MARKER *of the* MONTH

Exploring **known & novel associations of key biomarkers** using Sapient's **DynamiQ™ Insights Engine**

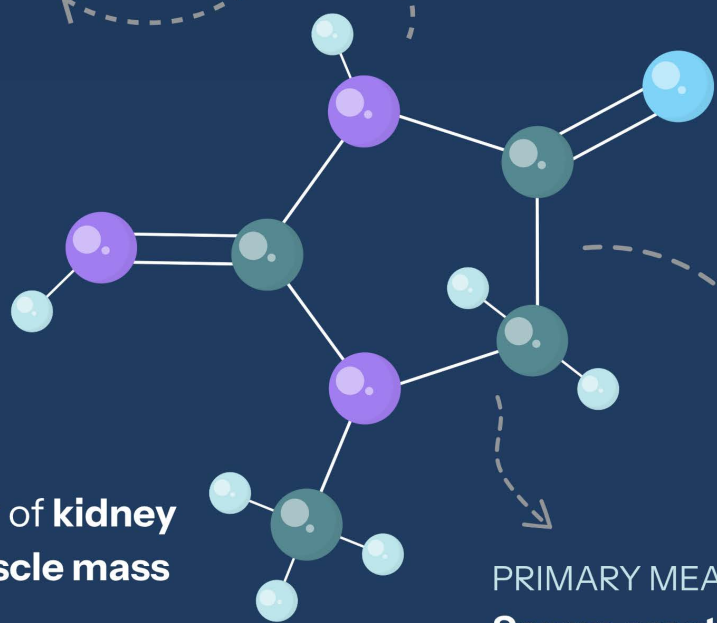
Creatinine

MOLECULAR FORMULA

$C_4H_7N_3O$

BIOLOGICAL CLASS

Small organic molecule (nitrogenous waste product)



KEY SOURCE

Muscle metabolism, formed from the breakdown of creatine phosphate

CLINICAL USE

Surrogate marker of **kidney function and muscle mass**

PRIMARY MEASUREMENT

Serum creatinine (SCr), **urinary creatinine**

Biological Origin and Physiological Role

Creatinine is the end product of creatine and creatine phosphate metabolism, representing a **normal waste product that the human body produces when muscle tissue breaks down.**

Creatine synthesis occurs mainly in the kidney, liver, and pancreas from glycine, arginine, and methionine, and is then transported to muscle tissue and phosphorylated to creatine phosphate. **During normal muscle metabolism, creatine and creatine phosphate undergo spontaneous, irreversible conversion to creatinine.** The creatinine enters the bloodstream and is subsequently filtered by the kidneys and released from the body via urine.

While creatinine itself has no active biological function, it is the most widely used surrogate biomarker of kidney function. Serum creatinine levels reflect glomerular filtration rate (GFR) efficiency: as filtration declines, creatinine rises, which can indicate impaired kidney health. Low levels of creatinine are also associated with reduced muscle mass and certain liver diseases.

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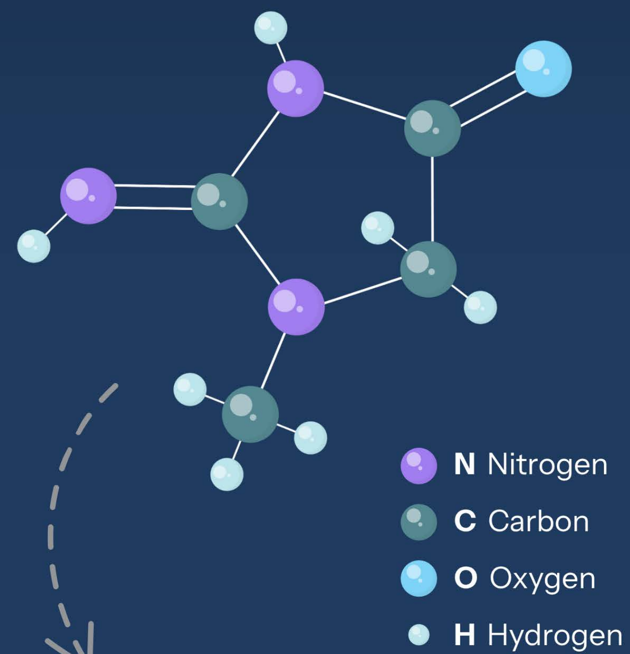
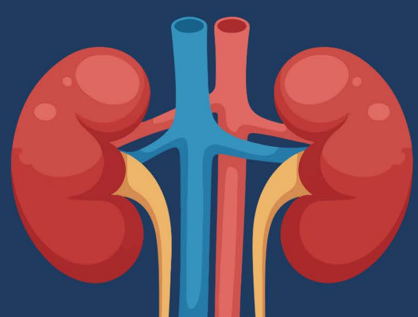
Creatinine





Creatinine Disease Associations

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Altered creatinine levels often reflect impaired kidney filtration, but can also be influenced by other systemic or muscular conditions. Key disease associations include:

Disease or Condition	Pathophysiological Link
Chronic Kidney Disease (CKD)	Reduced nephron filtration capacity in CKD leads to increased accumulation of creatinine. (Choi 2022)
Type 2 Diabetes (T2D)	High creatinine in patients with T2D often indicates diabetic nephropathy caused by chronic hyperglycemia and hypertension. (Butt 2024)
Cardiovascular Disease	Reduced renal prefusion can lead to elevated creatinine, which correlates with higher risk of stroke and myocardial infarction. (njp Cardiovasc Health 2024)
Systemic Lupus Erythematosus (SLE)	Autoimmune attacks on renal tissue can cause lupus nephritis, impairing creatinine filtration. (Musa 2025)
Sarcopenia and Muscle Wasting	Low muscle mass leads to decreased creatinine production. (Garcia-Torres 2020)
Liver Disease	Impaired creatine synthesis in the liver decreases creatinine production. (Slack 2010)

Clinical Significance

Estimating kidney function accurately and detecting changes in kidney performance in a timely fashion are critically important for a range of diseases. **Creatinine is a well-established and widely used biomarker to calculate estimated GFR (eGFR) in serum or for direct filtration estimation of creatinine clearance from 24-hour urine.** However, this marker *does have shortcomings* to be considered in clinical interpretation.

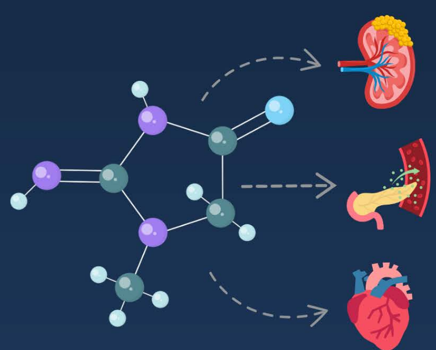
Most notably, creatinine levels can be influenced by muscle mass, diet, age, sex, and hydration. For example:

In cohorts with low muscle mass such as elderly patients, creatinine measures **may appear normal or low despite impaired kidney function.**

Creatinine provides limited sensitivity to detect early kidney dysfunction, as renal function can be **decreased by as much as 50% before a rise in serum creatinine** is observed.

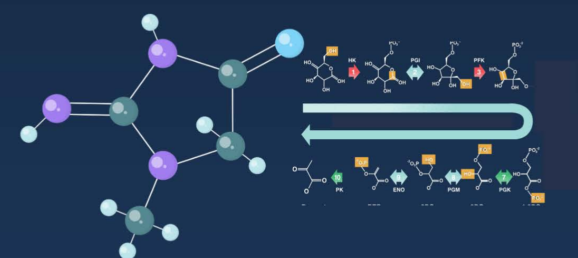
While creatinine remains an indispensable biomarker for clinical practice, **integration with additional or alternative biomarkers may offer a more precise and timely view of renal health.**

To that end, **Sapient has used our DynamiQ™ Insights Engine to profile creatinine in patients with CKD and T2D and to probe these questions:**



Can we **replicate known associations** between creatinine and these diseases in our DynamiQ cohorts?

Can we **identify other biomarkers beyond creatinine** that show similarly strong correlation with CKD and T2D?



What more **can we learn about creatinine within the broader context of metabolic disruptions** involved in these diseases?

Exploration of Creatinine in DynamiQ

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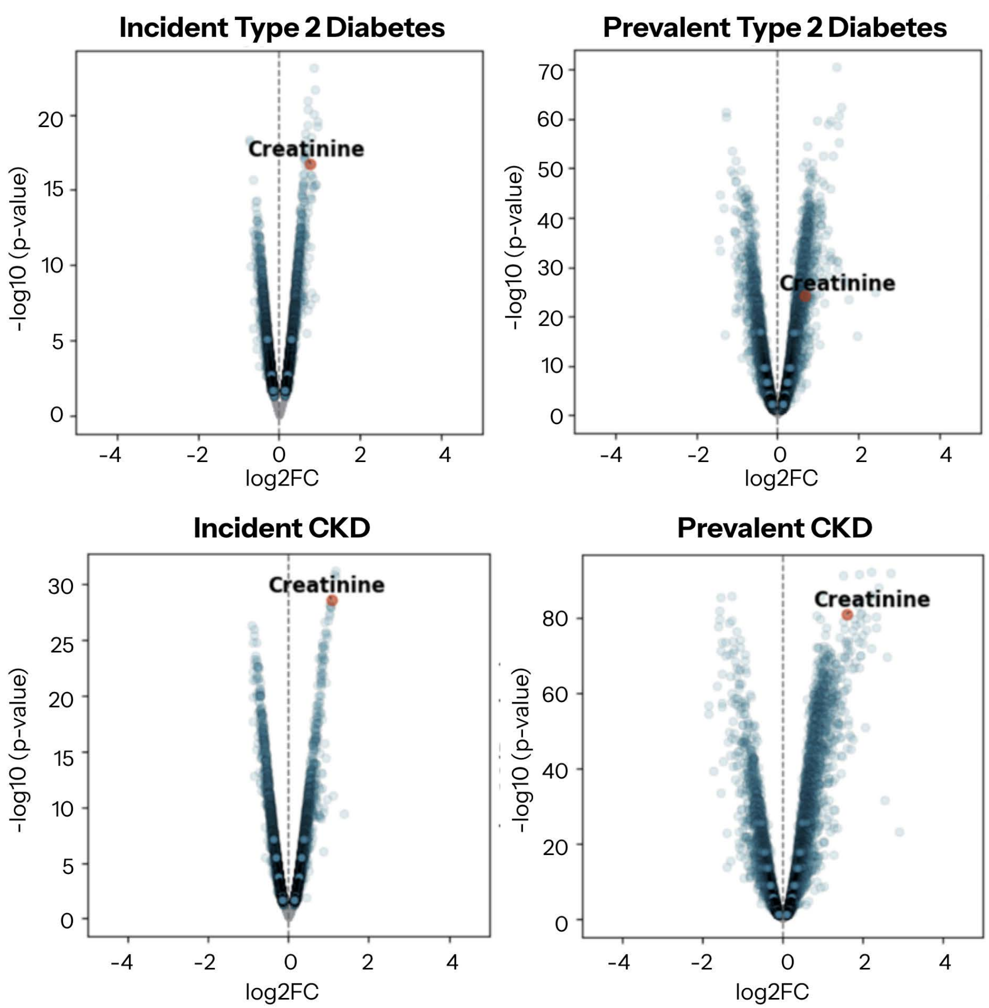
The following data is from analysis of 8,320 samples collected from 2,462 individuals.



Across more than 15,000 metabolites, we identified hundreds of molecules that are differentially expressed in both incident and prevalent T2D and CKD. **Creatinine ranks among the most significantly altered metabolites, consistent with well-established clinical reporting.**

We additionally find **multiple other metabolites that exhibit even larger effect sizes, which may represent novel biomarkers** with greater association strength than creatinine.

DynamiQ™

INSIGHTS ENGINE

Exploration of Creatinine in DynamiQ

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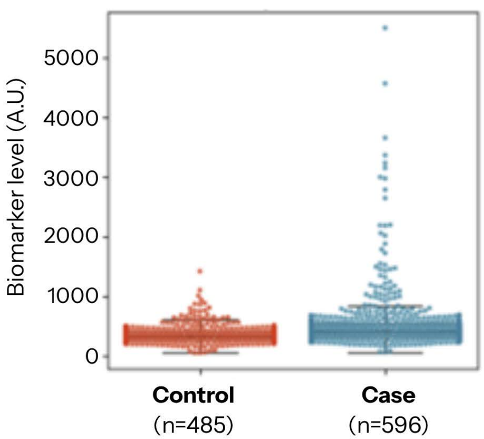
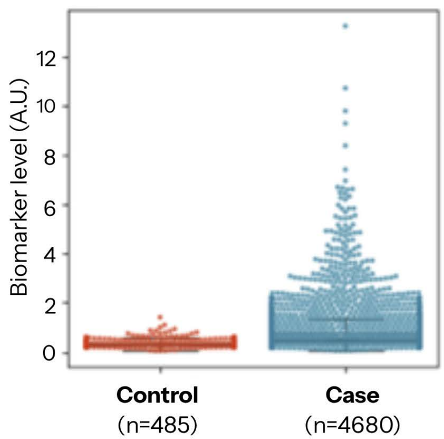
Taking a **closer look at key metabolites with effect sizes larger than creatinine,** we observe distinct distribution patterns between cases (individuals with T2D or CKD) and controls, with **biomarker levels significantly altered in disease groups compared to healthy individuals.**

METABOLITE A

Incident Type 2 Diabetes
P = 2.3E-22

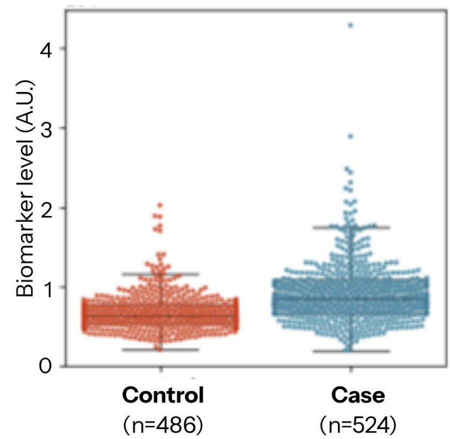


Prevalent Type 2 Diabetes
P = 3.2E-71

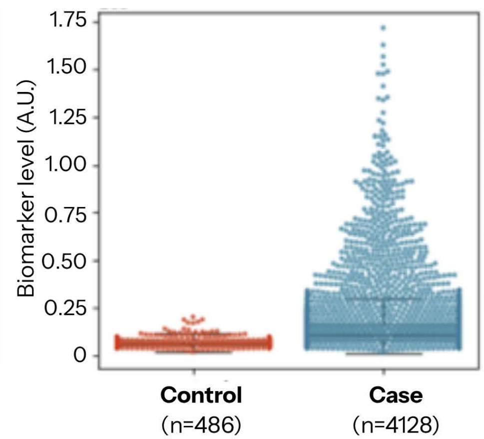


METABOLITE B

Incident CKD
P = 2.7E-22



Prevalent CKD
P = 5.8E-93



DynamiQ™
INSIGHTS ENGINE

Exploration of Creatinine in DynamiQ

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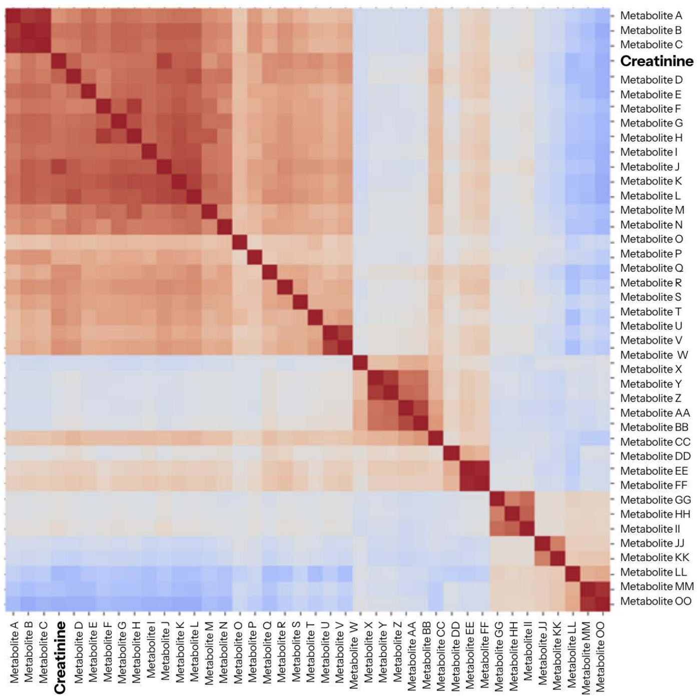
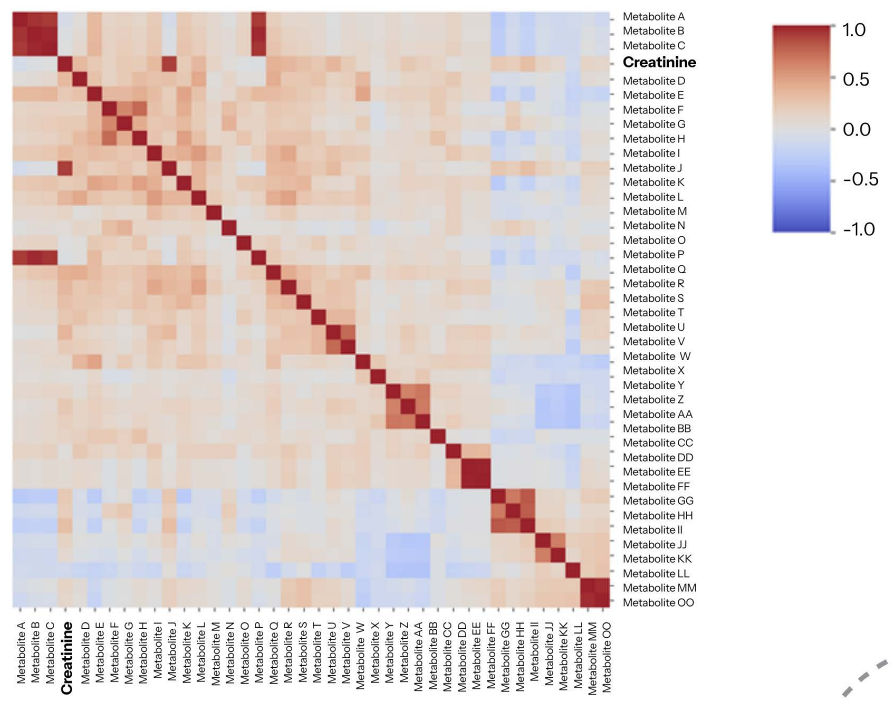
Correlation analysis of significantly changed metabolites, including creatinine, in patients with CKD reveals further metabolic variation compared to healthy individuals. In the disease group, **creatinine appears within a large cluster of co-dysregulated metabolites, suggesting it is part of a broader metabolic network disruption.** In contrast, healthy individuals exhibit weaker correlations, indicating these metabolites function more independently under normal conditions.

Prevalent CKD – Case



Prevalent CKD – Control



Exploration of Creatinine in DynamiQ

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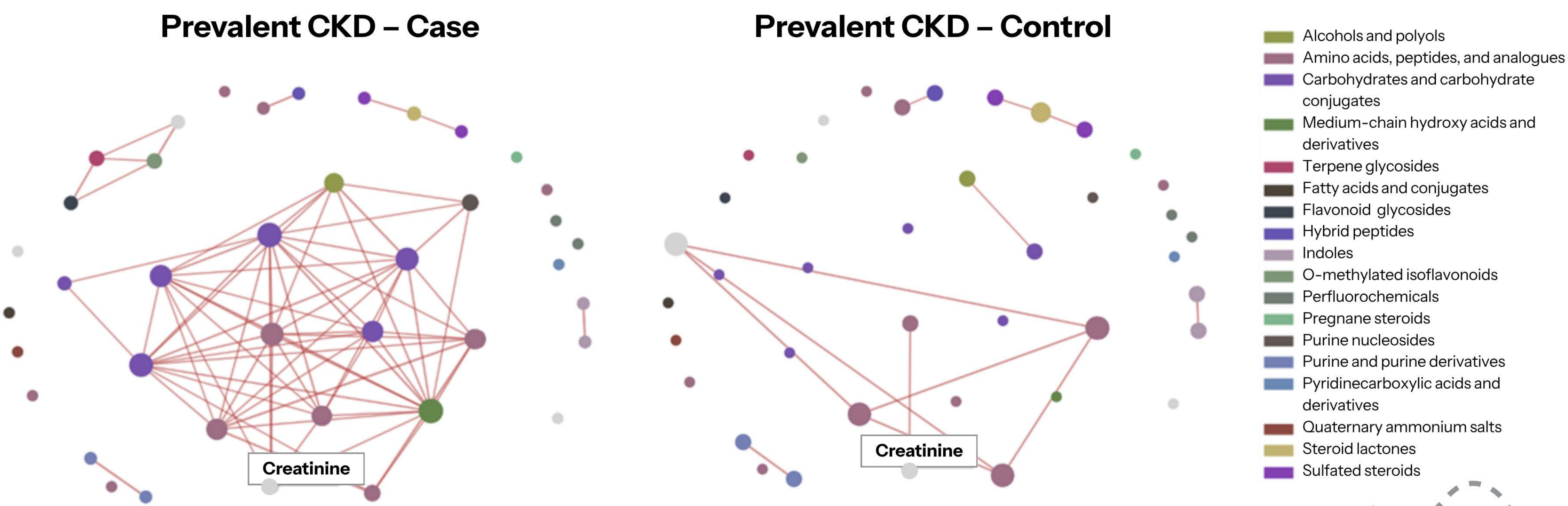
This is exemplified by the network plots below which **visualize inter-metabolite associations with creatinine in both CKD patients and healthy individuals. The disease population exhibits markedly stronger correlations among dysregulated metabolites,** suggesting coordinated metabolic changes that may provide insights into CKD pathophysiology.



DynamiQ™
INSIGHTS ENGINE

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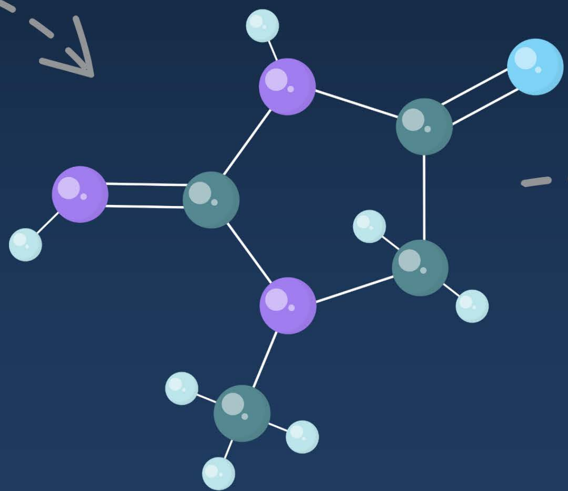

Creatinine

Extending Creatinine Insights with Novel Markers of the Future

Creatinine remains one of the most widely used and clinically validated biomarkers for assessing kidney function, owing to its clear physiological origin and established role in estimating GFR. However, its limitations – such as lack of sensitivity to detect early kidney dysfunction – highlight **the need for broader metabolic context.**

Our DynamiQ™ analysis confirms creatinine's strong association with CKD and T2D, consistent with clinical expectations, while also revealing metabolites with even greater effect sizes and distinct correlation patterns. These findings underscore the importance of discovery metabolomics to probe the broader landscape of human chemistry, revealing novel biomarkers and biomarker signatures that expand our disease understanding.

Such analyses can enable the **integration of creatinine with additional biomarkers to capture the broader metabolic disruptions underlying disease and improve diagnostic precision.** By expanding beyond traditional markers, we can advance toward more comprehensive and personalized approaches to address kidney and metabolic diseases.

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Exploring **known & novel associations of key biomarkers** using Sapient's **DynamiQ™ Insights Engine**

Interested in **exploring your marker of interest** in Sapient's DynamiQ database? Ready to expand the scope of your biomarker analyses to **reveal novel insights?**

Reach out to schedule a time to speak with our scientists.

BOOK A MEETING

SAPIENT

+ **sapient.bio/contact**
+ **discover@sapient.bio**
+ **858.290.7010**