

TargetMine Exercise and Tutorial

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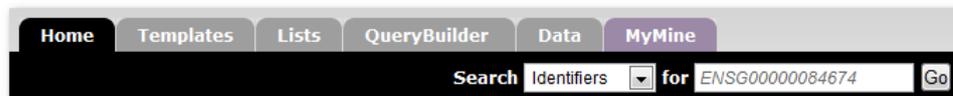
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Go to the TargetMine web site: targetmine.nibio.go.jp

All features are accessible from the toolbar on every TargetMine page:



I. Quick Search and report pages

A quick search box appears in the menu bar of all pages. Entering any object identifier (such as a gene name or identifier) in the quick search box will direct the user straight to the **report page** for that object. For example

Run a quick search for an ensembl id 'ENSG00000084674':



The report page for a particular object in the TargetMine database provides all the information that TargetMine has for that object. All report pages have the same basic structure

- The upper half summarises the information associated with each object

Summary for selected Gene

ncbiGeneNumber ? 338
 primaryIdentifier ? ENSG00000084674
 secondaryIdentifier ? HGNC:603
 symbol APOB
 name ? apolipoprotein B (including Ag(x) antigen)
 chromosomeLocation [unknown]
 organism.shortName H. sapiens
 description apo B-100|apoB-100|apoB-48|apolipoprotein B-100|apolipoprotein B48

Further information for this Gene

ensembl: ENSG00000084674
 Entrez Gene Entrez Gene: 338
 1 Organism [details...]
 3 Protein
 451 Publication
 7 Synonym

- The lower half 'Further information by category' provides more detailed information corresponding to data categories in TargetMine (which can be seen on the home page). This information is derived from a set of predefined queries known as templates (see below) related to specific data categories which are pre-run on the object of query.

transcripts 2 Transcript im:aspect:Genomics[x] Add tags

Class	Identifier	exonCount	length	chromosomeLocation
Transcript	ENST00000233242			[unknown]
Transcript	ENST00000399256			[unknown]

UTRs 0 UTR im:aspect:Genomics[x] Add tags

Gene --> GO terms and parents of those terms. 1092 results
 Gene --> GO terms. 28 results
 Gene --> Proteins. 3 results
 Show the proteins for a particular gene.

Gene > primaryIdentifier ?	Gene > symbol	Protein > primaryAccession	Protein > name
ENSG00000084674	APOB	P04114	Apolipoprotein B-100
ENSG00000084674	APOB	Q59HB3	Apolipoprotein B variant
ENSG00000084674	APOB	Q7Z7Q0	APOB protein

Showing all 3 rows.
 Gene --> Enzyme. no results
 Gene --> Pathway. no results

II. Lists and List Analysis pages

The 'list' function in TargetMine enables queries on user-supplied list(s) of objects (e.g., a list of genes/proteins). The user may either save lists from results pages or create them by uploading lists of identifiers. Lists can be used to **constrain queries** either a template query or in the query builder (see below), to perform **logical operations** (union, intersect, subtract) and exported. The users may also **search** and **copy** the lists.

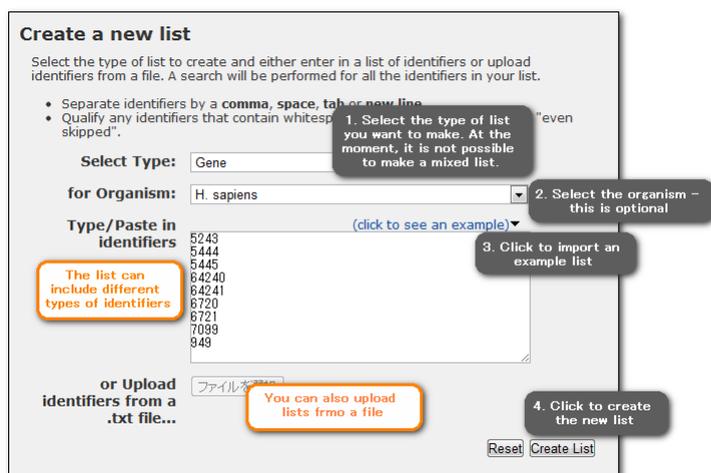
The Lists page is accessible via the 'Lists' tab on the TargetMine menu bar. The 'Upload' tab in the Lists page permits the user to create a list of objects either by 'Type/Paste in identifiers' or upload a file containing a list of objects.



A list can be created of only one 'type' of objects (e.g., genes, protein), which can be set from the drop-down list. However, it is possible for the list to contain a mix of identifier types (e.g., gene symbols and gene IDs). Optionally, the user may also set the organism for the list of identifiers.

This tutorial will deal with uploading an example list of genes. The list will then be used to view the 'List Analysis page', run a template query, save a further list from the results and employ the lists for a customised query using the query builder.

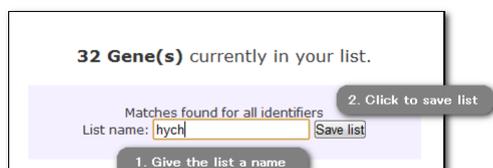
- Find the sample gene list at <http://targetmine.nibio.go.jp/workshop/hych>
- Select and copy the gene list and paste in "Type/Paste in identifiers" box. Then click on the "Create List" tab.



• List Confirmation Page

Before a list is created it is checked against the TargetMine database and any discrepancies are reported in the 'list confirmation page'. The user must

assign a name to the list. For example, the uploaded list contains 32 genes and for the purpose of this tutorial is saved as 'hych'.



• List Analysis Page

Details of the contents of the lists together with additional information about a list can be viewed through the 'List Analysis' page. The analysis page is automatically displayed when a list is created. It can also be accessed at other times by clicking on the list name on the 'list page'.

List Analysis page consists of three sections

- A **summary** of the contents of the list includes a table with the first 10 objects of the list, a list description, List Info, Convert tools and Link outs (if available). Above the table, there are Display/Export/Use options and a find box. Searching a list is case sensitive and wild cards cannot be used.
- A series of '**widgets**' providing more information on the list, for example, overrepresented KEGG pathway, Gene Ontology (GO), Drug and Disease Ontology associations, Protein-protein interactions (PPIs) and Associated Drugs.

Disease Ontology Enrichment

Disease ontology enriched for genes in this list. For more information about the math used in these calculations, see [here](#).
Number of Genes in this list not analysed in this widget: 11

Options
Multiple Hypothesis Test Correction: **Benjamini and Hochberg**
Maximum value to display: **0.01**

[View in results table](#) [Download](#)

DO Term	p-Value	
<input type="checkbox"/> hyperlipidemia [DOID:1168] ⓘ	4.6908E-24	16
<input type="checkbox"/> lipid disorder [DOID:9455] ⓘ	1.4971E-20	16
<input type="checkbox"/> hypercholesterolemia [DOID:2487] ⓘ	9.1811E-19	12
<input type="checkbox"/> coronary arteriosclerosis [DOID:3363] ⓘ	1.2849E-16	15
<input type="checkbox"/> coronary heart disease [DOID:3393] ⓘ	2.6044E-16	15
<input type="checkbox"/> extrinsic cardiomyopathy [DOID:3978] ⓘ	3.3505E-16	15
<input type="checkbox"/> myocardial ischemia [DOID:3394] ⓘ	3.5496E-16	15
<input type="checkbox"/> inborn errors lipid metabolism [DOID:3146] ⓘ	4.8004E-16	10
<input type="checkbox"/> familial combined hyperlipidemia [DOID:1168] ⓘ	6.6493E-16	9

Associated Drugs

Drugs which associated with genes in the list.
Number of Genes in this list not analysed in this widget: 21

[View in results table](#) [Download](#)

Drug.drugBankId	Targeted Genes
<input type="checkbox"/> DB00171	2
<input type="checkbox"/> DB00802	2
<input type="checkbox"/> DB01076	2
<input type="checkbox"/> DB03014	2
<input type="checkbox"/> DB00062	1
<input type="checkbox"/> DB00064	1
<input type="checkbox"/> DB00091	1
<input type="checkbox"/> DB00144	1
<input type="checkbox"/> DB00243	1
<input type="checkbox"/> DB00570	1
<input type="checkbox"/> DB00619	1
<input type="checkbox"/> DB00622	1
<input type="checkbox"/> DB00636	1
<input type="checkbox"/> DB00637	1

- A set of **template queries** that have been pre-run on the set of objects in the list.



III. Template queries

To enable the users to quickly and easily carry out diverse queries across data sources, TargetMine includes a library of **predefined Template queries**. These consist of a query form in which certain variables can be changed by imposing constraints (filters) on certain data types so as to restrict the queries to certain subsets of data.

Template queries can be accessed in different ways

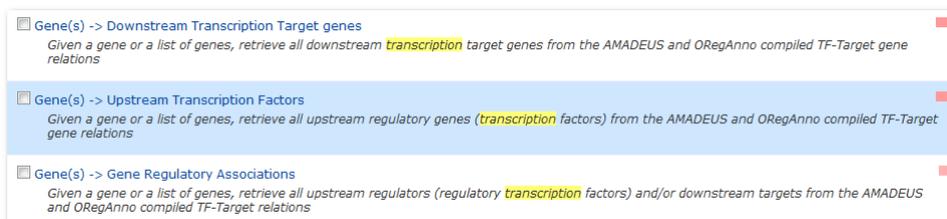
- Each **data category** page has a set of templates related to that data type.
- Templates appear on **report pages** and **list analysis pages**.
- Templates can be searched using the **Quick Search** available on every TargetMine page, by changing the drop-down list from 'Identifiers' to 'Templates'.
- The **templates page**, accessible from the TargetMine home page or via tabs in the menu bar, allows the users to search or browse for templates.



For example, search the template queries for 'transcription':

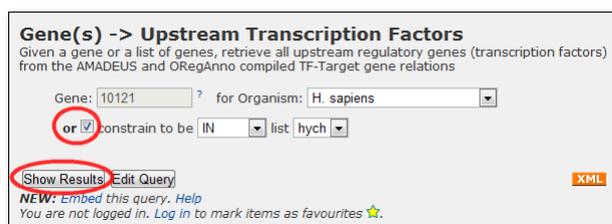


and select the template 'Gene(s) --> Upstream Transcription Factors':



Now that we have created a list the template query gives us the option to use it instead of entering an identifier.

Click the checkbox to select the demo list "hych" saved earlier, and then click on "Show Results" to run the query.



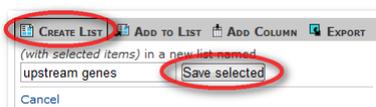
The results table shows the transcription factors that target the genes from our original list.

The user can also create new lists from results tables. We can save a list of the transcription factors from this query to view in the list analysis page or to use in more templates.

Click on the checkbox by 'Source > ncbiGeneNumber' to select all genes

Source > ncbiGeneNumber	Source > symbol	Source > name	Target > ncbiGeneNumber ?
<input checked="" type="checkbox"/> 1050	CEBPA	CCAAT/enhancer binding protein (C/EBP), alpha	<input type="checkbox"/> 338
<input checked="" type="checkbox"/> 3169		forkhead box A1	<input type="checkbox"/> 338
<input checked="" type="checkbox"/> 3172		hepatocyte nuclear factor 4, alpha	<input type="checkbox"/> 338
<input checked="" type="checkbox"/> 3172	HNF4A	hepatocyte nuclear factor 4, alpha	<input type="checkbox"/> 338
<input checked="" type="checkbox"/> 6927	HNF1A	HNF1 homeobox A	<input type="checkbox"/> 338
<input checked="" type="checkbox"/> 4790	NFKB1	nuclear factor of kappa light polypeptide gene enhancer in B-cells 1	<input type="checkbox"/> 7076

Click on the tab 'CREATE LIST' and choose a name for the saved list. For example, name it as 'upstream genes'. Then click 'Save selected' to save.



Using lists is an excellent way to retrieve information about a whole list of data. For example the users can also retrieve:

- Interactions for these genes
- Disease Ontology (DO) annotation for these genes

Please try it yourself.

IV. Query Builder

Aimed mostly at advanced users, the 'Query Builder' allows the users to

- construct new queries across multiple data sources in TargetMine
- modify existing template queries to change the output or add a filter as may be seen from the following example.

Click on 'Query' in the Trail to get back to the template form:

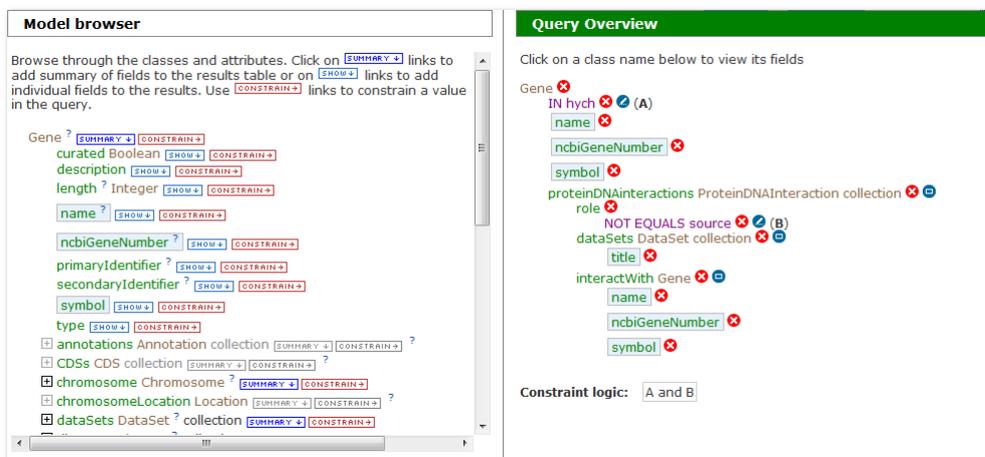


Now click 'Edit Query' to bring up the Query Builder:

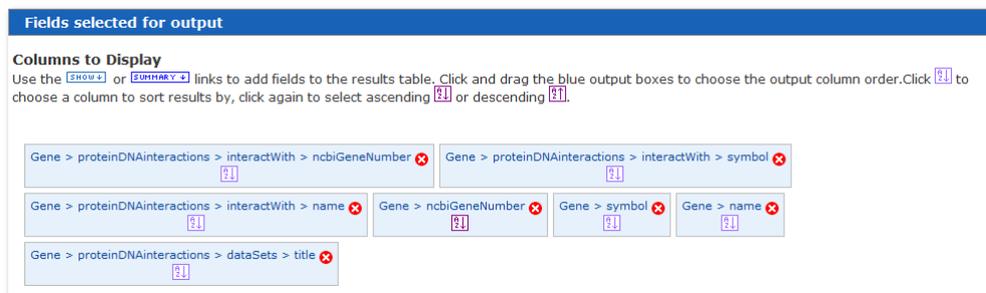


The 'Model browser' on the left permits the user to navigate the TargetMine data model. In this example, the model browser displays the initial Gene class and all its attributes (e.g., name, symbol) and related classes (e.g., organism, proteins). TargetMine uses an object based data model - biological types are termed 'classes' and individual entries are termed 'objects'.

The user can click  to open related classes and see their attributes. The [SHOW](#) tab may be used to add fields to the output. The [CONSTRAIN](#) tab allows the user to add constraints (filters).



Underneath the model browser, the 'Fields selected for output' displays the fields selected by the user to be displayed in the results. Each field is represented by a box which eventually corresponds to a column in the results table. The order of the fields in the column may be changed by drag and drop.



The 'Query Overview' section shows the constraints applied to this query. Notice that one of them says 'Gene' then 'IN demo list'. This indicates that the query is restricted to the genes from the sample list saved earlier.

What if the user wants to search for **all** genes in TargetMine for **any** upstream transcription factor that may regulate their gene expression? The user may simply remove this constraint and run the query again.

Click on the **X** button next to 'IN hych' to remove the constraint:



Now click 'Show results' to run the query:



The results table now shows all the upstream transcription factors in TargetMine and their target genes. The user can use the summary buttons  on the 'Source > symbol' and 'Target > symbol' columns to find more information about the numbers of each.