ALISTER – Application for Lipid Stability Evaluation and Research

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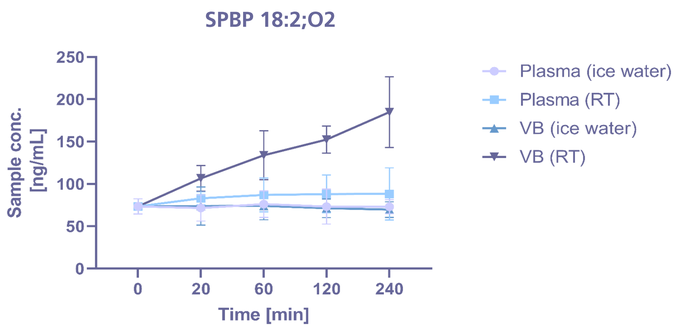
Introduction

The complexity of the lipidome and metabolome holds the potential to mirror diverse sets of internal and environmental influences in patients. This trait is of great interest when searching for potential biomarkers.

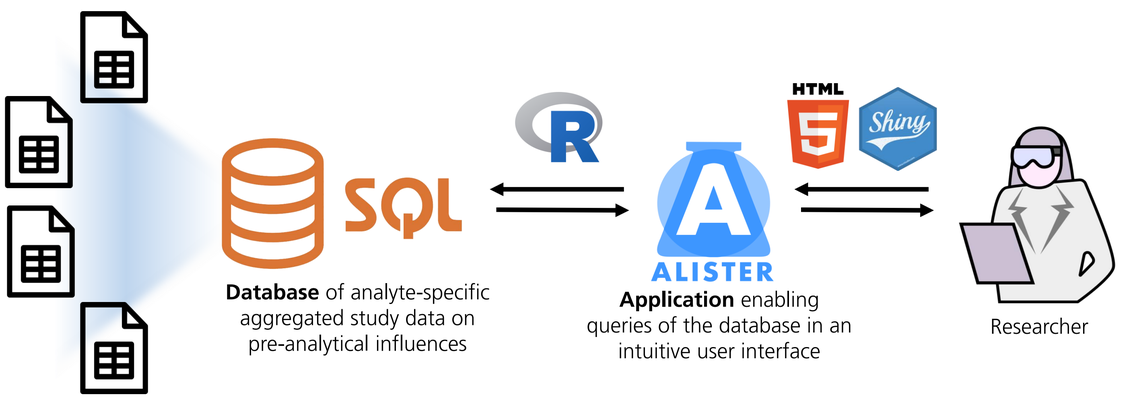
However, pre-analytical influences are known to cause *ex vivo* changes of analyte concentrations and are rarely accounted for in lipidomic and metabolomic studies.[1] Estimate suggests, that pre-analytical sample handling is a major issue causing low quality of blood samples. In certain cases, results might be skewed and could lead to waste of resources or even false conclusions.[2] Therefore, considering appropriate pre-analytical sample handling is a highly important part in LC-MS based clinical research.



SPBP 18:2;O2 is a well-known example of the impact of pre-analytical influences (e.g., storage temperature) on analyte levels.[3]

ALISTER (Application for lipid stability evaluation and research), is a data-driven tool for **assessing the influence of prominent pre-analytical variables on plasma (and serum) sample quality** to support reliable LC-MS based clinical research.

Methodology

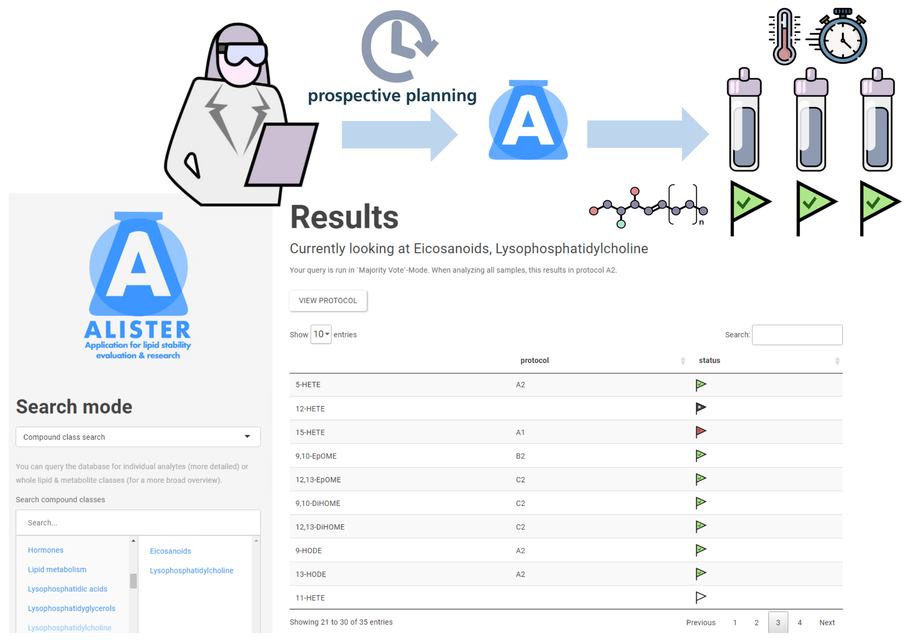


ALISTER is rooted in a SQL-database, that aggregates study data on pre-analytical impacts on lipid and metabolite concentrations.[4,5] Concentration changes are collected as fold changes (FC) towards properly collected baseline samples. Thus, each fold change holds information on the investigated pre-analytical impact (e.g., processing delay, intermediate storage temperature) on plasma and serum levels of a specific analyte.

Results

Compound class search

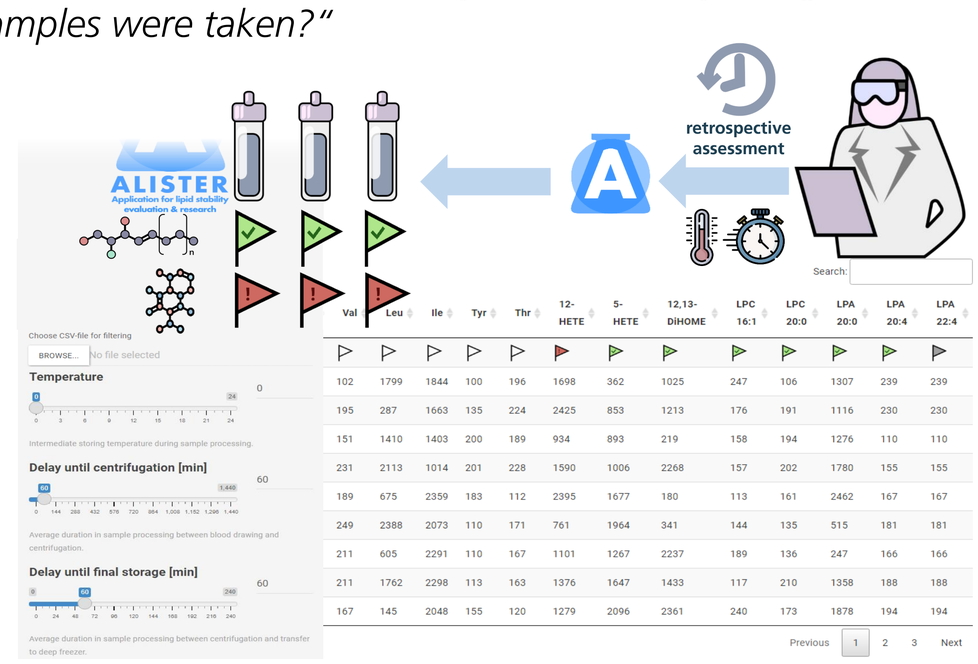
Methodological question: *„I am planning to investigate certain lipid/metabolite classes. How do I take and process samples in order to assure pre-analytical reliability?“*



ALISTER searches the database for processing conditions, where selected analytes were found to be stable (cut-offs). The most conservative estimation of stability-assuring conditions is given.

Sample search & Data filtering

Methodological question: *„I have measured samples that were obtained under a certain sampling and processing protocol. Do I need to be careful with any of the analytes, given how the samples were taken?“*



ALISTER looks into studies, where samples were analyzed similar to the input conditions and for the same analytes. A warning (or optional data filtering) is given for those analytes, that exceeded cut-offs due to the given pre-analytical influences.

Conclusion

ALISTER provides an additional **quality control/assurance layer in lipidomics and metabolomics studies**, by aggregating and evaluating data on pre-analytical plasma and serum sample stability. Analyte stability can be assessed in form of prospective study planning, as well as retrospective data assessments.

1 Lehmann, Rainer (2021): From bedside to bench-practical considerations to avoid pre-analytical pitfalls and assess sample quality for high-resolution metabolomics and lipidomics analyses of body fluids. In *Analytical and bioanalytical chemistry* 413, pp. 5567-. DOI: 10.1007/s00216-021-03450-0.
2 Burla, Bo; Arita, Makoto; Arita, Masanori; Bendt, Anne K.; Cazenave-Gassiot, Amaury; Dennis, Edward A. et al. (2018): MS-based lipidomics of human blood plasma: a community-initiated position paper to develop accepted guidelines. In *Journal of lipid research* 59 (10), pp. 2001–2017. DOI: 10.1194/jlr.S087163.
3 Liu, Xinyu; Hoene, Miriam; Yin, Peiyuan; Fritsche, Louise; Plomgaard, Peter et al. (2018): Quality Control of Serum and Plasma by Quantification of (4E,14Z)-Sphingadienine-C18-1-Phosphate Uncovers Common Preanalytical Errors During Handling of Whole Blood. In *Clinical chemistry* 64 (5), pp. 810–819. DOI: 10.1373/clinchem.2017.277905.
4 Hahnefeld, Lisa; Gurke, Robert; Thomas, Dominique; Schreiber, Yannick; Schäfer, Stephan M. G.; Trautmann, Sandra et al. (2020): Implementation of lipidomics in clinical routine: Can fluoride/citrate blood sampling tubes improve preanalytical stability? In *Talanta* 209, p. 120593. DOI: 10.1016/j.talanta.2019.120593.
5 Sens, Alena; Rischke, Samuel; Hahnefeld, Lisa; Dorochow, Erika; Schäfer, Stephan M. G.; Thomas, Dominique et al. (2023): Pre-analytical sample handling standardization for reliable measurement of metabolites and lipids in LC-MS-based clinical research. In *Journal of Mass Spectrometry and Advances in the Clinical Lab* 28, pp. 35–46. DOI: 10.1016/j.jmsacl.2023.02.002.

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