

# BBMRI-Omics hands on course

10:00-10:15 Introduction to available omics data within BBMRI-omics.nl. (Rick Jansen)

10.15-10.45: Introduction to the BBMRIomics R package for integrated analysis of BBMRI-omics data using R (Maarten van Iterson)

10:45-11.45: Practicum (Maarten van Iterson)

11.45-12:30: Lunch (demo: using BBMRI-Omics.nl online atlases (Jan-Bert van Klinken))

12.30-13.00: Joost Verlouw: QTL lookup of GWAS hits. Take the SNP hits from a recent GWAS, extract corresponding BIOS genotype data, run association with full Methylation, Expression and Metabolomics data sets.

13.00-14.00: Practicum (Joost Verlouw)

14.00-14.15- Tea break

14:15-14.: Introduction to the Brainshake 1H-NMR metabolomics platform (Marian Beekman)

14:45-15.30: Practicum. Analyzing Metabolomics data (Koen Dekker)

15:30-16:00: Allele specific expression (Niek de Klein & Freerk van Dijk)

16:00-17:00: Practicum (Niek de Klein & Freerk van Dijk))

17:00 Drinks

Wifi: eduroam or ask frontdesk. Course material:  
[http://wiki.bbmri.nl/wiki/BIOS\\_BBMRI-omics\\_course](http://wiki.bbmri.nl/wiki/BIOS_BBMRI-omics_course)



# BBMRI-omics = GONL + BIOS + BBMRI Metabolomics

GONL = Genotype sequencing ( $N=769$ )

BIOS = RNA-seq + Methylation + already measured genotypes and phenotypes

BBMRI Metabolomics = Brainshake 1H-NMR

**BIOS RNA-seq:** Illumina HiSeq 2000, >15M x 50bp Paired End, whole blood  
 $N = 3824$  BIOS samples, including 510 GONL,  $N = 2030$  non BIOS samples)

**BIOS Methylation:** Illumina 450k methylation, whole blood  
 $N = 4805$  BIOS samples, including 510 GONL,  $N = 1538$  non BIOS samples

**BBMRI Metabolomics:** Brainshake 1H-NMR (247 markers), whole blood  
( $N = 23,729$ , overlap with BIOS:  $N = 3880$  methylation,  $N = 2728$  RNA-seq,  $N = 2716$  both)

Samples from 6 biobanks: Twin Register (Amsterdam), Rotterdam Study, Leiden Longevity Study, LifeLines (Groningen), PAN (Utrecht), CODAM (Maastricht)



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Management teams:

**GONL** = Cisca Wijmenga (PI), Morris Swertz, P. Eline Slagboom, Gertjan B. van Ommen, Cornelia M. van Duijn, Jasper A. Bovenberg (ELSI), Dorret I. Boomsma, Paul I.W. de Bakker

**BIOS** = Bastiaan T. Heijmans (chair), Peter A.C. 't Hoen, Joyce van Meurs, Rick Jansen, Lude Franke.

**BBMRI Metabolomics** = Eline Slagboom, Dorret Boomsma, Cornelia van Duin



## BBMRI-omics: access to data

Work in progress: one central data sharing interface (<http://www.bbmri.nl/omics/>)

Currently:

**GONL:** request via <http://www.nlgenome.nl/>

**BIOS:** request via [http://wiki.bbmri.nl/wiki/BIOS\\_start-](http://wiki.bbmri.nl/wiki/BIOS_start-)

-BIOS data is available at a Sara Virtual Machines: 16 cores, 128 GB ram, 5TB storage

-BIOS data analysis has to be done at this VM (like today)

OR download freeze 1 at EGA (<https://www.ebi.ac.uk/ega/studies/EGAS00001001077>)

**Metabolomics:** Overlap with BIOS is accessible at the BIOS VM, data access procedure and website are being made.

Additional Phenotype data can be requested at the Biobanks!!

# Using the BIOS Virtual Machine (VM)

Three ways to access the VM: 1) ssh, 2) GUI, 3) R studio server

File locations: /viridir/Backup/RP3\_data/, see [http://wiki.bbmri.nl/wiki/BIOS\\_PreparedData](http://wiki.bbmri.nl/wiki/BIOS_PreparedData)

Genotype data is imputed vs GONL and HRC, present in vcf files.

When you work in R: use the package `BBMRIomics` by Maarten van Iterson.  
All data is available via this package and easy to link (we do this today)

Questions: we suggest our forum <https://www.biostars.org/t/bbmri-nl-bios/> (or email)



# Current research in BBMRI omics

GONL

nature  
genetics

PubMed.gov  
US National Library of Medicine  
National Institutes of Health

PubMed

## Whole-genome sequence variation, population structure and demographic history of the Dutch population

The Genome of the Netherlands Consortium\* (2014)

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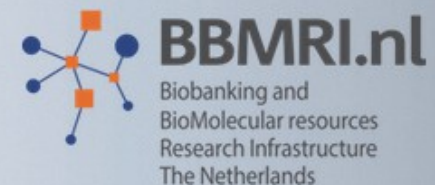
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- [A framework for the detection of de novo mutations in family-based sequencing data.](#)
- 1. Francioli LC, Cretu-Stancu M, Garimella KV, Fromer M, Kloosterman WP; **Genome of the Netherlands consortium.**, Samocha KE, Neale BM, Daly MJ, Banks E, DePristo MA, de Bakker PI. Eur J Hum Genet. 2017 Feb;25(2):227-233. doi: 10.1038/ejhg.2016.147. Epub 2016 Nov 23. PMID: 27876817 [Free PMC Article](#)  
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- [A high-quality human reference panel reveals the complexity and distribution of genomic structural variants.](#)
- 2. Hehir-Kwa JY, Marschall T, Kloosterman WP, Francioli LC, Baaijens JA, Dijkstra LJ, Abdellaoui A, Koval V, Thung DT, Wardenaar R, Renkens I, Coe BP, Deelen P, de Ligt J, Lameijer EW, van Dijk F, Hormozdiari F; **Genome of the Netherlands Consortium.**, Uitterlinden AG, van Duijn CM, Eichler EE, de Bakker PI, Swertz MA, Wijmenga C, van Ommen GB, Slagboom PE, Boomsma DI, Schönhuth A, Ye K, Guryev V. Nat Commun. 2016 Oct 6;7:12989. doi: 10.1038/ncomms12989. PMID: 27708267 [Free PMC Article](#)  
[Similar articles](#)
- [Uncompromised 10-year survival of oldest old carrying somatic mutations in DNMT3A and TET2.](#)
- 3. van den Akker EB, Pitts SJ, Deelen J, Moed MH, Potluri S, van Rooij J, Suchiman HE, Lakenberg N, de Dijkster WJ, Uitterlinden AG, Kraaij R, Hofman A, de Craen AJ, Houwing-Duistermaat JJ, van Ommen GJ; **Genome of The Netherlands Consortium.**, Cox DR, van Meurs JB, Beekman M, Reinders MJ, Slagboom PE. Blood. 2016 Mar 17;127(11):1512-5. doi: 10.1182/blood-2015-12-685925. Epub 2016 Jan 29. No abstract available. PMID: 26825711 [Free PMC Article](#)  
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# Current research in BBMRI omics

## Metabolomics

Several projects ongoing for the relation with:

Dementia (submitted)

Osteoarthritis

Ageing and mortality

Depression

Recurrent CVD risk

Complications in Type 2 diabetes

Migraine



# Current research in BBMRI omics

BIOS (> 70 data requests)

PubMed | BIOS consortium | Create RSS | Create alert | Advanced

Article types: Clinical Trial, Review, Customize ...  
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## Search results

Items: 18

- [Epigenome-wide association study \(EWAS\) on lipids: the Rotterdam Study.](#)  
1. Braun KV, Dhana K, de Vries PS, Voortman T, van Meurs JB, Uitterlinden AG; **BIOS consortium**, Hofman A, Hu FB, Franco OH, Dehghan A. *Clin Epigenetics*. 2017 Feb 7;9:15. doi: 10.1186/s13148-016-0304-4. eCollection 2017 Feb 7. PMID: 28194238 [Free PMC Article](#)  
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- [Genome-wide association analysis identifies novel blood pressure loci and offers biological insights into cardiovascular risk.](#)  
2. Warren HR, Evangelou E, Cabrera CP, Gao H, Ren M, Mifsud B, Ntalla I, Surendran P, Liu C, Cook JP, Kraja AT, Drenos F, Loh M, Verweij N, Marten J, Karaman I, Lepe MP, O'Reilly PF, Knight J, Snieder H, Kato N, He J, Tai ES, Said MA, Porteous D, Alver M, Poulter N, Farrall M, Gansevoort RT, Padmanabhan S, Mägi R, Stanton A, Connell J, Bakker SJ, Metspalu A, Shields DC, Thom S, Brown M, Sever P, Esko T, Hayward C, van der Harst P, Saleheen D, Chowdhury R, Chambers JC, Chasman DI, Chakravarti A, Newton-Cheh C, Lindgren CM, Levy D, Kooner JS, Keavney B, Tomaszewski M, Samani NJ, Howson JM, Tobin MD, Munroe PB, Ehret GB, Wain LV; International Consortium of Blood Pressure (ICBP) 1000G Analyses.; **BIOS Consortium**.; Lifelines Cohort Study.; Understanding Society Scientific group.; CHD Exome+ **Consortium**.; ExomeBP **Consortium**.; T2D-GENES **Consortium**.; GoT2DGenes **Consortium**.; Cohorts for Heart and Ageing Research in Genome Epidemiology (CHARGE) BP Exome **Consortium**.; International Genomics of Blood Pressure (iGEN-BP) **Consortium**.; UK Biobank CardioMetabolic **Consortium** BP working group.. *Nat Genet*. 2017 Mar;49(3):403-415. doi: 10.1038/ng.3768. Epub 2017 Jan 30. PMID: 28135244  
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- [Controlling bias and inflation in epigenome- and transcriptome-wide association studies using the empirical null distribution.](#)  
3. van Iterson M, van Zwet EW; **BIOS Consortium**., Heijmans BT. *Genome Biol*. 2017 Jan 27;18(1):19. doi: 10.1186/s13059-016-1131-9. PMID: 28129774 [Free PMC Article](#)  
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日本語要約

## Disease variants alter transcription factor levels and methylation of their binding sites

Marc Jan Bonder, René Luijk, Daria V Zhernakova, Matthijs Moed, Patrick Deelen, Martijn Vermaat, Maarten van Iterson, Freerk van Dijk, Michiel van Galen, Jan Bot, Roderick C Slieker, P Mila Jhamai, Michael Verbiest, H Eka D Suchiman, Marijn Verkerk, Ruud van der Breggen, Jeroen van Rooij, Nico Lakenberg, Wibowo Arindrarto, Szymon M Kielbasa, Iris Jonkers, Peter van 't Hof, Irene Nooren, Marian Beekman, Joris Deelen [et al.](#)

[Affiliations](#) | [Contributions](#) | [Corresponding authors](#)

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NATURE GENETICS | LETTER

日本語要約

## Identification of context-dependent expression quantitative trait loci in whole blood

Daria V Zhernakova, Patrick Deelen, Martijn Vermaat, Maarten van Iterson, Michiel van Galen, Wibowo Arindrarto, Peter van 't Hof, Hailiang Mei, Freerk van Dijk, Harm-Jan Westra, Marc Jan Bonder, Jeroen van Rooij, Marijn Verkerk, P Mila Jhamai, Matthijs Moed, Szymon M Kielbasa, Jan Bot, Irene Nooren, René Pool, Jenny van Dongen, Jouke J Hottenga, Coen D A Stehouwer, Carla J H van der Kallen, Casper G Schalkwijk, Alexandr Zhernakova [et al.](#)

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# BIOS QTL browser

This web page accompanies the manuscripts titled '[Disease variants alter transcription factor levels and methylation of their binding sites](#)', by *Bonder et al* and '[Identification of context-dependent expression quantitative trait loci in whole blood](#)', by *Zhernakova et al*, both have been published to Nature Genetics.

For further questions, contact the corresponding author: [lude@ludesign.nl](mailto:lude@ludesign.nl)

## Download meQTL results

You can download the independent top *cis*- and *trans*-meQTL and eQTMs, detected at a false-discovery rate of 0.05:

[Cis-meQTLs independent top effects](#)

[Cis-eQTMs independent top effects](#)

[Trans-meQTLs top effects](#)

## Download eQTL results

You can download the *cis*-eQTLs detected at a false-discovery rate of 0.05:

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## Query results

Or, you can query our independent eQTL, meQTL and eQTMs below (examples: rs3774937, cg10154826, ENSG00000226979 or *LTA*):

Gene or SNP name:

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