How comprehensive metabolic profiling can enrich the UK Biobank sample collection

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Making precision medicine a reality
How can we get the best research out of large biobank collections?

- Electronic medical records
- Genomic data

Molecular data
How can we get the best research out of large biobank collections?
Metabolic profiling of the entire UK Biobank collection
Announcing…

Nightingale and UK Biobank will embark on a major initiative to analyse 500,000 volunteer blood samples to facilitate global medical research.
Nightingale’s technology
One sample, One test, Comprehensive metabolic profile

Routine lipids
14 lipoprotein subclasses
Particle size
Apolipoproteins
Fatty acids
Omega-3 and -6
Amino acids
Ketones
Inflammation
Fluid balance
Glycolysis
### Comprehensive metabolic profiling

#### Cholesterol (mmol/l)
- Total cholesterol
- VLDL cholesterol
- IDL cholesterol
- LDL cholesterol
- HDL cholesterol
- HDL2 cholesterol
- HDL3 cholesterol
- Remnant cholesterol
- Free cholesterol
- Esterified cholesterol

#### Glycerides & phospholipids (mmol/l)
- Total triglycerides
- VLDL triglycerides
- IDL triglycerides
- LDL triglycerides
- HDL triglycerides
- Phosphoglycerides
- Ratio of triglycerides to phosphoglycerides
- Total cholines
- Phosphatidylcholines
- Sphingomyelins

#### Apolipoproteins (g/l)
- Apolipoprotein A-1
- Apolipoprotein B
- ApoB/ApoA-1

#### Fatty acids and saturation
- Total fatty acids
- Estimated degree of unsaturation

#### Fatty acids (mmol/l and % of total FAs)
- Omega-3 fatty acids
- Omega-6 fatty acids
- Polyunsaturated fatty acids
- Monounsaturated fatty acids
- Saturated fatty acids
- Docosahexaenoic acid
- Linoleic acid

#### Ketone bodies (mmol/l)
- Acetate
- Acetoacetate
- 3-hydroxybutyrate

#### Glycolysis related metabolites (mmol/l)
- Glucose
- Lactate
- Pyruvate
- Citrate
- Glycerol

#### Fluid balance
- Creatinine
- Albumin

#### Inflammation (mmol/l)
- Glycoprotein acetylation (GlyC)

#### Amino acids (mmol/l)
- Alanine
- Glutamine
- Glycine
- Histidine
- Branched-chain amino acids
- Isoleucine
- Leucine
- Valine
- Aromatic amino acids
- Phenylalanine
- Tyrosine

#### Lipoprotein particle size (nm)
- Mean diameter of VLDL particles
- Mean diameter of LDL particles
- Mean diameter of HDL particles

#### Particle concentration and lipid composition for 14 lipoprotein subclasses
- Total lipids (mmol/l)
- Particle concentration (µmol/l)
- Cholesterol (mmol/l and % of total lipids)
- Esterified cholesterol (mmol/l and % of total lipids)
- Free cholesterol (mmol/l and % of total lipids)
- Triglycerides (mmol/l and % of total lipids)
- Phospholipids (mmol/l and % of total lipids)

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**Lipid composition for each blood sample**

- **Chylomicrons and extremely large VLDL**: >75.0
- **Very large VLDL**: 64.0
- **Large VLDL**: 53.6
- **Medium VLDL**: 44.5
- **Small VLDL**: 36.8
- **Very small VLDL**: 31.3
- **IDL**: 28.6
- **Large LDL**: 25.5
- **Medium LDL**: 32.0
- **Small LDL**: 18.7
- **Very large HDL**: 14.3
- **Large HDL**: 121
- **Medium HDL**: 10.9
- **Small HDL**: 8.7

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**Average particle diameter (nm)**

- **<10**: Small particles
- **10-20**: Medium particles
- **>20**: Large particles

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**Nightingale**
Nightingale Health Ltd.

Specialized in comprehensive metabolic profiling by NMR.

500,000 blood samples analyzed.

150+ scientific publications.

From biomedical science towards clinical use.
# Endless scientific opportunities

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Combining metabolic profiling with genetics
Enhanced drug development

Studying drug effects with a genetic proxy

Metabolic profiling

- Treatment indication
- On- and off-target effects
- Molecular mechanisms

Randomized clinical trial
Biomarker discovery and risk prediction

Lipoprotein subclasses
- Extremely large VLDL
- Very large VLDL
- Large VLDL
- Medium VLDL
- Small VLDL
  - Very small HDL
  - Small HDL
  - Large HDL
  - Medium HDL
  - Small LDL
  - Very large HDL

Standard lipids
- Total C
- VLDL C
- IDL C
- LDL C
- HDL C
- Triglycerides

Fatty acids
- Omega-3 fatty acids (%)
- DHA(%) 
- Omega-6 fatty acids (%)
- Linoleic Acid (%)
- PUFA (%) 
- MUFA (%) 
- Saturated fatty acids (%)

Glycolysis related metabolites
- Glucose
- Lactate
- Pyruvate
- Citrate
- Glycerol

Inflammation
- Glycoprotein acetyl (GlyA)

Amino acids
- Alanine
- Glutamine
- Glycine
- Histidine
- Branched-chain amino acids
  - Isoleucine
  - Leucine
  - Valine
- Aromatic amino acids
  - Tyrosine
  - Phenylalanine

Phenylalanine, risk factor adjusted & stratification
- All ages, incidence of CVD
- Ages 25-50, incidence of CVD
- Ages 50-75, incidence of CVD
- All ages, death from CHD
- All ages, death from stroke

Nightingale
Better clinical decision-making

Type 2 diabetes risk
- Current risk level: High
  - Glutamine: 42
  - Alanine: 5

Heart disease risk
- Current risk level: Moderate
  - Phenylalanine: 80
  - Omega-6 FA: 2.2

Total fatty acids
- 72% of people in your reference group have higher values
- Alanine
- 51% of people in your reference group have higher values
- Tyrosine
- 21% of people in your reference group have higher values
- Glutamine
- 8% of people in your reference group have higher values

Nightingale
“It is time to advance NMR spectroscopy and mass spec technologies for lipoprotein and apolipoprotein profiling to meet the high throughput, low cost, and standardization required for potential clinical use.”

- Dr Manuel Mayr (Journal of American College of Cardiology 2018)
Thank you!

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