# Untargeted Metabolomics

## Technology introduction

The LC-MS untargeted metabolome is used for unbiased detection of metabolites in samples by liquid chromatography-mass spectrometry and to obtain their qualitative and quantitative information. The main research idea is to compare the case group with the control group to find the different metabolites and metabolic pathways between the groups, which can provide clues and directions for the research of disease biomarker development, pathogenesis and drug treatment mechanism.

## Technical Features

### Large curated database

Collected ultra-high sensitivity data of over 280000 metabolites. Each sample can typically identify 1500-3000 metabolites.

### Comprehensive identification strategy

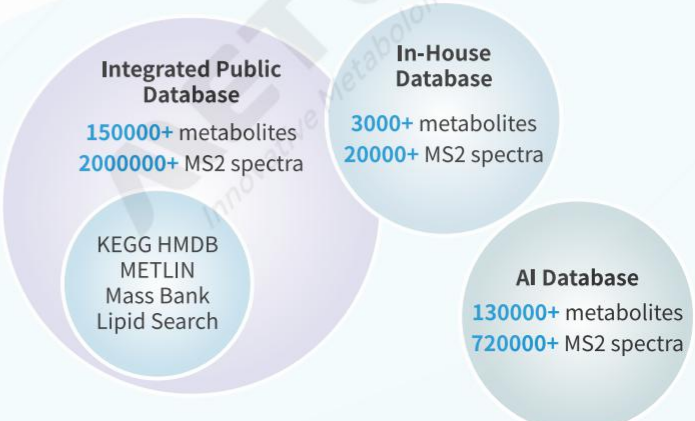
A comprehensive identification of metabolites was performed using four qualitative methods: ①matching in-house standard database;②matching integrated public database;③matching AI database; ④using the metDNA algorithm.

### Rigorous quality control

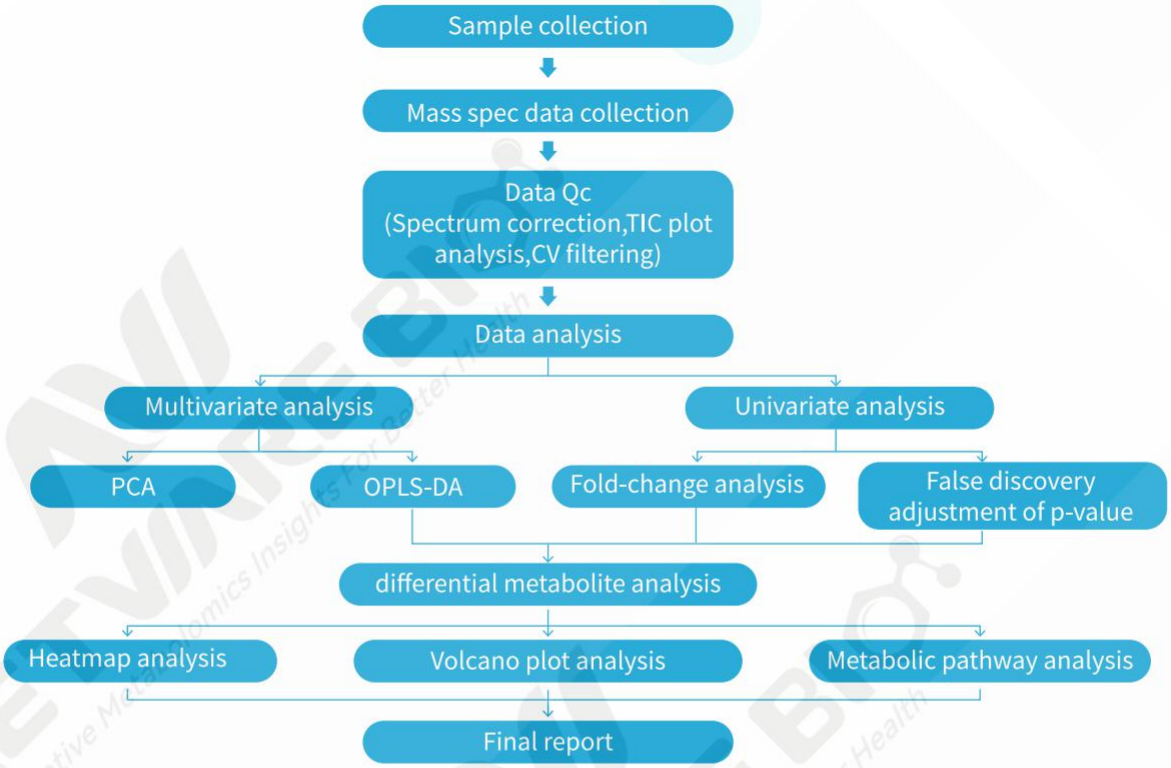
A mature quality control system monitoring all aspects of experimentation from sample preparation to data collection.

## List of metabolites

Our curated database contains over 280,000 metabolites, of which over 3,000 metabolites are from in-house standard database, over 150,000 metabolites from integrated public database, and over 130,000 metabolites from AI database. The integrated public database include KEGG, HMDB, Metlin, Mass Bank, Lipid Search and other common databases.



# Project workflow

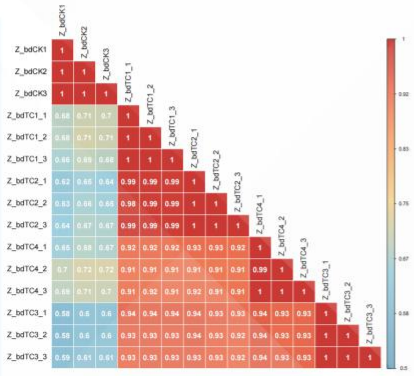



# Analysis content display

### Sample Correlation Analysis

Intuitively see the correlation of metabolite contents between samples and sample groups.

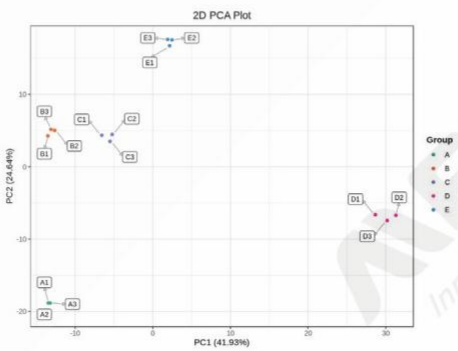
In this plot, the labels along the left and the diagonal represent sample names. The color boxes represent Pearson correlation coefficients. The darker the red, the stronger the correlation and the darker the blue, the weaker the correlation.



### Principal Component Analysis (PCA)

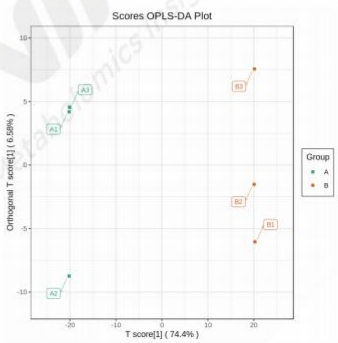
Quickly determine the variance between samples and sample groups.

In PCA plot, each dot represents a sample and samples in the same group are shown with the same color. PC1 and PC2 represent the first and second principal component, respectively. Percentage value describe how well a principal component can explain the sample variance.



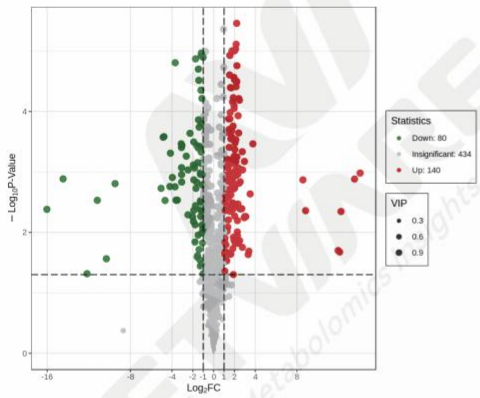

### Orthogonal Projections to Latent Structures Discriminant Analysis (OPLS-DA)

OPLS-DA is a statistical model to find which variables are driving the difference between two groups. In this plot, the X-axis represents the predicted principal component and measures the difference between groups. The Y-axis represents the orthogonal principal component and measures the difference within a group. Percentage value indicates the degree to which the component explains the data set. Each dot in the figure represents a sample, samples in the same group are shown with the same color.



### Volcano plot

A visual representation of relative differences and the statistical significance of metabolites between two samples or groups. Each point in the volcano plot represents a metabolite with green points represent significantly down-regulated metabolites, red points represent significantly up-regulated metabolites, and gray points represent detected metabolites with no significant differences. The X-axis represents the log2(fold-change) value of metabolites between two groups. The Y-axis represents the level of significance (-log10(p-value)). The size of each dot represents the Variable Importance in Projection (VIP) value.

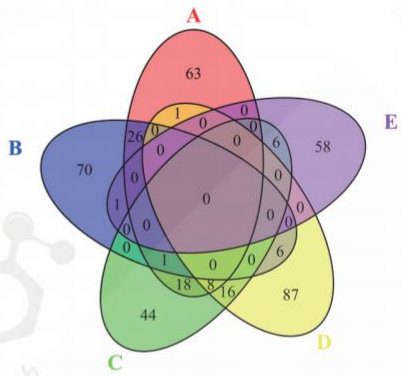



### Chord Plot

This plot captures the correlation of a metabolite with other metabolites. In this figure, the outermost layer shows the differential metabolites. The second layer shows log2FC value as circles and the circle size proportional to FC values. The color for the first and second layer represent different metabolite classification. The chords in the inner most layer reflect the Pearson correlation between the connected metabolites. Red chords represent positive correlation and the blue chords represent neg.

### Venn diagram

It is a powerful way to depict differential metabolites that are unique or shared between comparisons. Each enclosure represents a comparison group. The number in overlapped parts represent the number of common differential metabolites between comparison groups, and the number in non-overlapped parts represents the number of unique differential metabolites.




## Sample requirements

| Sample type | Sample | Recommended sample | Minimum sample | Biological duplication |
|---|---|---|---|---|
| liquid | Plasma, serum, hemolymph, milk, egg white | 100 μL | 20μL | samples>6<br>clinical samples>30 |
| | Cerebrospinal fluid, tear fluid, interstitial fluid, uterine fluid, pancreatic fluid and bile, pleural effusion, follicular fluid, corpse fluid | 100 μL | 20μL | samples>6<br>clinical samples>30 |
| | Seminal plasma, amniotic fluid, prostate fluid, rumen fluid, respiratory condensate, gastric lavage fluid, alveolar lavage fluid, urine, sweat, saliva, sputum | 500 μL | 100 μL | samples>6<br>clinical samples>30 |
| tissue | Animal tissue, placenta, thrombus, fish skin, mycelium, nematode | 100 mg | 20 mg | samples>6<br>clinical samples>30 |
| | Whole body, aircraft (wings), pupae | 500 mg | 20 mg | samples>6<br>clinical samples>30 |
| | Zebrafish organs, insect organs | 20 | 10 | samples>6<br>clinical samples>30 |
| cell | Adherent cells | 1*10^6 | 5*10^5 | samples>6 |
| | Escherichia coli and other microorganisms | 1*10^10 | 5*10^8 | samples>6 |
| stool | Feces, intestinal contents | 200 mg<br>(Wet weight) | 50 mg<br>(Wet weight) | samples>6<br>clinical samples>30 |

# Applications

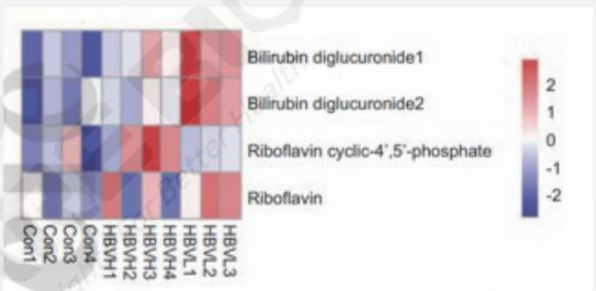
Untargeted Metabolomics is perfect for:

- Clinical marker discovery and development
- Understanding mechanisms behind disease progression
- Studying drug efficacy and toxicity
- Environmental toxicology research

# Selected publications

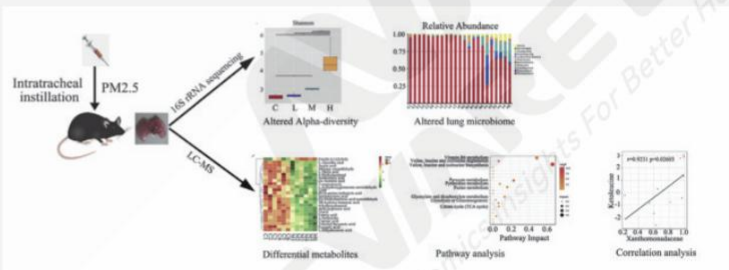
| Year | Journal | Title |
|---|---|---|
| 2020 | Hepatology | MAIT Cell Dysregulation Correlates with Conjugated Bilirubin Level in Chronic Hepatitis B Virus Infection |

This study reveal MR1-dependent anti-HBV potential of MAIT cells and identify conjugated bilirubin as a major factor dysregulating its frequency and function in chronic HBV-infected patients, suggesting a novel therapeutic target for MAIT cell-based immunity against chronic HBV infection.




| Year | Journal | Title |
|---|---|---|
| 2020 | Science of the Total Environment | PM2.5 exposure perturbs lung microbiome and its metabolic profile in mice |

In order to understand the mechanism underlying PM2.5-induced lung injury, 16S rRNA gene sequencing, and liquid chromatography-mass spectrometry (LC-MS) metabolomics analysis were conducted to investigate the impact of PM2.5 exposure on lung microbiome and its metabolic profile. 16S rRNA gene sequencing indicated that PM2.5 exposure significantly altered the richness, evenness, and composition of the lung microbiome. Metabolomics profiling showed that the levels of lung metabolites were perturbed after PM2.5 exposure.





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International Offices
8A Henshaw St., Woburn, MA, USA +1 (781)975-1541

www.metwarebio.com

support-global@metwarebio.com