

### Identification of Metabolic Biomarkers predictive of the severity of COVID-19 in hospitalized patients

Audrey Le Gouellec, Sylvie Berthier, Candice Trocme, V. Cunin, Florence Castelli, Caroline Plazy, Emeline Chu-Van, Federica Fiorini, Estelle Pujos-Guillot, François Fenaille, et al.

#### ▶ To cite this version:

Audrey Le Gouellec, Sylvie Berthier, Candice Trocme, V. Cunin, Florence Castelli, et al.. Identification of Metabolic Biomarkers predictive of the severity of COVID-19 in hospitalized patients. 14èmes JS RFMF, Nov 2021, Aussois, France. hal-04959019

#### HAL Id: hal-04959019 https://hal.science/hal-04959019v1

Submitted on 20 Feb 2025

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

# Identification of Metabolic Biomarkers predictive of the severity of COVID-19 in hospitalized patients

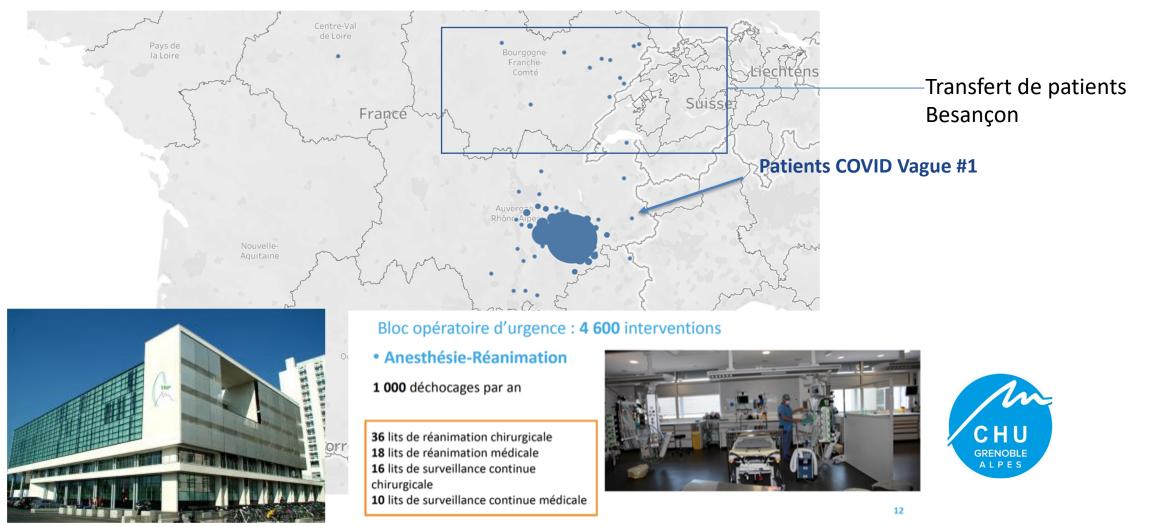
<u>Audrey Le Gouellec<sup>1,2</sup></u>, Sylvie Berthier<sup>2</sup>, Candice Trocme<sup>2</sup>, Florence Castelli<sup>4</sup>, Caroline Plazy<sup>1,2</sup>, Emeline Chu-Van<sup>4</sup>, Federica Fiorini<sup>2</sup>, Estelle Pujos-Guillot<sup>5</sup>, François Fenaille<sup>4</sup>, Bertrand Toussaint<sup>1,2</sup>, Olivier Epaulard<sup>3</sup>

<sup>1</sup> Laboratoire TIMC Recherche Translationnelle et Innovation en Médecine et Complexité, Univ. Grenoble Alpes, CNRS, UMR 5525, VetAgro Sup, Grenoble, France; <sup>2</sup> Plateforme de Métabolomique GEMELI-GExiM, Institut de Biologie et Pathologie – CHU Grenoble, Université Grenoble Alpes – France; <sup>3</sup>Service d'infectiologie CHU Grenoble Alpes, 38000 Grenoble, France; <sup>4</sup>CEA- Saclay – Commissariat à l'énergie atomique et aux énergies alternatives – France; <sup>5</sup>Université de Clermont-Ferrand Auvergne et CNRS – France

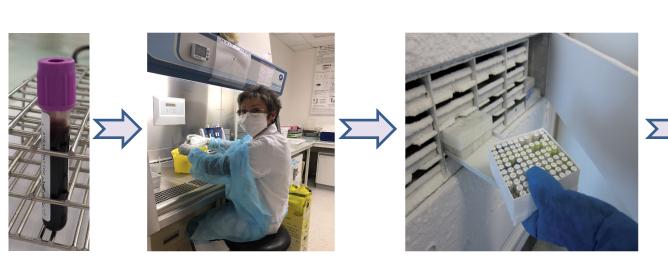
### Context

Since one year and a half, hospitals have been facing waves of varying intensity of new COVID-19 patients arriving, which are putting our healthcare system at risk (overwhelmed if no action was taken). We, infectious diseases physicians and hospital biologists, urgently need predictive biomarkers of the health trajectory of patients arriving at hospital's emergencies to better stratify risk and improve patient management. In particular, we need to identify as early as possible which hospitalized patients are at risk of developing a severe form of COVID-19 and requiring intensive care. To date, patient management has progressed, since evidence-based immunomodulatory treatments (dexamethasone, ...), provided at the right time, decrease the fatality rate for those with a severe disease. Almost all the severe cases are due to the onset of a delayed (after 7-10 days of mild symptoms usually) acute respiratory distress syndrome; this lung damage is due to an hyperinflammatory state secondary to an hyperactivation of the immune system. Classical markers of inflammation (C-reactive protein [CRP], Interleukin-6 [IL6], for instance with good sensitivity but low specificity 79% and 62% respectively) may participate in identifying, at the hospital admission, which patients will experience a worsening of lung functions; moreover, it has been clearly demonstrated that co-morbidities linked to dysmetabolic disorders (diabetes, obesity, hypertension, etc.) are risk factors severe forms. However, a more efficient identification of the most at-risk patients is needed.

### The hospital CHUGA is the reference establishment of the the Alpine arc, population 2 million inhabitants

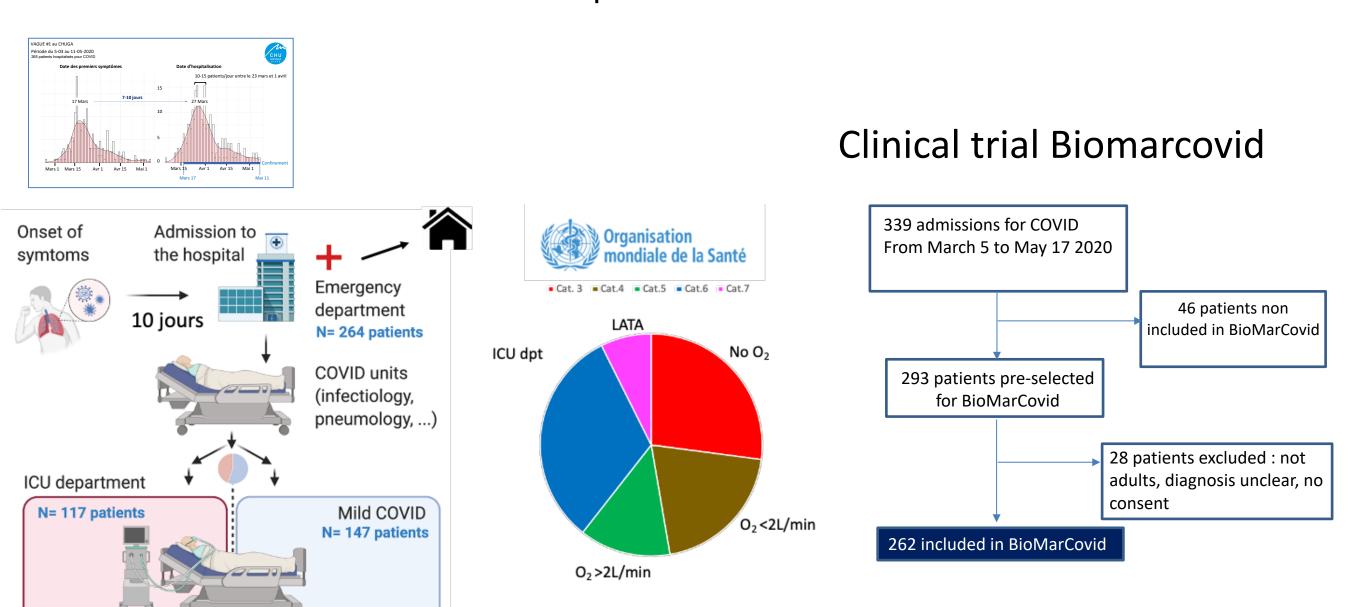


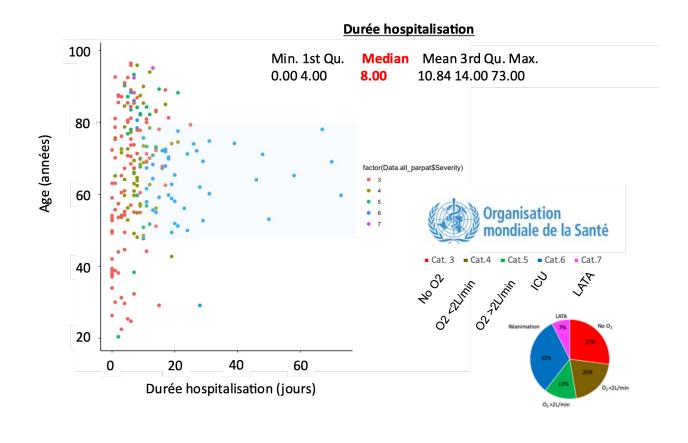
### Institute of Biology and Pathology



Biobanking

**749** clinical EDTA Blood samples stocked at -80°C for **513** patients (~ **4500** cryotubes)





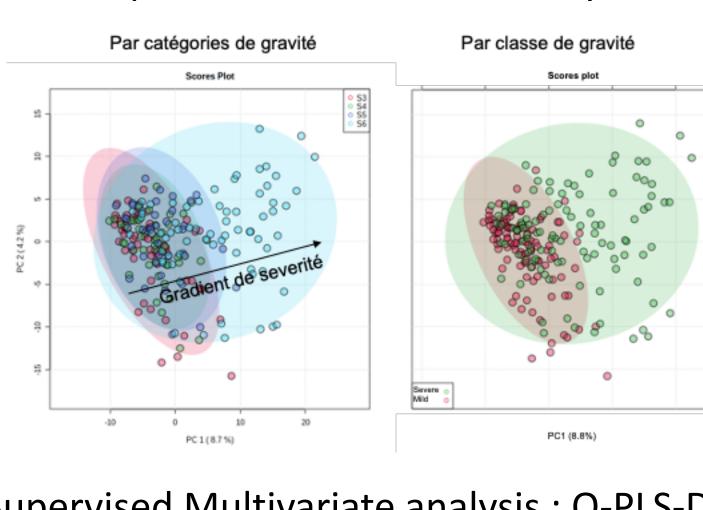
		Total (n=262)	Modérée (n=139)	Forme Sévère (n=123)	p.value
Genre, Homme (H)/Femme n(%)		149 / 113 (H : 56.87%)	66 / 73 (H : 47.48%)	83 / 40 (H : 67.48%)	p <0.001
Age (med)		70	68	72	.003
Comorbidités	IMC, (med [IQR])	26.4 [23.24;30.4]	24.9 [21.6;28.1]	28 [24.91;31]	.001
	Hypertension, n(%)	107 (53.23%)	44 (44.9%)	63 (61.17%)	p <0.003
	Diabète, n(%)	42 (16.03%)	17 (12.23%)	25 (20.33%)	p <0.001
Intervalle 1ers symptoms -		7	7	7	NS
hospitalisation (med [IQR])		[4;10]	[4;10]	[4;10]	INS

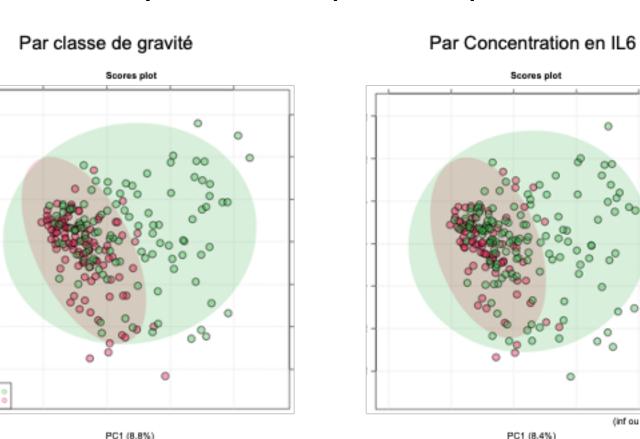
## Identify a set of clinical metabolic biomarkers for the severity of the disease, thus helping **Objectives** to stratify patients and anticipate the management of intensive care beds, which is now recognized as a critical point. Severe COVID? **Summary of the cohort of COVID-19** Patients biobanked early after admission Global view of the metabolism Platform Grenoble Expertise in Metabolomics

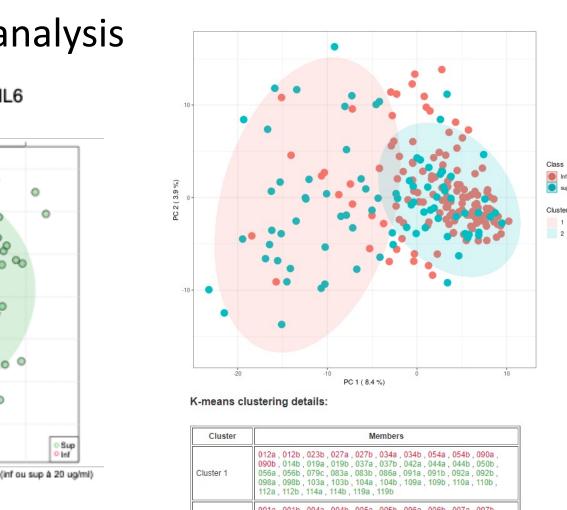
### **Preliminary results**

### LC-MS/MS (C18 Orbitrap ESI+)

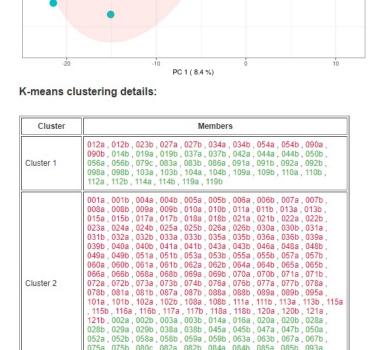
### Non supervised Multivariate analysis: Principal component analysis



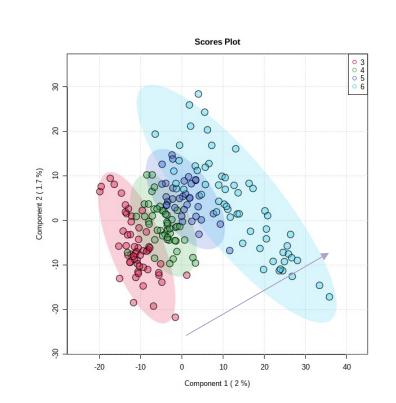


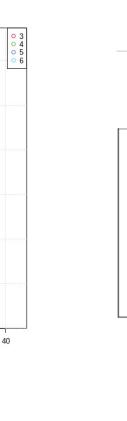


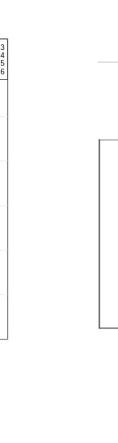
K-means clustering

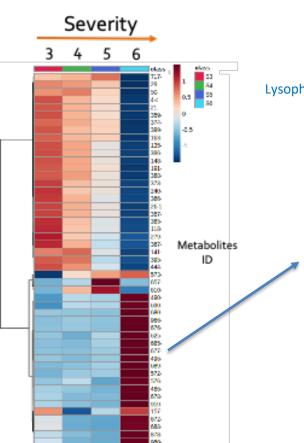


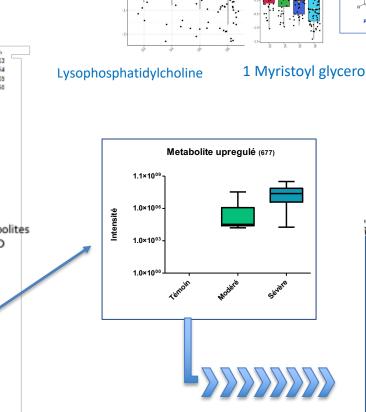
## Supervised Multivariate analysis: O-PLS-DA

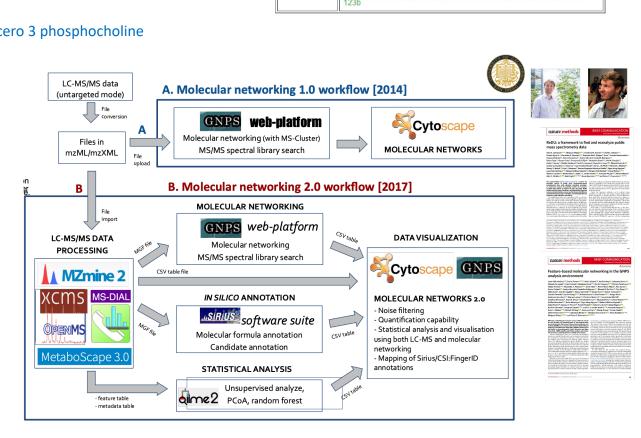




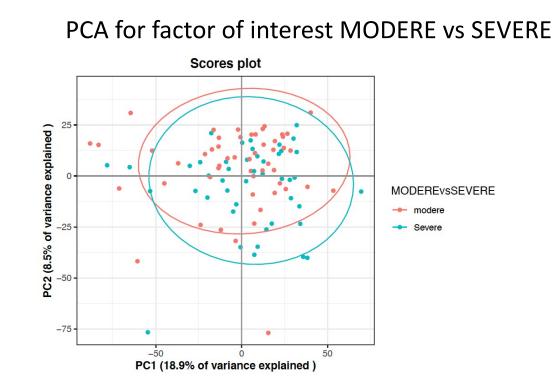


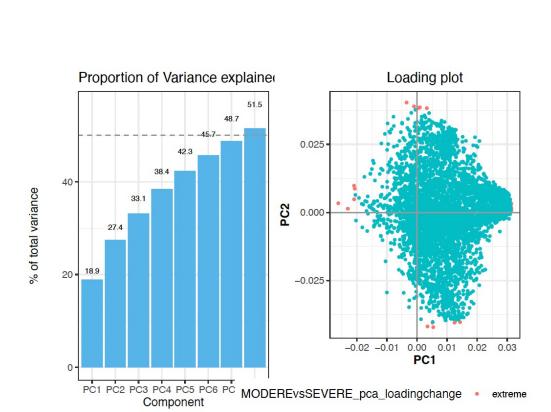




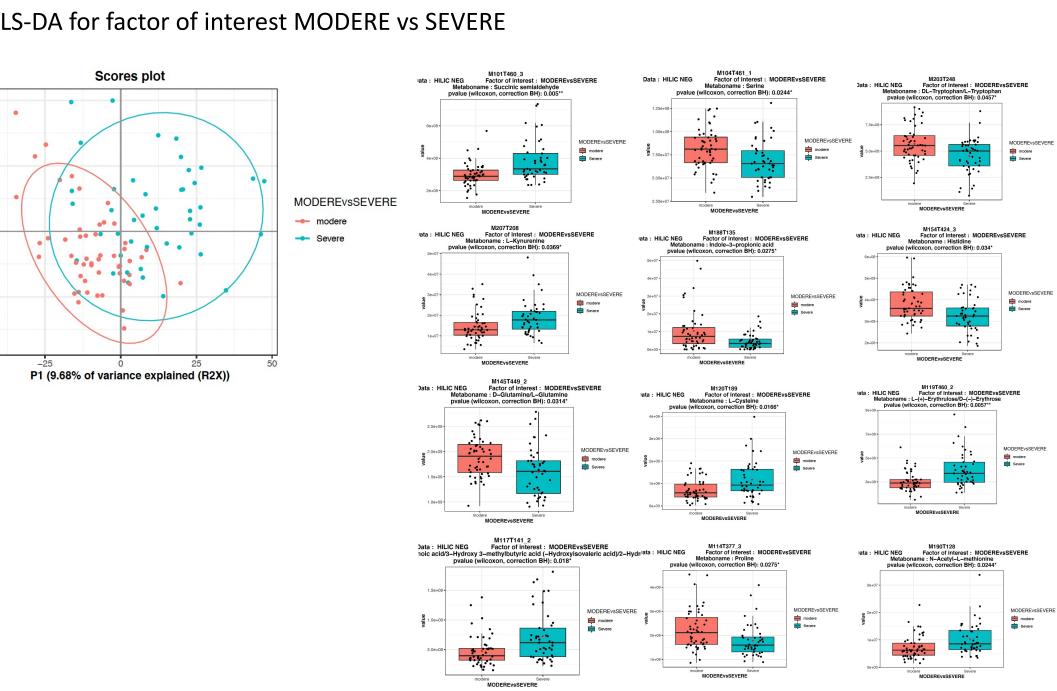


### LC-MS/MS (HILIC Orbitrap ESI-)





PLS-DA for factor of interest MODERE vs SEVERE



### **Conclusions and perspectives**

Two complementary metabolomics methods based on chromatography separation (Ultra High-Performance Liquid and Gas Chromatography) coupled to High Resolution (HR) Mass Spectrometry (MS) has been used to ensure a good metabolome coverage. In perspectives, Lipidomics or others columns will be used to increase the coverage.

Identification of VIP metabolites (ie Lysophoshphatidylcholine, Kynurenine, tryptophan, Glutamic acid, IPA, ...) has been done.

Identitification of an unknown metabolite is still missing. We need collaboration to find what is this metabolite ID #677.

A new cohort of validation of COVID-19 patients must be used to validate the identified biomarkers.









**Identification process** 













