

Annual Special Issue

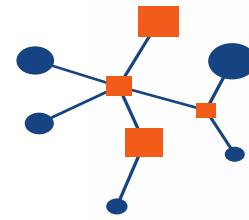
TIME

10 IDEAS CHANGING THE WORLD RIGHT NOW

The global economy is being remade before our eyes. Here's what's on the horizon

- WHY YOUR JOB IS YOUR MOST VALUABLE ASSET
- REPURPOSING THE SUBURBS
- ~~GLOBAL ECONOMIC SHOCKING~~
- **BIOBANKS: SAVING YOUR PARTS**
- NEED LAND? RENT A COUNTRY
- THE NEW CALVINISM
- ECOLOGICAL INTELLIGENCE
- AMORTALITY: FOREVER YOUNG
- AFRICA: OPEN FOR BUSINESS
- REINVENTING THE HIGHWAY





BBMRI.nl

Biobanking and
BioMolecular resources
Research Infrastructure
The Netherlands

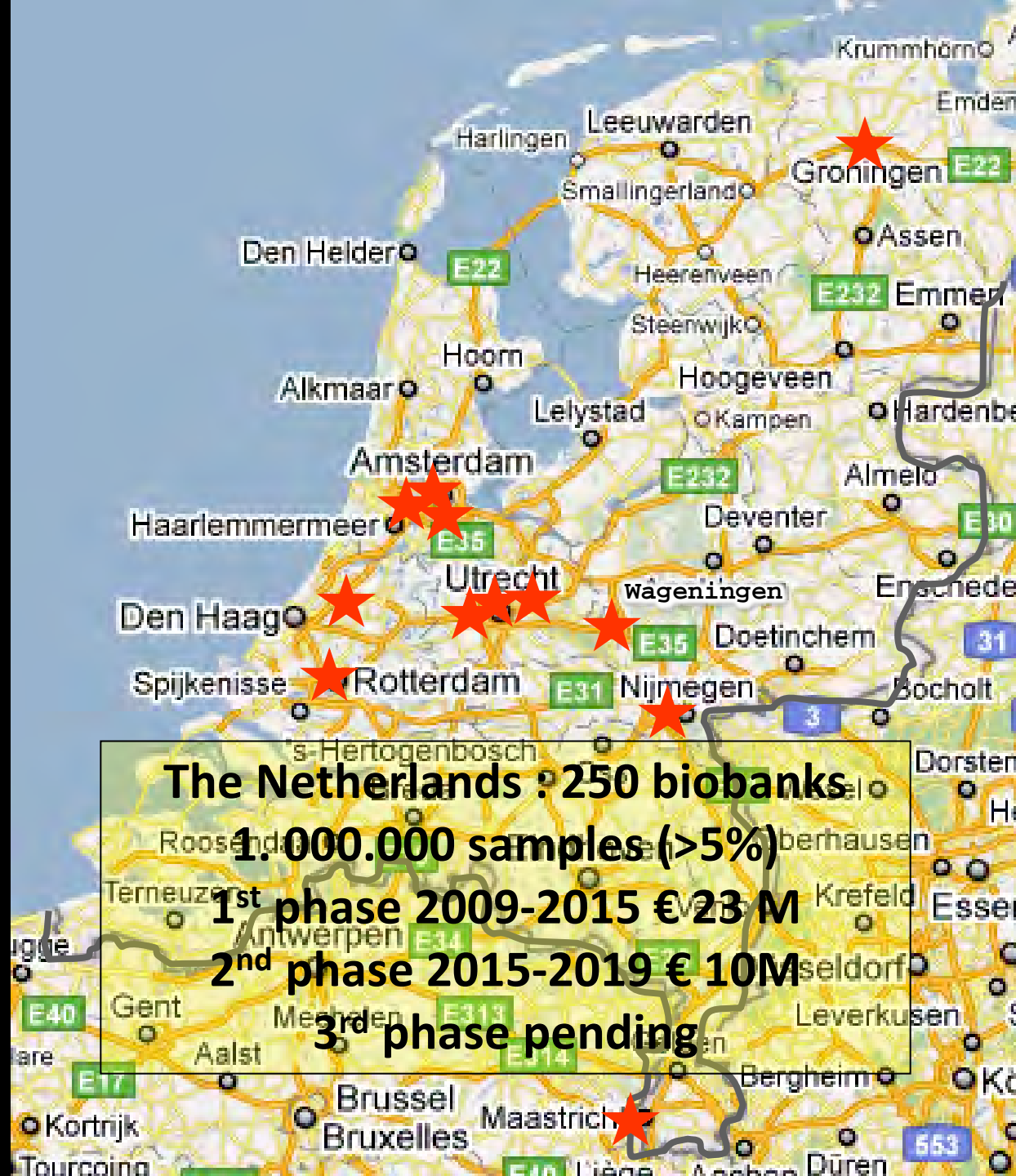
BBMRI.NL – A story of Sharing

BBMRI-NL

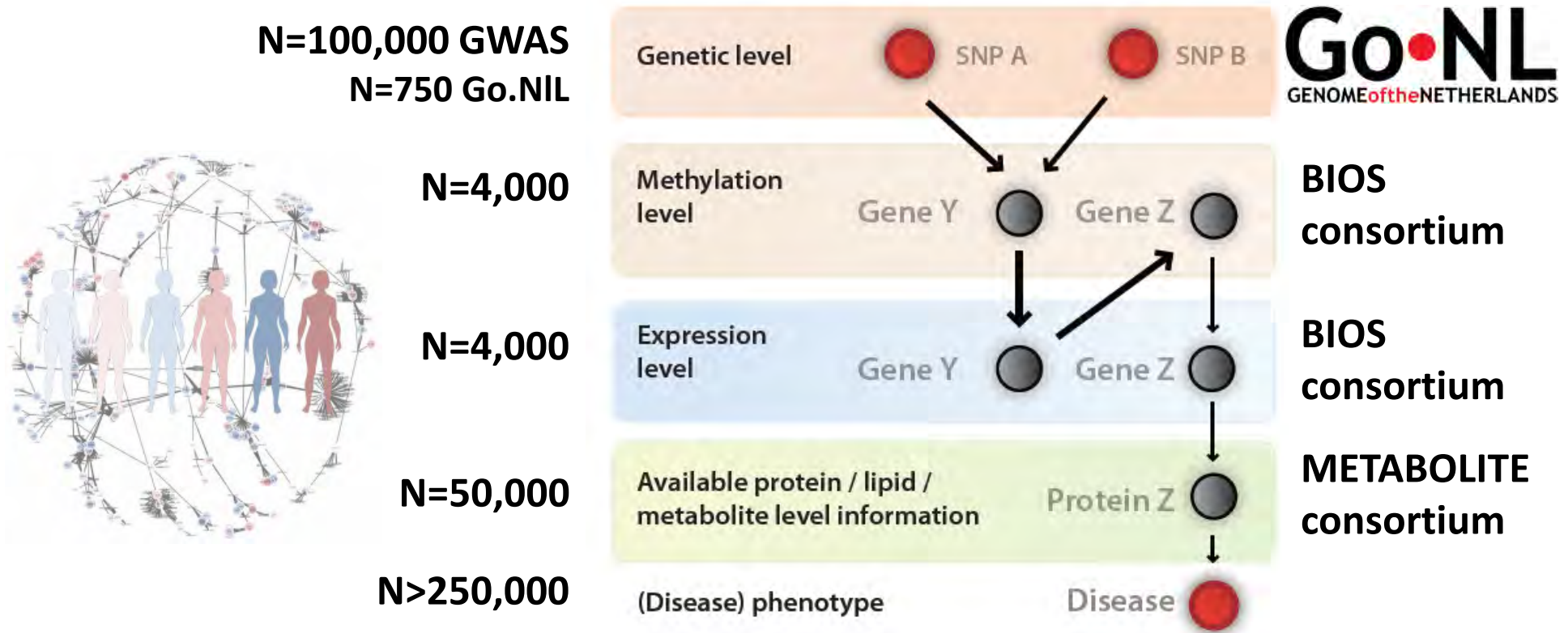
TOWARDS A NATIONAL BIOBANKING INFRASTRUCTURE

- Founded in 2009 as the Dutch node within the European BBMRI-ERIC
- Established to align, connect, complete and enrich biobanks
- Connecting > 250 Dutch biobanks
- Innovative integration of complementary efforts involving data, tissue, samples, population imaging and IT for translational research
- Aims to establish a sustainable nation-wide infrastructure for collecting, managing and providing access to data and samples for cutting-edge translational biomedical research





Highlights BBMRI-NL – molecular data



Building a central database for the research community

- To store raw and processed data
- Reference data for case-control studies and imputation
- Linking to clinical phenotypes

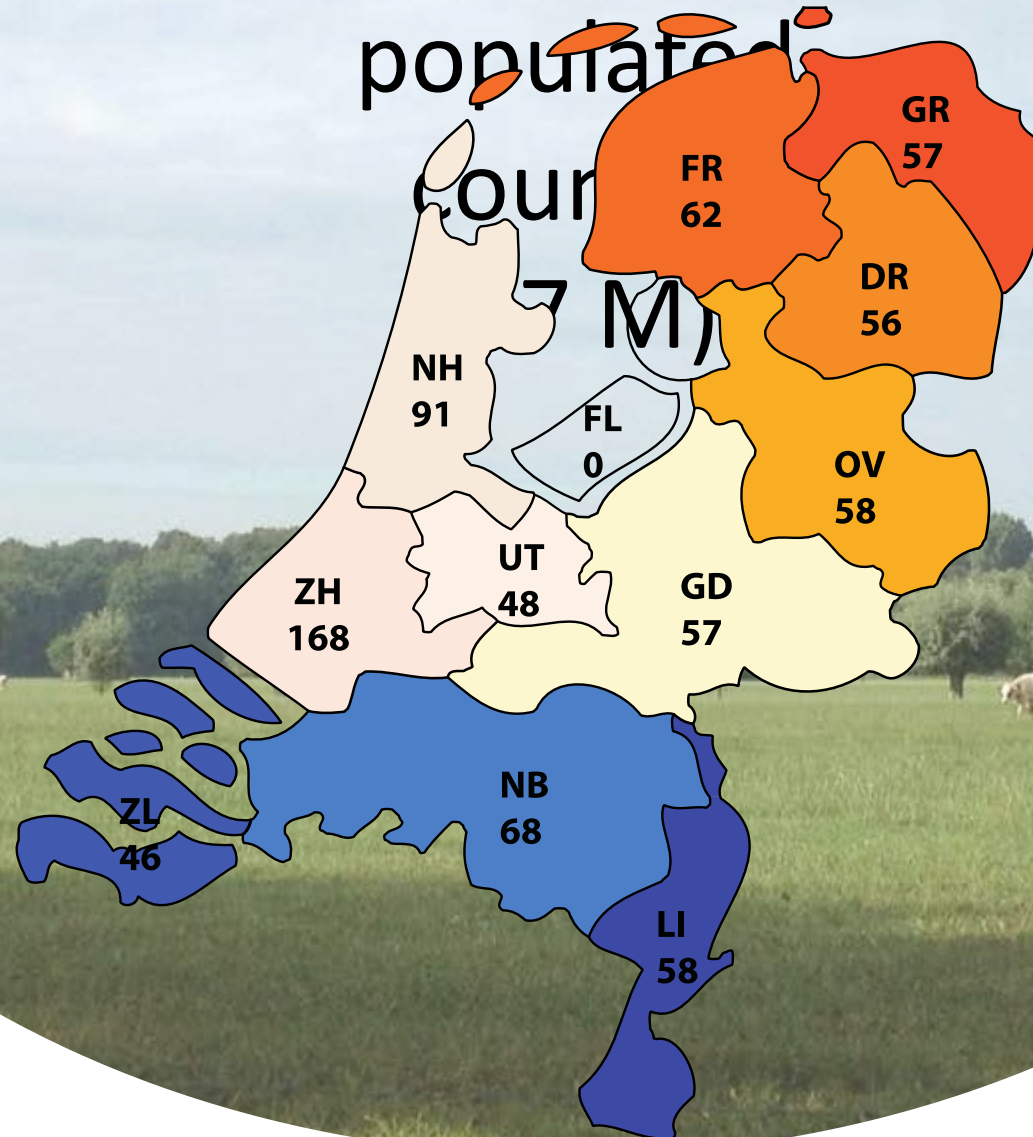
The Genome of the Netherlands:

A small (42,000 km²) but densely

populated

country

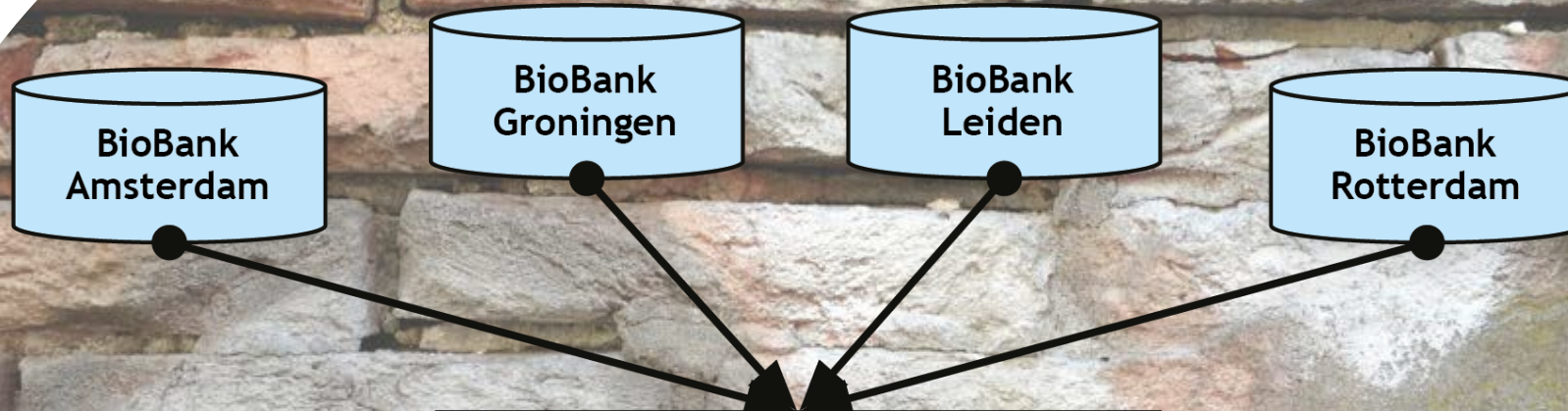
(7 M)






BBMRI.nl

Biobanking and
BioMolecular resources
Research Infrastructure
The Netherlands

GoNL



231 x  One Child
8 x  Dizygotic
Twins
11 x  Monozygotic
Twins +

769 Individuals

SELECT AN ERA TO EXPLORE

ATLAS OF THE HUMAN JOURNEY

When humans first ventured out of Africa some 60,000 years ago, they left genetic footprints still visible today. By mapping the appearance and frequency of genetic markers in modern peoples, we create a picture of when and where ancient humans moved around the world. These great migrations eventually led the descendants of a small group of Africans to occupy even the farthest reaches of the Earth.



GO TO:

[GENETIC MARKERS](#) +

[JOURNEY HIGHLIGHTS](#) +



Global field science supported by the Waitt Family Foundation



A research partnership of National Geographic and IBM

[NATIONALGEOGRAPHIC.COM](#)

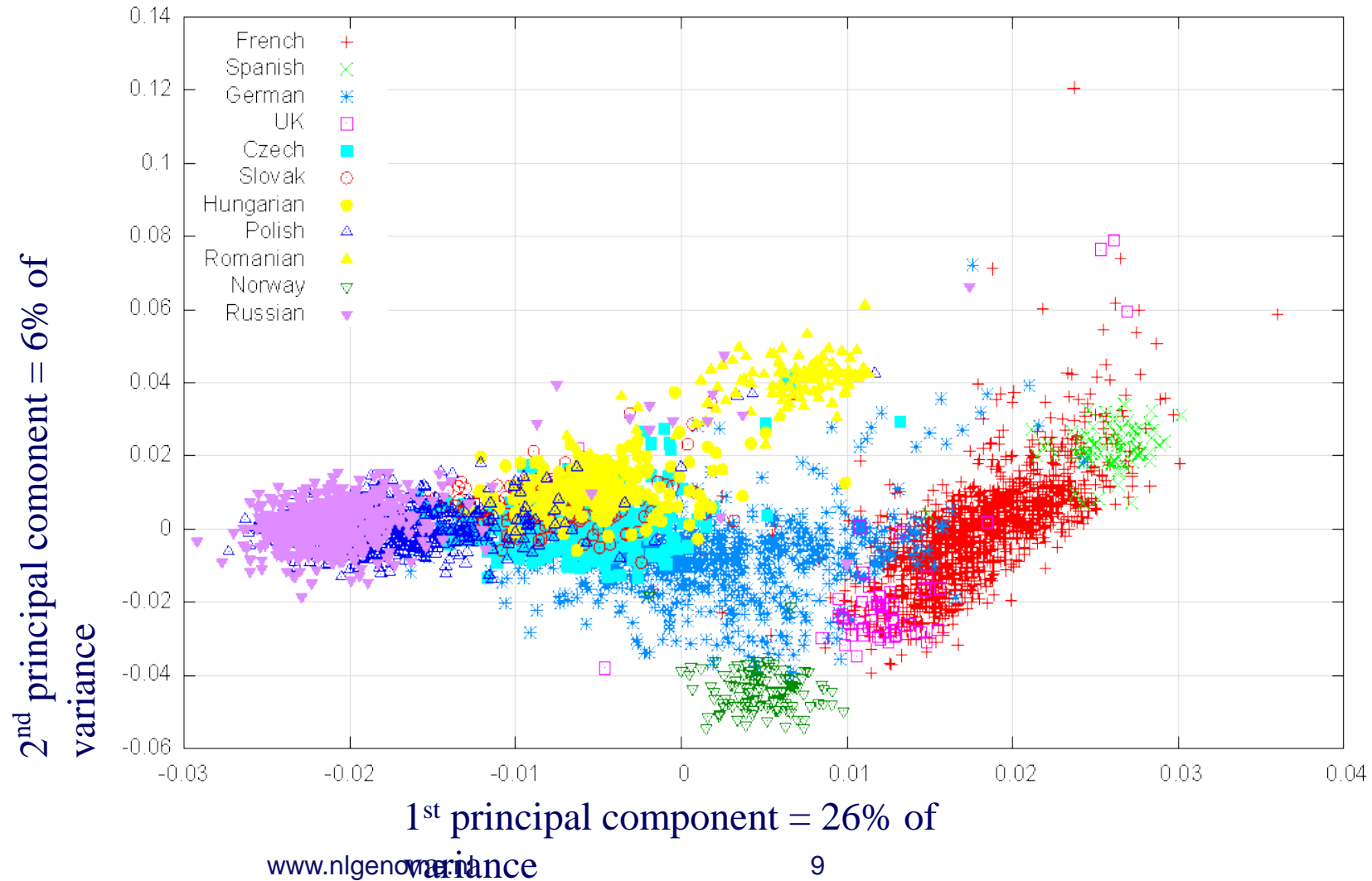
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www.nlgenome.nl

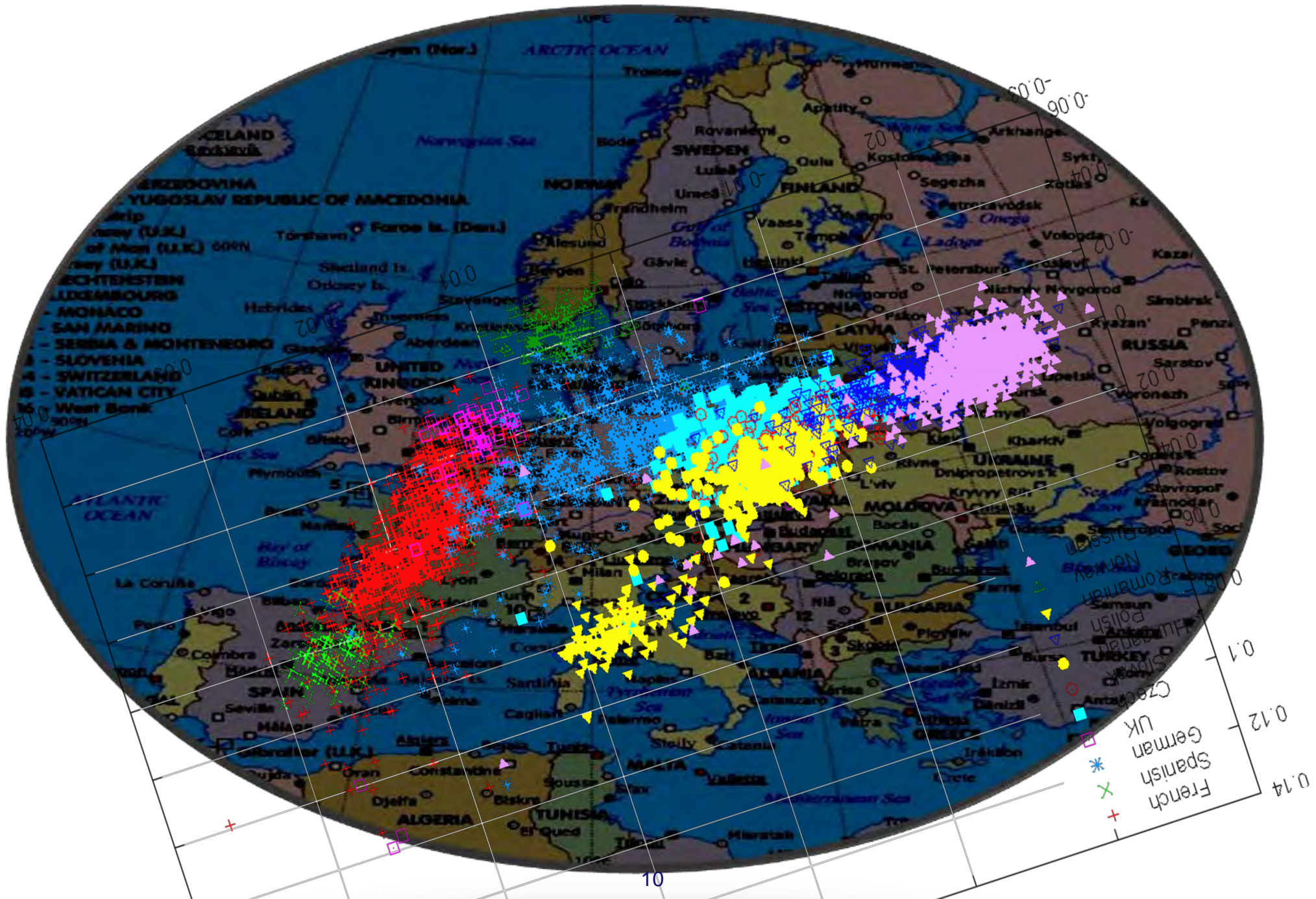
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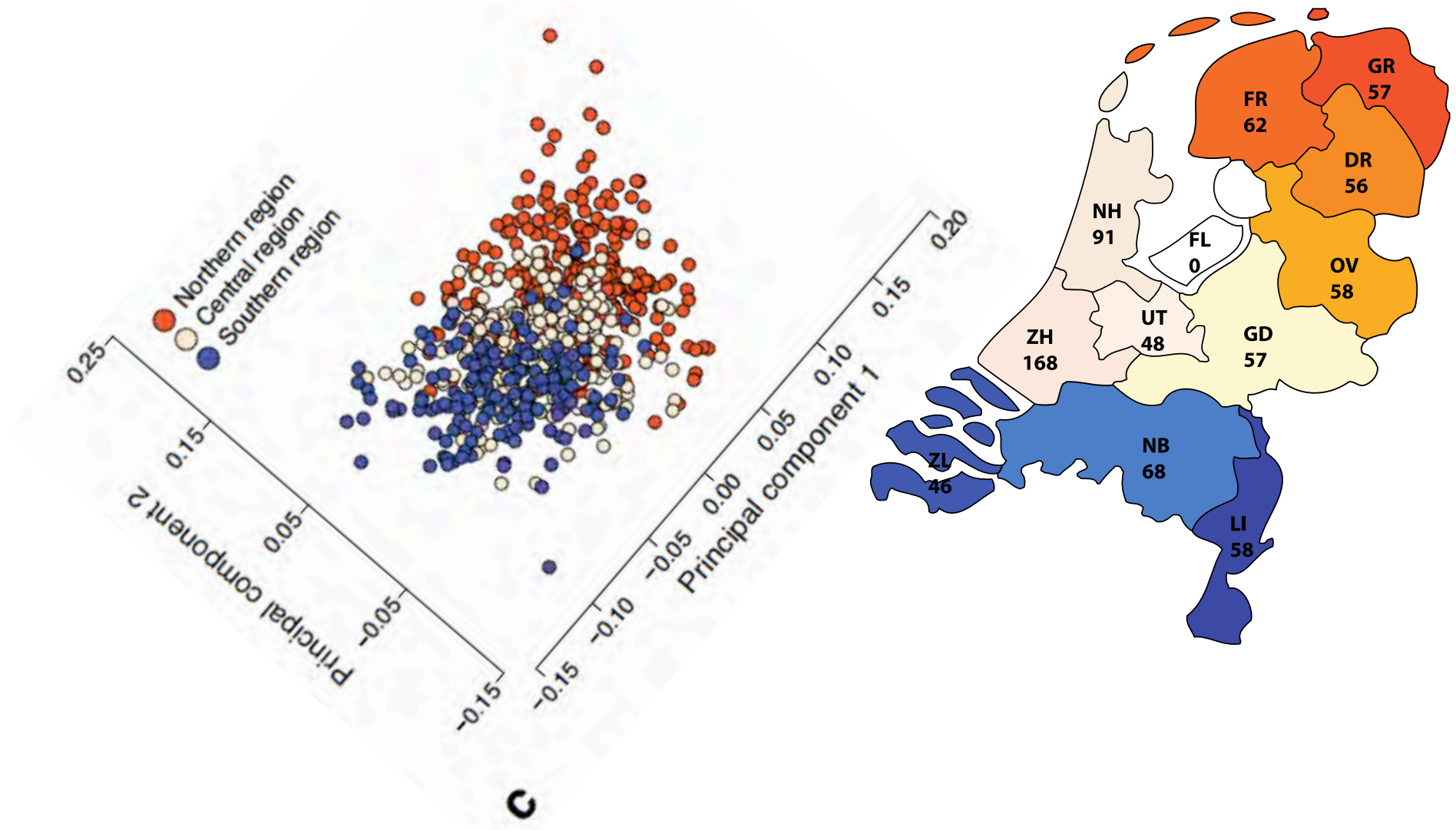
Principal component analysis of European populations

Simon Heath et al. (2008) EJHG 16, 1413 – 1429





PCA and ROH analysis show North-South gradient within Netherlands



2011001	Withoff, S.	UMCG
2011002	Sinke, R.J.	UMCG
2011004	Slagboom, P.	LUMC
2011005	Meulenbelt, I.	LUMC
2011006	Zhernakova, A.	LUMC
2011007	Boomsma/Abdellaoui	VU
2011008	Boomsma/Abdellaoui	VU
2011009	Bot, J.J.	LUMC
2011010	Lage, K.	Boston
2011012	Voight, B.	Pennsylvania
2011013	Kushner, S.	ErasmusMC
2012014	McCarroll/Handsaker	Harvard MS
2012015	Palamara, P.F.	Columbia
2012016	Baas, F.	AMC
2012017	Ophoff, R.A.	UMCU
2012019	Netea, M.	UMCN
2012021	Ridder, D. de	TU Delft
2012022	Reitsma/Rosendaal	LUMC
2012023	Zhang/Long	Gregor Mendel
2012024	Almomeni	UMCG
2012025	Schönhuth/Marschall	CWI
2012027	McCole, R	Harvard MS
2012028	Kok, K.	
2012029	Kiemeny/Franke/Coene	Radboud/UM
2013030	Swertz/Zhernakova	UMCG
2013031	Marchini c.s.	Oxford
2013033	Greevenbroek, M. van	Maastricht U
2013034	Vliet-Ostaptchouk, J. van	UMCG
2013035	Iperen, E. van	AMC
2013036	Meerman/Sikkema/Dier	UMCG
2013038	Durbin	Sanger

GoNL data is used by many researchers already



AVAILABLE: a reference dataset that combines the haplotypes from various public cohorts i.e. 1000G, GoT2D, UK10K **and GoNL**

**204 GoNL applications,
21 denied/rejected
~ 2000 users**

Biobank-based Integrative Omics Studies A second nation-wide data infrastructure

- **Data requests: 104 and counting**
- *All data* through SARA infrastructure (no downloads)
- *Post-publication RNA-seq/450k data* through EGA
- Downloadable
- Av approval time 1-2 months
- 41 publications including 'BIOS-Consortium'
(11 Nat. Genetics, 3 Nat. Comm, 3 AJHG, 3 in Genome Biol).

The screenshot shows the BIOS Consortium website. The top navigation bar includes links for Home, News, Publications, Agenda, Projects, Biobank catalogue, Contact, and About BBMRI-NL. A search bar on the right contains the text 'zoeken...' and a 'Zoeken' button. Below the navigation, the main content area features the title 'The BIOS Consortium' with a printer icon. The text below the title lists the members: 'Dr B. Heijmans (Chair), Dr L. Franke, Dr A. Isaacs, Dr R. Jansen'. A paragraph below describes the mission: 'The mission of the BIOS Consortium is to create a large-scale data infrastructure and to bring together BBMRI researchers focusing on integrative omics studies in Dutch Biobanks'. On the right side of the page, there is a sign-up form for the 'BBMRI-NL nieuwsbrief' (newsletter) with fields for 'Naam' (Name) and 'E-mail', and an 'Aanmelden' (Sign up) button.

BBMRI-NL BIOS Consortium

Biobank-based Integrative Omics Study

- 5,000 population based Dutch samples
- Genome-wide genotype data available
- Paired-end RNA-seq data generated in blood
- Methylation: 450k data generated in blood
- Effects of genetic variation on gene expression and methylation investigated

BBMRI Rainbow RP4 Metabolomics Applying Metabolomics in Dutch cohorts



**Phase 2 Metabolomics
1 platform 1H-NMR
Brainshake
N=25.000**

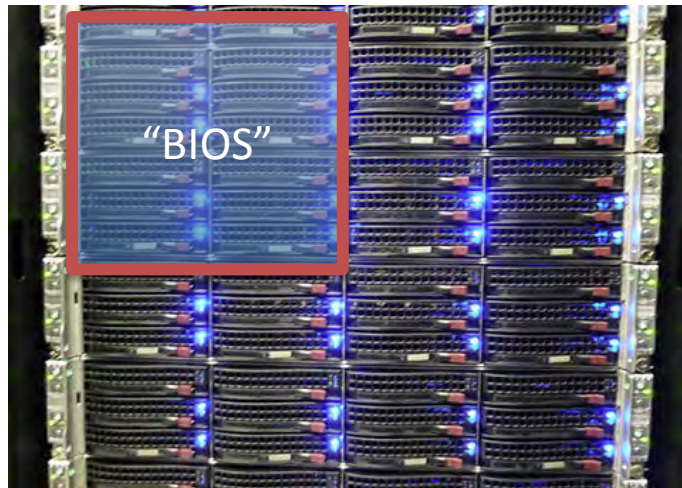
PI/PhDs of 22 cohorts

**Dorret Boomsma (VU)
Cornelia van Duijn (EUMC)
Eline Slagboom (LUMC)**

Highlights BBMRI-NL - ‘Cloud’ for controlled access multi-center studies

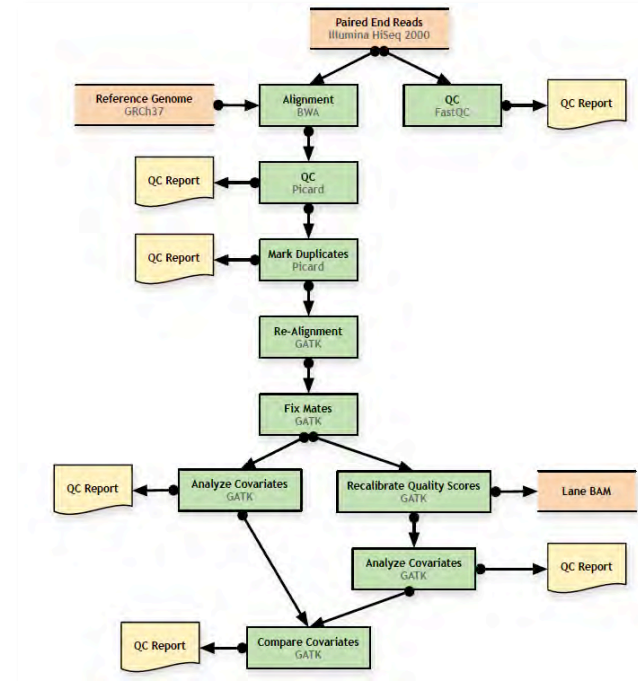
Storage & compute infrastructure services

(e.g. ‘virtual private cluster’ facilities at Groningen & Amsterdam)



Pipeline services

(e.g. imaging, DNA, RNA, metabolomics, microbiome)



Integration and warehouse services

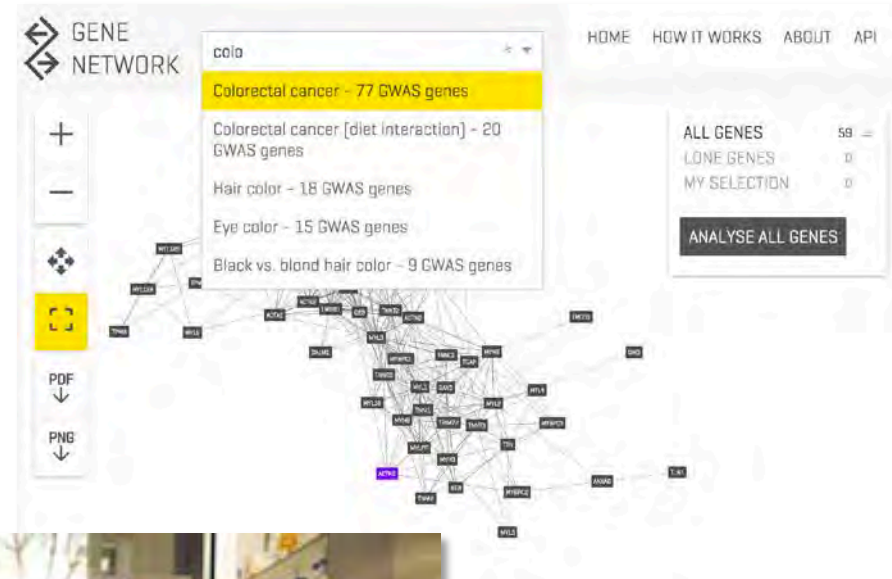
(e.g. clinical phenotypes, imaging phenotypes, molecular phenotypes, biobankconnect data harmonization, translational research toolbox)

Highlights BBMRI-NL – public access to BBMRI generated knowledge via ‘APPS’

Apps for the clinic

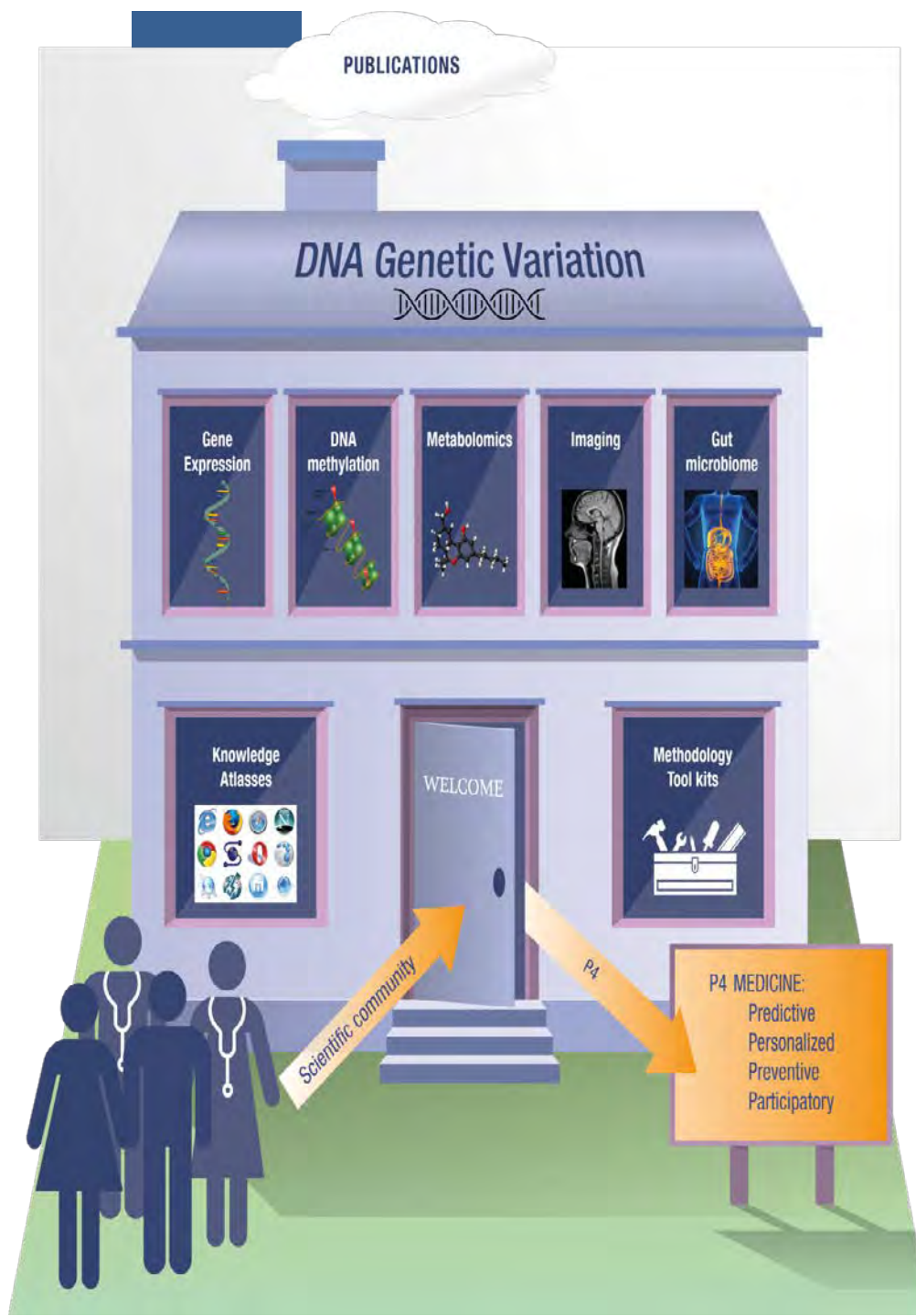


Apps for researchers



Apps for the public





Warehouse of
data
shared and
used by the
community

List of identifiers ?

NSD1

Identifier type

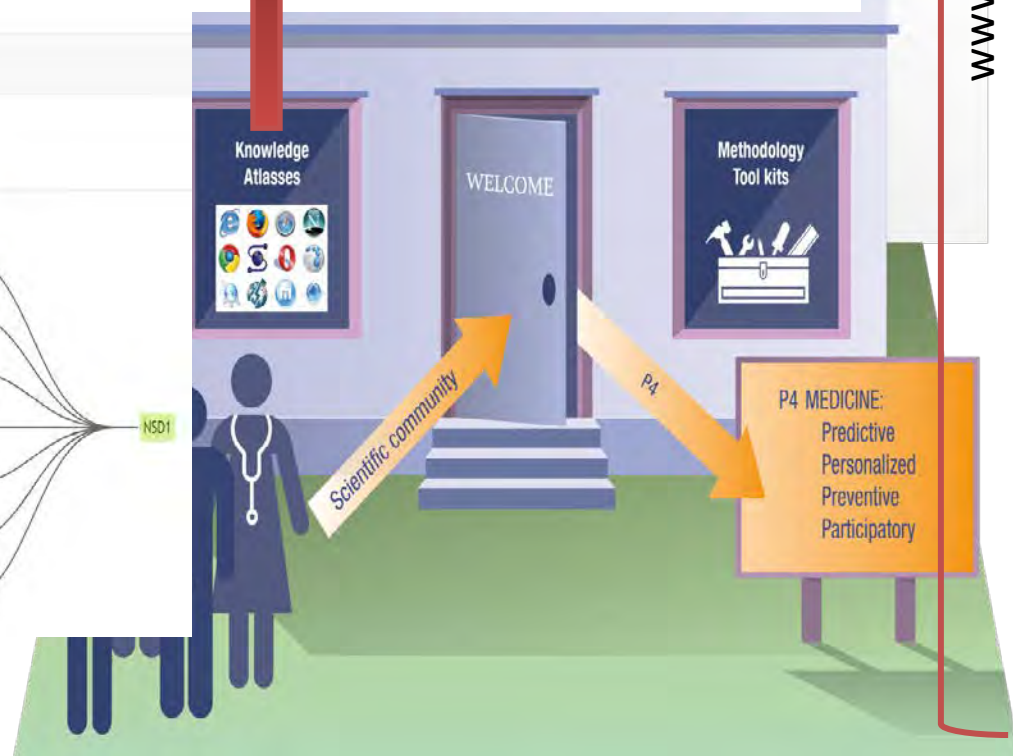
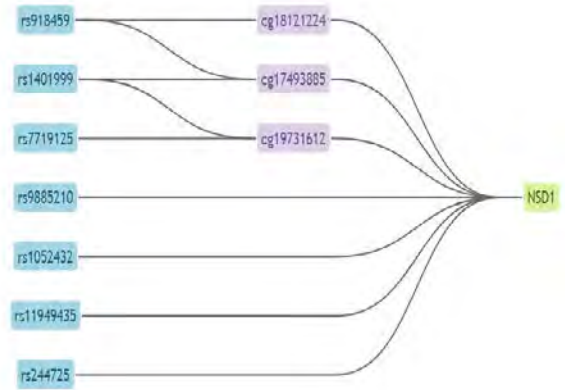
Gene

query **SNP-CpG** **SNP-Gene** CpG-Gene network ? Download

SNP	SNP (proxy)	LD R2	alleles	gene	type	p-value	Z-score	FDR
rs9885210	rs9885210	1	T/C	NSD1	gene	0.0000156	4.32	0.00885
rs1052432	rs1052432	1	G/A	NSD1	exon	0.00000168	4.79	0.00127
rs11949435	rs11949435	1	G/C	NSD1	exon	0.00000471	4.58	0.00328
rs244725	rs244725	1	T/C	NSD1	exon	0.0000721	3.97	0.0366

Search

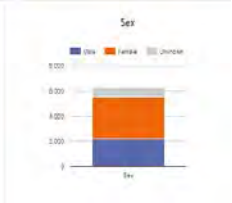
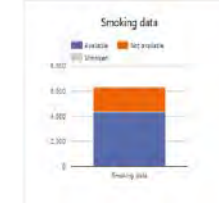
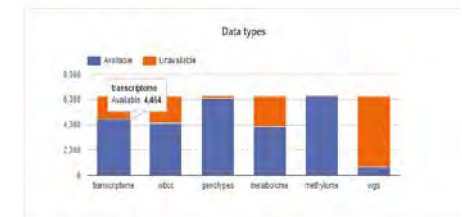
query **SNP-CpG** **SNP-Gene** CpG-Gene network



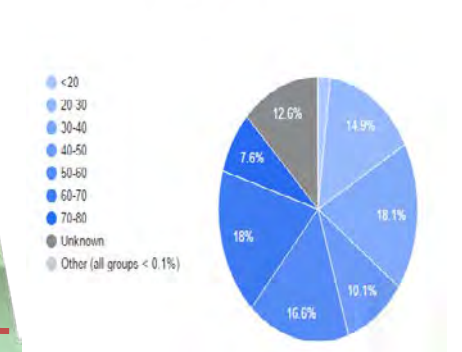
www.bbmri.nl/omics



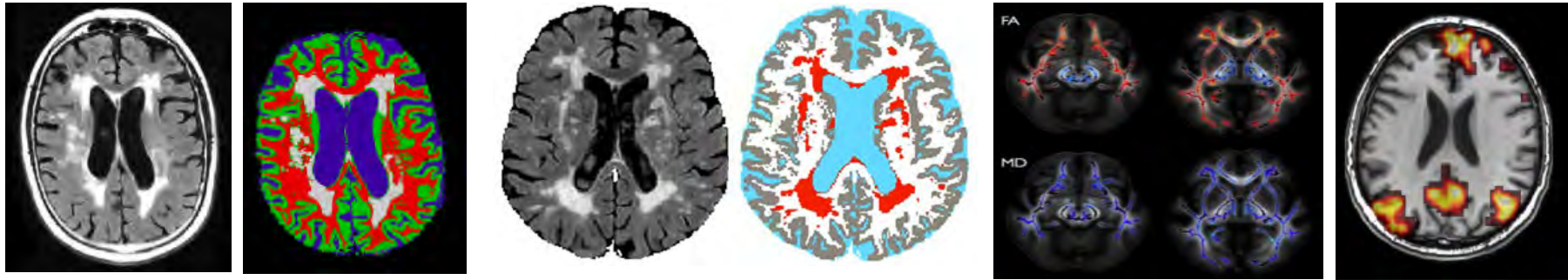
Sample makeup: All biobanks



Age distribution



Highlights BBMRI-NL – imaging data



Building a population imaging infrastructure

- Pool existing image data and generate new data
- Central database to store raw and processed data
- Procedures to harmonize data
- Development of reference data for case-control studies, spanning wide age range
- Linking image data to clinical and molecular phenotypes

Highlights BBMRI-NL – access to archival tumor material

Dutch National Tissuebank Portal

12 million tissue samples stored in
pathology archives
42 million records on almost 10 million
patients stored in the central data- bank



Judgment of Linkage requests by committees

- Linkage requests are judged by committees of individual biobanks, cohorts and registrations
- These follow:
 - Their own procedure
 - Their own criteria
 - Their own conditions
- -> divergent, conflicting judgments of the same linkage request
- **-> delay often takes years!**
- Aim: **Coordinated, uniform and simultaneous judgments of linkage requests**
- **Get (linkage) committees together!!**

BBMRI NL – BioLink :

Towards Joined Judgment of Linkage Requests



**Signing of Declaration of Intent Linkage Code, By
Scientific Board LifeLines and foundation
Perinatal Registration Nederlands,
Den Haag, 15 september 2015**



Engaging patients and publics in biobank governance

- Literature review & survey of the field
- Case studies of good practices
- Building up an advocacy & expert network for BBMRI
- Results: a widely distributed guideline
 - A context-sensitive how-to manual for biobanks
 - Engagement as a pragmatic endeavour, linked to specific patients/publics & research/organizational objectives
 - Routinizing engagement: building up relations, integration into organizational procedures
- **Stimulating practice a tougher nut to crack...**



SUMMARY - CURRENT

BBMRI-NL

- > 250 Dutch biobanks
- Clinical and general population samples, images and person data.
- International repository for the benefit of life sciences and clinical research.
- Developed common standards, interfaces and communication protocols, connected genomics, health, behavioural, molecular and imaging data.

Access to

- Cohort catalogue: (<https://catalogue.bbmri.nl/menu/main/app-molgenis-app-biobank-explorer/biobankexplorer>)
- Sequence data: (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3895638/>)
- Omics data: (<https://omics-explorer.bbmri.nl>)
- Analysis tools (<https://www.bbmri.nl/services/research-tools/omics-analysis-platform>) and an
- ELSI helpdesk for compliance with ELSI demands (<https://www.elsi.health-ri.nl/>).

More than 720 papers resulted from the BBMRI infrastructure, many high impact : (<https://www.bbmri.nl/services/knowledge/scientific-publications-2018>)



Samples, images, data Find & Access	Research tools Capture, Integrate & Analyse	Ethical, Legal & Social issues Support	Knowledge Share
<ul style="list-style-type: none">CatalogueOmics data setRequest portalPathology (PALGA) portalBiobank management	<ul style="list-style-type: none">Data captureData integrationOmics analysis platformImage analysis platformAtlases - Omics, Imaging	<ul style="list-style-type: none">ELSI Service deskPrivacy toolsPatient & Public Advisory CouncilDonor interactionPublic website	<ul style="list-style-type: none">Scientific publications 2018White papersGuidanceMoviesEducation

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Services

Samples, Images,
Data

Research tools

Ethical, Legal &
Social implications

Knowledge

Scientific
publications
2019

Archive

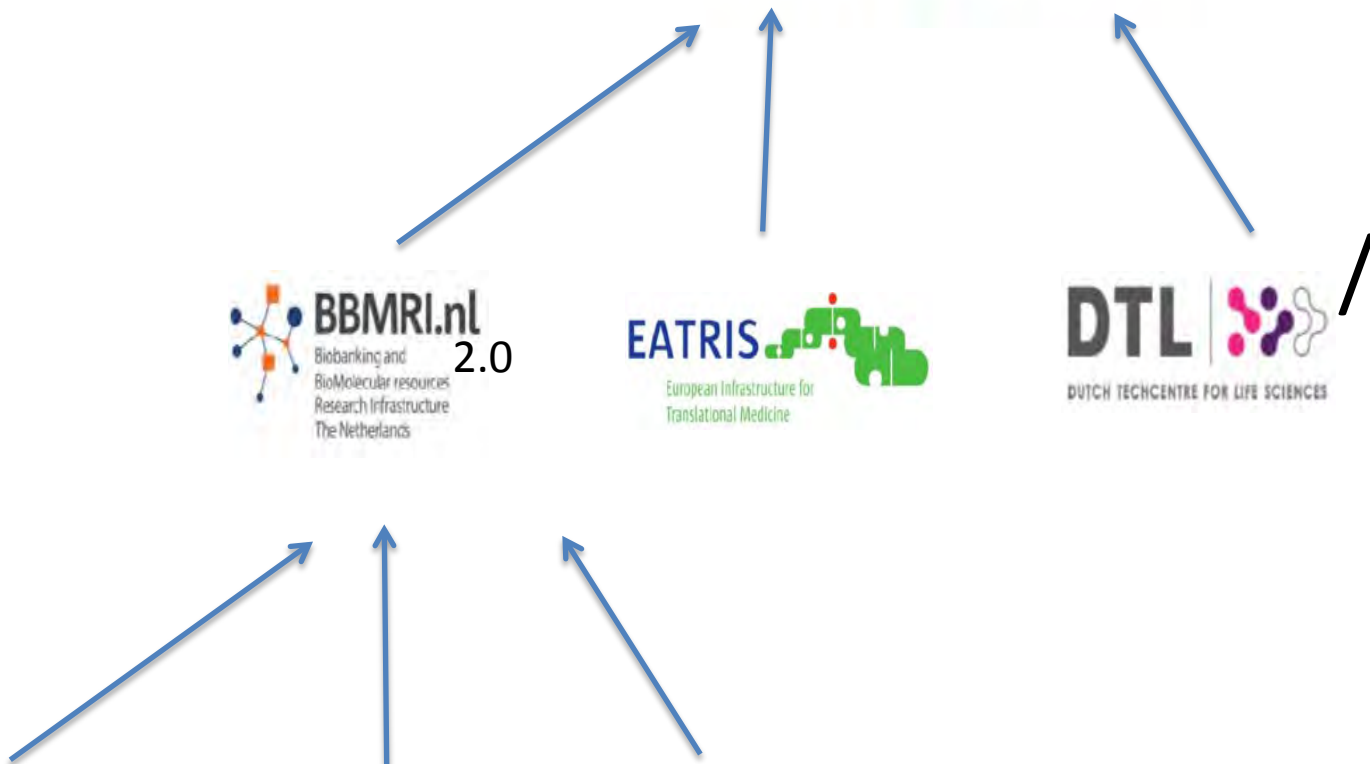
Publications

2019
2018
2017
2016
2015
2014
2013
2012
2011
2010

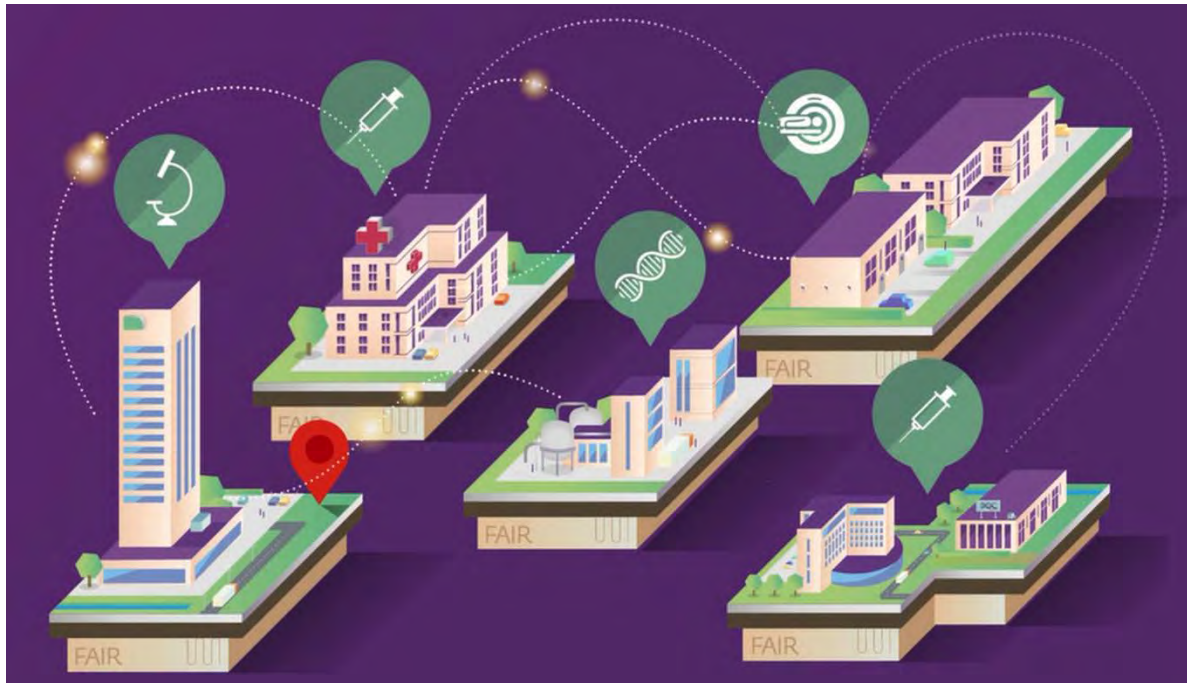
Scientific publications 2018

Below you will find an overview of BBMRI-NL Scientific publications in peer reviewed journals. We have only listed items that contain BBMRI-NL or the grant number in the affiliation, funding and/or acknowledgement section of the article. Items are listed per year in alphabetical order.

- Auwera van der, S., Peyrot, W.J., Milaneschi, Y., Hertel, J., Baune, B., Breen, G., Byrne, E., Dunn, E.C., Fisher, H., Homuth, G., *et al.* (2018). Genome-wide gene-environment interaction in depression: A systematic evaluation of candidate genes: The childhood trauma working-group of PGC-MDD. *American Journal of Medical Genetics Part B-Neuropsychiatric Genetics* 177, 40-49.
- Boeckhout, M., Scheltens, P., Manders, P., Smit, C., Bredenoord, A.L., and Zielhuis, G.A. (2018). Patients to learn from: on the need for systematic integration of research and care in academic health care. *J Clin Transl Res* 3, 401-406.
- Brouwer-Brolsma, E.M., Berendsen, A.A.M., Sluik, D., van de Wiel, A.M., Raben, A., de Vries, J.H.M., Brand-Miller, J., and Feskens, E.J.M. (2018). The Glycaemic Index-Food-Frequency Questionnaire: Development and Validation of a Food Frequency Questionnaire Designed to Estimate the Dietary Intake of Glycaemic Index and Glycaemic Load: An Effort by the PREVIEW Consortium. *Nutrients* 11.
- Chaker, L., Cremers, L.G.M., Korevaar, T.I.M., de Groot, M., Dehghan, A., Franco, O.H., Niessen, W.J., Ikram, M.A., Peeters, R.P., and Vernooij, M.W. (2018). Age-dependent association of thyroid function with brain morphology and microstructural organization: evidence from brain imaging. *Neurobiol Aging* 61, 44-51.
- Culverhouse, R.C., Saccone, N.L., Horton, A.C., Ma, Y., Anstey, K.J., Banaschewski, T., Burmeister, M., Cohen-Woods, S., Etain, B., Fisher, H.L., *et al.* (2018). Collaborative meta-analysis finds no evidence of a strong interaction between stress and 5-HTTLPR genotype contributing to the development of depression. *Molecular Psychiatry* 23, 133-142.
- Gudmundsdottir, V., Pedersen, H.K., Allebrandt, K.V., Brorsson, C., van Leeuwen, N., Banasik, K., Mahaian, A., Groves, C.J., van de Bunt, M., Dawed, A.Y., *et al.* (2018).



Health-RI: bundle and connect a wide range of resources including



- biobanks
- data collections
- image collections
- IT-technologies
- facilities
- processes

into one large-scale research infrastructure, to enable ground-breaking personalized medicine and health research



Next phase: DARE-4-LIFE

DARE-4-LIFE will make four major steps towards a more personalized, proactive approach to health:

- Enrich and connect novel microbiome data
- Tools for gene-gene and gene-environment interactions, imaging genetics and imaging-omics analyses by machine (deep) learning methods
- Distributed analysis → scalable analysis of comprehensive (global) health data
- Collaboration with data-driven life science initiatives worldwide

Proof of principle in three demonstrator projects, informing health professionals and citizens to take a more proactive approach to (their) health at different stages of life.