Hub 1

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Hub is the official newsletter of BBMRI-NL

European BBMRI news

Goodbye BBMRI-PP, hello BBMRI-ERIC

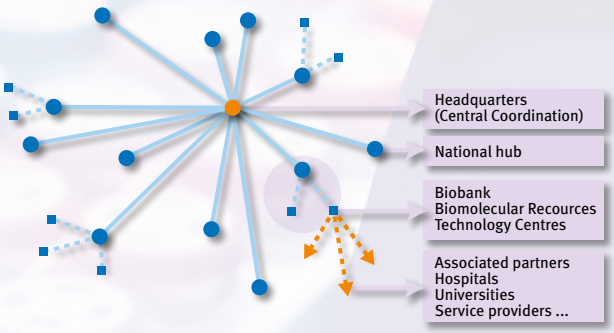
While BBMRI-NL is gathering speed, BBMRI on a European level is coming to the end of its preparatory phase in January 2011. A follow-up is in the make: as a part of the European Research Infrastructure Consortium (ERIC), BBMRI will continue its work from the spring/summer of 2011. The application for ERIC-status was filed in August. In the last 2.5 years BBMRI has grown into a 53-member consortium with over 280 associated organizations from over 30 countries, making it the largest research infrastructure project in Europe. The continuing interest of biobanks to join BBMRI suggests that it has been able to fill some of its key aims, such as bringing cohesion to the European biobanking community and making the existing and new high quality biological resources available for health research in Europe.

ERIC

The ERIC is an instrument specifically designed by the European Commission for the projects in the ESFRI roadmap, which allows consortia to operate in different Member States under one legislation and also offers VAT-free status. BBMRI-ERIC headquarters will coordinate the activities of National Hubs established in all Member States. Headquarters will provide a common access portal to resources available in Member States as well as appropriate facilities, support and expertise. The National Hubs are also established under the ERIC legal entity and will link the national scientific community (e.g., universities, hospitals, research institutions, resource centres) to BBMRI-ERIC in a so-called hub-and-spoke structure (see illustration). For now, it is uncertain where BBMRI-ERIC HQ will be established. Austria has offered to host, others may yet follow.

BBMRI-ERIC statutes are essentially ready, but some items remain unresolved and need to be decided at political level, for instance national contributions to joint budget and voting rights. Although the decision-making process to join BBMRI-ERIC is still in progress, official commitments towards the construction phase of BBMRI-ERIC have been received from six European Member States and biobanking is on the national roadmap in a further eight countries.

The Distributed Hub and Spoke Structure

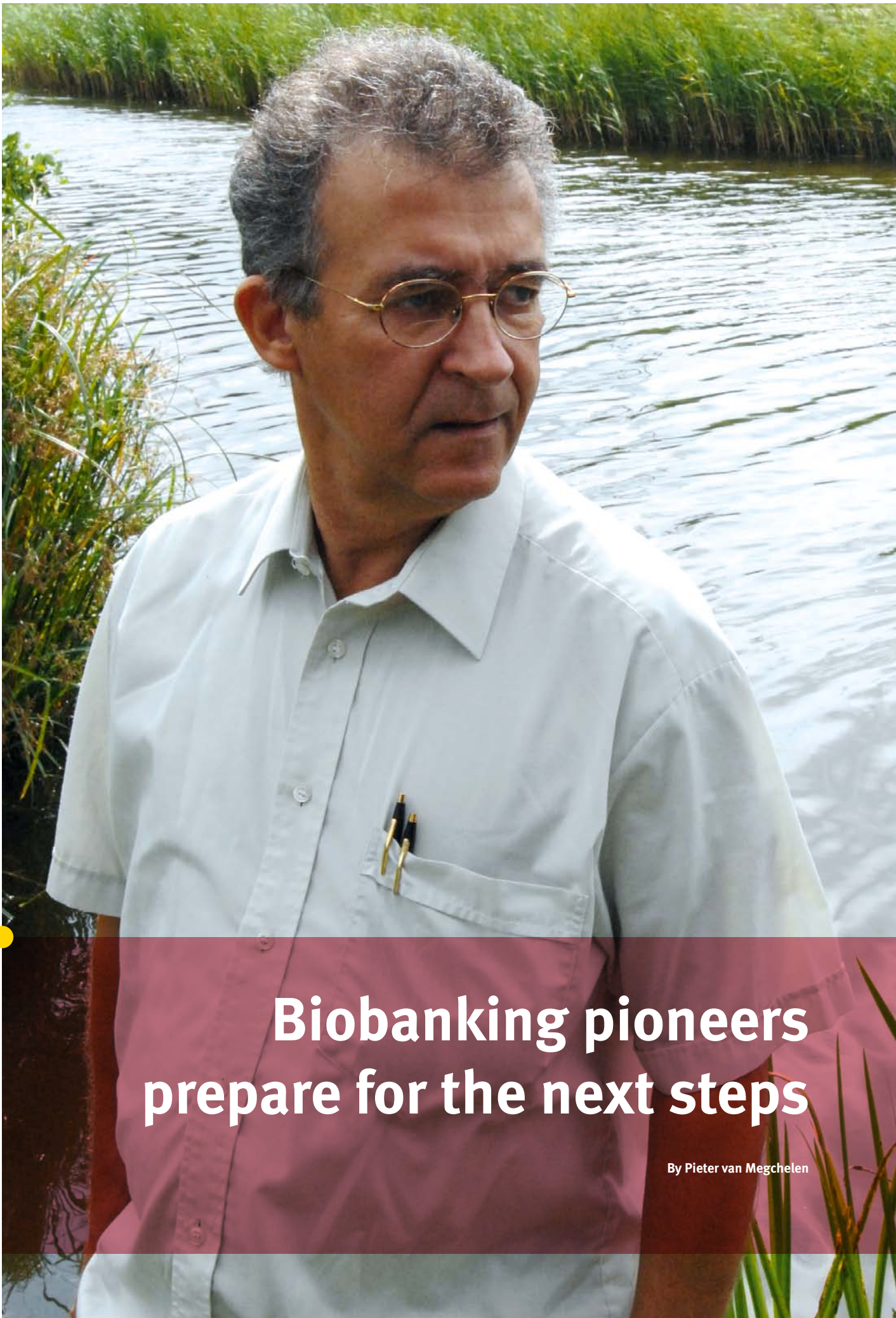


Access policy

Access policy is currently under discussion in BBMRI. The European Commission has very specific requirements in the ERIC guidelines that access should be open and fair to all scientific communities. This is a particular challenge in the field of biobanking as participating biobanks must follow their national legislation, ethical review and informed consent requirements that cannot be overruled by any European Directive. However, BBMRI is looking to develop a plan to integrate existing quality controlled biobanks, biomolecular resources and enabling technologies into a novel pan-European biomedical research infrastructure and provide access for the scientific community to the millions of samples and biobanks around Europe.

Heli Salminen-Mankonen, PhD

Keep up with the latest news on www.bbmri.eu.



Biobanking pioneers prepare for the next steps

By Pieter van Megchelen

BBMRI-NL is off to a flying start. In the past year, an organisation has been established, many promising projects have started and there are plans for even more daring endeavours. Special attention will be paid to clinical biobanking, the further development of expertise on legal, ethical and social aspects and last but not least the bioinformatics infrastructure needed to deal with the data tsunami that is being generated. BBMRI-NL scientific director prof. dr. Gert-Jan van Ommen: 'We have become an important factor in European biobanking.'

The BBMRI – Biobanking for Science conference Van Ommen and his team host in September 2010 in Amsterdam marks the end of the preparatory phase of the European BBMRI initiative. Van Ommen: 'With the backing of the Seventh Framework Program of the EU, a large international cooperation has been set up, with my colleague professor Kurt Zatloukal from the Medical University of Graz in Austria as leader. BBMRI-EU now needs to grow through the further development of national 'hubs', and over-arching hubs with a certain specialization, like clinical biobanking access, or ICT, financed by national funds, to build on this foundation of cooperation. In the Netherlands, we have initiated BBMRI-NL, making a flying start because we already had major existing biobanks like the Rotterdam ERGO and ERF studies, the Netherlands Twin Registry at the VU, as well as the 'String of Pearls' Initiative, a prospective clinical biobank that is being developed jointly in all the eight University medical centres. This major project is already generating a lot of expertise, for instance in the field of harmonisation and standardisation. Another large partner in BBMRI-NL is LifeLines, a population biobank being set up in Groningen. The main aim of BBMRI-NL is to connect the existing biobanks in the Netherlands, making them more readily accessible for research, nationally as well as in BBMRI-EU context. Our biobanks contain materials and data of over 400,000 participants. Several years ago, we already had the idea and the model for collaboration, so when the possibility arose to establish it, it didn't take much time to rekindle the enthusiasm of our colleagues.' With a large subsidy from the government through NWO, the Dutch organisation for scientific research, BBMRI-NL started in the autumn of 2009. Now, with program manager dr. Margreet Brandsma and communications officers Margot Heesakker-Heintz and Mascha Jansen, the staff is complete for now. 'We do not need a large office', Van Ommen explains. 'Most of the work is being done in the network of biobanks.

Professor dr. Gert-Jan van Ommen: 'Rainbow and Complementation projects greatly enhance the enthusiasm and commitment of researchers and biobankers.' (Photo: Edo Kooiman)

Large and small

To stimulate cooperation and enhance the value of existing biobanks, BBMRI-NL uses two parallel strategies, called 'Rainbow projects' and 'Complementation projects'. Van Ommen: 'The Rainbow projects are large endeavours, involving many centres. The title refers to the different colours, symbolizing the different forms and applications these projects may take. The 'Netherlands Genome Project' is the first Rainbow project, the building of a national biobanking and sequence analysis informatics infrastructure is another. Complementation projects on the other hand are small-scale investments in the quality and accessibility of various biobanks. When you establish a biobank, it typically starts with the refrigerator full of samples and a computer with the data that were relevant to your first enquiry. But then, others want a subsample of, say, white blood cells of all postmenopausal women. That may be a very reasonable request, but it often is a hell of a job to compile these samples, if your biobank is not structured that way. And there is no way you can get the financial means for this kind of work through the usual channels; however modest, often people are greatly helped by a 50 k€ impulse for one year. Now, we can provide this funding, so these necessary jobs on harmonisation and enrichment can be done. Forty-two Complementation projects have already been approved. We expect many useful results from these projects. And we have seen already that the stimulus greatly enhances the enthusiasm and commitment of researchers and biobankers.'

Bioinformatics challenge

The successful start of BBMRI-NL, together with related activities like PSI, LifeLines, BioSHaRe and the Netherlands Genome Project, is generating an unprecedented wealth of highly interesting biomedical data. 'With the Netherlands Genome Project, we are pioneering something that has not been done yet on the European mainland. The detailed and valid map of genetic variation it will provide will add greatly to the value of existing genetic data in our biobanks. The major challenge in the coming years will be to develop the bioinformatics tools, both in terms of hardware and software, to explore the enormous amounts of data, to sift through them and find the relevant patterns. This will be the next large Rainbow project.'

The enthusiasm and foresight of Van Ommen and his Dutch colleagues have put The Netherlands at the forefront of the European biobanking community. 'Our strengths lie in the field of both clinical and population biobanking, in dealing with the societal and legal aspects, and in unstructured text mining, a novel field in bioinformatics. These are important fields, so we have much to contribute to the larger community in BBMRI-EU. And that's important, for we need the international community to answer the important questions in biomedical sciences of today'.

BBMRI-NL funds 42 Complementation projects

BBMRI-NL has awarded funding to forty-two so-called Complementation projects, all to be conducted within a year from September 2010 at the eight Dutch academic medical centres, VU University Amsterdam, the University of Utrecht, the Netherlands Cancer Institute (NKI), and the National Institute for Public Health and the Environment (RIVM).

Dr. Schmidt's projects aim to enrich existing biobank materials.

Complementation projects are small scale projects aiming to give Dutch biobanks a quick quality impulse, making them ready for collaboration on a national and European scale. Some Complementation projects aim at harmonisation, that is to say, a better co-ordination of the way in which biobanks classify and save their data and materials. Other projects aim at enrichment, by adding information or matter to existing samples, so as to make them usable for more detailed research.
BBMRI-NL program manager dr. Margreet Brandsma: 'The Dutch biobanks contain a wealth of samples and data. Those are the basic materials for research into genetic and lifestyle factors that influence the development of for instance cardiovascular diseases, inflammatory diseases, and cancer. BBMRI-NL wants to make those basic materials more accessible to researchers, in the Netherlands as well as across Europe. By funding these Complementation projects we hope to improve the quality of individual biobanks and to create more unity.'
The result is a wide array of projects. At the RIVM, for instance, one Complementation project consists of the renovation of eight liquid nitrogen tanks that contain blood samples of the Morgen-Epic and the PROSPECT cohorts, a collaborative project between the RIVM and the University Medical Centre Utrecht (UMCU). Dr. Bas Bueno-de-Mesquita: 'Thanks to the BBMRI-NL funding, the tanks' lifespan has been extended with at least ten to fifteen years. We are very pleased that we were able to execute the renovation: it ensures the quality of almost half a million blood samples obtained from 35,000 participants that are used in international studies. And also, we have made the whole setup more (cost) efficient and user friendly.' The eight tanks were moved, so as to be more readily accessible. Also, the supply pipes were completely renewed and shortened. Bueno-de-Mesquita: 'Another main cost cutter was the placement of electronically tuned control panels on the tanks. Now they fill simultaneously, and that really makes a difference.'
Professor dr. Hanneke Schuitemaker (AMC) receives funding for her study 'Pump-up the number: Generation of additional GWA data for the Amsterdam Cohort Studies on HIV infection and AIDS'. The project uses existing DNA to try and find extra genetic factors that influence disease course in HIV infected persons. Professor Schuitemaker: 'Some HIV infected people get ill quickly, whereas others stay healthy for a long time. This research will try to identify the adverse or positive influence of genetic factors, other than the already known ones. The extra data gathered will also be used in a large-scale international collaboration. Hopefully, the results will generate new leads for the development of a vaccine or additional medicines.'
Dr. Marjanka Schmidt (NKI) is pleased to be able to collect

additional data for two studies with BBMRI-NL funding. 'In the national 'Breast cancer Outcome Study Of Mutation carriers (BOSOM)' we aim to evaluate the effect of genetic factors on breast cancer survival, treatment and the development of second tumors. In this study we have collected DNA and extensive clinical data and follow-up.

'Improving the data means more effective research'

We will now collect non-genetic risk factor data, for example smoking behavior and use of oral contraceptives. These data will be contributed to an international consortium with the acronym: BCAC (Breast Cancer Association Consortium). In BCAC we will investigate the interactive effect of polymorphisms (common hereditary variants in DNA) and life style factors on breast cancer risk and prognosis.'
'The second study includes breast cancer patients who were counseled and tested negative for BRCA1/2 mutations at our clinical genetic center. We will genotype thirteen known breast cancer susceptibility polymorphisms. These data will contribute to a national effort (HEBON) to develop breast cancer risk prediction models for breast cancer families.'

For a complete overview of the awarded projects, visit www.bbmri.nl/en-gb/activities/projects/87-complementation-projects-2010.

Agenda

CMSB Symposium
Leiden Naturalis, October 15, 2010
The Centre for Medical Systems Biology hosts its 7th annual symposium on October 15. Keynote speaker is Aarno Palotie of the Wellcome Trust Sanger Institute, who will discourse on 'Migraine and other complex disorders', foscussing on the medical and social impact of complex genetics. Registration is free. For more info visit www.boerhaavenet.nl.

NVHG Autumn Symposium
Amsterdam AMC, November 19, 2010
The Dutch Society for Human Genetics (NVHG) has its annual symposium on November 19 in college hall 4 of the AMC in Amsterdam. The programme is still under construction, but keep an eye on www.nvhg-nav.nl/agenda.aspx for updates.

'Connecting Biobanks'
Amsterdam AMC, November 22, 2010
Don't miss BBMRI-NL's official kick-off meeting! The event includes presentations by internationally renowned speakers such as David Cox and Josh Sommer, workshops, and the formal inauguration of the Concept Web Alliance. Organized by BBMRI-NL, NBIC, and CWA. To register, visit www.bbmri.nl/conference2010.

Life Sciences Momentum
Utrecht Media Plaza, November 23, 2010
The tenth edition of this networking conference has as its theme Global Connections. With keynote speaker Robert Jan Smits and parallel sessions on current topics, it promises to be well worth a visit. To register, go to www.momentum2010.nl/registration.html.

The liquid nitrogen tanks in their new and improved setup. (Photo: Ivar Pel)

Professor Cisca Wijmenga: 'Our trio design will help us to determine how a certain variant fits within the paternal and maternal patterns.' (Photo: Rob Huibers)

Unique in-depth perspective on regional genetic variants

By Pieter van Megchelen

The Netherlands Genome Project ('het Genoom van Nederland') is truly unique. Never before have so many genomes from one country been sequenced using such a 'trio' design. By sequencing the genomes of 250 couples and their offspring (the trio's), this project will map genetic variation in the Netherlands. It will provide a solid foundation for 'imputing' rare variants (i.e. deriving them by computation) in the more than 100,000 samples already stored in Dutch biobanks and resulting from conventional genome-wide association (GWA) studies.

Project leader Prof. Cisca Wijmenga: 'In the next ten years, whole genome sequencing will become a standard tool in research and molecular diagnostics. We hope to kick start the nationwide implementation of such tools with this project and build up the expertise needed to enable our scientists and the public to benefit from these future developments'.

'Since the start of the Human Genome Project in 1990, we have gained many new insights into the genetic variation between individuals', says Wijmenga. 'This has been very beneficial for biomedical research. To find the biochemical pathways involved in disease, we want to study the differences between individuals with and without a specific disease. With genome-wide association studies, focussing on SNP's, we are getting closer to the genes and variants involved. But we have also found that there are major regional differences in these variants, and we now need to find the actual variants protecting groups from a disease or predisposing them to developing it - and get even closer to identifying the genes themselves.' To do this, a more in-depth way to study genomic variation is needed. The gold standard, of course, would be to sequence the complete genomes of many people. Nowadays, with faster and less expensive new sequencing techniques coming onto the market, this is becoming feasible. But brute force alone is not enough to do the job, it needs to be combined with a clever approach.

Trio design

One of the potential pitfalls in using whole genome sequences to assess genetic variation is the fact that large parts of our DNA make for very boring reading: larger and smaller sequences tend to be repeated over and over again. Because of this, it can be difficult to pinpoint the exact location of a specific nucleotide and to determine whether it is a true variation on that particular spot or simply a sequence from somewhere else. 'Our trio design, in which we analyse the genomes of two parents and one offspring, will help us to determine how a certain variant fits within the paternal and maternal patterns', says Wijmenga. Just as looking with two eyes adds depth and perspective, the trio design adds certainty about the overall sequential order.
The trio approach makes the Netherlands Genome Project unique, even in comparison with similar projects like the '1000 genomes project' (www.1000genomes.org). Its advantages in terms of reliability are obvious. So why aren't geneticists all over the world doing trios? 'Many biobanks do not have this kind of material. Dutch biobanks have collected many samples of parents and their offspring. In other countries, this has not often been done on such a large scale', ventures Wijmenga.

Large yield

In the next few months, the genomes in 750 samples from Dutch biobanks will be analysed by BGI, the Beijing Genomics Institute, based in Shenzhen, which today has the best experience in high throughput sequencing. The sequencing machinery is provided by Illumina Inc. From the autumn of 2010 onwards, Dutch scientists will be busy checking and analysing the enormous amount of data generated by their Chinese colleagues. The samples will be taken from population biobanks, representing healthy people living in all the different regions of the Netherlands (equal numbers from all the original 11 provinces and a few extra from Amsterdam and Rotterdam). The results will therefore show the amount of genetic variation among the different regions. Not just single DNA base variants (SNPs), but also insertions, deletions, copy number variations and other ways the genomes of individuals may differ. Wijmenga: 'These data will be interesting in themselves, for we truly don't know how much genomic difference there is between people from Groningen and those from the province of Zeeland. For biomedical purposes, however, there is much more to gain. If we know the specific local variants, we can go back to the data we have from over 100,000 samples already used in GWA studies. Using 'imputation' techniques, we can get a lot closer to identifying the genes involved in health and disease. It's like driving on a highway: those small hectometer signs on the side of the road show you the exact location – but only if you already know roughly where you are. In genomic data, your location may be far from trivial. That's why the sequential order and its validity are so important. Once we have more insight into the variants, we could design a cheap DNA chip for many specific regional variants, and test their association with health and disease. We are now building an enormous reference database that will be very useful in the future.'

The biobanks participating in the Netherlands Genome Project ('het Genoom van Nederland') are LifeLines, the ERGO Rotterdam Cohort Study, the Netherlands Twin Registry, and the Leiden Longevity Study. The project is supervised by a steering committee in which all the participating organizations are represented.

Link

Human genome Project - www.ornl.gov/sci/techresources/Human_Genome/home.shtml

‘Conducting cross-border research? Consult BBMRI’s European legal wiki!’

Since June 2009, researchers, lawyers and other interested parties can find a treasure hoard of information, practical tools and templates on legal matters concerning biobanks, research across (non-) European borders, data protection, et cetera. Initiator dr. Jasper Bovenberg of Legal Pathways is enthusiastic about the wiki’s popularity, but warns that the platform requires constant and dedicated attention to remain up to date.

Jasper Bovenberg (Legal Pathways) has filled the wiki with all relevant EU policies and legislation. (Photo: Peter Koops)

‘There is a vast amount of tools and templates on legal matters available’, asserts Bovenberg, who started thinking about the wiki a couple of years back, when the European Science Foundation asked him to contribute to a report on European legislation surrounding biomedical research and biobanks. ‘The request was to come up with a solution to help researchers navigate the dazzling number of diverging rules and regulations in all Member States that govern their daily cross-border work.
Rather than compiling yet another overview of all EU and national regulations, the idea was to unearth and gather all existing practical tools and solutions in one place and keep them up to date. Writing a twenty-seven country report would have been a costly and laborious process, and would have presented more questions rather than provide hands on solutions. Plus, by the time you’re done chances are the information in it has already become obsolete.
That’s why I thought it would be a much better idea to start an online, 24/7, interactive collaborative application, in which everyone could share their own and their country’s tools, solutions and experiences. After all, the legislation available presents a multitude of grey areas. Having direct access to validated solutions of how other researchers and institutions have dealt with these grey areas can be of immense help.’

Applied knowledge

After a long deliberation on the architecture and technical setup and several tests, the wiki was launched as part of the BBMRI website. Successfully: the platform has over 150 members. There is an entry for every EU country, containing information on biobanking matters, such as access policies, and standard, EU approved, data transfer agreements, but also documentation: patient information leaflets, population consent forms, recruitment letters, and project descriptions. True to its mission, the platform provides ample documentation for doing biomedical research across EU borders.

Bovenberg: ‘The feedback I get is that people very much like to read about for instance the String of Pearls project. They find a lot of applied knowledge, ideas and observations there that they can apply to their own plans or projects. It saves them the trouble of having to find out all sorts of things themselves, and that is a good thing.’
Bovenberg doesn’t keep exact count of the number of downloads from the wiki, but he does know it is being used as a reference point by its members. ‘The user statistics show we have over 250 visits a month’, he says.
Still, there is always room for improvement, isn’t there?
Bovenberg: ‘In the first year and a half, I spent a lot of time putting ‘the basics’ online, that is to say, the European guidelines and regulations. The data on exchanging samples across EU borders, and the standard contracts for exchanges outside the EU are all to be found on the wiki. There is extensive information on the EU directive that permits free movement of data across Europe; a *sine qua non* for BBMRI’s continued existence and success.’

Sound system

‘The platform makes clear that, in spite of all the complaints about the hurdles to transfer data across borders, the EU in fact has a sound system in place, with practical contracts.’ While the passive use of the wiki is fantastic (the downloads) , Bovenberg would love to see more active contributions (the uploads). These are necessary to ensure that the information provided on the wiki is consistent,complete and up to date for all the countries. ‘The Netherlands, Italy and Hungary have done a good job, as well as several others; but there are some countries on which there is little information right now. Ideally, we should have a national correspondent for each country, but there is simply no funding for that.’
So far, only BBMRI in the Netherlands and Sweden have provided funding for such a national correspondent.
‘We applied for a grant with the EU, but it was denied’, Bovenberg says. ‘So perhaps we need to try for funding on a national basis in all twenty-seven member states. After all, we do have wiki members in each country, but these are people who have a lot of work on their hands and little time. You cannot ask them to take on the responsibility of providing accurate and up-to-date information without some kind of financial compensation. We all benefit from this type of collective, applied wisdom.’

The BBMRI legal wiki can be found at www.legalpathways.eu/index.php?option=com_joomlawiki&Itemid=53.

Colophon
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