

# Showcasing the utility of the BBMRI genomics infrastructure in daily science



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Opening up the BBMRI genomics infrastructure in The Netherlands, September 21, Amsterdam

# Platform of discovery

- Unique, large-scale multiple omics data infrastructure.
- Freely accessible to any PhD student or postdoc affiliated to BBMRI.

# The data

Methylome

*Illumina 450k array*

Genome

*Imputed (HRC)/WGS*

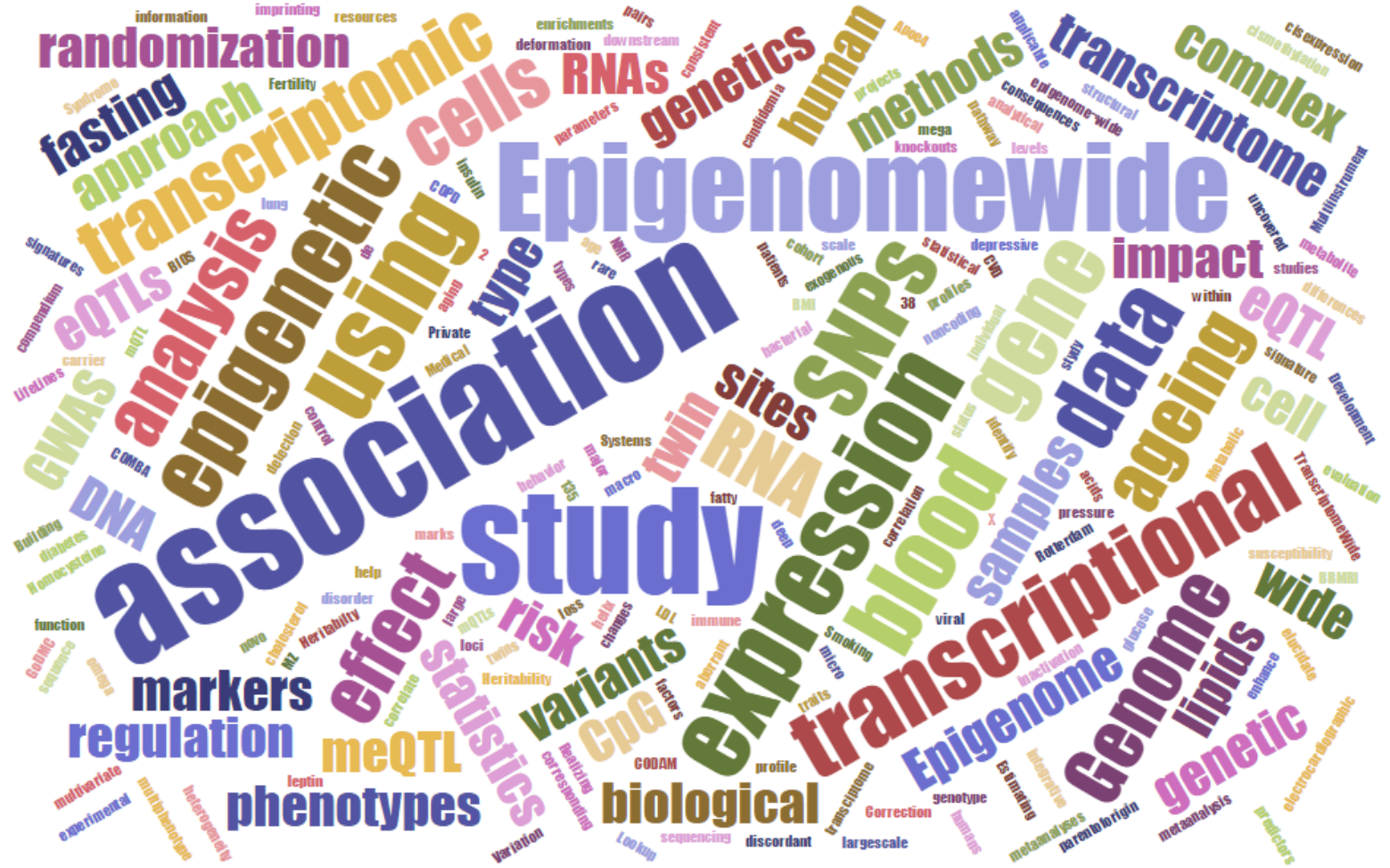
Phenotypes

*Lipids, height, weight,  
smoking, cell counts...*

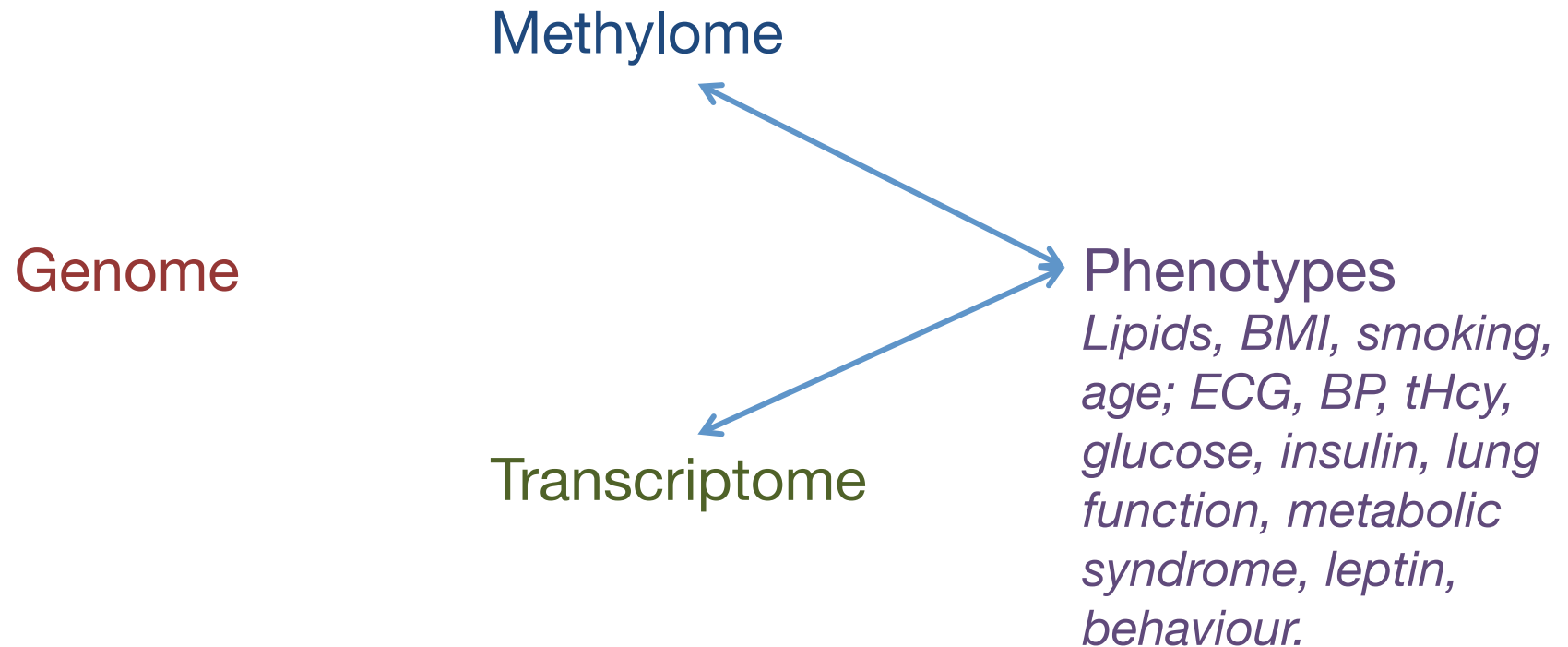
Transcriptome

*RNA-seq*

# 46 data request



# Epigenome- and transcriptome-wide association studies



# Scientific output

Twin Research and Human Genetics

page 1 of 13 | © The Author(s) 2015 | doi:10.1017/thg.2015.74

## Epigenome-Wide Association Study of Aggressive Behavior

Jenny van Dongen,<sup>1,2</sup> Michel G. Nivard,<sup>1</sup> Bart M. L. Baselmans,<sup>1,2</sup> Nuno R. Zilhão,<sup>1</sup> Lannie Ligthart,<sup>1</sup> BIOS Consortium,<sup>3</sup> Bastiaan T. Heijmans,<sup>4</sup> Meike Bartels,<sup>1,2</sup> and Dorret I. Boomsma<sup>1,2</sup>

ARTICLE

## Improving Phenotypic Prediction by Combining Genetic and Epigenetic Associations

Sonia Shah,<sup>1,2,14</sup> Marc J. Bonder,<sup>3,14</sup> Riccardo E. Marioni,<sup>1,4,5</sup> Zhihong Zhu,<sup>1</sup> Allan F. McRae,<sup>1,2</sup> Alexandra Zernakova,<sup>3</sup> Sarah E. Harris,<sup>4,5</sup> Dave Liewald,<sup>4</sup> Anjali K. Henders,<sup>6</sup> Michael M. Mendelson,<sup>7,8,9</sup> Chunyu Liu,<sup>10</sup> Roby Joeanes,<sup>11</sup> Liming Liang,<sup>12</sup> BIOS Consortium, Daniel Levy,<sup>9</sup> Nicholas G. Martin,<sup>6</sup> John M. Starr,<sup>4,13</sup> Cisca Wijmenga,<sup>3</sup> Naomi R. Wray,<sup>1</sup> Jian Yang,<sup>1</sup> Grant W. Montgomery,<sup>6,14</sup> Lude Franke,<sup>3,14</sup> Ian J. Deary,<sup>4,13,14</sup> and Peter M. Visscher<sup>1,2,4,14,\*</sup>

Sleker et al. *Genome Biology* (2016) 17:138  
DOI 10.1186/s13059-016-1000-6

Genome Biology

RESEARCH

Open Access



## Age-related accrual of methylomic variability is linked to fundamental ageing mechanisms

Roderick C. Sleker<sup>1</sup>, Maarten van IJterson<sup>1</sup>, René Luijk<sup>1</sup>, Marian Beekman<sup>1</sup>, Daria V. Zernakova<sup>2</sup>, Matthijs H. Moed<sup>1</sup>, Hailiang Mei<sup>3</sup>, Michiel van Galen<sup>4</sup>, Patrick Deelen<sup>5</sup>, Marc Jan Bonder<sup>2</sup>, Alexandra Zernakova<sup>2</sup>, André G. Uitterlinden<sup>5</sup>, Ettje F. Tigchelaar<sup>2</sup>, Coen D. A. Stehouwer<sup>6</sup>, Casper G. Schalkwijk<sup>6</sup>, Carla J. H. van der Kallen<sup>6</sup>, Albert Hofman<sup>7</sup>, Diana van Heemst<sup>8</sup>, Eco J. de Geus<sup>9</sup>, Jenny van Dongen<sup>9</sup>, Joris Deelen<sup>1</sup>, Leonard H. van den Berg<sup>10</sup>, Joyce van Meurs<sup>11</sup>, Rick Jansen<sup>11</sup>, Peter A. C. 't Hoen<sup>4</sup>, Lude Franke<sup>2</sup>, and Peter M. Visscher<sup>1,2,4,14,\*</sup>

Dekkers et al. *Genome Biology* (2016) 17:138  
DOI 10.1186/s13059-016-1000-6

Genome Biology

RESEARCH

Open Access



## Blood lipids influence DNA methylation in circulating cells

Koen F. Dekkers<sup>1</sup>, Maarten van IJterson<sup>1</sup>, Roderick C. Sleker<sup>1</sup>, Matthijs H. Moed<sup>1</sup>, Marc Jan Bonder<sup>2</sup>, Michiel van Galen<sup>3</sup>, Hailiang Mei<sup>4</sup>, Daria V. Zernakova<sup>2</sup>, Leonard H. van den Berg<sup>5</sup>, Joris Deelen<sup>1</sup>, Jenny van Dongen<sup>6</sup>, Diana van Heemst<sup>7</sup>, Albert Hofman<sup>8</sup>, Jouke J. Hottenga<sup>9</sup>, Carla J. H. van der Kallen<sup>9</sup>, Casper G. Schalkwijk<sup>9</sup>, Coen D. A. Stehouwer<sup>9</sup>, Ettje F. Tigchelaar<sup>2</sup>, André G. Uitterlinden<sup>10</sup>, Gonke Willemsen<sup>6</sup>, Alexandra Zernakova<sup>2</sup>, Lude Franke<sup>2</sup>, Peter A. C. 't Hoen<sup>3</sup>, Rick Jansen<sup>11</sup>, Joyce van Meurs<sup>10</sup>, Dorret I. Boomsma<sup>6</sup>, Cornelia M. van Duijn<sup>9</sup>, Marleen M. J. van Greevenbroek<sup>9</sup>, Jan H. Veldink<sup>9</sup>, Cisca Wijmenga<sup>2</sup>, BIOS Consortium<sup>12</sup>, Erik W. van Zwet<sup>13</sup>, P. Elise Slagboom<sup>1</sup>, J. Wouter Jukema<sup>14</sup> and Bastiaan T. Heijmans<sup>1\*</sup>

*Diabetologia* (2016) 59:998–1006  
DOI 10.1007/s00125-016-3872-0



ARTICLE

## Tobacco smoking is associated with DNA methylation of diabetes susceptibility genes

Symen Ligthart<sup>1</sup> · Rebecca V. Steenard<sup>1</sup> · Marjolijn J. Peters<sup>2,3</sup> · Joyce R. J. van Meurs<sup>2,3</sup> · Eric J. G. Sijbrands<sup>2</sup> · André G. Uitterlinden<sup>1,2,3</sup> · Marc J. Bonder<sup>4</sup> · BIOS consortium · Albert Hofman<sup>1</sup> · Oscar H. Franco<sup>1</sup> · Abbas Delghian<sup>1,2</sup>



ARTICLE

Received 10 Jun 2015 | Accepted 23 Feb 2016 | Published 7 Apr 2016

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OPEN

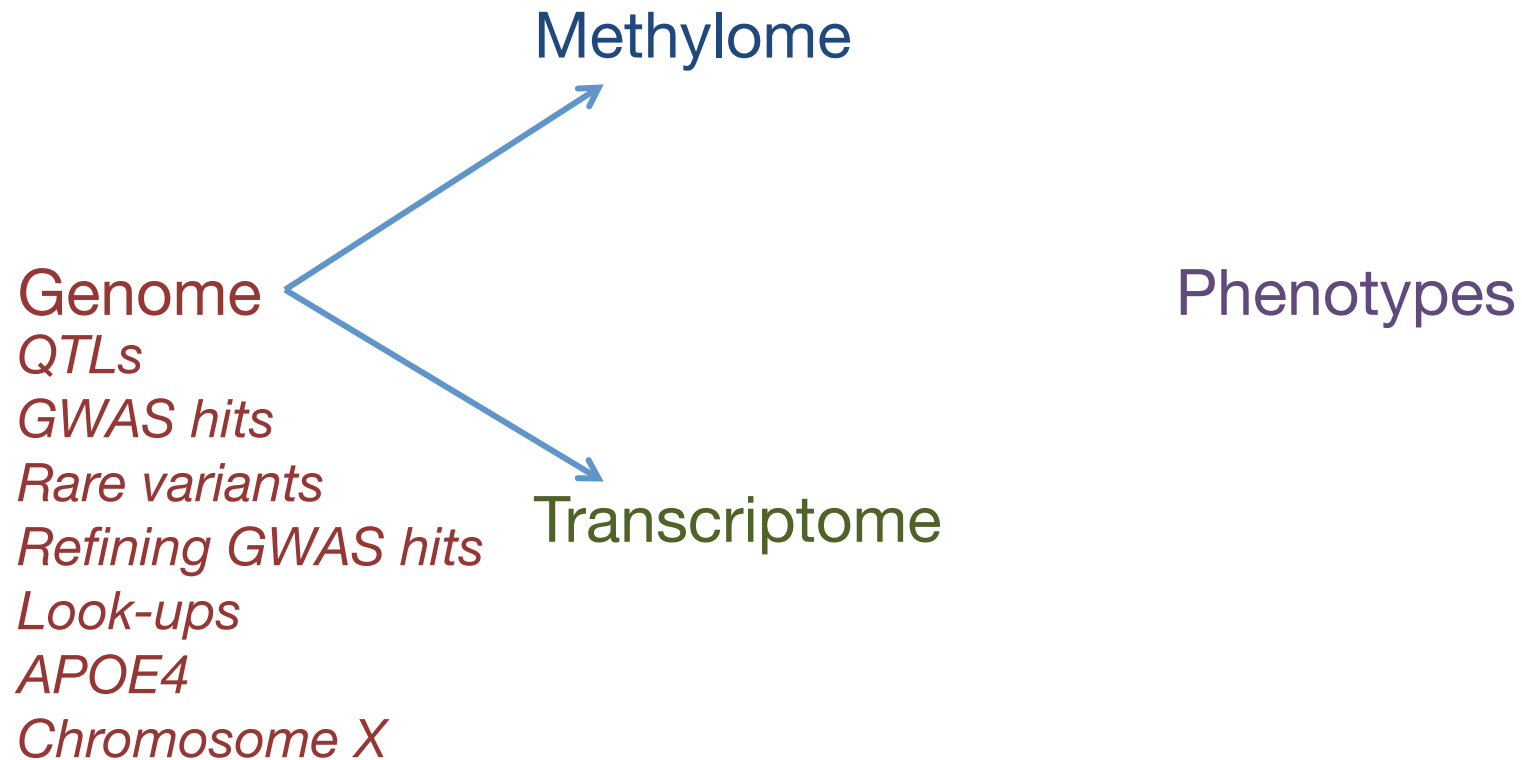
## Genetic and environmental influences interact with age and sex in shaping the human methylome

Jenny van Dongen<sup>1,\*</sup>, Michel G. Nivard<sup>1,\*</sup>, Gonke Willemsen<sup>1</sup>, Jouke-Jan Hottenga<sup>1</sup>, Quinta Helmer<sup>1</sup>, and Peter M. Visscher<sup>1,2,4,14,\*</sup>



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Biobanking and  
BioMolecular resources  
Research Infrastructure  
The Netherlands

# Downstream functional effects disease variants



# Scientific output



## ARTICLE

Received 10 Jun 2015 | Accepted 23 Feb 2016 | Published 7 Apr 2016

DOI: 10.1038/ncomms11115 OPEN

# Genetic and environmental influences interact with age and sex in shaping the human methylome

Jenny van Dongen<sup>1,\*</sup>, Michel G. Nivard<sup>1,\*</sup>, Gonneke Willemsen<sup>1</sup>, Jouke-Jan Hottenga<sup>1</sup>, Quinta Helmer<sup>1</sup>,  
<sup>1</sup>Department of Psychology, University of Groningen, 9712 CB Groningen, The Netherlands; <sup>2</sup>Department of Psychology, University of Amsterdam, 1018 CA Amsterdam, The Netherlands; <sup>3</sup>Department of Psychology, University of Leiden, 2300 RA Leiden, The Netherlands; <sup>4</sup>Department of Psychology, University of Oxford, 1018 CA Oxford, The Netherlands



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## New Results

### Hypothesis-free identification of modulators of genetic risk factors

Daria Zhernakova,  Patrick Deelen, Martijn Vermaat, Maarten van Iterson, Michiel van Galen, Wibowo Arindarto, Peter van t Hof, Hailing Mei, Freek van Dijk, Harm-Jan Westra,  Marc Jan Bonder, Jeroen van Rooij, Marijn Verkerk, P. Mila Jhamai, Matthijs

## New Results

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

 Marc Jan Bonder, René Luijk, Daria Zhernakova, Matthijs Moed,  Patrick Deelen, Martijn Vermaat, Maarten van Iterson, Freerk van Dijk, Michiel van Galen, Jan Bot,

## ARTICLES



Contents lists available at ScienceDirect

## Journal of Autoimmunity

journal homepage: [www.elsevier.com/locate/jautimm](http://www.elsevier.com/locate/jautimm)

# Trans-ancestry genome-wide association study identifies 12 genetic loci influencing blood pressure and implicates a role for DNA methylation

We carried out a trans-ancestry genome-wide association and replication study of blood pressure phenotypes among up to 320,251 individuals of East Asian, European and South Asian ancestry. We find genetic variants at 12 new loci to be associated

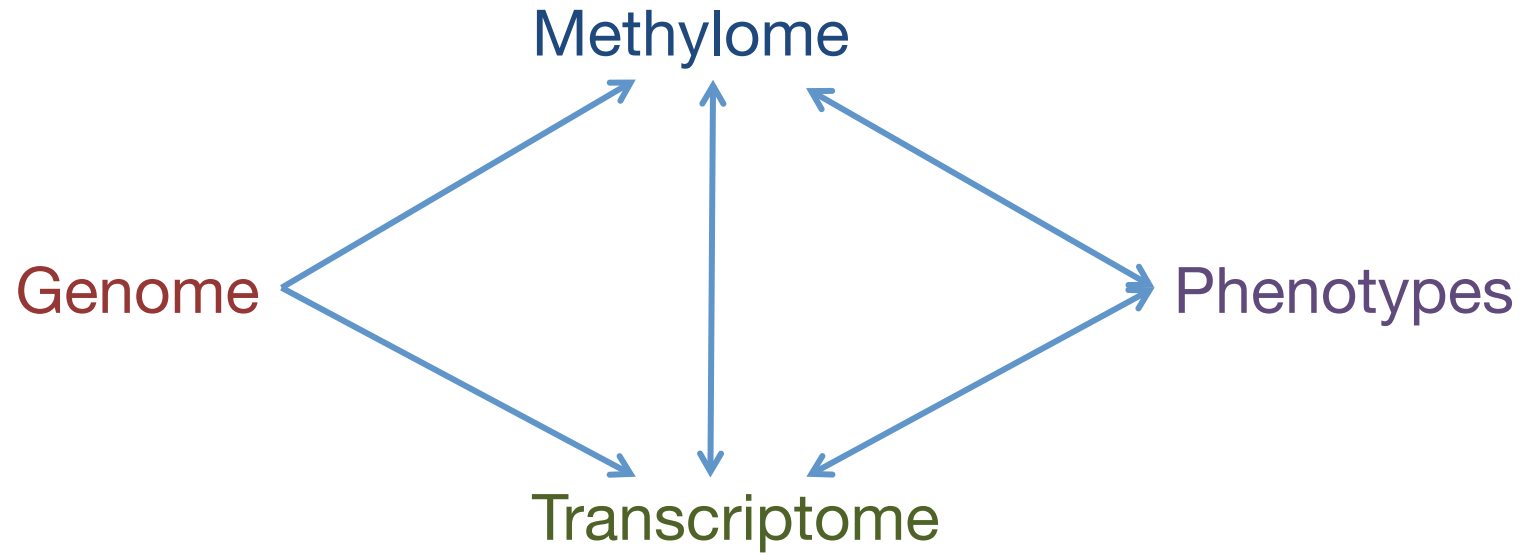
Refined mapping of autoimmune disease associated genetic variants with gene expression suggests an important role for non-coding RNA

Isis Ricaño-Ponce <sup>a</sup>, Daria V. Zhernakova <sup>a</sup>, Patrick Deelen <sup>a, b</sup>, Oscar Luo <sup>c</sup>, Xingwang Li <sup>c</sup>, Aaron Isaacs <sup>d</sup>, Juha Karjalainen <sup>a</sup>, Jennifer Di Tommaso <sup>a</sup>, Zuzanna Agnieszka Borek <sup>a</sup>





# Integrative genomics & causal inference approaches



# Scientific output

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DOI 10.1186/s13059-016-1000-6

Genome Biology

RESEARCH

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## Blood lipids influence DNA methylation in circulating cells



Koen F. Dekkers<sup>1</sup>, Maarten van Iterson<sup>1</sup>, Roderick C. Slieker<sup>1</sup>, Matthijs H. Moed<sup>1</sup>, Marc Jan Bonder<sup>2</sup>, Michiel van Galen<sup>3</sup>, Hailiang Mei<sup>4</sup>, Daria V. Zhernakova<sup>2</sup>, Leonard H. van den Berg<sup>3</sup>, Joris Deelen<sup>1</sup>, Jenny van Dongen<sup>5</sup>, Diana van Heemst<sup>7</sup>, Albert Hofman<sup>8</sup>, Jouke J. Hottenga<sup>6</sup>, Carla J. H. van der Kallen<sup>9</sup>, Casper G. Schalkwijk<sup>9</sup>, Coen D. A. Stehouwer<sup>9</sup>, Ettje F. Tigchelaar<sup>2</sup>, André G. Uitterlinden<sup>10</sup>, Gonneke Willemsen<sup>6</sup>, Alexandra Zhernakova<sup>2</sup>, Lude Franke<sup>2</sup>, Peter A. C. 't Hoen<sup>3</sup>, Rick Jansen<sup>11</sup>, Joyce van Meurs<sup>10</sup>, Dorret I. Boomsma<sup>6</sup>, Cornelia M. van Duijn<sup>8</sup>, Marleen M. J. van Greevenbroek<sup>9</sup>, Jan H. Veldink<sup>5</sup>, Cisca Wijmenga<sup>2</sup>, BIOS Consortium<sup>12</sup>, Erik W. van Zwet<sup>13</sup>, P. Eline Slagboom<sup>1</sup>, J. Wouter Jukema<sup>14</sup> and Bastiaan T. Heijmans<sup>1\*</sup>

Mendelian randomization (5x)

# Expertise & Methodology

nature  
genetics

nature  
genetics

Bonder et al. *BMC Genomics* 2014, **15**:860  
<http://www.biomedcentral.com/1471-2164/15/860>



## RESEARCH ARTICLE

### Systematic identification of drivers of known disease

Harm-Jan Westra<sup>1,40</sup>, Marjolein J Peters<sup>2,3,4</sup>, Johannes Kettunen<sup>7,8,40</sup>, Mark W Christian

### Heritability and genetic architecture of peripheral blood

Fred A Wright<sup>1-3,13</sup>, Patrick F Sullivan

### Genetic and epigenetic regulation of gene expression in fetal and adult human

Marc Jan Bonder<sup>1†</sup>, Silva Kasela<sup>2,3†</sup>, Mart Kals<sup>2,4</sup>, Riin Tamm<sup>2,3</sup>, Kaie Lokk<sup>3</sup>, Isabel Bai Patrick Deelen<sup>1,7</sup>, Jan-Willem Greve<sup>8</sup>, Maxim Ivanov<sup>5</sup>, Sander S Rensen<sup>6</sup>, Jana V var Rick Jansen<sup>7</sup>, Wonil Chung<sup>6</sup>, Yi-Hui Zhou<sup>1,2</sup>, Abdel Abdellaoui<sup>8</sup>, Sandra Batista<sup>9</sup>, Casey Butler<sup>9</sup>, Guanhua Che

## ARTICLE

Received 16 Jan 2015 | Accepted 7 Sep 2015 | Published 22 Oct 2015

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OPEN

### The transcriptional landscape of age in human peripheral blood

Marjolein J. Peters et al.<sup>#</sup>

## PERSPECTIVES

### OPINION

#### From promise to reality in epigenetic

Jonathan Mill and Bastiaan

Abstract | The epigenome aetiological puzzle for complex standard research approach

## BIOINFORMATICS

Genetics and population analysis

#### An alternative approach mapping reduces the pr

René Luijk<sup>1,2</sup>, Jelle J. Goeman<sup>3</sup>, Erik W. van Zwet<sup>2,\*</sup>

## BIOINFORMATICS

Genetics and population analysis

#### MethylAid: visual and 450k datasets

Maarten van Iterson\*, Elmar W P. Eline Slagboom and Bastiaan Department of Molecular Epidemiology Associate Editor: Jeffrey Barrett



## The multifaceted interplay between lipids and epigenetics

Koen F. Dekkers<sup>a</sup>, F and Bastiaan T. Heijmans

### Purpose of review

The interplay between lipids and epigenetics



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New Results

#### Controlling bias and inflation in epigenome- and transcriptome-wide association studies using the empirical null distribution

Maarten M. van Iterson, Erik W. van Zwet, The Bios Consortium, P. Eline Slagboom, Bastiaan T. Heijmans

21 peer-reviewed publications so far



# Showcases

13.15 – 13.30	Annique Claringbould (UMCG)	Trans-eQTL analysis.
13.30 – 13.45	Jenny van Dongen (VUMC)	Epigenome-wide association study of educational attainment.
13.45 – 14.00	Koen Dekkers (LUMC)	Identifying methylome-metabolome interactions
14.00 - 14.15	Marleen van Greevenbroek (MU)	Epigenetic and transcriptional markers of cardiometabolic disease.
14.15 – 14.30	Martijn Dekker (EMC)	Fetal differentially DNA-methylated regions, childhood lung function, and the risks of asthma and COPD across the life course.