Prices updated: April 2022

https://imsb.ethz.ch/research/zamboni/ext/clin.html

Activity of PHRT-CMAC

In a clinical setting, metabolomics and lipidomics can be used in discovery, validation, and diagnostics. Each of these tiers has different requirements and poses distinct challenges.

Our lab (CMAC) focuses on the discovery phase, and aims at providing fast, affordable, and possibly inclusive untargeted metabolomics and lipidomics to drive clinical and preclinical research.

Performing this type of analysis at scale demands specific (and expensive) instruments, technical knowhow, experience in operating sensitive equipment, and substantial software development which are **not** covered by existing facilities for clinical chemistry. Over >10 years, our lab specialized in these activities with own developments to enable data acquisition, processing, analysis, and visualisation. As a research lab, we analyzed > 1 Mio untargeted analyses, including >200 experiments with more than 1'000 samples each, many of which were external collaborations. This expertise sets us apart from other labs, and is the cornerstone of our service.

We perceive **speed, scale, and competitive costs as key factors** in clinical research. These are essential to provide statistically sound investigation of **complete clinical cohorts (up to 10'000 samples)** at affordable conditions. With our analysis, we pursue to quickly inform on potential markers or pathways that are of bio/medical interest.

Further information:

- Analytical services
- Metabolomics
- Lipidomics

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Analytical services

We currently offer the following analytical services:

- Metabolomics: Untargeted analysis of polar and moderately non-polar metabolites, including drugs, xenobiotics, etc.
- Lipidomics: Untargeted analysis of all major lipid classes (> 1000 lipid species detected in serum)

All of our services rely on high-throughput mass spectrometry methods that scale to thousands of samples without compromising quality and turnaround.

The readouts are semi-quantitative, i.e. provide relative changes of each detectable compound across the study. On demand and for limited compounds, approximative amounts (concentrations) can be approximated by spiking isotopically labeled (^{2}H or ^{13}C) standards. Specific needs should be discussed in advance.

The service includes the extraction of the metabolites from plasma, serum, or urine using automated liquid handling systems. Different type of samples (biopsies, in vitro tissue culture, feces, saliva, swabs, dried blood spots, ...) require special treatment that should be discussed.

The service includes data processing, QC/QA, putative annotation, expert curation, analysis of batch/drift effects, ev. normalization, and basic differential analysis in case samples groups have been provided (i.e. for unblinded studies).

Related information

- vertical_align_bottom General Term Conditions (PDF, 124 KB)
- chevron_right Fees
- chevron_right Infrastructure
- chevron_right Personalized Health and Related Technologies

https://imsb.ethz.ch/research/zamboni/ext/srv/metabolomics.html

Metabolomics

Methods

The analysis of primary metabolites (e.g. organic acids, amino acids, nucleotides, energy and redox cofactors) and xenobiotics is done by untargeted metabolomics, which allows to detect thousands of features in parallel, including unexpected compounds. We offer two standard configurations:

1) Untargeted metabolomics by LC-MSn

This approach includes a chromatographic separation that allows to discriminate between compounds with similar mass and reduce the interferences in complex samples. Specificially, we use a custom quaternary gradient that wss optimized to separate metabolites of all classes and chemical properties (up to logP <8). A sequence includes acquisition of MS2 data for structural confirmation, library matching, etc. **This is the recommended approach for clinical or complex samples, and for all studies with < 5000 samples.**

2) Untargeted metabolomics by flow injection (FIA)-MS

In flow injection analyses, the chromatographic separation is omitted. Thereby, much higher throughputs can be achieved at the cost of distinguishing compounds with the same molecular formula. This method is a unique speciality of our lab. The method was originally developed in 2011 and continuously improved with hardware and software ameliorations to maximize sensitivity and robustness. Over more than a decade we analyze ca. 1.5 Mio samples and published > 100 paperscall_made. The largest study performed was with ca. 75'000 samples. **This is the recommended approach for the analysis of cellular extracts (i.e. primary metabolism) or supernatants.**

Notes:

- The FIA method is about 75% cheaper than the LC-MSn method.
- All readouts are **semi-quantitative**, i.e. provide relative changes of each detectable compound across the study. On demand and for limited compounds, approximative amounts (concentrations) can be approximated by spiking isotopically labeled (^{2}H or ^{13}C) standards.
- Both methods can be run in either negative or positive mode. Normally, we recommend to use negative mode only in the analysis of most sample types. Analysis in positive mode is only recommended for the analysis of low abundance polyamines.

Sample types

- **Biofluids: serum, plasma, urine, CSF, saliva**
  - Requirements: 25 microL needed, 100 microL preferred
  - Sample preparation: done by us
  - Examples: DOI: 10.2337/db19-0131call_made
  - Example coverage: Plasma (ZIP, 1.6 MB)vertical_align_bottom

- **Solid samples: biopsies, fecal samples**
    - Requirements: 1 mg needed, 50 mg preferred
    - Sample preparation: to be discussed
    - Examples: DOI: 10.1126/science.aad0189call_made DOI: 10.1186/s12864-017-3547-3call_made
    - Example coverage: Muscle biopsy (ZIP, 1.4 MB)vertical_align_bottom
- **In vitro cell cultures, spheroids, organoids**
    - Requirements: 100'000 cells ok, more is advantageous for rare compounds
    - Sample preparation: to be discussed
    - Examples: DOI: 10.1016/j.cell.2016.09.031call_made DOI: 10.1016/j.ymben.2016.12.009call_made DOI: 10.1111/febs.14852call_made DOI: 10.1016/j.molcel.2015.06.017call_made
    - Example coverage: Cancer cell line (ZIP, 1.1 MB)vertical_align_bottom
- **Medium**
    - Requirements: 10 microL needed, 25 microL preferred)
    - Sample preparation: done by us
- **Dried blood spots**

https://imsb.ethz.ch/research/zamboni/ext/srv/lipidomics.html

Lipidomics

Main content

Method

In recent years, we have been developing innovative LC/MS workflows for untargeted and targeted lipidomics. In brief, we use reversed-phase liquid chromatography coupled to high-resolution mass spectrometry. The length of the each run can be as short as 2 minutes (500 samples/day), but longer runs might be necessary to resolve similar lipid species. The specifics are adjusted ad-hoc to optimized separation, throughput and coverage to each project's needs.

Using full scan and different fragmentation modes on Orbitrap (Q-Exactive HFx) and Q-TOF (Agilent 6546 Q-TOF) instruments, we can identify few thousand lipid species on the MS1 level while several hundreds can usually be confirmed on the MS2 level within each experiments. In addition, the excellent reproducibility of LC allows to identify features based on internal libraries and previous studies.

Example of lipids detected in a complex lipid extract. Ca. 500 are routinely confirmed by MS2 fragmentation in each study.

Notes

- Depending on the sample type and amount, we can detect and semi-quantify the following classes:
    - Acylcarnitines
    - Fatty acids
    - Lysophospholiipds (LPC, LPE, LPA, LPG and LPS and some of their ether counterparts)
    - Glycerolipids (MAG, DAG and TAG)
    - Phosphoglycerolipids (PC, PE, their ether forms and PA, PG, PS, and cardiolipins)
    - Sphingolipids (Sphingoid bases, dihydroceramides, ceramides, and their deoxy forms, sphingomyelins and different classes of glycosphingolipids such as mono- di- and tri- hexosyl-ceramides and gangliosides)
- The readouts are semi-quantitative, i.e. provide relative changes of each detectable compound across the study. By default, we also add internal standards for each lipid class.
- Sample preparation is done by us using high-throughput liquid handling stations (Hamilton Star and Agilent Bravo). Supported procedures include the standard MMC, MTBE, and BUME protocols as well as in-house modifications. Tissue homogenization is available (Precellys evolution).

Sample types

- **Plasma**
    - Preferably EDTA but also other anti-coagulants (e.g., Citrate or Heparin) can be used
    - Requirements: 20 µl needed, 100 µl preferred
    - Sample preparation: done by us
- **Serum**
    - Requirements: 20 µl needed, 100 µl preferred
    - Sample preparation: done by us
- **Cerebrospinal fluid**
    - Requirements: 50 µl needed
    - Sample preparation: done by us
- **Tissues and biopsies**
    - Requirements: 10 mg wet weight needed
    - Sample preparation: done by us
- **Tissue cultures:**
    - Requirements: 50,000 cells needed, 1 Mio preferred.
    - Sample preparation: done by us
- **Lower organisms (bacteria, yeasts)**
    - Requirements: 1 OD*mL (frozen pellet) preferred
    - Sample preparation: done by us
- ***C. elegans, Drosophila, Zebrafish, ...***
    - Contact us

Fees

Fees are calculated per sample to cover consumables, instrument usage and maintenance, and a part of labor. As of Feb 2022, the indicative fees for Academia are:

- **Metabolomics (LC-MS, untargeted): CHF 110 per sample and mode**. Normally, only negative mode analysis is needed.
- **HT Metabolomics (FIA-MS, untargeted): CHF 30 per sample and mode.** Normally, only negative mode analysis is needed. Recommended for cellular extracts and supernatants.
- **Lipidomics (LC-MS, untargeted): CHF 110 per sample and mode**.

Remarks:

- The minimum fee for a batch is CHF 5000 regardless of the number or type of samples.
- These fees are indicative, non-binding, and subject to change. An official quote will be issues upon discussing the details in person.
  Initial consultation regarding sample quality, recommended sample pre-preparation review of the experimental strategy, power analysis, as well as fast track data analysis are included in this pricing.
- We perform the extraction of the metabolites from plasma, serum, or urine. For solid samples (tumors, biopsies, feces), additional costs might occur depending on amount and size of samples.
- The fees are lower for larger studies (>1000 samples).
- The fees are double for Industry.
- Additional 10% overhead is charged by ETH Zurich for external services.
- Additional 8% VAT might apply for Swiss entities. Foreign entities are not subject to VAT.
- General Term Conditions (PDF, 124 KB)vertical_align_bottom apply.

If you are interested in using these services, we'll prepare a specific quote that matches the needs.