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The Mab001 data product

Original number of samples	3,000
Number of samples (per 27.11.2023)	2,989
Number of unique participants	2,989
Biological sample type	Plasma
Participant type(s)	MoBa mothers
Collection timepoint	Gestational week ~17
Case-control selection criteria	None
Biomarker type(s)	Vitamin B and one-carbon metabolites
Original reference article	<u>Nilsen <i>et al</i>. 2010</u>
Analytical method(s)	GS-MS, LC-MS, and microbiological assay
Related MoBaBIO product(s)	Mab004, Gtp001
FHI Project number(s)	PDB168



VERSION 1.0.0.

Mab001

The project that generated these data

Pregnancy, one-carbon metabolism and related single nucleotide polymorphisms (SNPs)

Project lead: Stein Emil Vollset

The purpose of this study was to measure B-vitamins, B-vitamin markers, and related onecarbon metabolites in pregnancy, and study the potential associations and effects of these on adverse prenatal and postnatal health conditions and outcomes.

Study population

The original Mab001 biomarker data source is based on plasma samples from **3,000 mothers** whose babies were born between July 2002 and December 2003. The mothers were selected at random, but inclusion required that mothers had donated a blood sample at the second trimester routine ultrasound appointment, were registered in the Medical Birth Registry of Norway (MBRN) and had completed and returned a baseline questionnaire and a Food Frequency Questionnaire (FFQ) administered during the second trimester.

Available biomarker measures (variable names in bold)

(Note: the single letters at the end of each variable name (A/B/C/D/F) refer to the analysis platform used for data generation - see section on analytical methodology below)

3'-Hydroxyanthranilic acid (**HAA_D**) 3'-Hydroxykynurenine (**HK D**) Anthranilic acid (**AA A**) Arginine (**Arg C**) Asymmetric dimethylarginine (ADMA C) Betaine (Betaine C) Choline (Choline_C) Cobalamin (Cob F) Cotinine (**Cot D**) Creatinine (Creat_C) Cystathionine (Cysta A) Cystathionine (Cysta_D) Dimethylglycine (**DMG_C**) Folate (**spFolate_F**) Glycine (**Glycine A**) Kynurenic acid (**KA_D**) Kynurenine (**Kyn A**) Methionine (Met_A) Methionine sulfoxide (MetSo_C) Methylmalonic acid (MMA A)

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Neopterin (Neopt_D) Pyridoxal (PL_D) Pyridoxal 5'-phosphate (PLP_D) Pyridoxamine (PM_D) Pyridoxic acid (PA_D) Pyridoxine (PN_D) Riboflavin (Ribo_D) Serine (Serine_A) Symmetric dimethylarginine (SDMA_C) Total cysteine (tCys_A) Total homocysteine (tHcy_A) Tryptophan (Trp_B) Xanthurenic acid (XA_D)

Biological sampling and processing

Non-fasting plasma from blood samples were collected from expecting mothers at 17-18 weeks' gestation. These samples were collected into ethylenediaminetetraacetic acid (EDTA) tubes, centrifuged within 30 minutes, and temporarily placed in a refrigerator at 4 °C. They were shipped from the collecting hospital overnight to MoBa's biobank at the Norwegian Institute of Public Health (NIPH). The samples most often arrived at the biobank within 1–2 days of blood donation, where EDTA plasma were aliquoted onto polypropylene microtiter plates (96-well format, 300 μ L per well), sealed with the use of heat-sealing foil sheets, and placed in long-term storage at –80 °C.

For more information on biological sampling, processing and storage, please refer to the original reference articles for NIPH's biobank by <u>Rønningen *et al.* 2006</u> and <u>Paltiel *et al.*</u> 2014.

Analytical methodology

Microbiological assay (Platform F)

Cobalamin: *Lactobacillus leichmannii* microbiological assay Folate: chloramphenicol-resistant *Lactobacillus casei* microbiological assay

Methods references: Kelleher et al. 1991, O'Broin et al. 1992

Gas chromatography - mass spectrometry

(Platforms A/B)

Anthranilic acid Cystathionine Glycine Kynurenine Methionine Methylmalonic acid Serine Total cysteine Total homocysteine Tryptophan

Methods references: Windelberg et al. 2005, Ueland et al. 2007

Liquid chromatography - mass spectrometry

(Platforms C/D)

3-Hydroxyanthranilic acid 3-Hydroxykynurenine Arginine Asymmetric dimethylarginine Betaine Choline Cotinine Creatinine Cystathionine Dimethylglycine Kynurenic acid Methionine sulfoxide Neopterin Pyridoxal phosphate **Pyridoxal** Pyridoxamine Pyridoxic acid Pyridoxine Riboflavin Symmetric dimethylarginine Xanthurenic acid

Methods references: Holm et al. 2003, Midttun et al. 2009, Midttun et al. 2013

Useful summary article for the analytical methods used in this study: Midttun et al. 2014

Measurement units:

3'-Hydroxyanthranilic acid, 3'-Hydroxykynurenine, Anthranilic acid, Cotinine, Cystathionine (measures on platform D), Folate, Kynurenic acid, Neopterin, Pyridoxal 5'-phosphate, Pyridoxal, Pyridoxamine, Pyridoxic acid, Pyridoxine, Riboflavin, Xanthurenic acid: **nmol/L**

Arginine, Asymmetric dimethylarginine, Betaine, Choline, Creatinine, Cystathionine (measured on platform A), Dimethylglycine, Glycine, Kynurenine, Methionine sulfoxide,

Methionine, Methylmalonic acid, Serine, Symmetric dimethylarginine, Total cysteine, Total homocysteine, Tryptophan: **µmol/L**

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Cobalamin: pmol/L

Limit of quantification (LOQ):

3'-Hydroxyanthranilic acid (HAA D): 2.0 nmol/L 3'-Hydroxykynurenine (HK D): 2.0 nmol/L Anthranilic acid (AA A): 2.0 nmol/L Arginine (Arg C): 0.25 µmol/L Asymmetric dimethylarginine (ADMA C): 0.08 µmol/L Betaine (Betaine C): 0.50 µmol/L Choline (Choline C): 0.50 µmol/L Cobalamin (Cob F): 30 pmol/L Cotinine (Cot D): 1.0 nmol/L Creatinine (Creat C): 0.25 µmol/L Cystathionine (Cysta A): 0.02 µmol/L Cystathionine (Cysta D): 0.02 nmol/L Dimethylglycine (DMG C): 0.25 µmol/L Folate (spFolate F): 2.0 nmol/L Glycine (Glycine A): 3.0 µmol/L Kynurenic acid (KA D): 0.4 nmol/L Kynurenine (Kyn A): 0.12 µmol/L Methionine (Met A): 1.0 µmol/L Methionine sulfoxide (MetSo C): 0.06 µmol/L Methylmalonic acid (MMA A): 0.03 µmol/L Neopterin (Neopt D): 0.7 nmol/L Pyridoxal (PL D): 0.2 nmol/L Pyridoxal 5'-phosphate (PLP D): 0.2 nmol/L Pyridoxamine (PM D): 0.1 nmol/L Pyridoxic acid (PA D): 0.5 nmol/L Pyridoxine (PN D): 0.5 nmol/L Riboflavin (Ribo D): 0.2 nmol/L Serine (Serine A): 5.0 µmol/L Symmetric dimethylarginine (SDMA C): 0.08 µmol/L Total cysteine (tCys A): 50 µmol/L Total homocysteine (tHcy A): 0.1 µmol/L Tryptophan (Trp B): 0.1 µmol/L Xanthurenic acid (XA D): 0.5 nmol/L

For more information on key data related to analytical platforms used by Bevital, visit https://bevital.no/key-data/

Published articles using Mab001

This section also includes articles related to study design, sampling, and data collection.

- Parr CL, Magnus MC, Karlstad Ø, et al. Maternal Folate Intake during Pregnancy and Childhood Asthma in a Population-based Cohort. Am J Respir Crit Care Med. 2017 Jan 15;195(2):221-228.
- Bjørke-Monsen AL, Ulvik A, Nilsen RM, et al. Impact of Pre-Pregnancy BMI on B Vitamin and Inflammatory Status in Early Pregnancy: An Observational Cohort Study. Nutrients. 2016 Nov 30;8(12):776.
- Sengpiel V, Bacelis J, Myhre R, et al. Folic acid supplementation, dietary folate intake during pregnancy and risk for spontaneous preterm delivery: a prospective observational cohort study. BMC Pregnancy Childbirth. 2014 Nov 2;14:375.
- Engel SM, Joubert BR, Wu MC, Olshan AF, Håberg SE, Ueland PM, Nystad W, Nilsen RM, Vollset SE, Peddada SD, London SJ. Neonatal genome-wide methylation patterns in relation to birth weight in the Norwegian Mother and Child Cohort. Am J Epidemiol. 2014 Apr 1;179(7):834-42.
- Roth C, Bjørke-Monsen AL, Reichborn-Kjennerud T, et al. Use of folic acid supplements in early pregnancy in relation to maternal plasma levels in week 18 of pregnancy. Mol Nutr Food Res. 2013 Apr;57(4):653-60.
- Bjørke-Monsen AL, Roth C, Magnus P, et al. Maternal B vitamin status in pregnancy week 18 according to reported use of folic acid supplements. Mol Nutr Food Res. 2013 Apr;57(4):645-52.
- Kvalvik LG, Nilsen RM, Skjærven R, Vollset SE, Midttun O, Ueland PM, Haug K. Selfreported smoking status and plasma cotinine concentrations among pregnant women in the Norwegian Mother and Child Cohort Study. Pediatr Res. 2012 Jul;72(1):101-7.
- Nilsen RM, Bjørke-Monsen AL, Midttun O, et al. Maternal tryptophan and kynurenine pathway metabolites and risk of preeclampsia. Obstet Gynecol. 2012 Jun;119(6):1243-50.
- Håberg SE, London SJ, Nafstad P, Nilsen RM, Ueland PM, Vollset SE, Nystad W. Maternal folate levels in pregnancy and asthma in children at age 3 years. J Allergy Clin Immunol. 2011 Jan;127(1):262-4, 264.e1.
- Nilsen RM, Vollset SE, Monsen AL, Ulvik A, Haugen M, Meltzer HM, Magnus P, Ueland PM. Infant birth size is not associated with maternal intake and status of folate during the second trimester in Norwegian pregnant women. J Nutr. 2010 Mar;140(3):572-9.

Restrictions for use

None currently known.

Acknowledgements recommended for use

We recommend that any use of these data in analyses that are presented in peer-review publications acknowledges the original articles describing sampling and data collection:



Nilsen RM, Vollset SE, Monsen AL, Ulvik A, Haugen M, Meltzer HM, Magnus P, Ueland PM. Infant birth size is not associated with maternal intake and status of folate during the second trimester in Norwegian pregnant women. J Nutr. 2010 Mar;140(3):572-9.

Disclaimer

The data in Mab001 that are available for use are provided by MoBa on an *as is* basis as they were received from the generating laboratory and have not been curated or quality controlled prior to release. FHI does not provide any guarantees related to data quality and assurance of the original dataset. We reserve the right to periodically remove samples from the dataset belonging to participants who have retracted their consent to participate in this cohort study, and may alter the contents of the associated documentation accordingly.