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### ► To cite this version:

Nina Lager-lachaud, George Alzeeb, Noémie Butin, Thibaud Lante, Hanna Kulyk, et al.. Miniaturisation of metabolomic and fluxomic workflow on spheroids cultures applied to the treatment of gastric cancer.. Analytics 2022, Sep 2022, Nantes, France. hal-03894052

**HAL Id: hal-03894052**

**<https://hal.science/hal-03894052>**

Submitted on 12 Dec 2022

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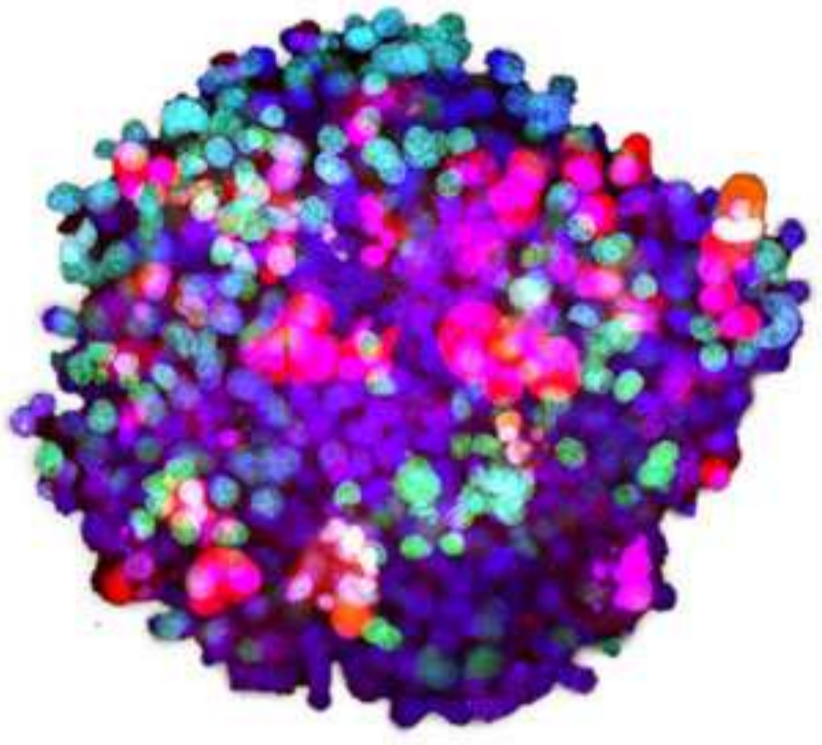
# Miniaturisation of metabolomic and fluxomic workflow on spheroids cultures applied to the treatment of gastric cancer



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## Introduction

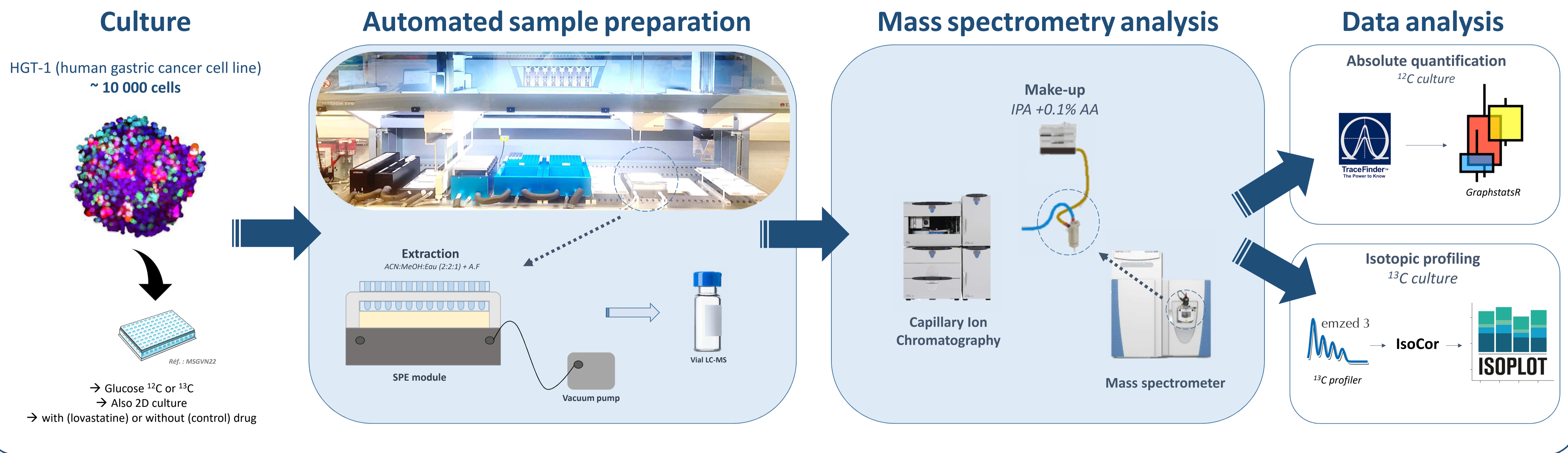


Single spheroid

Spheroid (3D) culture models are becoming essential to mimic what happens in tissues *in vivo*. They are more representative of the cell-cell contact, dynamic interactions and reduce the impact of plastic compared to traditional 2D cultures. According to the models of cultures, metabolic differences were observed (in glycolytic activity, ATP production and sugar nucleotides synthesis). Expression of drug resistance genes may be also different and spheroids are often more resistant to the drug than 2D cultures. Culture of single spheroids are used to analyse with high throughput a large number of conditions. The challenge of this project was to be able to perform a study of metabolism for single spheroid (metabolomics and <sup>13</sup>C metabolomics) of gastric cancer cell line.

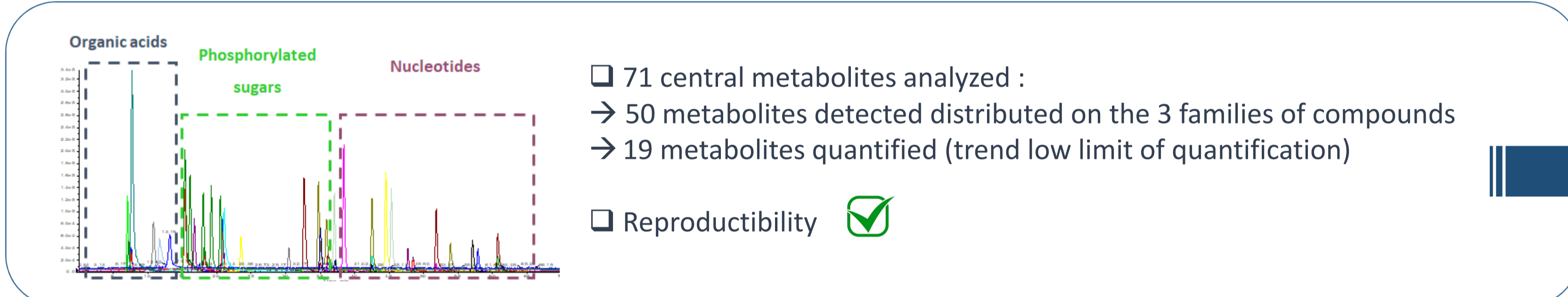
→ **Objective : Development of automated workflow (sample preparation and mass spectrometry) to analyse a single spheroid**

## Material and methods

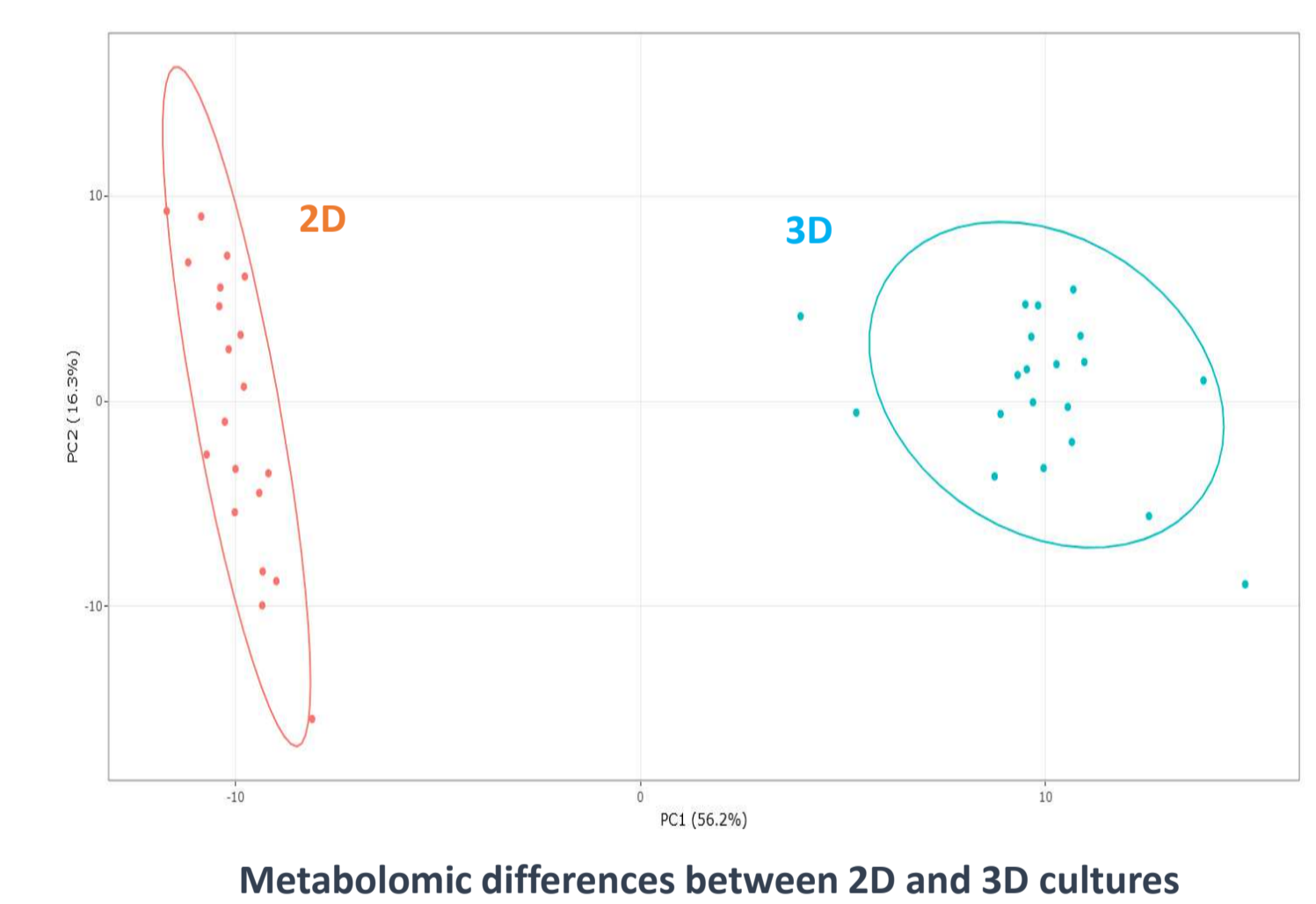


## Results and discussion

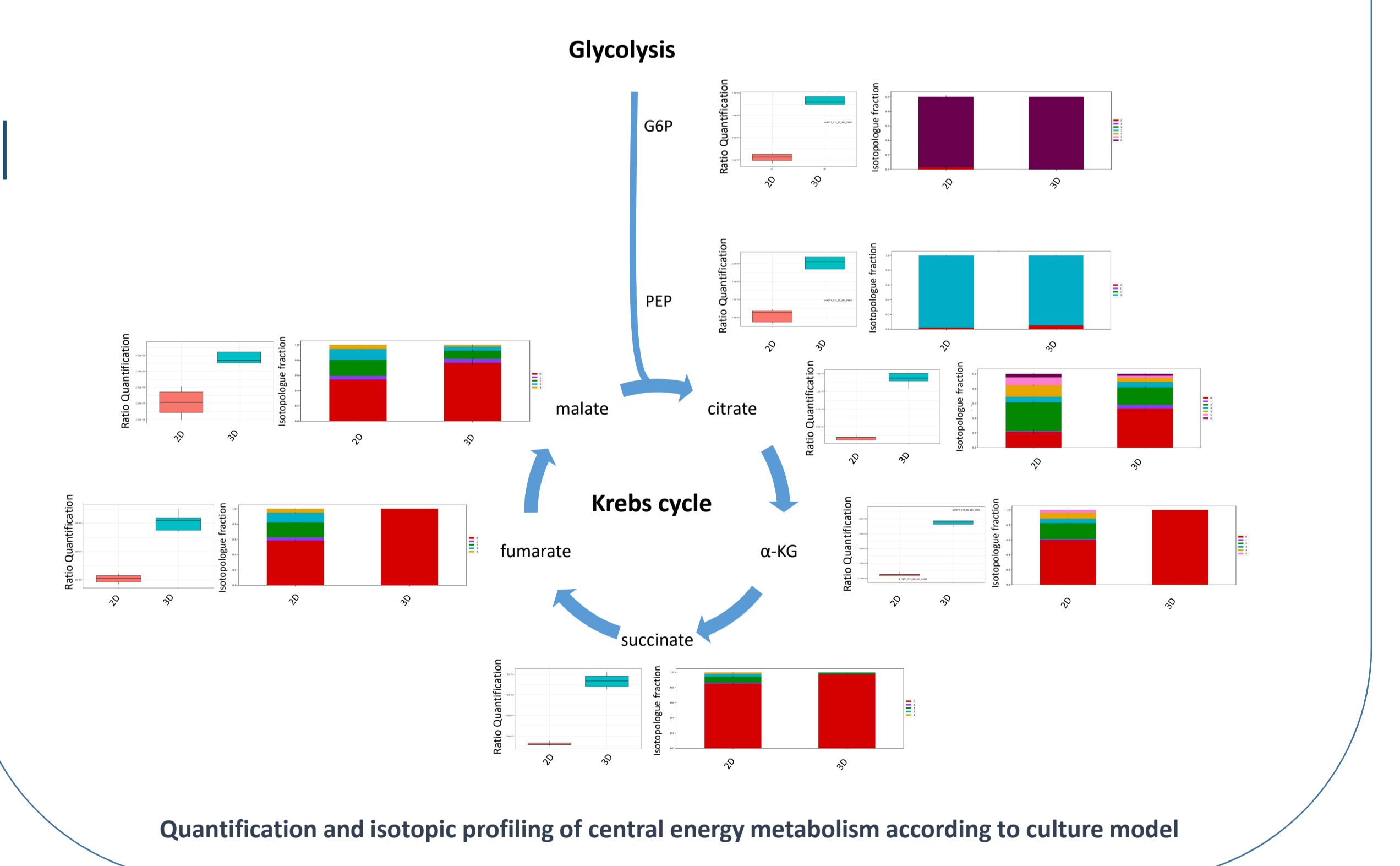
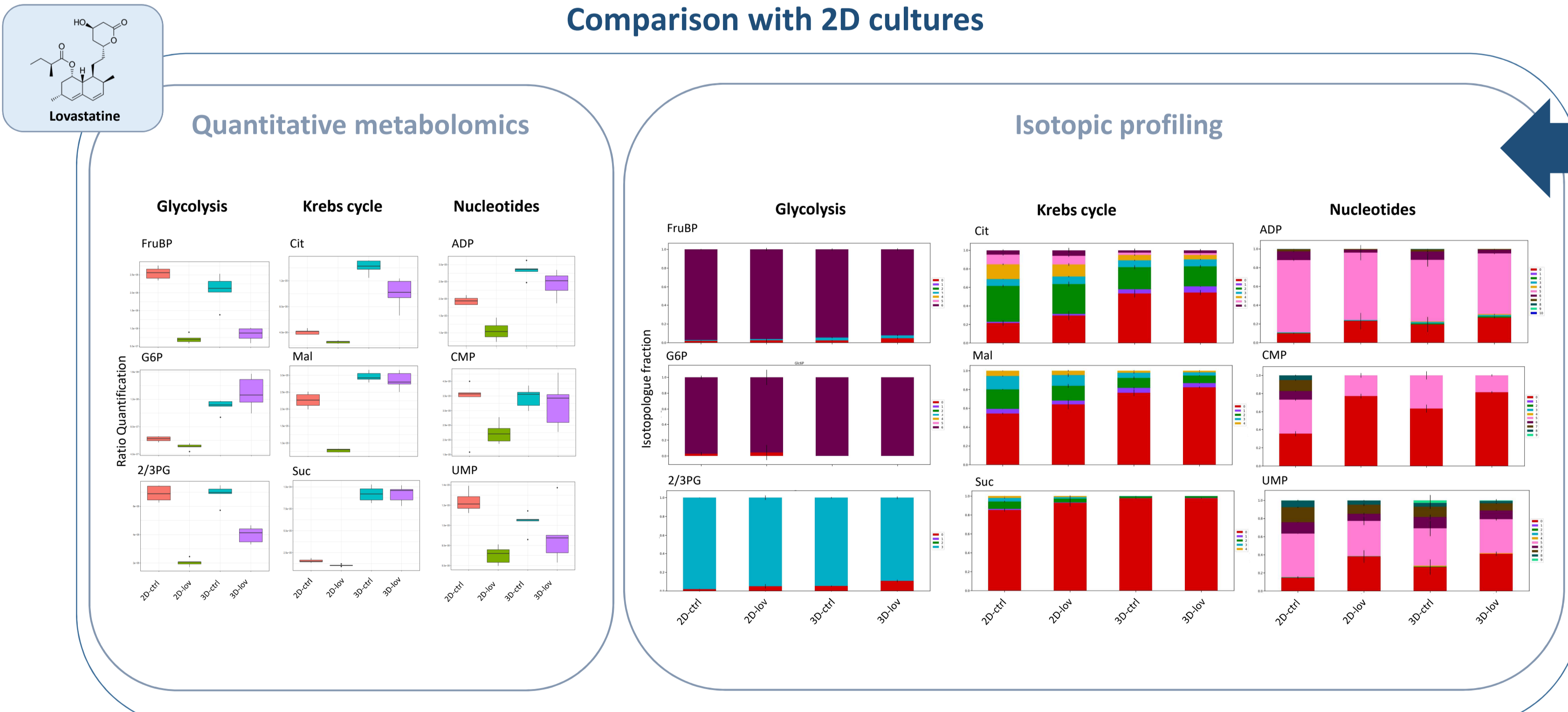
### Spheroids metabolome coverage



### Spheroids metabolism analysis Comparison with 2D cultures



### Drug impact on spheroid metabolism Comparison with 2D cultures



## Conclusions

- Validation of a high throughput sample preparation protocol applied to single spheroid.
- Ability to analyze a single spheroid (400 cells injected) for absolute quantification and isotopic profiling by mass spectrometry. 😊
- Metabolic differences between 2D and 3D cultures : Higher level of most central metabolites in spheroids / Stronger impact of drugs on 2D than on 3D cultures.
- Non targeted analysis in process... 🌱

## References

- [1] Gastric cancer cell death analyzed by live cell imaging of spheroids. Alzeeb, *et al.* 2022
- [2] Metabolic flux analysis of 3D spheroids reveals significant differences in glucose metabolism from matched 2D cultures of colorectal cancer and pancreatic ductal adenocarcinoma cell lines. Tidwell, *et al.* 2022
- [3] The use of a double coaxial electrospray ionization sprayer improves the peak resolutions of anionic metabolites in capillary ion chromatography-mass spectrometry. Hirayama, *et al.* 2020
- [4] Single Spheroid Metabolomics: Optimizing Sample Preparation of Three-Dimensional Multicellular Tumor Spheroids. Rusz, *et al.* 2019

## Acknowledgments

MetaboHUB (MetaboHUB-ANR-11-INBS-0010)

