the studies (DTT Report Pages) and links to downloadable data.

- Useful Links
  - DTT Report Page (optional): the link redirects the user to the DTT Page containing ulterior information and data from the study

**Note: If no report page is available for the selected study, there will not be a link present in this section**
- Accumulation Plot Coordinate Files
  - BMDMedian Coordinates: the coordinate file used to generate the Accumulation Plot with the Most Affected Genes ordered by BMD Median
  - Maxfold Coordinates: the coordinate file used to generate the Accumulation Plot with the Most Affected Genes ordered by Maximum Fold Change
  - Maxfold Absolute Coordinates: the coordinate file used to generate the Accumulation Plot with the Most Affected Genes ordered by Absolute Value of the Maximum Fold Change
  - GO Pathway Coordinates: the coordinate file used to generate the Accumulation Plot with the Most Affected Biological Processes ordered by BMD Median
- Data Downloads
  - Input Data: A zipped folder containing two files:
    - BMDExpress Individual Probe Set BMD Results.txt: contains full BMDExpress results for the individual probe sets
    - BMDExpress GO Biological Process BMD Results.txt: contains full BMDExpress results for the Biological Process

**Note:** All Input Data files for the 'TGx Benchmark Dose Guided Search' are the output of BMDEExpress software. For a detailed description of the data files refer to the BMDEExpress user manual (<https://github.com/auerbachs/BMDEExpress-2/wiki>).