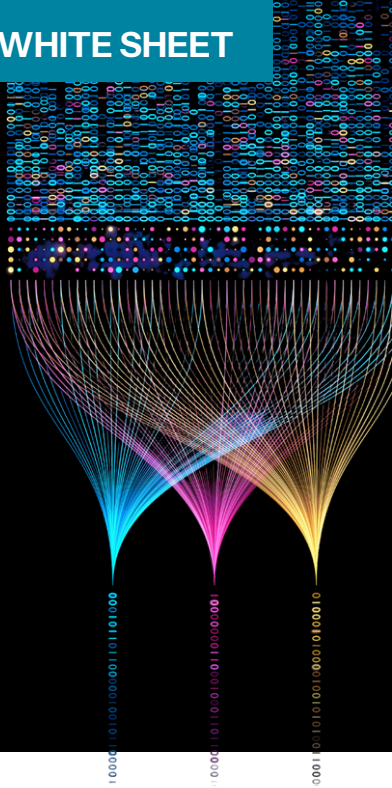
WHITE SHEET

SAPIENT

DynamiQ™ Metabolic Foundation Model

A foundation AI model of human metabolic state for de-risking drug development



The DynamiQ™ metabolic foundation model reads the dynamic physiology of a patient from a single blood sample, **revealing the metabolic state that determines disease trajectory, drug response, and toxicity.** It gives drug development teams a powerful tool to enrich trials, discontinue failing programs earlier, and detect safety signals that are hidden to genomic, structural, and clinical record models.

Patients who share the same diagnosis, driver mutation, or baseline lab value can respond to the same therapy in markedly different ways and progress along distinct trajectories. **That heterogeneity is a primary driver of the industry's most expensive failures:** pivotal trials diluted by patients the drug was never going to help, molecules advanced into late-stage development without ever engaging their intended biology, and safety signals identified too late to address. The differences lie in each patient's physiological state: **the integrated, real-time output of genotype, microbiome, diet, exposure, and organ function.**

The DynamiQ metabolic foundation model closes this gap. It learns a reusable representation of the circulating metabolome – the functional layer that reflects a patient's dynamic physiology – and applies it to answer critical questions that drug development teams are asking each day: which patients to enroll, whether a molecule is engaging its intended biology, and whether a safety liability is emerging.

The representation is learned once and reused across therapeutic areas, programs, and development phases, **providing a physiology-based readout that no other licensed model can deliver.**

What Existing Foundation Models Measure – and What They Miss

A new class of asset has arrived in drug discovery: the biological foundation model, licensed to pharma on recurring commercial terms. These models are powerful, but the data that trains them defines both their strengths and their limits.

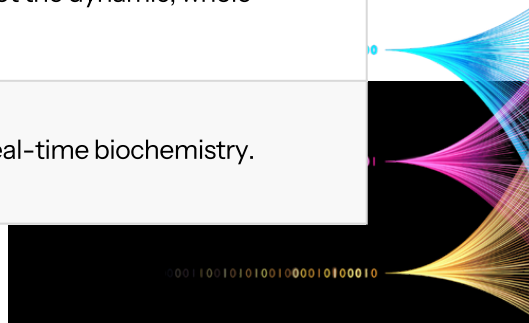
Existing Model Class	Key Limitaton for Patient-Level Decisions
Genomic models	Describe inherited risk and expression potential, not the physiological state a patient is actually in.
RNA-based models	Encompass intermediate signals in singular tissues rather than whole-body physiology.
Spatial and single-cell tumor atlases	Capture tissue morphology in a single biopsy, not the dynamic, whole-body circulating state.
Clinical and multimodal record models	Summarize documented medical history, not real-time biochemistry.

Most of these models capture a static or localized property, such as a sequence, an inherited variant, or a snapshot of a single tissue. None measure the dynamic, whole-body physiological state that separates one patient from another once a program is underway.

That systemic state is carried by the circulating metabolome as the functional integrator in which genotype, microbiome, diet, exposure, and physiology converge into a single measurable readout. The DynamiQ model is built to capture this state, giving drug development teams a systemic view of each patient rather than one that is static or tissue-bound.

The Power of the DynamiQ Metabolic Foundation Model

The model is trained by self-supervised learning on Sapient's DynamiQ database, the largest standardized resource of human metabolism assembled for this purpose. During training it learns to reconstruct masked metabolites and preserve the covariation structure across pathways, mapping the intrinsic



PREDICTIONS AND MEASUREMENTS, NOT TARGET HYPOTHESES

The DynamiQ model outputs **predictions** – which patients will respond, which are at high risk – and **measurements** – whether a drug is engaging its intended biochemistry, or whether an organ injury signature is emerging.

organization of human metabolic biology rather than optimizing for a single labeled outcome. **Because the representation is learned from population-scale metabolic structure, it is robust to cohort shift, missing data, and sparsely observed phenotypes, and it captures the latent states that drive differential drug response and disease progression.**

The defensibility of the model rests on the data beneath it. Model architectures are commoditizing quickly, but the input is not. Broad, standardized metabolomics at this scale cannot be assembled without a purpose-built analytical platform and years of harmonized data collection. **The DynamiQ database comprises:**

Over 67,000 human plasma samples collected longitudinally from more than 13,000 individuals.

15,000+ metabolite and lipid features per sample, including thousands of unannotated features that encode biochemical activity invisible to genomics, transcriptomics, and proteomics.

Matched EHR data and clinical outcomes across more than 60 diseases, spanning cardiometabolic, hepatic, renal, immune-mediated, inflammatory, and neurodegenerative conditions.

Standardized rLC-MS acquisition engineered for batch and collection site invariance – the properties that makes a metabolomic model trustworthy across trials.

DynamiQ™
INSIGHTS ENGINE

A BLOOD-BASED MODEL FOR SYSTEMIC DISEASE

Cardiometabolic, hepatic, renal, immune-mediated, and inflammatory diseases do not localize to a single tissue – their biology is expressed throughout the body. **Blood is the only practical window into that whole-body state, and the circulating metabolome provides the richest functional readout.**

The DynamiQ model is built for exactly this space, giving development teams a systemic, tissue-independent view of diseases that tissue-based models alone cannot resolve.

Key Applications in Drug Development

Read in different ways, the DynamiQ metabolic foundation model addresses three of the most consequential problems in clinical development.

Patient Stratification and Trial Enrichment

Response to metabolic and immune therapies is itself largely a metabolic phenotype, so **a baseline blood signature can separate likely responders from non-responders before enrollment and focus a trial on those patients most likely to benefit from the drug.**

The same capability supports prognostic enrichment for event-driven trials. Cardiovascular outcome trials, for example, commonly enroll 10,000 to 14,000 patients over three to six years because modern background therapy suppresses event rates. Enriching for a higher-risk population decreases the required trial size. By lifting the annual event rate from roughly 3.5% to 5.25% enrollment can be reduced from about 14,000 patients to about 9,300, which on a study costing hundreds of millions of dollars represents tens to well over a hundred million dollars in savings.

Baseline metabolic signatures identify likely responders and high-risk patients, ***concentrating and shrinking trials.***

Disease State and Pharmacodynamics

Because mass spectrometry measures what is present in the blood at a given moment, the model reads out biological state directly and non-invasively. This is particularly beneficial for disease states such as metabolic-associated liver disease, where tissue sampling is difficult. **On treatment, it detects whether a molecule is shifting the metabolome along its intended mechanistic axis,** providing a pharmacodynamic and target engagement (TE) readout weeks before a clinical endpoint moves. This converts a slow and expensive failure into an early, low-cost go or no-go decision.

On-treatment metabolome shifts read TE ***weeks before the clinical endpoint.***

Safety and Toxicity Profiling

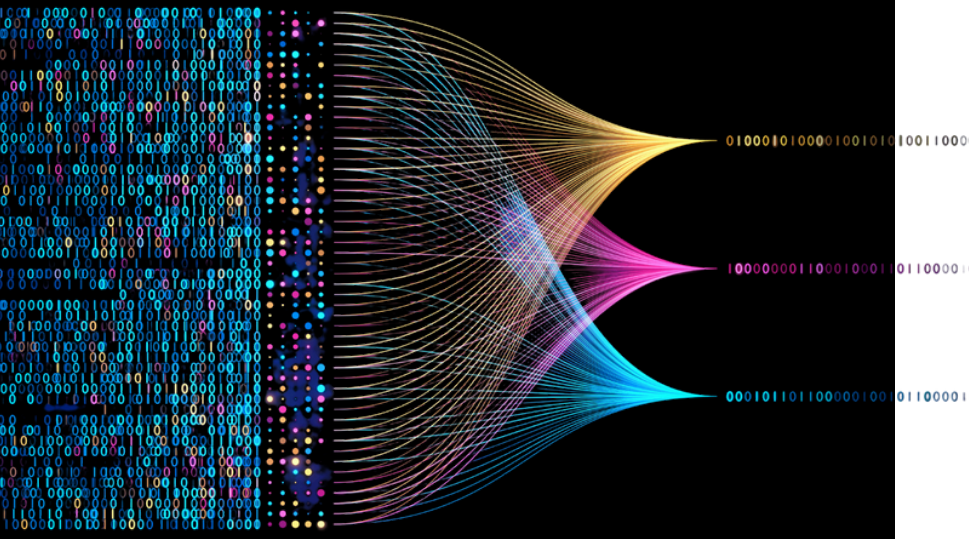
Human toxicity is a leading cause of program failure but still difficult to predict with standard omics measures. Muscle and lean-mass catabolism, drug-induced liver injury, and nephrotoxic or metabolic signatures appear in circulating biochemistry – often before standard clinical measures register them – and **the DynamiQ foundation model captures this chemistry to read out emerging organ injury and metabolic stress.** Continuous metabolic safety monitoring surfaces these signals while they are still a protocol decision in early development, rather than a label restriction or cause for program withdrawal.

Injury and metabolic-stress signatures ***flag toxicity while it is still a protocol decision.***

De-Risking Drug Development with DynamiQ Data

Historically, patient heterogeneity in a trial has been **approached through the lens of diagnosis, genotype, and standard laboratory values.**

The DynamiQ metabolic foundation model **reframes it around a direct question: what is each patient's metabolic state, and how does that state predict response, risk, and tolerability?** Answering those questions align patient selection and trial interpretation with the physiology that actually drives outcomes.



Evaluate the Model with Your Own Samples

Sapient can scope a retrospective analysis on a subset of your banked baseline samples from a completed or ongoing program to demonstrate the model's results and how it can be applied to answer critical questions across discovery, translational, and clinical development including:

- Which patients are most likely to respond to a given therapy?
- Can an outcome trial be enriched to reduce trial size and costs?
- Is a metabolic safety signal emerging before it becomes a label or franchise risk?
- Why did a completed trial succeed or fail in the patients it enrolled?

To discuss a scientific collaboration or model licensing engagement, contact discover@sapient.bio.

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