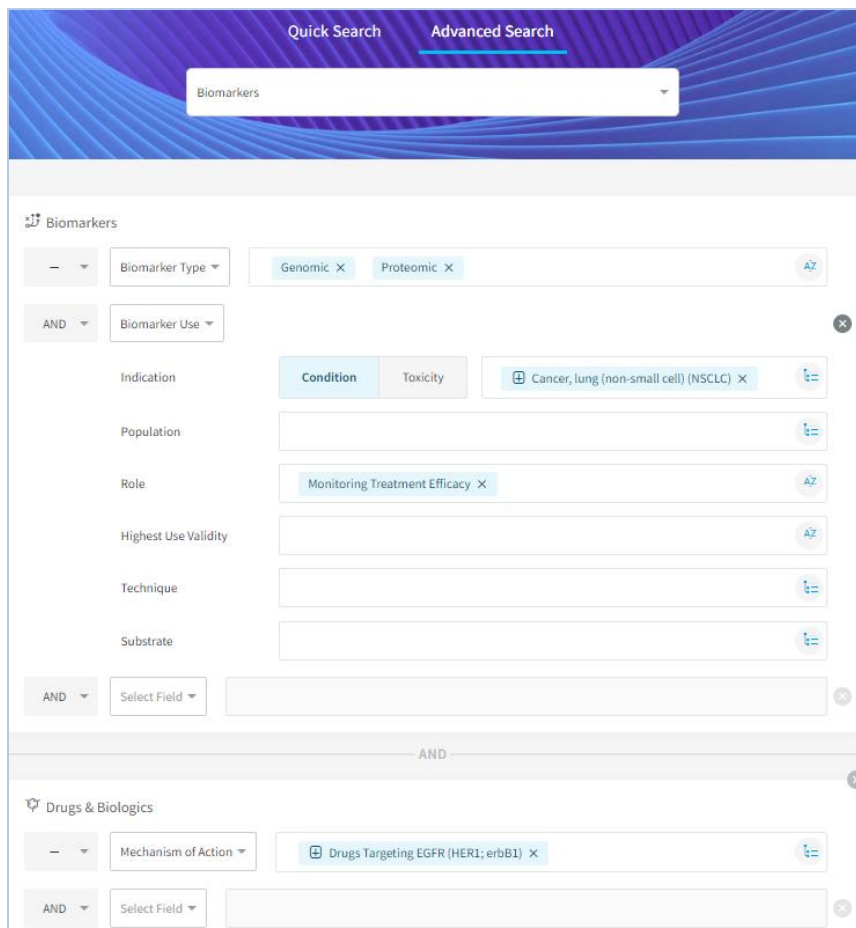![Clarivate™]

Selecting biomarkers by mechanistic rationale

Cortellis Drug Discovery Intelligence & MetaCore

If you have a long list of biomarkers from the **Cortellis Drug Discovery Intelligence Biomarkers Module**, you can reduce the list using **MetaCore's** enrichment analysis (separate subscription required) to identify those biomarkers that are related to a common signaling pathway or process.

Use Advanced Search in Cortellis Drug Discovery Intelligence to find your biomarkers of interest

In this example, we are searching for genomic/proteomic biomarkers to monitor the efficacy of drugs that target Epidermal Growth Factor Receptors in the context of non-small cell lung cancer:

Despite applying multiple search parameters, we still have a long list of potential biomarkers, almost 1,800 in this example.

Showing **1-50** of **1769** **Biomarkers** records for **Biomarker Type:** Genomic *OR* Proteomic AND (**Biomarker Use Condition:** Cancer, lung (non-small cell) (NSCLC) AND **Biomarker Use Role:** Monitoring Treatment Efficacy) AND **Mechanism of Action:** Drugs Targeting EGFR (HER1; erbB1)
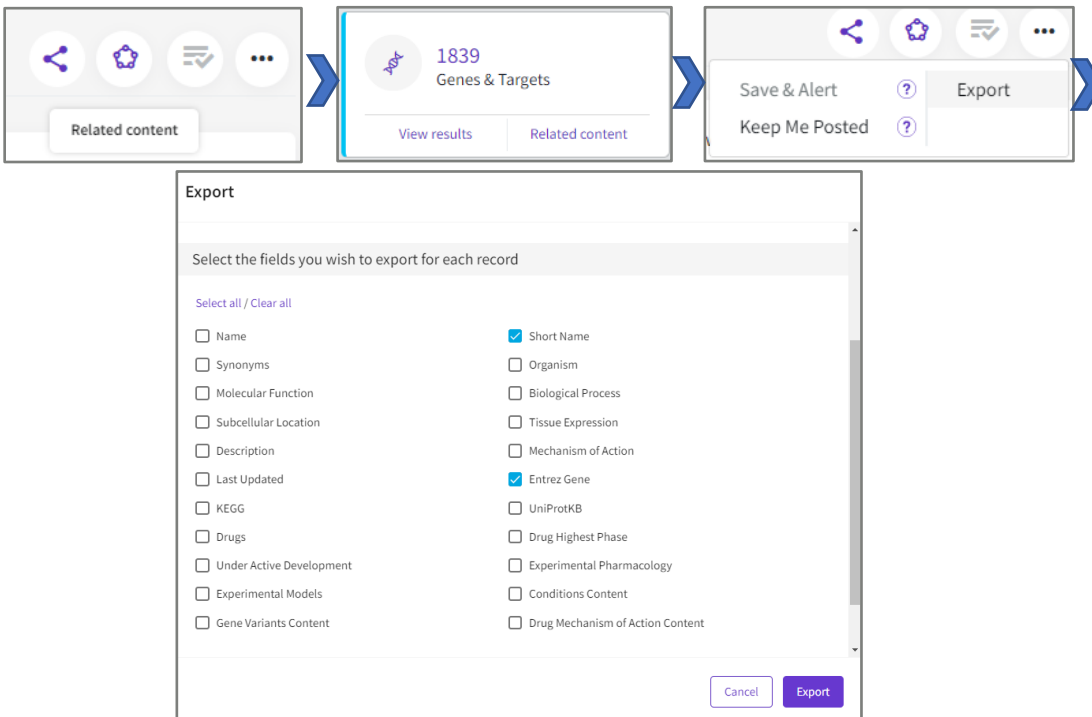
Export the list to MetaCore for analysis

1. From the Biomarker results page, click the *Related content* button > select Genes & Targets > Options, Export > Then select the Short name and Entrez gene ID to export to excel

2. Re-format the list ready for uploading to MetaCore

   a. Open the downloaded Excel > Enable editing > Delete the sheet "Export Information"
   b. File > Save as > Save as Type = Text (Tab delimited)

3. From the **MetaCore** home page > Upload > Upload Experiments with Gene or Protein IDs and follow the workflow steps > Once the upload is complete, click the Experiment name to activate your list

Use MetaCore's enrichment analysis to identify processes and pathways that are over-represented in your biomarker list

MetaCore's home page > Workflows & Reports > Biomarker Assessment > Follow the guided setup. In this example, because I am interested in biomarkers of EGFR inhibition, I will select target = EGFR (optional step); and disease group = Cancer. The final step is to allow you to select thresholds and P-values, but this does not apply as we just have a gene list without any experimental data > Apply. The calculation can take some time.

- When the cancer disease name is green, this indicates that EGFR (the target we selected in the biomarker
- assessment setup) is one of the biomarkers for this disease.
- Ratio: the red number is the total number of biomarkers in MetaCore associated with that disease, and the green number is the number of biomarkers in our list for that disease
- The top 10 results are displayed. Pick from the drop-down menu to see more
- Note, although we selected this list for NSCLC, there is a very strong enrichment for other cancers, implying common mechanisms for all these cancers

Pathway Maps and Process Networks are a good mechanism to filter your biomarker list based on co-occurrence in the same causal pathway.
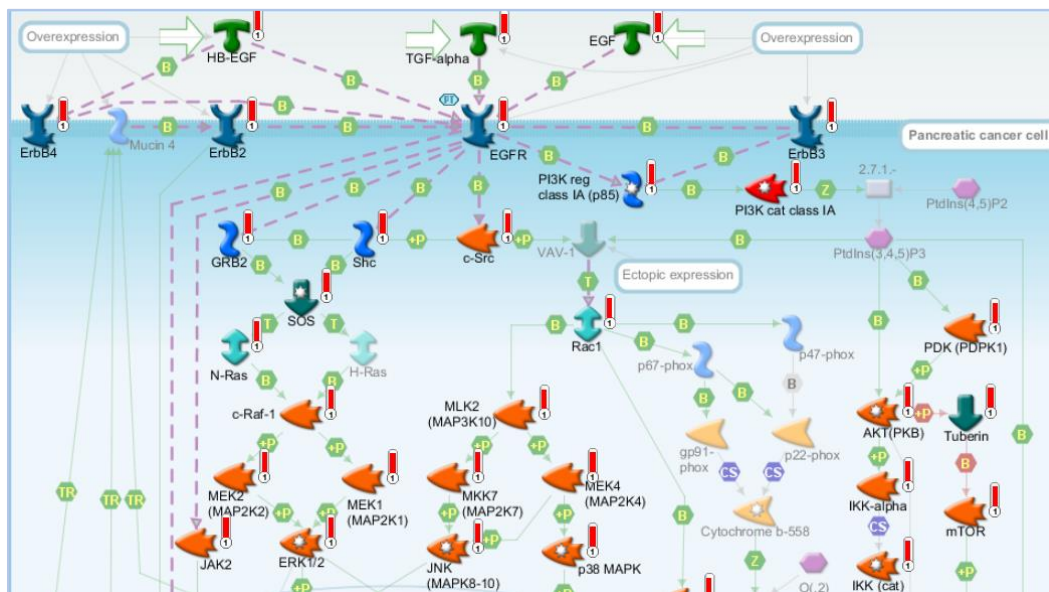

- Click on the map title to view the map and see how biomarkers from your list are related in a mechanistic pathway

Clarivate™

- Click the green number under *Ratio* to export the shortlist of biomarkers, or to save it for further analysis.

Using this approach, we have quickly reduced a list of almost 1800 biomarkers to around 50 or 60 mechanistically related pharmacodynamic markers of response to EGFR inhibitors.

For more information contact Customer Service at **LS Product Support.**