WHITE SHEET

SAPIENT

What Discovery Metabolomics Reveals About Human Biology

Using metabolomics to **uncover disease mechanisms, risk states,** and **biological heterogeneity**

The Core Problem in Human Biology

Current molecular profiling approaches **remain insufficient to explain phenotypic variability** among individuals who share similar genetic backgrounds, clinical diagnoses, or lab values.

Across nearly every therapeutic area – from neurology to cardiometabolic disease, oncology, renal disease, inflammation, and aging-related disorders – investigators face **the same constraints:**

- Genomics explains risk, not necessarily actual state
- Proteomics captures regulation, but not exposure or flux
- Clinical labs collapse biology into blunt averages
- Animal models fail to reproduce human heterogeneity

What **Discovery Metabolomics** Makes **Possible**

Nontargeted, longitudinal plasma metabolomics **reveals how biological processes manifest in real people,** rather than how they are inferred or predicted.

Novel biology is the key to discovery. Sapient's metabolomics approaches provide a **scalable way to measure functional metabolic states in humans**, which enables researchers to:

- Define **biologically distinct** human subpopulations
- Separate **disease presence from disease mechanism**
- Reveal **system-wide effects** invisible to tissue-specific markers
- Capture **environmental, microbial, and drug-related biology** simultaneously

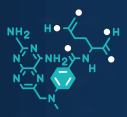
Key discovery metabolomics use cases

Define biologically distinct human subpopulations

Metabolomics data identifies stable "metabotypes" – distinct metabolic states – across human populations that **reflect fundamentally different characteristic metabolic phenotypes.**

- Individuals with similar demographics, genomics, and laboratory values can **have distinct molecular states correlating to very different disease risk**

KEY INSIGHT



Disease categories defined by diagnosis or lab cutoffs obscure real biological subgroups. **Metabolomics recovers them.**

Separate disease presence from disease mechanism

Metabolomics can **identify subpopulations of disease with distinct, differing pathobiology.** For example, multiple cardiometabolic risk states have non-overlapping lipid, fatty acid, and microbiome-linked metabolites.

- In cardiovascular disease, Alzheimer's disease, autoimmune disease, and cancer, metabolomics can **identify different subpopulations with distinct disease biology**

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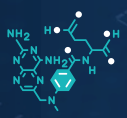

Metabolomics **distinguishes *how* disease manifests,** not just *whether* it is present.

Reveal system-wide effects invisible to tissue-specific markers

Plasma metabolites **integrate signals from multiple tissue beds** including the liver, kidneys, muscle, and adipose, as well from the immune system, gut microbiome, and environmental and dietary exposures.

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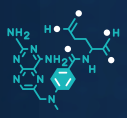


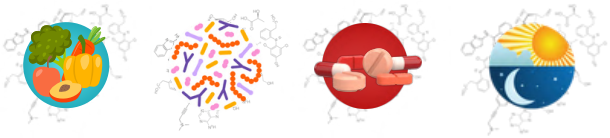
Many organ-specific diseases have systemic effects. Metabolomics allows for **early detection of whole-body physiological stress.**

Capture environmental, microbial, and drug-related biology simultaneously

Unlike genomics or transcriptomics, metabolomics **captures non-genetic factors and exposure biology** that influence disease by detecting:

- **Dietary** compounds
- **Microbiome-derived** metabolites
- **Drug** metabolites
- **Environmental** exposures (e.g., PFAS)

These biomarkers reflect dynamic **host-environment exposures** which traditional omics cannot reveal.



KEY INSIGHT

Metabolomics **closes the gap between environment, host biology, and disease phenotype.**

Sapient's discovery metabolomics workflows

With unmatched metabolome coverage and rapid, high-throughput workflows, we enable metabolite and lipid biomarker discovery at an **entirely new speed and scale.**

Category	Technical Specification
Metabolites Captured	**>15,000 features** per plasma sample including **polar metabolites, polar lipids, nonpolar lipids, and bioactive lipids**
Metabolite Identification	**Up to 1,400 metabolites identified** using our library of **>13,000 reference standards**
Unknown Molecules	**Putative structural identification** using our database of **>6M MS2 spectra** representing more than **850,000 compounds**
Throughput	Capacity to analyze **>2,000 samples per day**
Quality Metrics	**Continuous monitoring of >500 parameters** including pooled replicate samples and exogenous system performance standards introduced to each sample
Pathways Annotated	Common pathways include **amino acids, fatty acids, triacylglycerols, phosphatidylcholines, eicosanoids, carbohydrates and conjugates, bile acids, alcohols and derivatives, sphingomyelins, diacylglycerols, ceramides, oxylipins, perfluorochemicals, benzoic acids, hydroxysteroids, and steroid esters**

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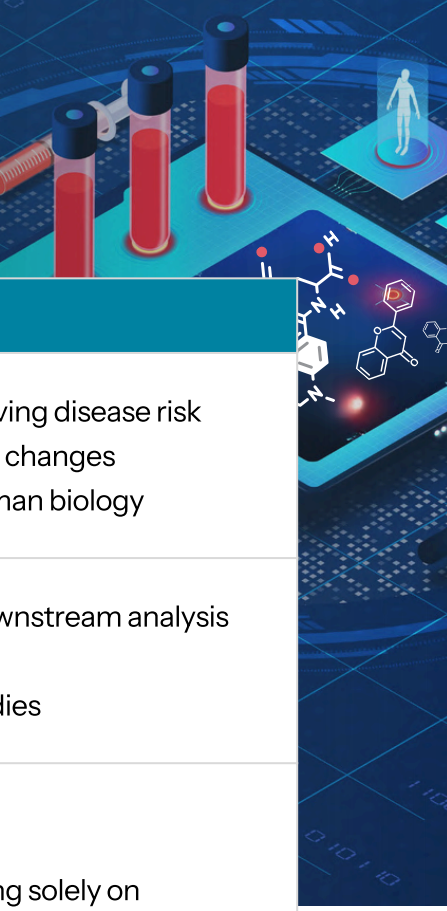
Insights enabled by robust discovery metabolomics data



Application	Insights Enabled
Human disease mechanism discovery	• Identify **previously unrecognized pathways** driving disease risk • Distinguish **causal vs. compensatory** metabolic changes • Generate **testable hypotheses** grounded in human biology
Patient stratification for translational studies	• Define **molecularly coherent subgroups** for downstream analysis • **Reduce noise** from heterogeneous cohorts • **Improve signal detection** in underpowered studies
Longitudinal biology	• Track within-person **metabolic trajectories** • Study **disease progression vs. remission** • **Measure response** to intervention without relying solely on clinical endpoints
Cross-disciplinary research	• **Integrate metabolomics** with genomics, proteomics, imaging, or clinical data for deeper biological context • Enable **systems-level models** of human physiology

This is **not a targeted assay** looking for known answers. It is a **discovery framework** that lets investigators ask:

- Why do some patients respond to a given therapy and others don't?
- What exposure signals modify genetic risk?
- Which biological processes actually differ between phenotypically similar people?
- Which metabolic signals precede clinical disease, and what contributes to disease progression?

Sapient's metabolomics to advance your research

Our robust discovery approaches can help you **resolve heterogeneity, mechanism, or trajectory** that other omics have not, with:

- Access to **population-scale reference biology** for statistically powered discovery
- **Biology-first interpretation,** not just feature tables
- Reusable datasets for **multiple hypotheses**

Contact discover@sapient.bio to discuss your study needs.