

Bioinformatics tool: Standalone interface – R package (Bioconductor)

« ***BiomiX**, a user-friendly bioinformatic tool for automatized multiomics data analysis and integration* »

LBAI: [Lymphocytes B, Autoimmunité et Immunothérapies - UMR 1227](#)

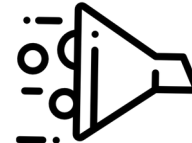
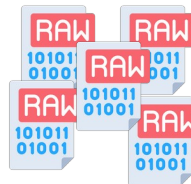
Authors: Cristian Iperi **Supervisors:** Álvaro Fernández-Ochoa, Anne Bordon, Christophe Jamin

Why BiomiX?



*The usage of high-throughput technology in health and biological sciences boosted the amount of information obtainable from samples, ensuring highly robust disease diagnosis and consistent research approaches. The increased dependency on these technologies **revealed how data analysis represents the bottleneck step both in time and in skilled bioinformatics users.***

*The **BiomiX** offers an efficient and fast pipeline to **analyze -omics data individually and integrate multi-omics data** from the same patients **within the same tool.***



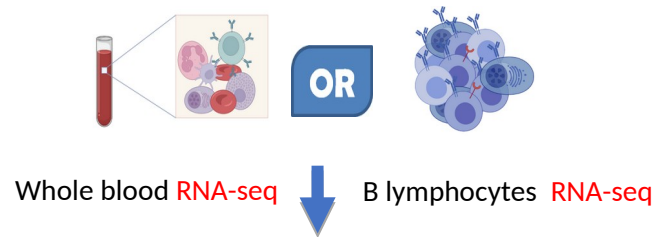
The Input



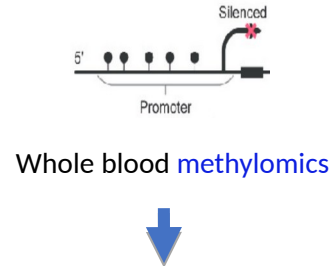
Pipeline on PRECISEADS consortium datasets

Raw matrices + Metadata tables

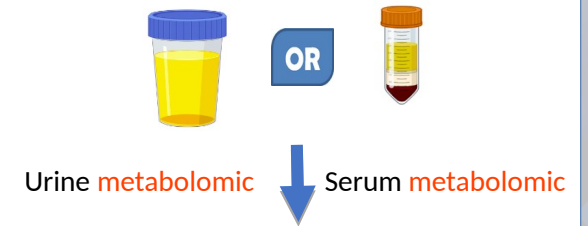
Transcriptomic data*



Methylomics data*

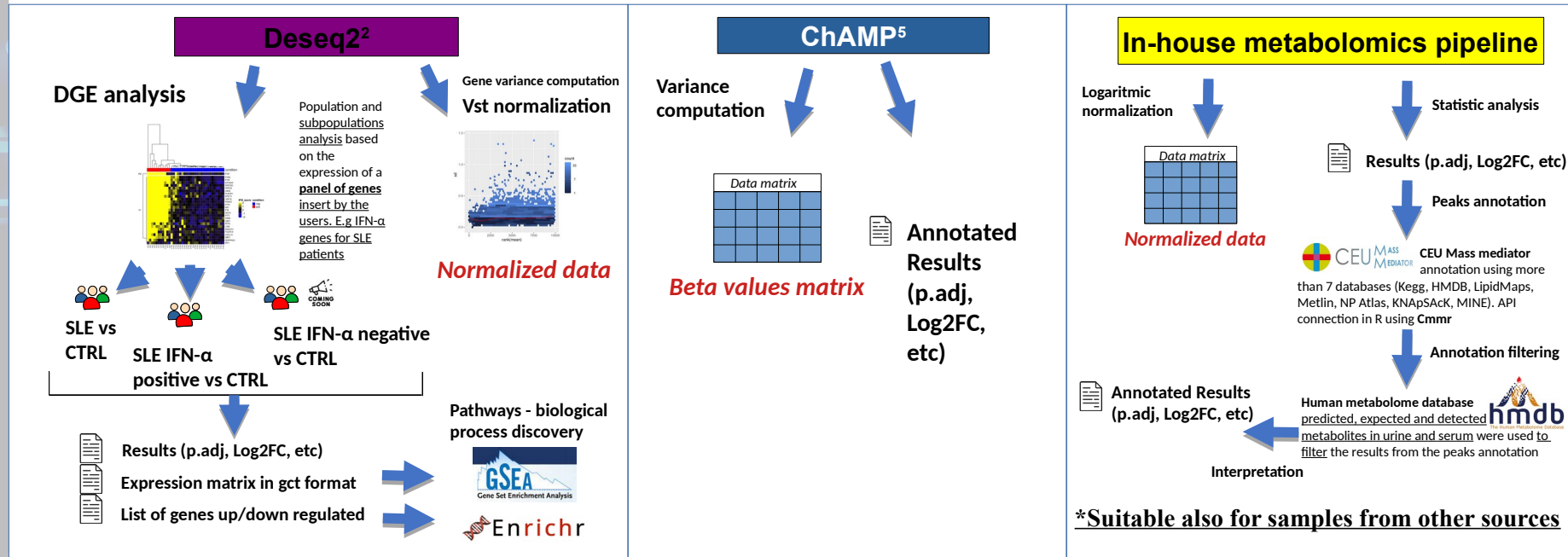


Metabolomic data*



*Suitable also for samples from other sources

The single -omics Pipeline



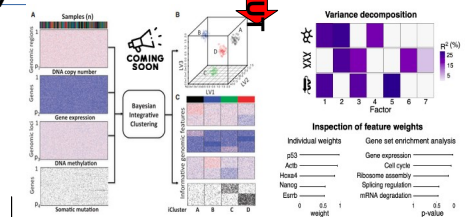
The integration Pipeline



Transcriptomic data*

Methylomics data*

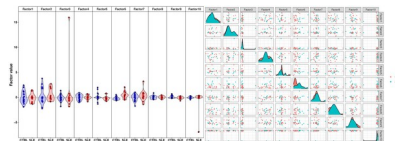
Metabolomic data*



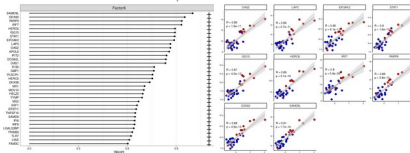
IclusterPlus

MOFA

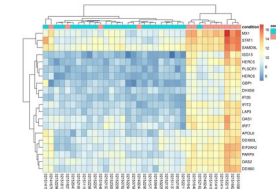
Multomics data integration



Identification discriminant factors



Identification features contributing to discriminant factors



Clustering and heatmap based on discriminant factors

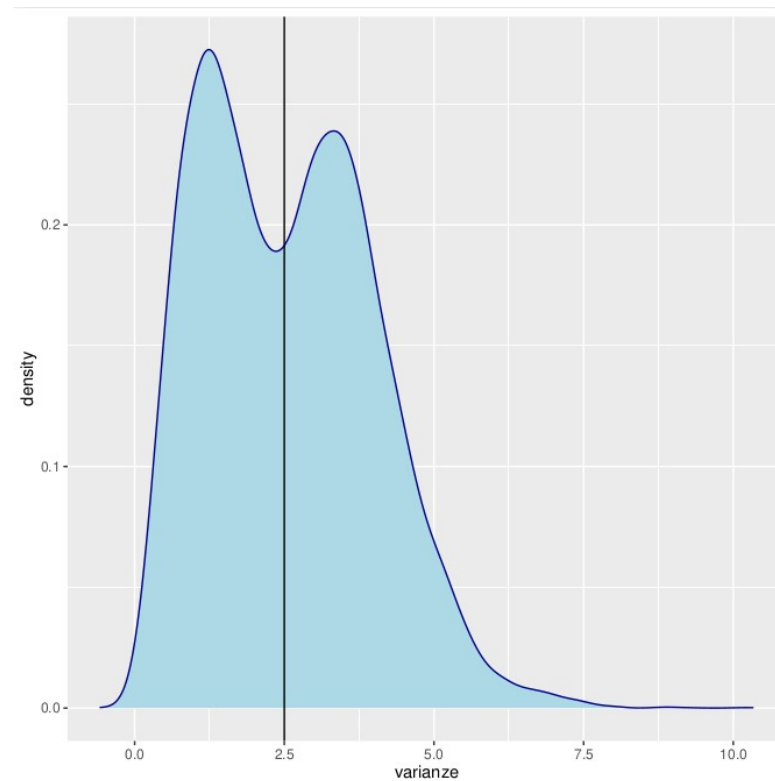
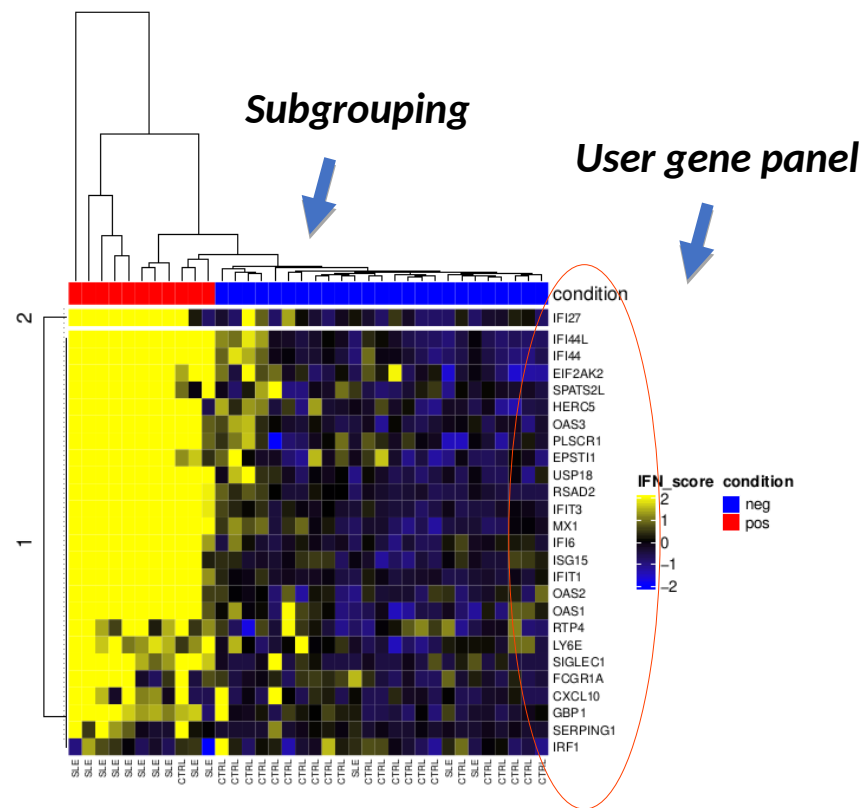
Transcriptomics analysis in details

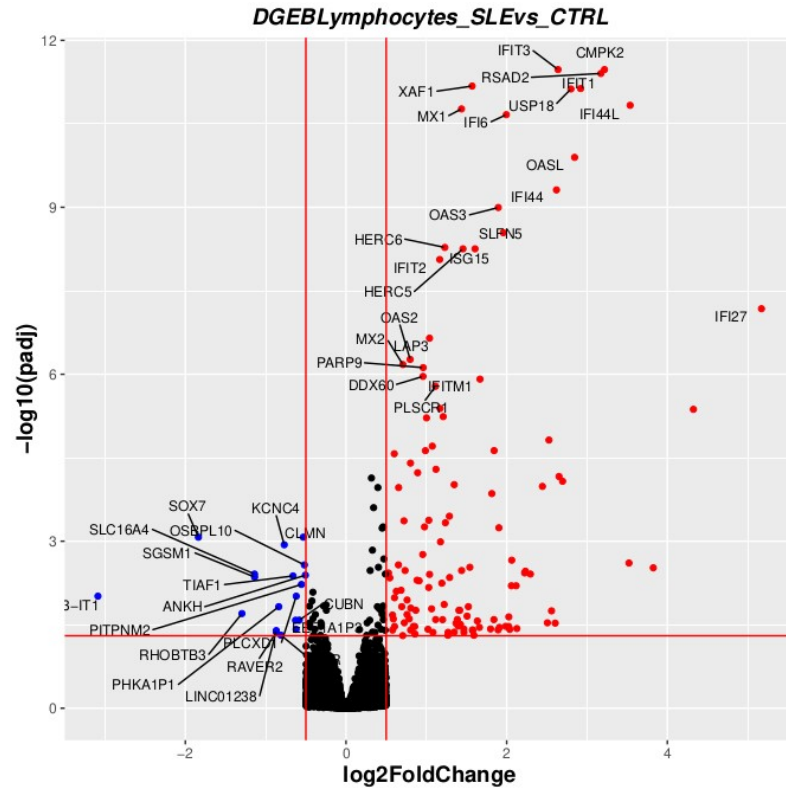


The differential gene expression analysis is made using Deseq2. The threshold is set to provide results with $\text{Log2FC} > |0.5|$ and adjusted p.value < 0.05 .

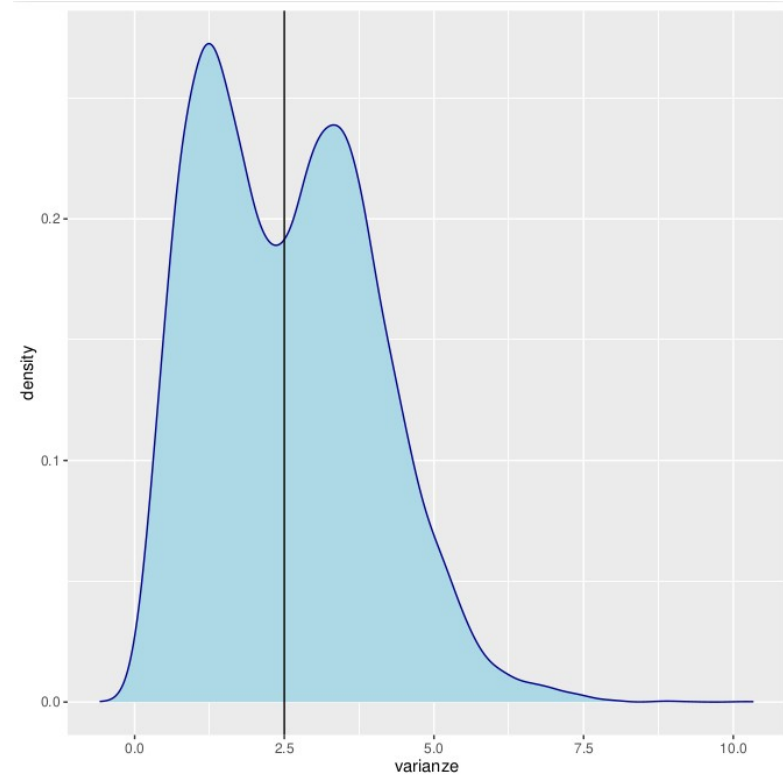
*The **panel of genes** allows to study subpopulations together with the whole population (e.i Interferon-alpha positive/negative). For each comparison the output includes the results file, the data matrix in .gct format for the **GSEA analysis** and the list of the genes up/downregulated for the **EnrichR** analysis. Also, a **volcano plot** is drawn for each condition*

*The subgrouping plot using the gene panel is provided, also with threshold parameters to increase and improve the subgrouping sensibility. It is **possible to use an external marker to validate** the belonging of the **subgroups**. A **plot** resuming the **genes variances** is also produced.*





Volcano plot differential gene expression (ggplot)



Gene variance distribution

Metabolomics analysis in details



The peaks signal analysis is made using an in-house script calculating Log2FC and adjusted p.values from Mann-Whitney corrected with FDR. . The threshold is set to provide results with $\text{Log2FC} > |0.5|$ and adjusted p.value < 0.05 .

*The script seeks a match between the peaks annotations and the 7 databases linked to **CEU MASS MEDIATOR** (Kegg, HMDB, LipidMaps, Metlin, NP Atlas, KNApSack, MINE) and retrieves the candidate metabolites. The **candidate metabolites in urine and serum metabolomics can be filtered** using the metabolites previously predicted or detected in the scientific community, **to reduce the number of candidates**.*

The output file contains adducts, names, mass and links for the 7 databases for each metabolite.

Name	Formula	Adduct	Molecular Weight	PPM Error	Ionization Score	Final Score	Keeg	Keeg_URI	HMDB_URI	LipidMaps	LipidMaps_URI
Hydroxychloroquine	C18H26ClN3O	M+H	335.176440176	1	-2	-2	C07043	http://www.genome.jp/kegg/compound/show?C07043	http://www.hmdb.ca/metabolites/HMDB000000000	NA	NA
OR-1896	C13H15N3O2	M+H	245.116426739	1	-2	-2	NA	NA	http://www.hmdb.ca/metabolites/HMDB000000000	NA	NA
PC(14:0/22:5(4Z,7Z,10Z,13Z,16Z))	C44H78NO8P	M+Na	779.546504989	8	11.489675	NA	NA	NA	http://www.hmdb.ca/metabolites/HMDB000000000	LMGP01012130	http://www.lipidmaps.org/di
PC(14:0/22:5(7Z,10Z,13Z,16Z,19Z))	C44H78NO8P	M+Na	779.546504989	8	11.489675	NA	NA	NA	http://www.hmdb.ca/metabolites/HMDB000000000	LMGP01012131	http://www.lipidmaps.org/di
PC(14:1(9Z)/22:4(7Z,10Z,13Z,16Z))	C44H78NO8P	M+Na	779.546504989	8	11.489675	NA	NA	NA	http://www.hmdb.ca/metabolites/HMDB000000000	LMGP01011407	http://www.lipidmaps.org/di
PC(16:0/20:5(5Z,8Z,11Z,14Z,17Z))	C44H78NO8P	M+Na	779.546504989	8	11.489675	NA	NA	NA	http://www.hmdb.ca/metabolites/HMDB000000000	LMGP01010633	http://www.lipidmaps.org/di
PC(16:1(9Z)/20:4(5Z,8Z,11Z,14Z))	C44H78NO8P	M+Na	779.546504989	8	11.489675	NA	NA	NA	http://www.hmdb.ca/metabolites/HMDB000000000	LMGP01010695	http://www.lipidmaps.org/di
PC(16:1(9Z)/20:4(8Z,11Z,14Z,17Z))	C44H78NO8P	M+Na	779.546504989	8	11.489675	NA	NA	NA	http://www.hmdb.ca/metabolites/HMDB000000000	LMGP01012139	http://www.lipidmaps.org/di
PC(18:1(11Z)/18:4(6Z,9Z,12Z,15Z))	C44H78NO8P	M+Na	779.546504989	8	11.489675	NA	NA	NA	http://www.hmdb.ca/metabolites/HMDB000000000	LMGP01012152	http://www.lipidmaps.org/di
PC(18:1(9Z)/18:4(6Z,9Z,12Z,15Z))	C44H78NO8P	M+Na	779.546504989	8	11.489675	NA	NA	NA	http://www.hmdb.ca/metabolites/HMDB000000000	LMGP01011604	http://www.lipidmaps.org/di
PC(18:2(9Z,12Z)/18:3(6Z,9Z,12Z))	C44H78NO8P	M+Na	779.546504989	8	11.489675	NA	NA	NA	http://www.hmdb.ca/metabolites/HMDB000000000	LMGP01011625	http://www.lipidmaps.org/di
PC(18:2(9Z,12Z)/18:3(9Z,12Z,15Z))	C44H78NO8P	M+Na	779.546504989	8	11.489675	NA	NA	NA	http://www.hmdb.ca/metabolites/HMDB000000000	LMGP01011626	http://www.lipidmaps.org/di
PC(18:3(6Z,9Z,12Z)/18:2(9Z,12Z))	C44H78NO8P	M+Na	779.546504989	8	11.489675	NA	NA	NA	http://www.hmdb.ca/metabolites/HMDB000000000	LMGP01011653	http://www.lipidmaps.org/di
PC(18:3(9Z,12Z,15Z)/18:2(9Z,12Z))	C44H78NO8P	M+Na	779.546504989	8	11.489675	NA	NA	NA	http://www.hmdb.ca/metabolites/HMDB000000000	LMGP01011683	http://www.lipidmaps.org/di

Example partial metabolomics results table

Methylomics analysis in details



The evaluation of the different methylations in the CpG island was made using ChAMP. And so the annotation and the linkage with the genes. For further information, we suggest you take a look at the article and the package.

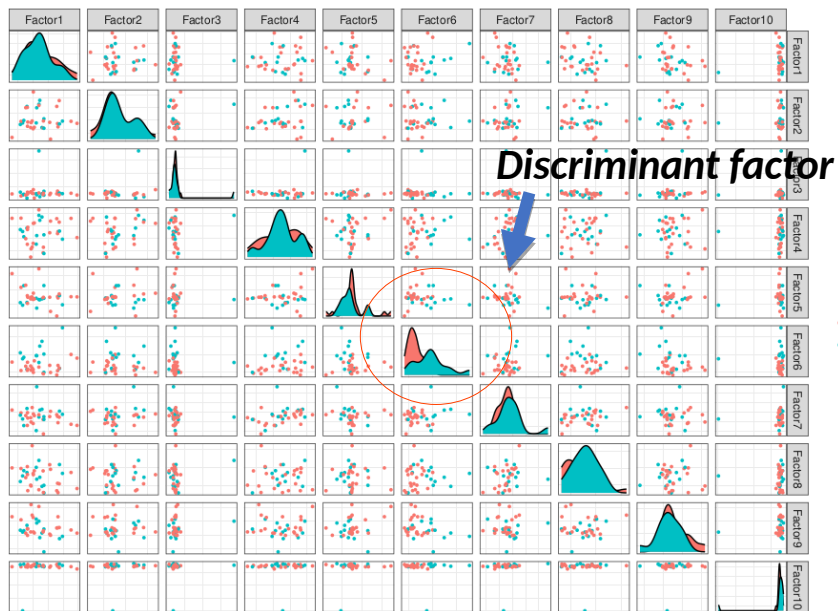
<https://www.bioconductor.org/packages/devel/bioc/vignettes/ChAMP/inst/doc/ChAMP.html>

MOFA analysis in details

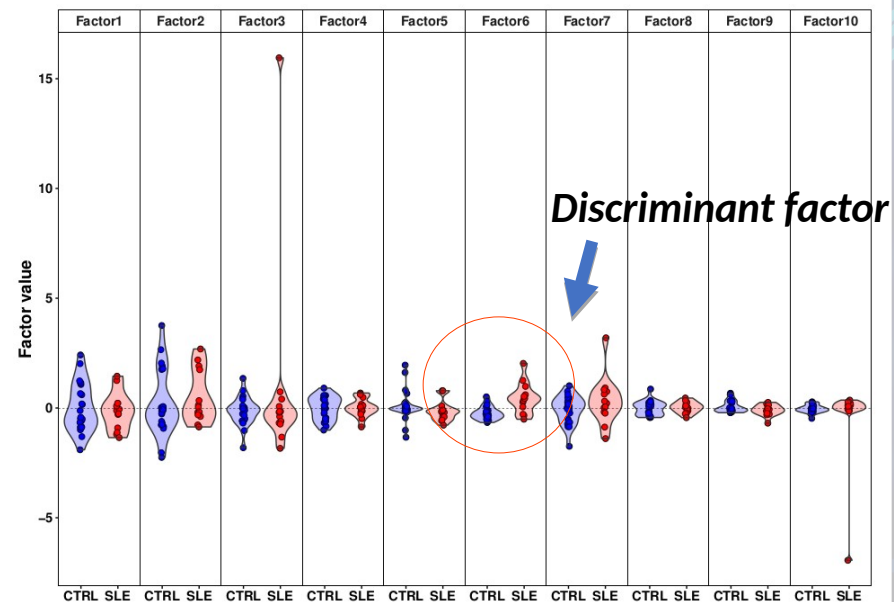


The usage of MOFA is based on the identification of factors to distinguish the two **conditions/populations** that we are interested in. The tool allows selecting the number of factors calculated and the ones on which we want to focus further analysis (**discriminating factor**).

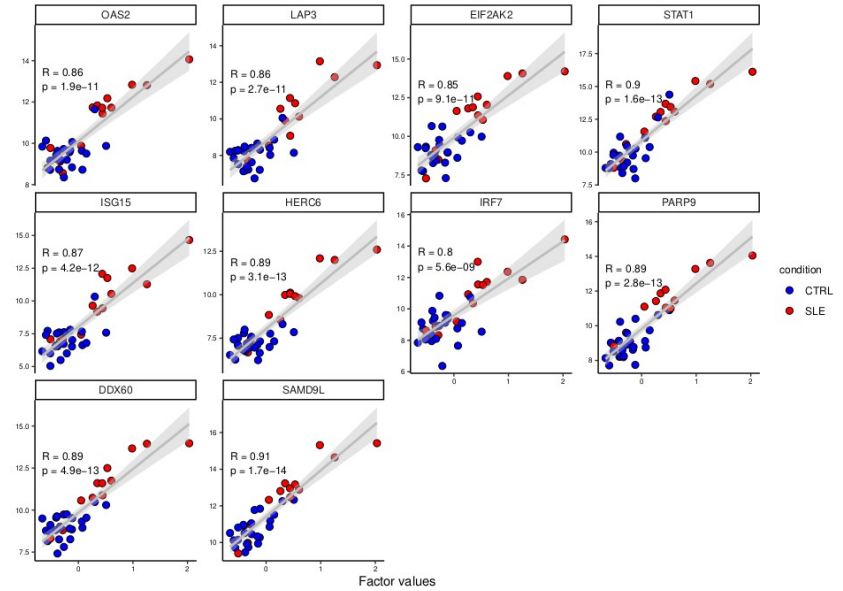
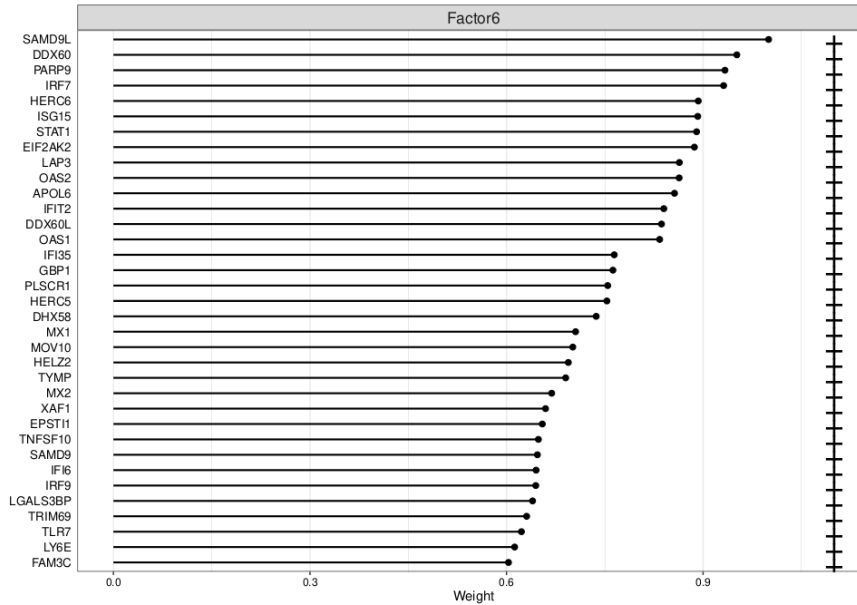
MOFA allows **testing the clustering efficiency** of our conditions in the -Omics contributing to the **chosen discriminating factor**, by heatmaps. It also shows the top features (genes/peaks/CpG island) with higher weight in the selected factor.



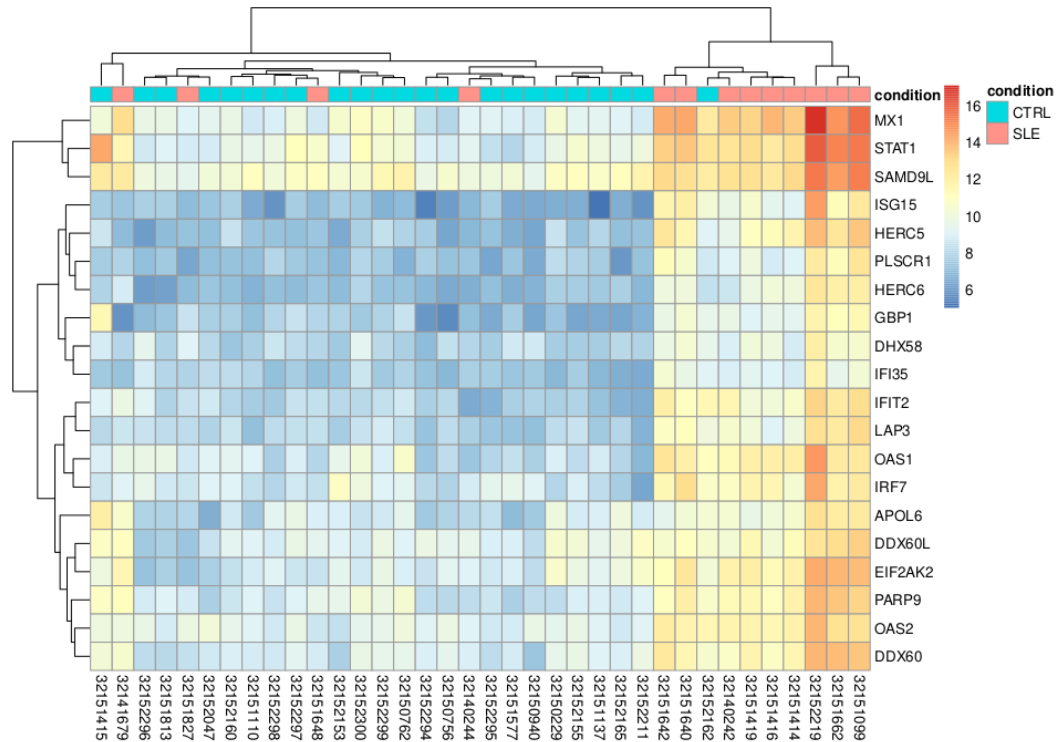
Ggally plot to select the discriminant factor



Violin plot to select the discriminant factor



B cell top genes contributing to discriminant factor and their scatter plot



Whole blood heatmap and clustering of top genes contributing to discriminant factor

Further information and usage?



BiomiX is written in R language, and the interface in python.

If you are interested in using it please write your e-mail and name into the google document here.

https://docs.google.com/spreadsheets/d/10V0QF5leqdT5fhG_nhh-NLuyGzWELbFNLWzP4a3YwTc/edit?usp=sharing

If you want to use the beta-version, please contact me:

cristian.iperi@univ-brest.fr/cristian.iperi@gmail.com

