online}Ce message contient des images, Si vous ne les voyez pas, consultez-le en ligne{/readonline}

METABOHUB

Newsletter-1

Juillet 2014

Dear readers,

MetaboHUB is the French infrastructure in Metabolomics & Fluxomics created in 2013 in the framework of the Program "Investissements d'Avenir" (Investment for the Future) launched by the French Ministry of Research and Higher Education and the National Agency for Science (ANR).

MetaboHUB aims at providing state-of-the-art tools, *services* and support in metabolomics and fluxomics to academic research teams and industrial partners in the fields of *nutrition, health, agriculture and biotechnology*.

MetaboHUB will be developed in two phases, a construction and an operational phase. We are moving forward the construction phase to harmonizing, implementing and up-grading the *four existing platforms* with common metabolomics and fluxomics tools, and methods in order to build a world-class national research center and database in metabolomics.

We hope you enjoy reading this newsletter.

Kind regards,

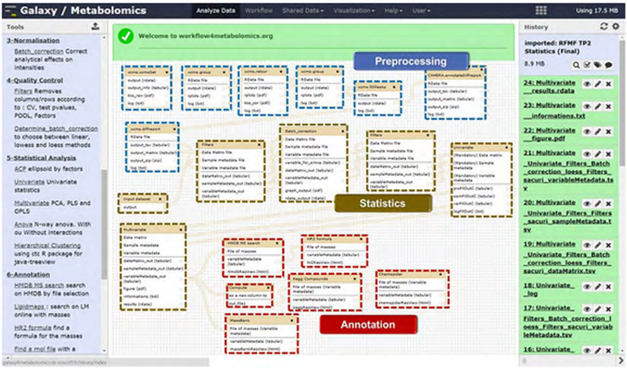
Dominique Rolin

MetaboHUB Coordinator

Innovation

Launch of the workflow4metabolomics online bioinformatics IFB-MetaboHUB platform for metabolomics data processing, analysis and annotation

Jointly developed by the French Bioinformatics Institute (*ABiMS* platform) and MetaboHUB, the workflow4metabolomics (W4M) collaborative portal dedicated to metabolomics data processing, analysis and annotation was officially launched in May 2014. The Galaxy environment provides user-friendly interface (e.g. a workflow editor) as well as convenient functionalities to store and share workflows (modules and their parameters) and histories (input and output data from each analysis). Modules necessary to build a full LC-MS workflow (pre-processing with XCMS and CAMERA, analytical drift correction, uni- and multivariate analysis, and annotation with public databases) are already available.


Galaxy / Metabolomics
Analyze Data
Workflow
Shared Data
Visualization
Help
User
Using 17.5 MB
Tools
3-Normalisation
Batch_correction Correct analytical effects on intensities
4-Quality Control
Filters Removes columns/rows according to : CV, test pvalues, POOL, Factors
Determine_batch_correction to choose between linear, lowess and loess methods
5-Statistical Analysis
ACP ellipsoid by factors
Univariate Univariate statistics
Multivariate PCA, PLS and OPLS
Anova N-way anova. With ou Without interactions
Hierarchical Clustering using ctc R package for java-treeview
6-Annotation
HMDB MS search search on HMDB by file selection
Lipidmaps : search on LM online with masses
HR2 formula find a formula for the masses
Find a mol file with a
Welcome to workflow4metabolomics.org
Preprocessing
Statistics
Annotation
History
imported: RFMF TP2 Statistics (Final)
8.9 MB
24: Multivariate__results.rdata
23: Multivariate__informations.txt
22: Multivariate__figure.pdf
21: Multivariate_Univariate_Filters_Batch_correction_loess_Filters_sacuri_variableMetadata.tsv
20: Multivariate_Univariate_Filters_Filters_sacuri_sampleMetadata.tsv
19: Multivariate_Univariate_Filters_Batch_correction_loess_Filters_sacuri_dataMatrix.tsv
18: Univariate__log
17: Univariate_Filters_Batch_correction_loess_Filters_sacuri_variableMetadata.tsv
16: Univariate_

Web portal of the workflow4metabolomics enabling users to select the analysis modules, create their own workflow, run the analyzes and save their data (http://workflow4metabolomics.org)

Monsoor M., Le Corguille G., Landi M., Petera M., Pericard P., Duperier C., Tremblay-Franco M., Martin J., Goulitquer S., Thévenot E., Giacomoni F. and Caron C. (2014). workflow4metabolomics.org. Galaxy Community Conference, Baltimore (poster).

In the coming months, new modules will be added to allow NMR pre-processing, provide a connection to the MetaboHUB spectral database (under construction) and to the *MetExplore* resource for pathway analysis.

A novel platform for automated high-throughput fluxome profiling of metabolic variants

Heux Stéphaniea, b, c , Poinot Juliettea, b, c, Massou Stéphanea, b, c, Sokol Sergueia, b, c, Portais Jean-Charlesa, b, c

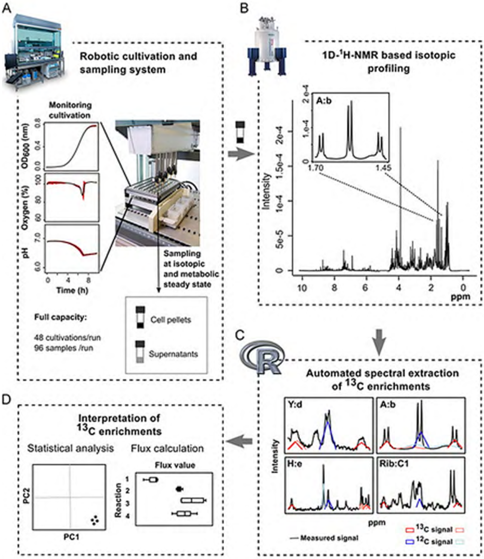
Metabolic Engineering, In Press, Uncorrected Proof

a Université de Toulouse; INSA, UPS, INP; LISBP, 135 Avenue de Rangueil, F-31077 Toulouse, France

b INRA, UMR792, Ingénierie des Systèmes Biologiques et des Procédés, F-31400 Toulouse, France

c CNRS, UMR5504, F-31400 Toulouse, France

Advances in metabolic engineering are enabling the creation of a large number of cell factories. However, high-throughput platforms do not yet exist for rapidly analyzing the metabolic network of the engineered cells. To fill the gap, we developed an integrated solution for fluxome profiling of large sets of biological systems and conditions. This platform combines a robotic system for 13C-labelling experiments and sampling of labelled material with NMR-based isotopic fingerprinting and automated data interpretation. As a proof-of-concept, this workflow was applied to discriminate between Escherichia coli mutants with gradual expression of the glucose-6-phosphate dehydrogenase. Metabolic variants were clearly discriminated while pathways that support metabolic flexibility towards modulation of a single enzyme were elucidating. By directly connecting the data flow between cell cultivation and flux quantification, considerable advances in throughput, robustness, release of resources and screening capacity were achieved. This will undoubtedly facilitate the development of efficient cell factories.


A
Robotic cultivation and sampling system
Monitoring cultivation
OD600 (nm)
0.0
0.4
0.8
Oxygen (%)
60
80
100
pH
6.0
7.0
0
4
8
Time (h)
Sampling at isotopic and metabolic steady state
Full capacity:
48 cultivations/run
96 samples /run
Cell pellets
Supernatants
B
1D-¹H-NMR based isotopic profiling
A:b
1.70
1.45
Intensity
0
5e-5
1e-4
1.50e-4
2e-4
10
8
6
4
2
0
ppm
C
Automated spectral extraction of ¹³C enrichments
Y:d
A:b
H:e
Rib:C1
Intensity
ppm
Measured signal
¹³C signal
¹²C signal
D
Interpretation of ¹³C enrichments
Statistical analysis
Flux calculation
PC1
PC2
Flux value
Reaction
1
2
3
4

Integrated platform for fluxome profiling

(A) E. coli cells were grown and harvested on a robotic platform. This platform allowed the preparation, running, monitoring (growth, pH and oxygen) and control (pH, temperature, stirrer speed) of 48 parallel micro-scale (10 ml) cultivations with ^{13}C-labelled substrates. An automated process allowed harvesting of biomass at targeted optical density (OD_{600}) and preparation of samples (i.e. supernatant and cell pellets) for further analysis. Examples of offline measurement of growth (OD at 600 nm) and online measurement of pH and oxygen during batch cultivation of a wild type (WT) E. coli strain on ^{13}C-labelled glucose in the bioreaction block (V=15 ml, T=37 °C, stirred at 2200 rpm) are presented. Mean and standard deviations (red area) of 4 replicates are shown.

(B) Labelling patterns were measured on a high resolution (800 MHz) NMR spectrometer equipped with a cryoprobe and an autosampler. A representative 1D–^{1}H-NMR spectrum of labeled biomass hydrolysates (1.5 mg of dry biomass) obtained from WT E. coli cells grown on labelled glucose is shown.

(C) Spectral data were automatically processed using a program developed in R. This allows automatic quantification of ^{13}C enrichments from the spectra by incorporating ^{1}H–^{13}C and ^{1}H–^{12}C signals using triangle modelling. A subset of 4 protonated carbon positions is shown as an example. Triangles for ^{1}H–^{13}C and ^{1}H–^{12}C signals of the corresponding carbon position are dark gray and triangles for others signals are pale gray.

(D) Processed data are delivered in formats suitable for statistical and flux analysis.

Aquisition of an OrbitrapTM FusionTM

The metabolome IDF platform develops analytical tools for metabolomic and lipidomic analysis by the use of high resolution mass spectrometry coupled with ultra- and high-performance liquid chromatography systems (LC-HRMS). This platform aims to participate in the metabolomic analysis of biological samples collected from medical cohorts in order to discover biomarkers for the diagnosis and follow-up of diseases, but also to monitor the efficacy of drug treatments. It's also involved in the development of quantification methods of metabolites, and in building relational databases of metabolites and metabolic signatures under various physiological and pathological conditions. Our platform also supports clinical laboratories for a better medical monitoring of patients.

Acquiring an OrbitrapTM FusionTM in the laboratory will enable to access to very high mass resolution capabilities (in the order of 450.000 FWHM at m/z 200) to resolve complex mixtures of isobar lipids and metabolites as well as to increase the detection sensitivity of molecules with very low abundances in complex biological samples. Furthermore the ability to use different activation modes such as Collision-Induced Dissociation « CID » or Higher-energy Collisional Dissociation « HCD » for MSn experiments at high resolution will improve metabolite identification.The Orbitrap Fusion will be installed at the end of July on the site of Saclay.

Training & education

Challenges and advance in the annotation and de novo identification of small biological molecules: 23 & 24 October 2014 - Gif sur Yvette, France

This first workshop is designed to promote the emergence of a community involved in the development and standardization of methods and recommendations for the characterization of natural products and the identification of small molecules, including metabolites . The annotation of metabolites and their identification is essential for the study of metabolism in a large variety of organisms and plays a central role in the discovery of bioactive molecules.

Programme and registration at the following link: *http://www.icsn.cnrs-gif.fr/spip.php?article966*

Communication

Internal events

Merlion metabolomics workshop Singapore 2014 on 19-21 November at the University of Singapour: *http://137.132.165.245/metabolomics2014/index.html*

"This Merlion Metabolomics Workshop will leverage on the strong infrastructure towards applying metabolomics technology in environment, food science and technology, and human health at National University of Singapore (NUS) (acting through NUS Environmental Research Institute (NERI)) and the well-established expertise in the area of nutrition, toxicology at the National Research Institute of Agronomy (acting through MetaboHUB), to encourage technical exchanges and catalyze the development of research collaboration in the field of metabolomics between Singapore and France. This workshop also provides opportunities for the knowledge and technologies developed in Europe to be applied in the Asian context."

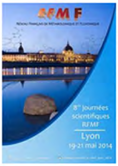
2nd MetaboHUB scientific days gathering all the MetaboHub partners organised on 4th and 5th June 2014 at Clermont-Ferrand, France

Scientific day on mass spectrometry imaging: "Principles, advantages and limitations". Examples on proteomics, metabolomicsandlipidomics have been presented in Toulouse, France on 13 & 14 February 2014 in Toulouse, France : *http://www.transbio-sudoe.eu/transbio-events.php?n=9*

External events

Several MetaboHUB members attended the 62nd conference on Mass Spectrometry and Allied Topics which was held in Baltimore (MD) from 15th to 19th of June 2014.

http://www.asms.org/conferences/annual-conference


RFMF
8e journées scientifiques RFMF
Lyon
19-21 mai 2014

Several MetaboHUB members actively participated in the organization and the scientific exchanges during the 8th Scientific Meeting of Réseau Français de Métabolomique et Fluxomique (*https://colloque6.inra.fr/8_js_rfmf_lyon_2014*) in Lyon on 19th to 21th May 2014. This meeting dedicated to applications in and developments for metabolomics, lipidomics and fluxomics gathered about 250 participants. More than 20 MetaboHUB members participated in this meeting presenting 22 posters and giving 5 oral communications.

Publication

See the last publications on the MetaboHUB web site:

http://www.metabohub.fr/en/research/about-metabolomics-and-fluxomics

Job opportunity

An Application Engineer position (TOU-IE-4-WP2B) will be available on the MetaToul platform for the development, validation, and operation of a High-Throughput fluxomics robotic platform (deadline for submitting august 25th 2014): see *Job opportunity*

Contact : *contact@metabohub.fr*

More information : *http://www.metabohub.fr/en/*

ANR-11-INBS-0010

Vous ne voulez plus recevoir cette newsletter ? *Se désinscrire*