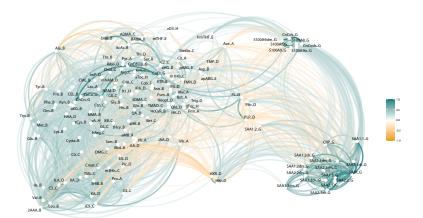
# BEVITAL

# Assessment of Disease Risk by Targeted Metabolomics



#### High precision data

BEVITAL's methods have been developed by our scientists and technicians, and have been published in leading scientific journals within the fields of analytical technology. BEVITAL's analytical repertoire covers high to low abundance biomarkers which are quantified by targeted metabolomics. Our methods use authentic isotopelabelled internal standards which deliver highly precise biomarker quantification with superior CVs in comparison to methods based on non authentic standards.

#### Disease related biomarkers and comprehensive coverage of whole pathways

The analytical repertoire of BEVITAL covers defined, cross-talking pathways, cofactors involved, and biomarkers reflecting key lifestyle factors, nutritional status, kidney and endothelial function, and inflammation. Biomarkers are allocated to complementary platforms characterized by multiplexing, high capacity, large dynamic range, and low volume consumption to save precious biobank material. More than 130 biomarkers are measured in less than 500 µL.

#### Scientific support from analysis planning to data interpretation

Most scientists at BEVITAL have for decades been involved in scientific projects and can provide academic support, including collaboration and contributions to writing of funding applications and scientific articles. If requested, we also offer support in statistical data analysis using sophisticated methods based on R and Shiny apps.

#### Track record in international, EU-, and NIH-funded projects

BEVITAL was founded in 2003 by members of a research group with more than 25 years experience in bioanalytical technology, including chromatography and mass spectrometry. BEVITAL has been partner in several international projects that involve instrument development, establishment of new technologies, and their application in large epidemiological projects, such as the lung cancer consortium (LC3).

#### **Platform specifications**

Technology (n): GC-MS/MS (2), LC-MS/MS (5), MALDI-TOF MS (1), Microbiological (1)

Sample type: Serum and plasma; cerebrospinal fluid, urine, and whole blood for

selected biomarkers

Sample volume: 15 - 500µL, depending on number of platforms

Number of biomarkers: 137

**Quantification:** Absolute biomarker quantification from pM to mM

**Between-run precision (median):** 2.7% on GC-MS/MS and 4.4-5.9% on LC-MS/MS

#### Vitamins & Lifestyle

#### B vitamins

- Cobalamin
- · Folate species and catabolites
- · Folate, erythrocyte
- Folate, serum
- Functional B6 marker, HK:XA
- · Functional B6 marker. HKr
- HCC index
- mNAM
- RBC-folate as pABG equivalents
- Serum folate as pABG equivalents
- Vitamin B1
- Vitamin B2 (riboflavins)
- Vitamin B3
- · Vitamin B6 species

#### Fat soluble vitamins

- A vitamer
- D vitamers
- E vitamers
- K vitamers

#### Folate and cobalamin

- Cobalamin
- · Folate, erythrocyte
- · Folate, serum
- HCC index
- Homocysteine
- Methylmalonic acid
- RBC-folate as pABG equivalents
- Serum folate as pABG equivalents

#### Meat and fish

- 1-Methylhistidine
- 3-Methylhistidine
- Trimethylamine-N-oxide
- β-Alanine

#### Tobacco and coffee

- 3-Hydroxycotinine
- Cotinine
- Trigonelline

#### **Pathology & Physiology**

#### Diabetes

- · 2-Aminoadipic acid
- · 2-Hydroxybutyrate
- 3-Hydroxybutyrate
- 3-Hydroxyisobutyrate
- Acetoacetate
- · Branched-chain amino acids
- HbA1c
- · Imidazole propionate

#### Endothelial function

- Arginine
- · Asymmetric dimethylarginine
- Homoarginine
- · Symmetric dimethylarginine

#### Inflammation

- · C-reactive protein
- Calprotectin and variants
- · Kynurenine/tryptophan ratio
- Neopterin
- PAr index
- Serum amyloid A and variants

#### Keton bodies

- 3-Hydroxybutyrate
- Acetoacetate

#### Liver pathology

· Amino acid ratios

#### Neuroactive

- 3-Hydroxykynurenine
- · Kynurenic acid
- Picolinic acid
- · Quinolinic acid

#### Oncometabolites

- Fumarate
   α-Hydroxyglutaric acid
- Lactate
- Succinate

#### Renal function

- Creatinine
- · Cystatin C and variants
- · Symmetric dimethylarginine

#### Uremic toxin

· 3-Indoxyl sulfate

#### **AGEs**

- · Carboxyethyllysine
- Carboxymethyllysine

#### Amino acids and metabolites

- 1-Methylhistidine
- · 2-Aminoadipic acid
- · 3-Hydroxyisobutyrate
- · 3-Methylhistidine
- Arginine
- Citrulline
- Cysteine
- Glycine
- Histidine
- · Imidazole propionate
- Methionine
- · Methionine sulfoxide
- Ornithine
- · Other amino acids

Aspartic acid (Asp), glutamic acid (Glu), lysine (Lys), alanine acid (Ala), phenylalanine (Phe), isoleucine (Ile), leucine (Leu), proline (Pro), valine (Val), asparagine (Asn), glutamine (Gln), threonine (Thr), and tyrosine (Tyr).

- Serine
- Tryptophan
- β-Aminoisobutyrate

#### Acylcarnitines

- Carnitine
- · Carnitine, total
- · Short-, medium-, and long-chain acylcarnitines

#### **Metabolites & Pathways**

#### Choline oxidation pathway

- Betaine
- · Choline, free
- · Choline, total
- Dimethylglycine
- Glycine
- Sarcosine
- Serine
- Trimethylamine-N-oxide

#### Citric acid cycle

- Citrate
- Fumarate
- Isocitrate
- Lactate
- Malate
- Pvruvate
- Succinate
- α-Hydroxyglutarate
- α-Ketoglutarate

#### Microbiota-derived

- 3-Indoxyl sulfate
- · Imidazole propionate
- Indole-3-acetamide
- Indole-3-acetate
- Indole-3-aldehyde
- Indole-3-lactate
- Indole-3-propionate
- · Short-chain fatty acids Trimethylamine-N-oxide

#### One carbon metabolism

- Betaine
- · Choline, free
- Cobalamin
- Dimethylglycine
- Folate, erythrocyte
- · Folate, serum
- Formate
- Glycine
- HCC index

- Homocysteine
  - Methionine
  - Methylmalonic acid
- RBC-folate as pABG equivalents
- Sarcosine
- Serine
- · Serum folate as pABG equivalents

#### Transsulfuration

- Cystathionine
- Cysteine

#### Tryptophan metabolites

- · 3-Indoxyl sulfate
- · Indole-3-acetamide
- · Indole-3-acetate
- Indole-3-aldehyde
- Indole-3-lactate
- · Indole-3-propionate
- Kynurenine
- Kvnurenines Tryptophan

#### Urea cycle

- Arginine
- Aspartate
- Citrulline Ornithine

#### Others

- Creatine
- · Trimethyllysine



### Platform A GC-MS/MS Short-chain fatty acids.

Sample vol.: 50 µL

Concentrations in µmol/L

- Acetate
- Butyrate
- Formate
- Isobutyrate

- Isovalerate
- Propionate
- Valerate

Pyruvate

Sarcosine

Total cysteine

Tryptophan

α-Ketoglutarateβ-Alanine

β-Aminoisobutyrate

Total homocysteine

α-Hydroxyglutaric acid

Serine

α-Methylbutyrate

Concentrations in µmol/L

# Platform B GC-MS/MS TCA metabolites and intermediates. Amino and carboxylic acids.

Sample vol.: 50 µL

- 2-Aminoadipic acid
- 2-Hydroxybutyrate
- 3-Hydroxybutyrate
- 3-Hydroxyisobutyrate
- Acetoacetate
- Carboxyethyllysine
- Carboxymethyllysine
- Citrate
- Cystathionine
- Fumarate
- Glycine
- Histidine
- Isocitrate
- Kynurenines
- Lactate
- Malate
- Methionine
- Methylmalonic acid
- Ornithine
- Other amino acids:

Aspartic acid (Asp), glutamic acid (Glu), lysine (Lys), alanine acid (Ala), phenylalanine (Phe), isoleucine (Ile), leucine (Leu), proline (Pro), valine (Val), asparagine (Asn), glutamine (Gln), threonine (Thr), and tyrosine (Tyr).

Platform I LC (HILIC)-MS/MS

Short-, medium-, and long-chain
acylcarnitines.

New platform under development

# Platform C Choline derivates. Charged, methylated or sulfur amino acids. Short- and medium-chain acylcarnitines.

Sample vol.: 35 µL

- · 1-Methylhistidine
- 3-Methylhistidine
- Arginine
- · Asymmetric dimethylarginine
- Betaine
- Carnitine
- · Carnitine, total
- Choline
- Choline, total
- Citrulline
- Creatine
- Creatinine

Concentrations in µmol/L

- Dimethylglycine
- Histidine
- Homoarginine
- Methionine
- · Methionine sulfoxide
- · Short- and medium-chain acylcarnitines

LC-MS/MS

- · Symmetric dimethylarginine
- Total cysteine
- Total homocysteine
- Trimethylamine N-oxide
- Trimethyllysine

#### Platform D

## Kynurenine pathway and B vitamins (B1, B2, B3, B6).

Sample vol.: 60 µL

4-Pyridoxic acid

- Cotinine
- Cystathionine\*
- · Flavin mononucleotide
- Imidazole propionate\*
- Kynurenines\*
- Microbiota-derived indoles
- N1-methylnicotinamide
- Neopterin
- Nicotinamide
- Nicotinic acid

Concentrations in µmol/L (\*) or nmol/L

- Pyridoxal
- Pyridoxal 5-phosphate
- Pyridoxine
- Riboflavin
- Succinate
- Thiamine
- Thiamine monophosphate
- Trans-3-hydroxycotinine
- Trigonelline\*
- Trimethylamine N-oxide\*
- Tryptophan\*
- · Derived indexes:

HK:XA ratio

HKr

Kyn/Trp ratio

PAr

## Platform E LC-MS/MS Folate species and catabolites.

Sample vol.: 60 µL

Concentrations in nmol/L

- 4-Alfa-hydroxy-5-methyl-THF
- 5-Formyl-tetrahydrofolate
- 5-Methyl-tetrahydrofolate
- · Acetamidobenzoylglutamate
- · Folic acid
- · Para-aminobenzoylglutamate
- RBC-folate as pABG equivalents
- Serum folate as pABG equivalents

## Platform F Microbiological assay Folate (B9) and cobalamin (B12).

Sample vol.: 15–35 µL

Concentrations in nmol/L or pmol/L (\*)

- Erythrocyte folate
- Serum cobalamin\*
- Serum folate

## Platform G MALDI-TOF MS **Proteins and proteoforms.**

Sample vol.: 30 µL

Concentrations in µmol/L

LC-MS/MS

- C-reactive protein
- Calprotectin and variants
- Cystatin C and variants
- HbA1c
- Serum amyloid A and variants

# Platform H Lipid-soluble vitamins and long-chain acylcarnities.

Sample vol.: 50–100 µL

· All-trans retinol

Concentrations in µmol/L or nmol/L (\*)

- 25-hydroxy vitamin D2\*
- OF hardness with main DO\*
- 25-hydroxy vitamin D3\*
- α-tocopherol

· Phylloquinone\*

- arnitinaa
- · Long-chain acylcarnitines
- γ-tocopherol