

The toolbox of TRANSFAC 2.0

User guide release 2.0

Table of contents

Getting started	2
Welcome to MATCH Suite	2
Basic interface	2
Gene set analysis	3
Launching the analysis Selecting the input gene list	
Composing an input gene list in the TRANSFAC® database	3
Selecting input gene list from the MATCH Suite interface	4
Specifying the launch parameters	8
Optimizing the input gene set by GO functional classification (optional step)	9
Confirming the launch parameters and starting the analysis	10
Viewing the results Operating in the Launch history	
Results visualization	13
Factor view table	15
Factor view Pro table	16
Matrix view table	17
Genes table	
Genome Browser	19

Heatmaps	22
Single gene analysis	25
Launching the analysis Selecting the input gene	
Selecting the input gene in the TRANSFAC® database	25
Specifying the input gene from the MATCH Suite interface	26
Specifying the launch parameters	27
Confirming the launch parameters and starting the analysis	29
Viewing the results Operating in the Launch history	
-	30
Operating in the Launch history	30 32
Operating in the Launch history Results visualization	30 32 33
Operating in the Launch history Results visualization Factor view table	30 32 33 34
Operating in the Launch history Results visualization Factor view table Matrix view table	30 32 33 34 36



Getting started

Welcome to MATCH Suite

Welcome to MATCH Suite – the toolbox of TRANSFAC 2.0, which comprehensively addresses the syntax and semantics of gene regulation and allows you to identify the transcription factors regulating the genes(s) of your interest.

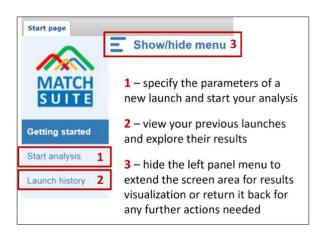
MATCH Suite can be launched on an individual human gene or on a list of human genes. Depending on your selection, different analyses will be ran to identify the activation patterns of your input (see Methods document linked to the analysis report of each run for further details).

Explore the functional enrichment of your gene set, find only transcription factors (TFs) expressed in the tissue of your interest, filter the predicted TFs by those intersecting with conservative regions of the genome and much more! Navigate to *Start analysis* to immediately launch the comprehensive and fully automatized gene regulation study.

Basic interface

The MATCH Suite interface is based on two main sections:

- (1) **Start analysis** navigate to this section to launch a new analysis
- (2) **Launch history** navigate to this section to view the history of your previous launches and open their results



The **Show/hide** menu button at the top of the screen (3) allows you to hide the left panel menu for extending the useful screen area when this is needed (this function is of particular importance when visualizing the analysis results).



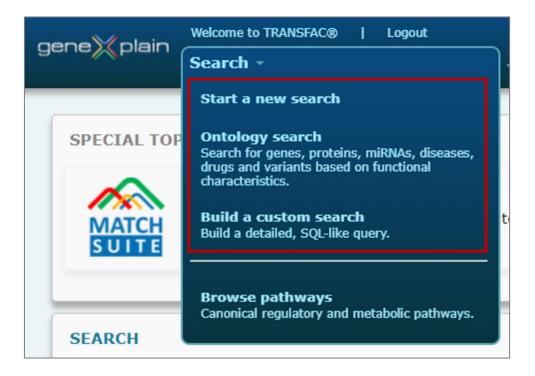
Gene set analysis

Launching the analysis

Selecting the input gene list

Composing an input gene list in the TRANSFAC® database

A particularly convenient way to compose a gene list for analysis is to run the MATCH Suite on your search results in the TRANSFAC[®] database. For instance, when you search for a certain disease in the standard Search field or select genes belonging to a certain Gene Ontology (GO) category (Search > Ontology search), you end up with a list of genes.



In the search result inside TRANSFAC[®] database you can view all found entries on one page (select "All" in the "Hits on page" list) and then select the search results of your interest to launch the MATCH Suite gene set analysis on a respective gene list (you can use the *Mark all on page* option and then only human genes from your selection will be automatically taken to the MATCH Suite analysis upon launching it).



ene <mark>)(</mark>	plain Welcome to	o TRANSFAC® Logou h - MATCH Suite	Tools - My Data -	Home Taskbar <mark>Help +</mark>
► Vie Found 12 Search	IRC w more search opt 28 results for "BRC" in 3 th results nes and proteins NAs	ions if you want to do i 3 categories: 16 Transcripti 14 Matrices	Still searching?	example searches: gene BRCA1 mRNA mir-155 disease ovarian cancer pathway JNK pathway drug Simvastatin transcription factor FOXA1 matrix STAT When you search, you will look for information from all available source. Learn more. Choose more search options to specifically limit your search to Julg one source, like chere and proteins or selected source.
25 of 9 Save the First	ese results Export the	ese results Pathfinder	d view as: Contrology Autor Suite gene set Launch MATCH Suite on the search results Description	rgene V Search Filter Hits on page V 25 50 100
	br	Drosophila melanogaster	broad [matched: 'BRC' (GENES_AND_PROTEINS, MATRICES)]	200
	Arid4b	Mus musculus	Protein with high similarity to human ARID4B, which inhibits transcription and cell proliferation, and is associated with lu binding activity-knot of a chromodomain containing family, contains an RBBINT (NUCI62) domain [metedet: BKC (DKB_AND_PROTEINS]]	ng neoplasm, member of the RNA All
	brn	Drosophila melanogaster	brainiac [matched: BRC' (GENES_AND_PROTEINS)]	
	BRCA1	Homo sapiens	Breast cancer 1 early onset, a transcription regulator that acts in double-strand break repair, apoptosis, protein folding, breast, ovary, and prostatic neoplasms; mRNA is downregulated in melanoma (matched: "BRC (DRES_ML0, PROTENS_MATRICE))	and mRNA cleavage, upregulated in

When you have selected the search results of your interest, press the button "Match Suite gene set" and you will be automatically transferred to the MATCH Suite tool, where you will be asked to assign a name to your gene list prior to proceeding to the next step of the analysis launch wizard:

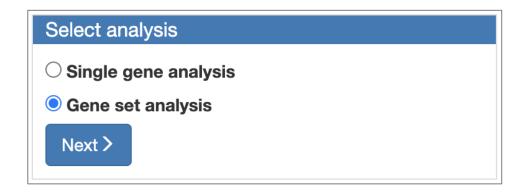
Please name the selected gene list	
Gene list name: gene list(1)	
	Cancel

After giving a name to your gene list, the wizard will immediately take you to the *Specifying the launch parameters* step of the MATCH Suite analysis launch wizard.

Selecting input gene list from the MATCH Suite interface

When you click on the *Start analysis* section, the system immediately navigates you to the analysis launch wizard. At the very first step of this wizard you will be asked to select the type of the analysis you would like to perform:





If you will select the *Gene set analysis* option, you will be taken to the next step of the wizard, where you will be asked to select the gene list which should be used for the analysis.

Start page			
\sim	Show/hide menu		
	Specify input data		
<u>MATCH</u>	O Use demo gene list 1		
SUITE	Use my data 2	Supported input	
	○ Construct tissue-specific gene lis	st from scratch (requires subscriptio	on to HumanPSD™) 4
Getting started	+ Upload files Browse	stored data Textual input	Next >
Start analysis	5	6 7	11
Launch history		Name	Delete
,	• 8	My gene list 1 9	10 🗙
	0	My gene list 2	×
	0	My gene list 3	×
	0	My gene list 4	×
\wedge	0	My gene list 5	×
TRANSFAC 2.0	0	My gene list 6	×

You can try launching the analysis using the **Use demo gene list** (1) option, or you can specify your own gene list by selecting the **Use my data** (2). The demo gene list contains 50 Ensembl genes, you can view them by clicking on the *demo gene list* blue link. The **Supported input formats** (3) link also is clickable, it provides you with the information about the requested format of the gene list, which can be analyzed with the MATCH Suite 1.1:



Supported input form	ats ×
	lysis from any human gene o 1000 genes, all coming in nats:
Gene symbols	e.g. TNMD
Genes Ensembl	e.g. ENSG0000000005
Genes Entrez	e.g. 64102
	ok

Lists of 20 to 2000 genes coming in Ensembl ID, Entrez ID or Gene symbols format are accepted by the MATCH Suite 1.1. The system will select automatically the human genes from your list, only these will be subject to the further analysis.

.

A tissue-specific gene list can be automatically constructed for further analysis using the **Construct tissue-specific gene list from scratch** (4) option.

O and list a	construction by tissue
Gene list o	construction by tissue
<	Back
Please	select the tissue of your interest to proceed
amygo	tala -
	you see the diagram that represents the top 488 genes highly relevant for the amygdala tissue. These genes were among the top 10% of all genes known to be expressed in the amygdala tissue and highest tissue specificity values among others for the amygdala tissue.
located how sp	ot on the diagram below represents the gene with respective gene expression and tissue specificity values for the amygdala tissue. The most highly expressed and tissue specific genes are thus in the top upper corner of the diagram. Values of relative gene expression in a given tissue are taken from the Protein Attas. General expression specificity value demonstrates on a scale from 0 to 1 ecifically expressed is the gene in a certain tissue (values closer to 1) or how generally expressed it is across all supported tissues (values closer to 0). See Methods section for details on how sion specificity value was calculated.
	select the genes you would like to proceed with to further analysis by selecting the area of your interest with the mouse. Just navigate to the diagram, click on your mouse and, keeping the mouse , select the area where the genes of your interest are located. You can further widen or narrow the selected area by adjusting the edges of the rectangular selection.
	ave selected 73 genes select at least 20 genes to proceed with the analysis Proceed with selected genes
1.0 e.o cificity	
tissue specificity	
Relative tis	
0.6	
0.5	
0.4	
0.3 -	
0.2	
0.1 -	
0.0	20 40 60 80 100 120 140 160 180 200 220 240 200 Expression

This option provides you with the ability to select any tissue among the 61 supported tissues and visualize the most tissue-specific genes among the top 10%



of all genes known to be expressed in the selected tissue according to the information about relative gene expression levels provided by the Protein Atlas. You can further select the genes of your interest on the interactive diagram to either proceed with them to the analysis launch or just save the selected genes into the inputs of your project (both options managed by the *Proceed with selected genes* button). Please note that tissue-specific gene list construction option is available only to the <u>HumanPSDTM</u> database subscription owners.

The gene list for your analysis can be uploaded from your local computer using the **Upload files** (5) option, it can be also selected from the data stored in any geneXplain platform project accessible to you by using the **Browse stored data** (6) option. In such case the selected gene list will be copied to the MATCH Suite project and taken for further analysis. The next option for input gene list specification is **Textual input** (7). This function provides you with an ability to simply copy and paste any gene list of your interest (in Ensembl, Entrez or Gene symbols format) to the dedicated textual input form:

Textual input		
Gene list name: my gene list		
Type or copy+paste your genes here, e.g.		
ENSG0000000005		
ENSG0000000419		
ENSG0000000457		
	Cancel Upload	

The last option to specify an input gene list is to select it from the gene lists that were previously used by you as inputs for the MATCH Suite analysis (8). The names of the previously used gene lists are clickable and the respective gene list will open upon the click on its name (9). You can manage the gene lists stored in your project and permanently delete the unnecessary ones using the **Delete** option (10). Please note that the maximum size of your MATCH Suite project is 2 GB. You can free up space by deleting the unnecessary gene lists and analysis results if that would be needed (see *Operating in the Launch history* section below for further info)

To select the gene list for the current analysis run, mark it with the radio button in the list of all currently available inputs (8) (any newly uploaded gene list will automatically appear in this list).



Please note that regardless of the input gene list source, the selected gene list will be checked by the MATCH Suite for correspondence to the input gene lists requirements and only human gene lists containing from 20 to 2000 human genes in supported formats will be accepted for further analysis.

After selecting the input, click **Next** (11) to proceed.

Specifying the launch parameters

In the next step of the analysis launch wizard the MATCH Suite will ask you to fill in the following form:

Start page	Show/hide menu
	Specify parameters
MATCH	Name of the analysis demo-gene-list 1
	Studied tissue 2 Nothing selected -
Getting started	Tissue selection will allow to use tissue-specific promoters from the FANTOM5 database and
Start analysis	identify the transcription factors regulating your gene set that are known to be expressed in the selected tissue.
Launch history	Promoter range Use default promoter range [-500,+100] Customized promoter range From Key 5000 to Key 1000
	Gene set optimization Max -5000 Max +1000 Max +1000 A A Categories
TRANSFAC 2.0	< Back Next > 5

You can give a name to your analysis launch or keep the default name suggested by the system in the **Name of the analysis launch** field (1). This name will be further used in the launches history for easy selection of the run of your interest.

Optionally you can specify the tissue of your interest from the dropdown list of supported tissues in the **Studied tissue** field (2). The provided tissues are the tissues from <u>FANTOM5</u> database with specific coordinates for the transcription start sites (TSSs) that allow to select tissue-specific promoters for the subsequent analysis. The selected tissue is also used further for identification of transcription factors that are known to be expressed in the tissue of your interest. Please refer to the <u>Methods</u> document for further details.

The promoter range that will be used for the search of TFBS in your analysis run is specified by the **Promoter range** parameter (3). By default the promoter range used by the MATCH Suite is [-500,100] relative to the TSS. You can specify a



customized promoter range limited to the maximum of -5000 and +1000 from TSS.

Your input gene set can be optimized by functional enrichment using the **Gene set optimization** option (4). Having clicked on it, you will be offered to select between the supported GO categories:

Gene set opt	timization
	 Narrow my gene list to genes coming from certain GO categories biological process cellular component molecular function

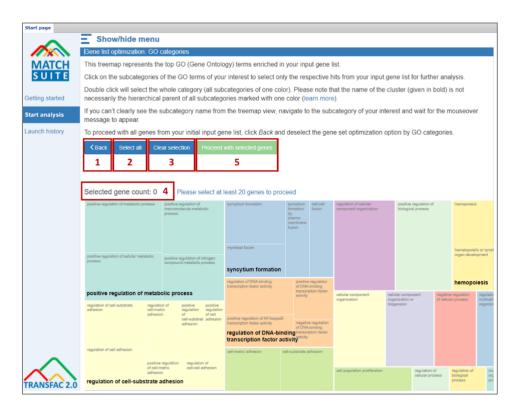
Depending on your selection, the tree map visualization of functional classification of your input gene set will be built either on biological processes, or on cellular components, or on molecular functions. If you do not wish to optimize your input gene set by functional categories, simply do not tick the *Gene set optimization* option.

When done with parameters selection, click on **Next** (5) to proceed either to GO functional optimization of your input gene set or skip this step and start the analysis immediately by confirming the selected analysis launch parameters.

Optimizing the input gene set by GO functional classification (optional step)

In case you have selected to optimize your input gene list by GO functional classification at the parameters specification step, the tree map of GO biological processes, cellular components or molecular functions will be constructed for your input gene set depending on your selection.





You can click **Back** (1) to return to the parameters specification step and cancel the GO optimization of your input gene list by unticking the *Gene set optimization* option. Otherwise you are requested to select the GO categories of your interest, following the instructions provided at the top of the screen. Only genes belonging to the selected GO categories will be taken by the MATCH Suite for further analysis.

The **Select all** (2) button will allow you to select for further analysis all genes, belonging to all GO categories enriched in your input gene set (genes belonging to all GO categories visualized on the tree map). The **Clear selection** (3) button will deselect all previously selected GO categories and will reset the gene count to 0. The number you will see next to the **Selected gene count** (4) will show you the total amount of genes underlying the currently selected GO categories. Once this number will reach the minimum of 20 genes that are requested for launching the analysis, the **Proceed with selected genes** (5) button will become active and you will be able to launch the analysis using the optimized gene set.

Confirming the launch parameters and starting the analysis

After specifying all parameters for your launch, the MATCH Suite wizard will ask you to confirm your selection:



	Show/hide menu elected launch parameters	
MATCH	Launch name:	demo-gene-list 1 1
SUITE	Input gene list:	demo-gene-list optimized by GO categories
	Selected tissue:	Nothing selected
Getting started	Promoter range:	[-500,+100]
Start analysis Launch history	Selected GO categories:	positive regulation of metabolic process <go:0009893> positive regulation of metabolic process <go:0031325> positive regulation of cellular metabolic process <go:0010604> positive regulation of macromolecule metabolic process <go:0051173> positive regulation of nitrogen compound metabolic process</go:0051173></go:0010604></go:0031325></go:0009893>
TRANSFAC 2.0		2 Back Launch analysis 3

All parameters that you selected for the current launch will be shown on the screen (1). You can check the genes that were eventually selected for the analysis launch after GO functional classification (if it was applied) by clicking on the name of the input gene list.

If you want to apply any changes to the specified parameters of the launch, click on **Back** (2), otherwise you are ready to start your analysis by clicking on the **Launch analysis** button (3).

Viewing the results

Operating in the Launch history

Once your analysis was launched, you will be redirected to the *Launch history* section, also accessible by the direct link at the left menu panel. The Launch history allows you to view the results of all your previous analysis runs and to follow the progress of the currently running analyses.



	Show/hide m	ienu					
MATCH	Recent launch Select the analysis la	nes aunch you want to view or sta	art a new analy	sis			
	Date	Name		Parameters	Status	Results	Terminate/Delete
ting started	2021.08.28 12:00:09	demo-gene-list 1	1	Gene set analysis View input parameters	Running: 8%	2 In progress	X 3
nch history	2021.08.27 22:10:35	My launch 3		Single gene analysis View input parameters	Completed	View results	
	2021.08.27 21:59:00	My launch 3		Single gene analysis View input parameters	Completed 4	View results	
	2021.08.26 13:16:13	demo-gene-list		Gene set analysis View input parameters	Completed	View results	5
\sim	2021.08.26 13:13:09	My launch 1		Single gene analysis View input parameters	Completed	View results	
ANSFAC 2.0				Start new analysis 6			

You can check the parameters used for the launch by clicking on the **View input parameters** link (1). The following pop-up form will appear:

Launch parameters		×
demo-gene-lis	st 1 2021.08.28 12:00:09	
Input gene list:	demo-gene-list optimized by GO categories	
Tissue selected during the analysis launch:	none	
Promoter range:	[-1000,+100]	
GO categories selected to narrow the input gene list:	show	
		ok

The gene set used for the current run can be viewed by clicking on the respective link in the *Input gene list* field. In case you have selected to optimize your input gene list by certain GO categories, you can view them by clicking on the *show* link next to the *Categories selected to narrow the input gene list field*. If no GO functional categories optimization was done, the respective field will display *none*.

The progress of the currently running analysis will be displayed in the **Status** column (2). Please note that the progress is displayed in percentage of the finished steps of the underlying workflow and it has no direct correlation with the time left for the analysis to finish. Commonly one analysis run will take several hours, but this time interval is highly dependent on the input gene set and other parameters selected for the respective analysis launch.



It is not recommended to have several analysis launches running in parallel. Analysis runs will finish faster when launched consecutively one after another.

If you wish to terminate the launched analysis, you can click on the **Terminate** button (3).

To view the results of a finished analysis please click on the **View results** button (4).

You can manage the stored analysis results and delete the unnecessary data by clicking on the **Delete** icon (5). This action will delete all results of the respective analysis launch. The input gene list used for this analysis launch will still be accessible in the available list of inputs, which is viewed at the very first step of the start analysis wizard (see the *Selecting the input gene list* section of this document). By default, your MATCH Suite account is equipped with 2 GB disk space for storing your analysis results and input gene lists used. You can extend this volume by contacting us via info@genexplain.com with a respective request.

You can launch a new analysis run directly from the *Launch history* section by clicking on the **Start new analysis** (6) button.

Results visualization

Having selected in the *Launch history* section the analysis result which you want to view, it will open in the results visualization mode on your screen.

In the results visualization mode the screen will be divided into four different segments with the following functions:

- (1) The **identified transcription factors** regulating your gene set and respective **matrices tables**
- (2) The **table of your input genes** and found site hits in their promoters
- (3) The **info box** displaying the information about the currently selected object
- (4) The **genome browser**, allowing to visualize the tracks of found sites and additional annotation tracks for further results interpretation



User guide	Download tables 5										
	Show/hide menu										
	demo-gene-list 3: factor/matrix vi	ew			demo-gene-list 3: ge	ene view					
MATCH	Factor view Factor view Pro	Matrix view			Show 10 • entries	1	F	irst Prev	ious 1	2 3 Next	Last
SUITE	Best factors on top O Remove a	Il filters 🛛 Apply c	hanges 🛛	1	Showing 1 to 10 of 27	entries	2				
etting started	Show 10 • entries	Prev	ious 1 2 3	4 5 6 Next					Total	V\$AIOLOS_03 0	V\$DEAF
art analysis	Showing 1 to 10 of 56 entries				Ensembl ID	Gene symbol 🔅	Gene description () O	CMA Score 🗸	number of sites	lkaros, ikzfő	DEAF1
aunch history	Enrichment Factor name analysis	Combinatorial	Average factor expression across	Expression specificity (rank of					Θ		
ew results		Ø	all tissues O	average) O	ENSG0000067606	PRKCZ	protein kinase C zeta	5.36	21		4
Visualization Report 6	DP-2	-	12.46	0.10 13/62 0.12	ENSG0000074964	ARHGEF10L	Rho guanine nucleotide exchange factor 10 like	5.26	19		2
	MAZ	-	34.69	18/62 0.03 22/62	ENSG00000100142	POLR2F	RNA polymerase II subunit F	4.98	14	1	
	FOSB		22.99	0.18			remodeling				
	Info box		Genome browser	* 7 82*1	<u>-</u>						
\sim	Track Enriched sites Sequence collection: databases/EnsemblHuman100/Seque GRCh38	3	Sequence (chromosome): 1 4 Promoters	9411 204			enblid ENSG000 2050 III PRKCZ		Go 20	1	2050
ANSFAC 2.0	Site count: 428		CMA sites	0			V\$DEAF1_01		V\$RFX1	_05 V\$KLF7_07	

The Factor, Matrix and Gene tables that you see on the screen can be exported with the applied filters (see filtering instructions below) using the **Download tables button** (5). The archive containing these three tables in tab-separated text format will be downloaded to your local computer.

You can open the comprehensive analysis report about the respective run by clicking on the **Report** (6) link in the left menu panel. The self-explaining report will contain the factor, matrix and gene tables you see in the results visualization section along with supplementary tables and analysis steps description.

You can extend or narrow certain segments of the screen by moving the splitter lines. At this point you might want to use the *Show/hide menu* button, which will hide the left panel menu from view and will broaden the results area of the screen.

art page	Download tables									
	Show/hide menu									
🔊 🖌	demo-gene-list 3: factor/matrix view			demo-gene-list 3: ge	ene view					
MATCH	Factor view Factor view Pro Matri	c view		Show 10 • entries		F	rst Prev	ious 1	2 3 Next	Last
SUITE	Best factors on top O Remove all filters	Apply changes		Showing 1 to 10 of 27	entries					2001
etting started	Show 10 • entries	Previous 1 2 3	4 5 6 Next					Total	V\$AIOLOS_03	V\$DEA
tart analysis	Showing 1 to 10 of 56 entries			Ensembl ID	Gene symbol 🕴	Gene description () O	CMA Score 🚽	number of sites	lkaros, ikzf5	DEAF1
aunch history		inatorial Average factor expression across	Expression specificity (rank of		•	•	•	Θ		
ew results	Factor name analysis 🔅 analy O	all tissues	average)	ENSG0200067606	PRKCZ	protein kinase C zeta	5.36	21		4
Visualization Report	DP-2 •	- 12.46 - 14.96	13/62	ENSG0000074964	ARHGEF10L	Rho guanine nucleotide exchange factor 10 like	5.26	19		2
	MAZ	34.69	18/62 0.03 22/62	ENSG0000100142	POLR2F	RNA polymerase II subunit F	4.98		1	
	FOSB	22.99	0.18			remodeling				
	Info box	Genome browser		******				din se		
•	Track Enriched sites Sequence collection:		Filter No filter Position: 1:20494115 3411 20			cted • embl id • ENSG0000 20500		20	50200	2050
\sim	databases/EnsemblHuman100/Sequences/chr GRCh38	mosomes Promoter	\$4}			PRKCZ			-	



In the screen segment, which visualizes the tables of predicted factors and respective matrices, you will find three accessible tables: Factor view, Factor view Pro and Matrix view.

Factor view table

In the **Factor view** (1) table you will see a simplified summary of the transcription factors predicted to be regulating your input gene set. By default top 10 factors will be shown, this can be changed in **Show <number> entries** (2) field. The total number of factors identified will be displayed in (3). You can navigate through the predicted factors using the pages in (4). The columns of the *Factor view* table are fully matching the *Table 1* given in the analysis report of the respective run. You can refer to the analysis report for denominations of column names and their contents or use the info hints provided in the results visualization interface as a mouseover message that will appear upon hovering above the **?** sign (5) available at multiple places in the interface.

demo-gene-list 1: factor/ma	trix view				
Factor view 1 Factor view	Pro Matrix view	Best factors on top ?	Remove all filters ?	Apply changes 🚱	
Show 10 v entries 2	L	7		4 Previous 1 2	3 4 5 6 Next
Showing 1 to 10 of 56 entries	3				
Factor name	Enrichment analysis O		analysis	Average factor expression across all tissues Θ	Expression specificity (rank of average) Θ
DP-2	•		-	12.46	<mark>0.10</mark> 13/62
c-Ets-1	•		-	14.96	<mark>0.12</mark> 18/62
MAZ	•		-	34.69	0.03 22/62
FOSB	•		~	22.99	0.18 17/62
c-Fos	•		~	63.36	0.10 19/62
ZNF-24	•		-	22.57	0.01 21/62
BTEB2	•		×	15.2 <mark>3</mark>	0.20 21/62
Sox-10	•		*	10.14	0.24 16/62

The columns of tables have in-built sorting option (6) which allows to sort the values within one column by ascending or descending order or by alphabetical order in case of textual contents. Simply click on the gray arrows for the sorting to be applied. By default, best factors (or matrices) are brought to the top (please see the analysis report and the <u>Methods</u> document for explanations on the factors



and matrices ranking procedures). If you want to return to the original order of factors, click on the **Best factors on top** button (7).

Factor view Pro table

The **Factor view Pro** table (1) provides a deeper look into the transcription factors identified to be regulating the input gene set. It fully corresponds to the *Table 3* of the analysis report, where you can find the denominations of its column names and their contents description. Respective info is also summarized in the **?** hints available as mouseover messages upon navigating on them, similar to the *Factor view* table.

Factor view	Factor view P	ro Matrix	view Be:	st factors on top 😯	Remove all fil	ters 😗 🛛 Ap	oply changes 🔞		
Tissue 😡	2	Select a tissue	-		3		4		
Show 10 🗸	entries				Firs	t Previous	s 1 2	3 4 5	6 Next Last
Showing 1 to 10 Factor name	of 56 entries Gene symbol	⇔ TF cl	assification O	⊜ Site model €	¢	Factor enric	hment 🛓 exp	erage factor pression across ∳ ∳	Expression specificity (rank of average) $oldsymbol{\Theta}$
DP-2	TFDP2	Fork h helix f 3.3.2.2		V\$E2F6_03		2.83		2.46	0.10 13/62
c-Ets-1	ETS1	Trypto factors 3.5.2.1		V\$GCM1ERG	_01	2.85		4.96	<mark>0.12</mark> 18/62
MAZ	MAZ	C2H2 factors 2.3.4.0		V\$MAZ_Q5		2.69		34.69	0.03 22/62
FOSB	FOSB		leucine zipper (bZIP) 1.2	V\$FOS_06		1.31		22.99	<mark>0.18</mark> 17/62
c-Fos	FOS		leucine zipper (bZIP) I.1	V\$FOS_06		1.31	-	63.36	<mark>0.10</mark> 19/62
ZNF-24	ZNF24	C2H2 factors		V\$ZNF24_01		2.37		22.57	0.01 21/62

The *Factor view Pro* table allows you to apply the **Tissue** filter (2). You can select the tissues(s) of your interest from the dropdown list in (2) and click on the **Apply changes** button (4) to recalculate the factors and genes tables, as well as the track of found sites in the genome browser, leaving only those factors and their sites, which are known to be expressed in the tissue(s) of your selection. Respective columns with expression values of factors in the selected tissue(s) will be added to the table. You can refer to the <u>Methods</u> document for information on the expression values origin. To remove the filtering of factors by selected tissues, click on the **Remove all filters** button (3).



Please note that the tissue expression filter will be also auto applied to all tables and tracks when you will switch from the Factor view Pro table to either of the Factor view or Matrix view tables. To cancel the filters, click on the *Remove all filters* button.

Matrix view table

The **Matrix view** table (1) shows the PWMs (positional weight matrices) of the TRANSFAC[®] library, the respective sites of which were identified in the promoters of the studied gene set.

Similar to the factors table, the *Best matrices on top* button allows to bring the best matrices to the top of the matrix table in case their order was changed while sorting the values in individual columns. This table fully corresponds to the *Table 4* of the analysis report, where you can find the denominations of its column names and their contents description. Respective info is also summarized in the ? hints available as mouseover messages upon hovering above them, similar to the *Factor view and Factor view Pro* tables.

demo-gene-list	1: factor/matrix view								
Factor view	Factor view Pro 1 Matrix view Best matrices of	n top 😯	Re	move all filters ?	Apply change	es 😧			
1.0	enrichment 2 1.6 2.2 2.8 3.4		Adjus	ted sequence enr 0.5	ichment	3 1.5 2.0			Â
Show 10 ✓ e						F	irst Previous	1 2 1	Next Last
Showing 1 to 10 o	♦ Matrix logo		¢	Adjusted site enrichment	Site enrichment 🎙 🅑	Site enrichment FDR O	Adjusted sequence enrichment	Sequence enrichment FDR O	Composite model ∲ ₽
V\$PPARD_02				2.10	5.31	2.37e-4	2.28	1.22e-3	yes
V\$SOX8_04	ATTCAT			2.03	3.93	5.68e-10	0.47	3.61e-1	yes
V\$KLF7_07	<u>_</u>			1.91	3.59	8.11e-11	1.29	1.61e-3	yes
V\$DEAF1_01	CTCGP9_STTTCCG		_	1.59	3.20	6.64e-6	1.32	1.01e-3	yes
V\$FOS_06				1.31	2.36	2.23e-8	0.45	6.78e-1	yes
V\$RFX1_05	GTIGCCA_GGAS			1.17	2.55	3.93e-3	0.76	2.22e-2	yes
	0000								-

The **Adjusted site enrichment filter** (2) allows to leave only matrices with the adjusted site enrichment values higher than the threshold specified by the filter. The set filter will be first applied exclusively to the *Matrix view* table. To recalculate the factors and the genes tables, as well as the track of the found sites in the



genome browser, only with matrices that were left after applying the filter, you should click on the *Apply changes* button.

The **Adjusted sequence enrichment filter** (3) allows to leave only matrices with the adjusted sequence enrichment values higher than the threshold specified by the filter. The set filter will be first applied exclusively to the *Matrix view* table. To recalculate the factors and the genes tables, as well as the track of the found sites in the genome browser, only with matrices that were left after applying the filter, you should click on the *Apply changes* button.

Filters will be also auto applied to all tables and tracks when you will switch from matrix table to either of the factor tables. To cancel the filters, click on the *Remove all filters* button.

Genes table

The genes table presented in the results visualization section fully corresponds to the gene table provided in the *Table 5* of the analysis report, where you can find the denominations of its column names and their contents description. Respective info is also summarized in the **?** hints available as mouseover messages upon navigating on them, similar to the *Factor view*, *Factor view Pro* and *Matrix view* tables.

demo-gene-list 1: ge	ene view								
Show 10 v entries	5					First	Previous	1 2 3	Next Last
Showing 1 to 10 of 27	entries								
	Gene	Gene	СМА	Total -	V\$AIOLOS_03	V\$DEAF1_01 \$	V\$E2F6_03	V\$EGR1_19	V\$ERR1_Q3
Ensembl ID ₽	symbol ≑ Ø	description ≑ ₽	Score v	number of sites ∲	lkaros, ikzf5	DEAF1	DP-2	Egr-1	ERR1
ENSG0000067606	PRKCZ	protein kinase C zeta	5.36	21		4	1	3	2
ENSG0000074964	ARHGEF10L	Rho guanine nucleotide exchange factor 10 like	5.26	19		2	1	7	
ENSG00000100142	POLR2F	RNA polymerase II subunit F	4.98	14	1			2	1
ENSG0000048649	RSF1	remodeling and spacing factor 1	4.96	19	1	2		2	
ENSG00000051523	СҮВА	cytochrome b-245 alpha	4.90	21		1		4	

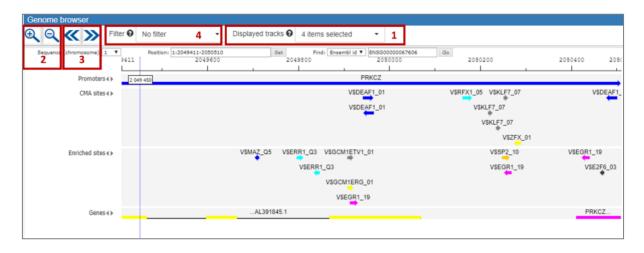
To visualize in genome browser the sites found in the promoter of any gene, just click on the line with the gene of your interest inside the genes table and refer to the genome browser below to explore the predicted regulation model of the respective gene.



Genome Browser

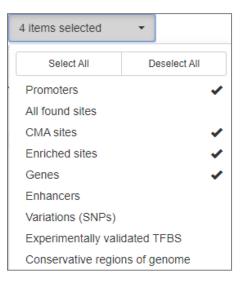
The genome browser provides you with visualizations of the predicted gene regulation models for each gene from the input gene set. Having clicked on any gene from the *Genes table*, the promoter model of the respective gene will be automatically opened in the genome browser with visualization of the sites found within the respective promoter. By default the displayed tracks include:

- **Promoters** the track of all promoters that were used for the performed analysis
- **CMA sites** the track of sites belonging to the combinatorial matrices of the constructed CMA model (see <u>Methods</u> for further info)
- **Enriched sites** the track of the remaining sites found to be enriched in the promoters of the studied genes



- **Genes** – the track with all Ensembl genes

Displayed tracks can be customized using the **Displayed tracks** dropdown list (1)





You can zoom in and zoom out for a more generalized or a more detailed view of the promoter model using the **zoom in** and **zoom out** buttons (2). In case navigation in genome browser is lost due to multiple zoom clicks, you can always return to the promoter of your interest by selecting the respective gene in the genes table once again.

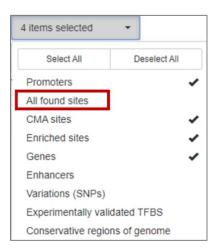
Navigation through the track is supported by the **Shift to the left** and **Shift to the right** buttons (3)

Filtering can be applied to the displayed sites using the **Filter** option (4):

No filter 👻
No filter
View only sites intersecting with enhancer regions
View only sites near the conservative regions of genome

Depending on your selection, only sites intersecting with the conservative regions of the genome or those intersecting with the enhancer regions will be displayed. The genes table will be automatically recalculated leaving only the hits for the sites left after applying the respective filter. To cancel the applied filter, select the *No filter* option in the dropdown list of filters.

Please note that the *CMA sites* track shows only the best sites relevant to the identified CMA combinatorial model. The genes table will contain the full counts for all sites identified, both enriched and combinatorial. To view the respective full track of all found sites, you can add the *All found sites* track to the visualization:



For receiving additional information about any of the found sites, you can click on the site of your interest and explore the contents displayed in the *Info box* section:



Info box	Genome browser	
Site ID: 278	(€) (€) (€) (€) (€) (€) (€) (€) (€) (€)	
Type: TF binding site Sequence name: 1 Sequence: AGGCGGGAAGT Position: 17539416 - 17539426 (11)	Sequence (chromosome)(1 Position(1:1753698-17539797) Set Find(1Ensemblid *) ENS00000074964 Go Promoters+} ARHOEF10L ARHOEF10L	
Properties: • coreScore: 1.0 • score: 0.991601 • siteModel: V\$E2F6_03	CMA sites () VSDEAF1_01	
Model V\$E2F6_03		
Binding element: E2F-6 Threshold: 0.9538317285805532 Matrix: V5E2F6_03 Matrix length: 11	Enriched sites () V\$EGR1_19 V\$GCM1ERG_01 V\$EGR1_19 V\$EGR1_19	
<u> </u>	Genes∢≽	

A right click on the track name in genome browser will open a context menu allowing you to remove the track from the visualization or open it as a table (function supported only for tracks of predicted sites or promoter track):

CMA sites∢ ▶	V\$DEAF1_01			
📷 Open tabl 👔 Remove fi				
Enriched sites∢ ▶		V\$EGR1_19	V\$GCM1ERG_01	
		V\$EGR1_19	V\$EGR1_19	
			V\$E2F6_	.03
Genes∢ ▶				

Tracks opened as table can be exported using the *Export* button at the top menu panel or used for further analysis from the geneXplain platform perspective.

Start	User guide Bage Page Finriched sites X								
First	Previous Page 1 of 9 Next Last	Show	ving 1 to 50	of 428 entrie	5				Show 50 • entrie
ID 🔺	Sequence (chromosome) name 🍦	From \$	To 🔶	Length 🔶	Strand 🔶	Туре 🔶	Property: coreScore	Property: score	Property: siteModel
1	16	1307882	1307892	11	+	TF binding site	1	0.95586	V\$E2F6 03
2	16	1307882	1307890	9	+	TF binding site	1	0.99915	V\$AIOLOS 03
3	16	1307884	1307896	13	-	TF binding site	1	0.79395	V\$ZNF24 01
4	16	1307888	1307900	13	-	TF binding site	0.80889	0.80562	A V\$ZNF24 01
5	16	1307889	1307906	18	+	TF binding site	0.92998	0.89941	* V\$EGR1 19
6	16	1307894	1307908	15	+	TF binding site	0.92684	0.86619	V\$GCM1ERG 01
7	16	1307898	1307908	11	-	TF binding site	0.95972	0.97675	VSMAZ Q5
8	16	1307902	1307910	9	+	TF binding site	1	1	V\$AIOLOS 03
9	16	1307904	1307916	13	-	TF binding site	1	0.80844	A V\$ZNF24 01
10	16	1307908	1307920	13		TF binding site	1	0.9057	★ V\$ZNF24 01
11	16	1307913	1307930	18	+	TF binding site	0.92998	0.90011	V\$EGR1 19
12	16	1307914	1307928	15	+	TF binding site	0.92684	0.86466	V\$GCM1ERG 01
13	16	1307914	1307924	11	-	TF binding site	1	0.98093	VSMAZ Q5

The list of available export formats is as follows:



Export	Export document								
Format:	FASTA sequences (*.fasta)]							
	FASTA sequences (*.fasta)	[
	BED format (*.bed)								
	Interval format (*.interval)	cel							
	General Feature Format (*.gff)								
	Gene Transfer Format (*.gtf)								
	Match format (*.match)								
	Variant Call Format (*.vcf)								
	Wiggle format (*.wig)								

Heatmaps

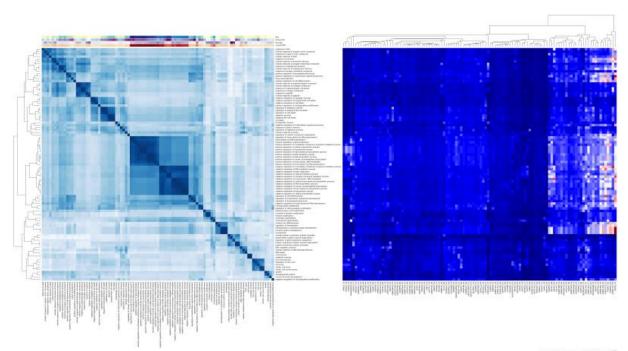
If the functional classification of your input gene set by GO terms produced reliable results (by p-values and by the number of genes in each functional category), heatmaps for the respective GO categorization will be included in the optional section *Functional Analysis of Gene Regulation* of the analysis report.

The constructed image will contain two parts:

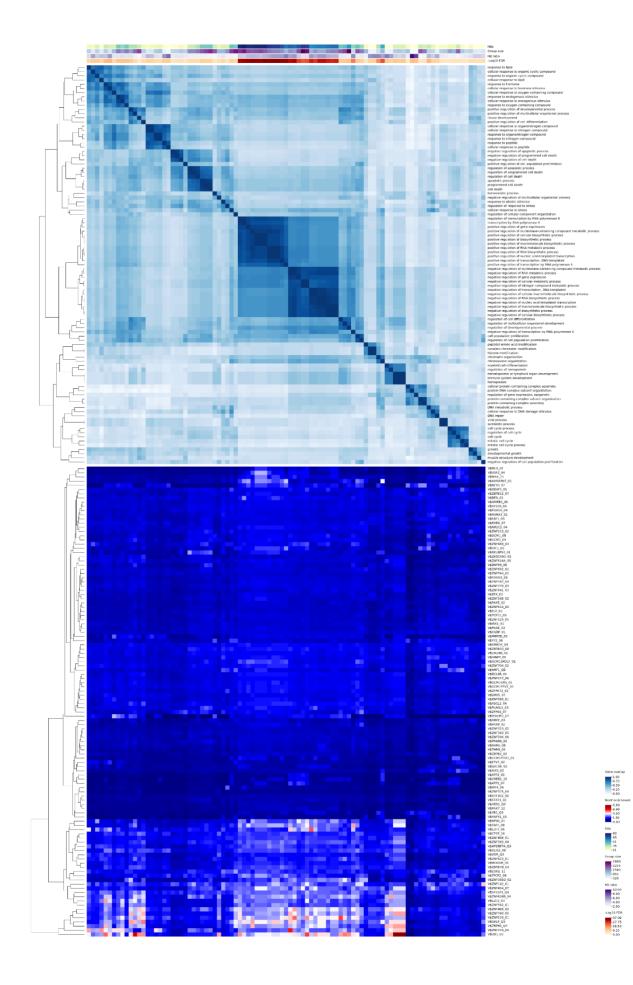
- (1) *The* heatmap of GO to GO terms mapping for the GO terms overrepresented among the studied gene set;
- (2) The heatmap visualizing how enriched motifs are associated with the respective GO categories.

The visualization examples of such heatmaps is given below. Depending on your preference, you can use either of the heatmaps: the one with the horizontal layout (provided in the analysis report as a clickable image), or the one with the vertical layout (provided under the link to alternative view in the report text):











Single gene analysis

Launching the analysis

Specifying the input gene

Sspecifying the input gene in the TRANSFAC[®] database

A particularly convenient way to launch the MATCH Suite single gene analysis is to select the gene of your interest from the search results in the TRANSFAC[®] database. For instance, you can select any human gene in the results of your search in TRANSFAC[®] database and launch the MATCH Suite single gene analysis on a respective gene:

eneX	plain	me to TRANSFAC® + Huma		Logout Iy Data -				Home Taskbar	Help 👻
1	RC	options if you want to	do a more specific searc	search			example searc gene miRNA disease pathway drug transcription factor	BRCA1 mir-155 ovarian cancer JNK pathway Simvastatin	
Searc 105 G 0 miRi 5 Path S Path Save the First	ways es and prote o5 total ese results Expo	16 Tran 14 Mat eins Select re t these results \$\$ Path 4 5 10 Last	suits and view as:	0 Variants 96 Diseases 14 Drugs Hatch Match Suite	Still searching? More search options Ontology search Custom search gene set Launch MATCH Suite on the Suite on the	🏹 PASTA 🖡 Profiles	available sources lis Choose more search search to just one s	STAT ou will look for information ted above. Learn more. options to specifically upper look option options to specifically options of specifically v Search Filtz Hits on page [limit your proteins or ins for the er
		ype Species/Taxon	Description	, mark none.)	search result				
0	br	Drosophila melanogaster	broad	5_AND_PROTEINS, MATRICES)	01				
	Arid4b	Mus musculus		not of a chromodomain	ID4B, which inhibits transcription and c containing family, contains an RBB1NT		associated with lung neoplasm, me	mber of the RNA	
	brn	Drosophila melanogaster	brainiac [matched: 'BRC' (GENES	5_AND_PROTEINS)]					
	BRCA1	Homo sapiens	breast, ovary, and		ion regulator that acts in double-strand mRNA is downregulated in melanoma	l break repair, apoptosis	, protein folding, and mRNA cleava	ge, upregulated in	
	BRCC3	Homo sapiens							

or start the MATCH Suite single gene analysis from a locus report of the gene of your interest:



geneXplain Docus Report - Human BRCA1 (BRCA1)		logout help -	
Transcriptional Regulation what is this? Regulation of BRCA1 gene expression			
Analyze BRCA1 with MATCH Suite → Launch MATCH Suite from the locus report of the gene			
Predicted promoter sequences : 🚊 Match 🐳			
Best supported : PM000854077			
All promoters for the gene : PM000643642, PM000854077			
ER-apha(h) pSSBP1(h) EXP-1(h) EXP-1(h) EXP-1(h) GABP-stopha(h) GAP-stopha		¢	ł
-70 -80 -50 -40 -30 -20 -10 0 10 20 30	40 50	60 70	
Viewing nucleotides -81 to 81			
* Note: Only binding sites whose location is relative to the TSS are graphically displayed. Binding sites with an asterisk (*) are not included in the graphically displayed.	ical display.		

When you have selected the gene of your interest, press the button "Match Suite single gene" in the search results or click on the "Analyze <gene name> with MATCH Suite" button in the *Transcriptional regulation* section of the locus report of the selected gene, and you will be automatically transferred to the MATCH Suite tool. The wizard will automatically save and process the gene you have selected and in several seconds you will be taken to the *Specifying the launch parameters* step of the MATCH Suite single gene analysis wizard.

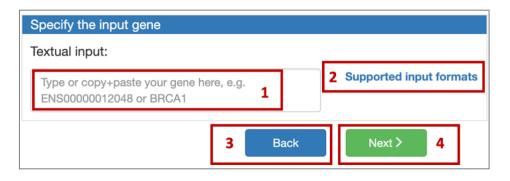
Specifying the input gene from the MATCH Suite interface

When you click on the *Start analysis* section, the system immediately navigates you to the analysis launch wizard. At the very first step of this wizard, you will be asked to select the type of the analysis you would like to perform:

Select an	alysis							
Single gene analysis								
\bigcirc Gene set analysis								
Next >								



If you will select the *Single gene analysis* option, you will be taken to the next step of the wizard, where you will be asked to specify the gene you want to use for the analysis:



You can launch the analysis by typing any gene symbol, Entrez gene ID or Ensembl gene ID into the **textual input field** (1). The **Supported input formats** (2) will assist you in providing the input gene in the correct format:

Supported input formats ×									
You can launch the analysis from any human gene coming in one of the following formats:									
Gene symbol	e.g. TNMD								
Gene Ensembl	e.g. ENSG0000000005								
Gene Entrez	e.g. 64102								
typed in the Textual i	input field								
	ok								

You can return to the MATCH Suite analysis type selection using the **Back** (3) button or click on **Next** (4) to proceed with specifying the launch parameters of the MATCH Suite single gene analysis.

Specifying the launch parameters

In the next step of the analysis launch wizard the MATCH Suite will ask you to fill in the following form:



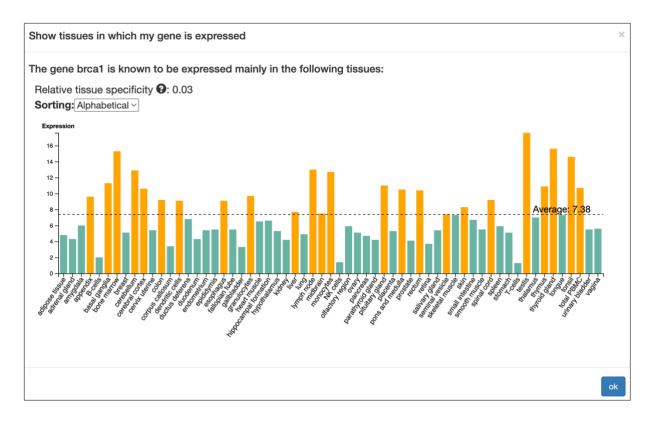
Name of the analysis launch					
	a1 1				
Studied tissue No	thing selected	•	2		
Sh	ow tissues in which	my gene is exp	pressed	3	
Tissue selection will allow to use tissue-sp identify the transcription factors regulation					
Tissue selection will also provide considera	tion of tissue-specif	ic enhancers/si	ilencers in c	ase any are kn	own to
be active for input gene in the selected tiss will l	ue. If tissue will not be considered in the		I known enh	ancers of inpu	t gene
Promoter range					
Use default promoter range	-500,+100]		4		
○ Customized promoter range					
From Max -5000	to	Max +1000			
Promoter type					
est supported promoter					
◯ most 5 prime	5				
O most 3 prime					
Profile optimization					
Narrow transcription factors se	arch to certain GO c		1		
Nothing selected	-	6	1		
			-		
7	< Back	Next >	8		

You can give a name to your analysis launch or keep the default name suggested by the system based on the gene you have submitted for the analysis in the **Name of the analysis launch** field (1). This name will be further used in the launches history for easy selection of the run of your interest.

Optionally you can specify the tissue of your interest from the dropdown list of supported tissues in the **Studied tissue** field (2). The provided tissues are the tissues from <u>FANTOM5</u> database with specific coordinates for the transcription start sites (TSSs) that allow to select tissue-specific promoters for the subsequent analysis. Tissue selection will also provide consideration of tissue-specific enhancers/silencers in case any are known to be active for input gene in the selected tissue. If tissue will not be selected, all known enhancers of input gene will be considered in the analysis. The selected tissue is also used further for identification of transcription factors that are known to be expressed in the tissue of your interest. Please refer to the <u>Methods</u> document for further details.

You can view the tissues in which the input gene is known to be mainly expressed by clicking on the **Show tissues in which my gene is expressed** (3) button:





The promoter range that will be used for the search of TFBS in your analysis run is specified by the **Promoter range** parameter (4). By default the promoter range used by the MATCH Suite is [-500,100] relative to the TSS. You can specify a customized promoter range limited to the maximum of -5000 and +1000 from TSS. The **Promoter type** (5) parameter allows you to specify which type of the promoter should be used in the analysis: best supported / most 5 prime / most 3 prime.

The search for transcription factors that are regulating the input gene can be narrowed to transcription factors that are encoded by genes belonging to the certain Gene Ontology (GO) categories. For this you can specify the GO categories of your interest from the provided dropdown list in the **Profile optimization** (6) field.

When done with parameters selection, click on **Next** (8) to proceed to the analysis launch confirmation or click on **Back** (7) to return to the input gene specification.

Confirming the launch parameters and starting the analysis

After specifying all parameters for your launch, the MATCH Suite wizard will ask you to confirm your selection:



Launch name:brca1 demo runInput:brca1Selected tissue:Nothing selectedPromoter range:[-500;+100]Promoter type:best supported promoterSelected GO categories:GO:0000003 reproduction • GO:0007049 cell cycle	cted launch parameter	s		
Selected tissue: Nothing selected Promoter [-500;+100] range: Promoter type: best supported promoter Selected GO • GO:0000003 reproduction	Launch name:	brca1 demo run	1	
Promoter [-500;+100] range: Promoter type: best supported promoter Selected GO • GO:0000003 reproduction	Input:	brca1	*	
range: Promoter type: best supported promoter Selected GO • GO:0000003 reproduction	Selected tissue:	Nothing selected		
Selected GO • GO:0000003 reproduction		[-500;+100]		
	Promoter type:	best supported promoter		

All parameters that you selected for the current launch will be shown on the screen (1). If you want to apply any changes to the specified parameters of the launch, click on **Back** (2), otherwise you are ready to start your analysis by clicking on the **Launch analysis** button (3).

Viewing the results

Operating in the Launch history

Once your analysis was launched, you will be redirected to the *Launch history* section, also accessible by the direct link at the left menu panel. The Launch history allows you to view the results of all your previous analysis runs and to follow the progress of the currently running analyses.

	Show/hide m	enu				
TCH I T E	Recent launch Select the analysis la	nes unch you want to view or start	a new analysis			
	Date	Name	Parameters	Status	Results	Terminate/Delet
t	2021.08.28 12:00:09	brca1 demo run	1 Single gene analysis View input parameters	Running: 8%	02 In progress	X 3
	2021.08.27 22:10:35	My launch 3	Single gene analysis View input parameters	Completed	View results	
	2021.08.27 21:59:00	My launch 3	Single gene analysis View input parameters	Completed	4 View results	
	2021.08.26 13:16:13	demo-gene-list	Gene set analysis View input parameters	Completed	View results	5
	2021.08.26 13:13:09	My launch 1	Single gene analysis View input parameters	Completed	View results	
C 2.0			Start new analysis 6			



You can check the parameters used for the launch by clicking on the **View input parameters** link (1). The following pop-up form will appear:

Launch parameters		×
brca1 demo	run 2022.03.31 22:58:57	
Input:	brca1	
Tissue selected during the analysis launch:	none	
Promoter range:	[-500,+100]	
Promoter type:	Most active	
GO categories selected to optimize the input profile:	show	
		ok

In case you have selected to optimize the profile used for the site search by certain GO categories, you can view them by clicking on the *show* link next to the *GO categories selected to optimize the input profile*. If no GO categories were selected, respective field will display *none*.

The progress of the currently running analysis will be displayed in the **Status** column (2). Please note that the progress is displayed in percentage of the finished steps of the underlying workflow and it has no direct correlation with the time left for the analysis to finish. Commonly one analysis run will take several hours, but this time interval is highly dependent on the input gene set and other parameters selected for the respective analysis launch.

It is not recommended to have several analysis launches running in parallel. Analysis runs will finish faster when launched consecutively one after another.

If you wish to terminate the launched analysis, you can click on the **Terminate** button (3).

To view the results of a finished analysis please click on the **View results** button (4).

You can manage the stored analysis results and delete the unnecessary data by clicking on the **Delete** icon (5). This action will delete all results of the respective analysis launch. By default, your MATCH Suite account is equipped with 2 GB disk space for storing your analysis results and inputs. You can extend this volume by contacting us via info@genexplain.com with a respective request.

You can launch a new analysis run directly from the *Launch history* section by clicking on the **Start new analysis** (6) button.



Results visualization

Having selected in the *Launch history* section the analysis result which you want to view, it will open in the results visualization mode on your screen.

In the results visualization mode the screen will be divided into four different segments with the following functions:

- (1) The **identified transcription factors** regulating your gene and respective **matrices tables**
- (2) The **table of analyzed regulatory regions of the input gene** and site hits found within them
- (3) The **info box** displaying the information about the currently selected object
- (4) The **genome browser**, allowing to visualize the tracks of found sites and additional annotation tracks for further results interpretation

		hide menu												
		o run: factor/ma						brca	1 demo run	: regulatory reg	ions view			
TCH ITE	Factor viev	Matrix view	Best factors on t	Remove all	filters 🖸 Apply ch	anges 🕢		Sho	w 10 ~ en	tries		First Pre	avious 1 N	ext L
5	Show 10	v entries		1	First Previous	1 2 3 4	Next Last	Sho	ving 1 to 7 of	7 entries	2		V\$GKLF_Q4	V\$IK_C
ysis	Factor name	Gene symbol	TF classification ↓ ♀	Site model	-log(affinity p- value) ✔	Average factor expression across all tissues	Expression specificity (rank of average)	•	Type ⊖ 0	Accession	Coordinates €	Total number of sites	KLF13, KLF15, KLF5	IKZF1, IKZF3, IKZF5
ults			High-mobility			U	•	1	promoter	BRCA1	17:43170146- 43170745	37	1	1
6	SOX-2	SOX2	group (HMG) domain factors 4.1.1.2.2	V\$SOX2_Q6	4.04	7.24	0.22 15/62	2	enhancer	EN000176039	17:43321712- 43324211	182	2	7
	ARNT2	ARNT2	Basic helix-loop- helix factors (bHLH)	V\$ARNTL_01	5.57	7.16	0.19	3	enhancer	EN000176018	17:43314502- 43317001	171	2	8
			1.2.5.2.2				17/62	4	enhancer	EN000176016	17:43318322- 43320821	149		15
	MondoB	MLXIPL	Basic helix-loop- helix factors (bHLH) 1.2.6.6.3	V\$CHREBP_Q6	3.1 <mark>4</mark>	6.82	0.27 13/62	5	enhancer	EN000176063	17:43328836- 43331085	73	1	1
			Basic helix-loop- helix factors					6	enhancer	EN000176064	17:43333120- 43334602	59	2	
	Mad1	MXD1	(bHLH)	V\$MYCMAX_03	2.86	10.89	0.17 17/62	7	enhancer	EN000024071	17:42886296-	18	3	

The Factor, Matrix and Regulatory regions tables that you see on the screen can be exported with the applied filters (see filtering instructions below) using the **Download tables button** (5). The archive containing these three tables in tabseparated text format will be downloaded to your local computer.



You can open the comprehensive analysis report about the respective run by clicking on the **Report** (6) link in the left menu panel. The self-explaining report will contain the factor, matrix and regulatory regions tables you see in the results visualization section along with supplementary tables and analysis steps description.

You can extend or narrow certain segments of the screen by moving the splitter lines. At this point you might want to use the *Show/hide menu* button, which will hide the left panel menu from view and will broaden the results area of the screen.

<u> </u>	Show/hi	de menu							_						
<i>*^/\</i> _	brca1 demo	run: factor/ma		_		_			brca	1 demo ru	n: regulatory reg	ions view			
TCH ITE	Factor view	Matrix view	Best factors on t	op 🤁 🛛 Remove a	all filters	Apply chan	ges 😯		Show	/ 10 ~ e	entries		First Pre	evious 1 N	lext Last
IIE	Show 10 $$ $$	entries			First	Previous	2 3 4	Next Last	Show	ing 1 to 7 o	f 7 entries				
d	Showing 1 to 1	0 of 40 entries							÷ .					V\$GKLF_Q4	V\$IK_Q5_
	Factor ¢	Gene symbol	TF classification 0	Site model		log(affinity p- alue) ∲ ₽	Average factor expression across all tissues	Expression specificity (rank of average)	*	Type ♀	Accession	Coordinates €	Total number of sites	KLF13, KLF15, KLF5 more	IKZF1, IKZF3, IKZF5
			High-mobility				•	v	1	promoter	BRCA1	17:43170146- 43170745	37	1	1
	SOX-2	SOX2	group (HMG) domain factors 4.1.1.2.2	V\$SOX2_Q6	8	04	7.24	22		Cor	EN000176039	17:43321712- 43324211	182	2	7
	ARNT2	ARNT2	Basic helix-loop- helix factors (bHLH)	V\$ARNTL_01	6	3.57	7.16	0.19	3	enhancer	EN000176018	17:43314502- 43317001	171	2	8
			1.2.5.2.2					17/62	4	enhancer	EN000176016	17:43318322- 43320821	149		15
	MondoB	MLXIPL	Basic helix-loop- helix factors (bHLH) 1.2.6.6.3	V\$CHREBP_Q6	3	14	6.82	0.27 13/62	5	enhancer	EN000176063	17:43328836- 43331085	73	1	1
			Basic helix-loop-						6	enhancer	EN000176064	17:43332 9- 43334	59	2	
	Mad1	MXD1	helix factors (bHLH) 1.2.6.7.1	V\$MYCMAX_03	e e	86	10.89	0.17 17/62	7	enhancer	EN000024071	17:4288	18	3	
	Info box			Genome	browse	yr			••••						
	Track Foun	deitee		Q Q	. «	Filter 🛛	No filter	 Displayed trac 	cks 😡	3 items sele	ected -				
	Sequence col					Chrom 0146	osome: 17 ✓ Po 43170200	sition: 17:43170146-431 43170300	70745	4317040		embl id	4317060		3170700 43
	databases/Ens GRCh38	emblHuman104	/Sequences/ch				43170200							· · · · · · · · · ·	

In the screen segment, which visualizes the tables of predicted factors and respective matrices, you will find two accessible tables: Factor view and Matrix view.

Factor view table

The **Factor view** table (1) provides the information on transcription factors identified to be regulating the input gene in the specified conditions. By default top 10 factors will be shown, this can be changed in **Show <number> entries** (2) field. The total number of factors identified will be displayed in (3). For single gene analysis in MATCH Suite this number will be always equal to 40, see <u>Methods</u> document for details. You can navigate through the predicted factors using the pages in (4). The columns of the *Factor view* table are fully matching the *Table 1* given in the analysis report of the respective run. You can refer to the analysis



report for denominations of column names and their contents or use the info hints provided in the results visualization interface as a mouseover message that will appear upon hovering above the **?** sign (5) available at multiple places in the interface.

brca1 demo run	: factor/matrix	view				
Factor view 1	Matrix view	Best factors on top 3	Remove all filters ?	Apply changes 3		
Show 10	Show 10 \sim entries 2		8	First 4 Previous	1 2 3 4	Next Last
Showing 1 to 10 of	f 40 entries 3]		L		
Factor name 🍦	Gene symbol	TF classification	Site model	-log(affinity p- value) ≑ ₢	Average factor expression across all tissues	Expression specificity (rank of average)
SOX-2	SOX2	High-mobility group (HMG) domain factors 4.1.1.2.2	V\$SOX2_Q6	4.04	7.24	<mark>0.22</mark> 15/62
ARNT2	ARNT2	Basic helix-loop- helix factors (bHLH) 1.2.5.2.2	V\$ARNTL_01	5.57	7.16	0.19 17/62
MondoB	MLXIPL	Basic helix-loop- helix factors (bHLH) 1.2.6.6.3	V\$CHREBP_Q6	3.14	6.82	<mark>0.27</mark> 13/62
Mad1	MXD1	Basic helix-loop- helix factors (bHLH) 1.2.6.7.1	V\$MYCMAX_03	2.86	10.89	0.17 17/62
KLF15	KLF15	C2H2 zinc finger factors 2.3.1.2.15	V\$GKLF_Q4	18.00	11.82	0.07 22/62

The columns of tables have in-built sorting option (6) which allows to sort the values within one column by ascending or descending order or by alphabetical order in case of textual contents. Simply click on the gray arrows for the sorting to be applied. By default, best factors (or matrices) are brought to the top (please see the analysis report and the <u>Methods</u> document for explanations on the factors and matrices ranking procedures). If you want to return to the original order of factors, click on the **Best factors on top** button (7). If filters were applied using the matrix table or the genome browser visualization, you can cancel the applied filtering by clicking on the **Remove all filters** button (8).

Matrix view table

The **Matrix view** table (1) shows the PWMs (positional weight matrices) of the TRANSFAC[®] library, the respective sites of which were identified in the studied regulatory regions of the input gene.



Similar to the factors table, the *Best matrices on top* button allows to bring the best matrices to the top of the matrix table in case their order was changed while sorting the values in individual columns. This table fully corresponds to the *Table 2* of the analysis report, where you can find the denominations of its column names and their contents description. Respective info is also summarized in the ? hints available as mouseover messages upon hovering above them, similar to the *Factor view* table.

brca1 demo run: fac	tor/matrix viev	v										
Factor view 1 Mat	trix view Be	st matrices on top ?	Remove all filters ?	Apply changes	94							
-log(affinity p-value	e) 😯	2	Site score 🕢		3							
1.8 5.0 8.2	11.4 14.6	17.8	0 .8	0.9	1.0							
Show 10 ~ entries	5			First Prev	vious 1	2 3 Next	Last					
Showing 1 to 10 of 24	Showing 1 to 10 of 24 entries											
Matrix ID		Matrix log P	jo	Number of sites	Affinity score	-log(affinity p-value) <mark>♥</mark>	Site score 🍦					
V\$GKLF_Q4		2		11	5.92	18.00	1.00					
V\$IK_Q5_01	<u>_</u> GG _G A_	-		32	5.79	11.54	1.00					
V\$AP2GAMMA_Q5	_ <mark>GCC</mark> _			1	4.23	9.09	1.00					
V\$PATZ1_04	유수수모요		SC-	23	13.94	7.19	0.98					
V\$BCL6_01	Z	· · · · · · · · · · · · · · · · · · ·	T.	18	6.22	6.87	0.97					
V\$TAF1_07	Gecec	<u>Gc</u>		53	3.95	6.85	1.00					

The **-log(affinity p-value) filter** (2) allows to leave only matrices with -log(affinity p-value) values higher than the threshold specified by the filter. The set filter will be first applied exclusively to the *Matrix view* table. To recalculate the factors and the regulatory regions tables, as well as the track of the found sites in the genome browser, only with matrices that were left after applying the filter, you should click on the *Apply changes* button.

The **Site score filter** (3) allows to leave only matrices with site score values higher than the threshold specified by the filter. The set filter will be first applied exclusively to the *Matrix view* table. To recalculate the factors and the regulatory regions tables, as well as the track of the found sites in the genome browser, only with matrices that were left after applying the filter, you should click on the **Apply changes** (4) button.



Filters will be also auto applied to all tables and tracks when you will switch from matrix table to the factor table or vice versa. To cancel the filters, click on the *Remove all filters* button.

Regulatory regions table

The regulatory regions table presented in the results visualization section fully corresponds to the regulatory regions table provided in the *Table 3* of the analysis report, where you can find the denominations of its column names and their contents description. Respective info is also summarized in the **?** hints available as mouseover messages upon navigating on them, similar to the *Factor view* and *Matrix view* tables.

brca	brca1 demo run: regulatory regions view										
Show	w 10 ~ er	ntries						First	Previous 1	Next	Last
Show	Showing 1 to 7 of 7 entries										
				Total - number of sites	V\$GKLF_Q4	V\$IK_Q5_01	V\$AP2GAMMA_Q5	V\$PATZ1_04	V\$BCL6_01 🔅	V\$TAF1_07 🔅	v
	Type ✔	Accession	Coordinates		KLF13, KLF15, KLF5 more	IKZF1, IKZF3, IKZF5	AP-2alpha	MAZ, VEZF1	BCL-6	LEF-1, TCF-7	D
1	promoter	BRCA1	17:43170146- 43170745	37	1	1			2	2	
2	enhancer	EN000176039	17:43321712- 43324211	182	2	7		3	7	14	
3	enhancer	EN000176018	17:43314502- 43317001	171	2	8		13	3	18	
4	enhancer	EN000176016	17:43318322- 43320821	149		15		5	1	14	
5	enhancer	EN000176063	17:43328836- 43331085	73	1	1		1	4	3	
6	enhancer	EN000176064	17:43333120- 43334602	59	2		1	1	1	1	
7	enhancer	EN000024071	17:42886296- 42886595	18	3					1	

To visualize in genome browser the sites found in the certain regulatory region (promoter / enhancer / silencer), just click on the line with the regulatory region of your interest inside the regulatory regions table and refer to the genome browser below to explore the predicted regulation model of the respective region.

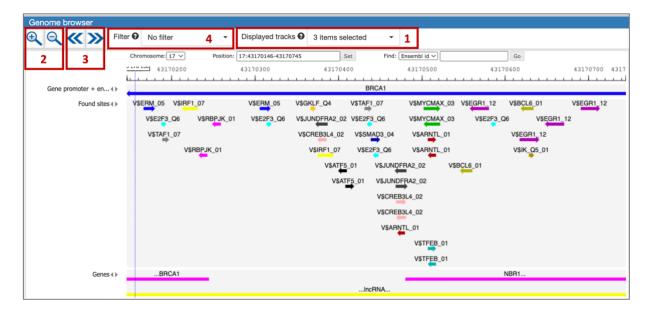
Genome Browser

The genome browser provides you with visualizations of the predicted regulation models for each of the studied regulatory regions of the input. Having clicked on any regulatory region from the *Regulatory regions table*, the model of the

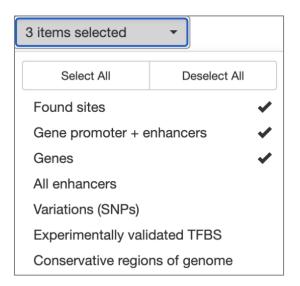


respective regulatory regions will be automatically opened in the genome browser with visualization of the sites found within the respective regions. By default the displayed tracks include:

- **Gene promoter + enhancers** the track of all regulatory regions that were used for the performed analysis
- **Found sites** the track of all sites found to have cumulative binding affinity to the studied regulatory regions (see <u>Methods</u> for further info)
- Genes the track with all Ensembl genes



Displayed tracks can be customized using the **Displayed tracks** dropdown list (1)



You can zoom in and zoom out for a more generalized or a more detailed view of the regulatory region model using the **zoom in** and **zoom out** buttons (2). In case navigation in genome browser is lost due to multiple zoom clicks, you can always



return to the regulatory region of your interest by selecting the respective regulatory regions entry in the table of regulatory regions.

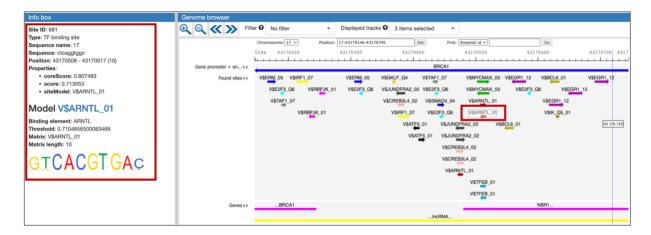
Navigation through the track is supported by the **Shift to the left** and **Shift to the right** buttons (3)

Filtering can be applied to the displayed sites using the **Filter** option (4):

No filter -
No filter
View only sites near the conservative regions of genome

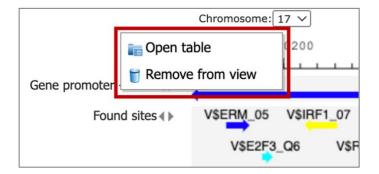
Depending on your selection, only sites intersecting with the conservative regions of the genome can be displayed. The regulatory regions table will be automatically recalculated leaving only the hits for the sites left after applying the respective filter. To cancel the applied filter, select the *No filter* option in the dropdown list of filters.

For receiving additional information about any of the found sites, you can click on the site of your interest and explore the contents displayed in the *Info box* section:



A right click on the track name in genome browser will open a context menu allowing you to remove the track from the visualization or open it as a table (function supported only for track of found sites or regulatory regions track):





Tracks opened as table can be exported using the *Export* button at the top menu panel or used for further analysis from the geneXplain platform perspective.

≏	⑦ User guide								MATCH Suite
Start	age 🛷 Found sites X								
									Select all Select pag
First	Previous Page 1 of 14 Next	Last Show	ing 1 to 50 of	689 entries				:	Show 50 🗸 entries
ID 🔺	Sequence (chromosome) name	🔷 From 🔶	То 🔶	Length 🔷	Strand 🔷	Туре 🍦	Property: coreScore 🔶	Property: score 🍦	Property: siteModel 🍦
1	17	42886310	42886324	15	+	TF binding site	0.8181	0.85072	V\$JUNDFRA2_02
2	17	42886311	42886322	12	+	TF binding site	1	0.96061	V\$NFE2L1_Q5
3	17	42886311	42886322	12	+	TF binding site	0.74828	0.81669	V\$CREB3L4_02
4	17	42886391	42886401	11	+	TF binding site	0.94133	0.86479	🕿 <u>V\$ATF5 01</u>
5	17	42886394	42886400	7	+	TF binding site	1	1	V\$GKLF_Q4
6	17	42886411	42886421	11		TF binding site	1	0.92022	V\$RBPJK 01
7	17	42886426	42886434	9	+	TF binding site	0.92074	0.94714	V\$TAF1 07
	17	42886444	42886457	14	-	TF binding site	0.91624	0.81753	V\$ERM 05

The list of available export formats is as follows:

Export document X							
Format:	FASTA sequences (*.fasta)	۲	1				
	FASTA sequences (*.fasta)		ſ				
	BED format (*.bed)						
	Interval format (*.interval)		cel				
	General Feature Format (*.gff)						
	Gene Transfer Format (*.gtf)						
	Match format (*.match)						
	Variant Call Format (*.vcf)						
	Wiggle format (*.wig)						



Switching to geneXplain platform

All results received with the MATCH Suite can be further analyzed in the geneXplain platform tool, access to which is provided to all users of the MATCH Suite. GeneXplain platform is a comprehensive online toolbox and workflow management system for a broad range of bioinformatics and systems biology applications.

For switching from the MATCH Suite perspective view to the geneXplain platform view, please use the perspectives switcher located at the top upper corner of the screen:

MATCH S	Suite 🗸					
Platform						
MATCH Suite						

Please, refer to the User Guide of the geneXplain platform for detailed description of its functions.

