

Minutes of the Genomeutwin steering group meeting, Copenhagen 8.5.2003
Notes taken by Markus Perola, National Public Health Institute (NPHI), Finland.
Please e-mail comments to markus.perola@ktl.fi

Present:

Bernard Mulligan (EC)(BM)

Leena Peltonen (NPHI, PI)(LP)

Antonia Stazi (Istituto Superiore di Sanità, Rome)(AS)

Jennifer Harris (FHI, Norway)

Alun Evans (University of Belfast)(AE)

Markus Perola (NPHI)(MP)

Kirsten Ohm Kyvik (University of Southern Denmark)(KOK)

Kaare Christensen (University of Southern Denmark)(KC)

Kari Kuulasmaa (NPHI)(KK)

Ann-Christine Syvänen (University of Uppsala)(AS)

Jan-Erik Litton (Karolinska Institute)(JEL)

Dorret Boomsma (Free University of Amsterdam)(DB)

Jaakko Kaprio (University of Helsinki)(JK)

Nancy Pedersen (Karolinska Institute)(NP)

Aarno Palotie (University of Helsinki)(AP)

Hans Howelingen (University of Leiden)(HH)

Tim Spector (St Thomas Hospital, London)

LP started the meeting with general matters:

-the progress report needs to be in Brussels in August

-Scientific Advisory board (SAB) will meet in September/October to evaluate the progress made during the first year

-suggested dates were: Sept. 21.-23; Sept. 29.-30; Oct 5.-7.; Oct 12.-14.

-LP presented a schedule for progress in preparing the report:

-data to LP from participants Aug. 1st

-1st draft to participants by Aug. 10th, response time 5 days

-2nd draft to participants by Aug. 20., response time 5 days

-final submission August 27th.

-a combined GSG&SAB meeting will be held on some of the above listed dates.

-city to be decided (suggested: Amsterdam/London)

BM presented greetings from Brussels and described EU related matters.

-Genomeutwin as one of the flagship projects for EU

-excellence beyond state of the art, critical mass

-Genomeutwin-related and –based projects should apply for the next round in 6th framework

-not Genomeutwin as a project, but projects made possible by it

-BM presented data from the first round of calls:

NOE/IP 47 proposals on 15 topics, averaging 11,9M€

STREP/CA 52 proposals, av. 2,8M€

SSA 7 proposals, av. 381.800€

- Genomeutwin could apply for funding for example in organizing workshops (SSA) or coordinator actions (CA)
- 2nd call letters in mid June 2003, deadline November 2003., budget ~415M€
- also Marie Curie actions (see: <http://www.cordis.lu/fp6/mobility.htm>)

MP gave a presentation on the deliverables and milestones (see presentation at the genomeutwin website)

A discussion on the EU funding details followed:

- EUs instruments for providing support for infrastructure very much lacking, large support not allowed but infrastructural matters should not be forgotten from proposals (BM).
- Genomeutwin can and should apply for the next round of calls as a background infrastructure and facilitator, not as a project (BM)
- BM pointed out that if applying for extra funds, for example for additional partners, in FP6, the application should not be “Genomeutwin 2” but be a part of or represent a new program
- also it would be a good idea to evaluate the possibilities to apply funds via other than functional genomics programs
 - Brussels would like to know of the deliverables met even before the deadlines
 - the timing can be changed if very good scientific reason
- LP mentioned the sad passing of Dr. Sandkuijl, which has somewhat affected the start-up of the statistical core.

ACTION ITEM 1: MP to send information of the Genomeutwin and MORGAM websites to BM

JK told details about the exchange student program:

- about 30.000€ a year
- needs a decision structure
- A training grant committee was formed: JK, Caroline van Baal, AE

ACTION ITEM 2: Training grant committee forms a plan for student exchange before summer.

KC summarized the status for the epidemiological core:

- EpiCore is extending its effort to new partners
- summary of the current status: we are in a very good situation to find interesting twin pairs
- expert groups formed on phenotypes, headed by people from twin registries who know about the registries and the phenotype in question
- draft manuscripts for the special issue in Twin Research (October 2003) circulated
- BMI, height, migraine phenotypes in very good shape, we can move forward.
- first DNAs delivered from Denmark and Finland for genome-wide scans
- we need to think of intermediate phenotypes
- CHD, stroke, longevity will take a longer time to establish cohorts
- new co-operation been successful and new papers are already planned

ACTION ITEM 3: A list of papers of the special issue to be delivered to BM (TS)

DB told that a plan to open the Mx script website for public use has been made. This was seen as a good idea, however the users should acknowledge the website and Genomeutwin when publishing data where the scripts have helped.

ACTION ITEM 4: The website address for Mx scripts to be delivered to BM (MP)

A discussion of a list of phenotypes to be collected for studies followed. This list is needed for ethical applications at least in Sweden. Denmark and Finland have the greater flexibility here (JK). A broad, general application was suggested to be used, and also a side note that “these are the current instruments, if new are developed they can be applied”.

ACTION ITEM 5: KK delivers a suggestion of a minimum list of phenotypes collected for cardiovascular studies.

For **new** ethical applications, it was seen useful that the coordinating centre would apply for acceptance of the whole project in its national ethical board. It was agreed that the coordinator should deliver the original application to The Finnish National Advisory Board on Health Care Ethics (ETENE) or other more applicable Finnish ethical board. (see <http://www.etene.org/e/index.shtml>)

ACTION ITEM 6: KTL delivers the original application for ETENE review (LP)

It was noted, that EC ethical panel has already accepted the plan and this can be mentioned in coming ethical applications (BM).

ACTION ITEM 7: EU Contract; having the ethical approval, will be scanned and added to the website (MP)

ACTION ITEM 8: JH prepares a statement for progress in ethical matters.

A discussion followed of what phenotypes can be analysed at this stage from already scanned materials.

ACTION ITEM 9: KC and MP prepare a list of phenotypes available to the website

AP and AC gave an update of the genotyping progress (see presentation at website)

The results were seen as very reasonable and applicable for many trait analyses. By August we should have 4500 pairs genome-scanned, excluding Australia. AC stressed that selection of SNPs to be genotyped is a burning issue and some decisions need to be made. However, it was agreed that we should first analyze the existing data by linkage and the concentrate on the interesting peaks. Some decisions are needed in the next steering committee meeting.

JEL gave an update of the database issues.

Federated db and datawarehouse systems are being developed in parallel. Eventually we want to go into a federated solution, but now the first action is that all centers provide data from 100 pairs to db core.

ACTION ITEM 10: Db core sends description of the federated db system to centers for the long time plans (JEL)

LP gave an update on the discussions with IBM and their federated database system Discovery Link. IBM has proposed 25k cost for the first implementation of the system. With that, we will build a trial system between Sweden and Finland and have access to the analytical tools as well (such as IBM's OLAP cube solutions). IBM will provide (loan) also 2-4 servers for this test trial. After trial each centre who wants to join the system, needs to invest 25-30k for its infrastructure. LP suggested that coordinator invests the trial fee (25k) and reviews with the db core whether the system works for us or not. IBM representative could come to the db core meeting May 26th.

The GSG gave a unanimous green light to LP to proceed with the IBM contract.

ACTION ITEM 11: LP organizes a conference call between IBM and relevant experts in GenomeTwin for the DL solution.

HH presented the happenings in the statistical core. The statistical core will have a satellite meeting May 9th, where many relevant issues will be discussed, the presentations will be placed on GenomeTwin website.

The matter of including discordant sibs in the analyses was discussed and seen as an important angle in this study, however *unascertained* samples should be included as well. The latter is especially important for future studies, which will concentrate on different phenotypes that for what the ascertainment was done.

LP presented a suggestion (distributed to participants at the meeting) prepared by NPHI and UK Twin Study to start marker map harmonization for linkage analyses immediately, the natural first step being the combination of different genome scans. A lively discussion followed.

Following points were agreed upon:

- merging and cleaning the genotype data is very important
- there should be joint analysis of all the produced genotypes, not only merging IBD data from individual centres. This does not exclude the analyses each participant can do with their own data.

How the scans would be combined and who would do the analyses was discussed. It was agreed, that the genotyping centres should be involved in combining the genotype data and marker maps. Here, both pooling the allele data or MIBD data approaches should be used. Genotype-phenotype analyses will be coordinated by Leiden and coordinator. However, LP stressed that the experience the genotyping centres and St Thomas+Australia have on linkage analyses should not be dismissed.

TS was enquired about the commercial attachments UK Twin Study might have. He explained that only the following traits have restrictions on use: osteoporosis, osteoarthritis, acne.

ACTION ITEM 12: The steering group accepted the use of 12 months of salary for marker set harmonization for the performed genome scans and the concept of the pooled data analysis of the genotypes. This should be started immediately with the scan data available. Leiden will coordinate also these statistical analyses.

KOK reviewed the publication rules. Three kind of papers were listed:

1. individual partners analyzing their data
2. data formed by collaboration between centres
3. Collaborative Genomeutwin publications

-a deadline for delivering the planned publication was seen necessary, as well as a monitoring structure.

- the manuscript proposal should include planned date for publication
- the GSG will be the ultimate monitor of the publications

-all papers, which use Genomeutwin resources, should acknowledge it

-Genomeutwin should be listed as a keyword where possible

-a mechanism to inform people of planned manuscripts would be the website.

-the website will list the publications produced in the project

- pdf files for them when possible will be placed on the website

- the first author is responsible for informing MP of the publication and producing the pdf-file

ACTION ITEM 13: Publication rules will be placed on the website.

ACTION ITEM 14: AE will give MORGAM material transfer agreement to JH

It was noted, that the centres own the genotype data of their cohorts.

Forthcoming special issue of Twin Research was discussed

TS will be the special editor.

The deadline of the final manuscripts is the end of May

All phenotypic papers should have heritabilities and variances listed

The GSG made suggestions of the referees to each paper. One would be internal and one external.

Coronary Heart Disease (AE):

AE presented the manuscript for CHD. It would need some data from the participants, blood pressure was selected as an interesting phenotype. All cohorts had some data on it and will provide AE requested data, when asked.

Referees: Ulf DeFaire and Tim Spector's postdoc

Stature (JK):

Situation stable and good, some parts missing.

Referees: endocrinologist from Norway (JH), Tim Spector's postdoc

BMI (JH)

Logged BMI was agreed to be used. Sex-specific models were agreed to be used.

Referees: JK, Hermine H. Maes

Longevity (KC):

Some form of heritabilities will be presented, however another publication is under planning for higher-impact journal

Referees: HH, Harold Schnieder

Stroke (leader David Gaist, KC presented)

Not much end-points available, more of a review and discussion on the phenotype

Referees: Kjell Asplund, a member from Decode paper

Migraine (DB):

Results look good, manuscript well going

Referees: NP, Rune Frants

Legal&Ethical (JH)

Proceeding well

Referees: Bertha Knoppers, Mats Hannson

Genotyping (AC):

Validation, genomics, strategy considered

Referees: MP, Ivo Gut

Statistics I (DB)

80-90% finished

Referees: Nick Martin, Mike Neale

Statistics II (HH)

More of a review

Referees: Pak Sham, AI Yashin

Db (JEL)

-first version circulated

Referees: Juha Saharinen, Eric Sobel

General description (LP)

-number of DNA samples needed

ACTION ITEM 15: KC delivers the number to LP

Referees: JH, Nick Martin

Also, a short letter from EC will be produced by BM

ACTION ITEM16: the EC letter requested by the editor (TS)

A working group for the Genomeutwin manual was formed on voluntary basis: AS, KK, and a lab person to be named by AC+AP

ACTION ITEM 17: lab person for the manual (AC+AP)

Jan-Eric Litton was announced as a new member of the steering group (the updated list can be found from: http://www.genomeutwin.org/member/member_steering.htm)

Two statistics workshops are being organized. First one on advanced analyses of genetic statistics will be in Finland September 8-12, second on basic tools of twin statistics in Netherlands September 15-19. Genomeutwin participants have a priority for attendance, at least one from each centre should be accepted.

ACTION ITEM 18: generic e-mail addresses for application (MP)

Several calls for funding will be open. It is necessary to apply for many of those.

ACTION ITEM 19: everybody thinks of possible headings by the next steering committee meeting in June

The process will be discussed in the next GSG meeting.

AP and AC brought out the item of the necessity to genotype more variants in the scanned individuals and it was agreed that at least 10 mikrograms should be available for each individual selected for scans for Genomeutwin purposes.

ACTION ITEM 20: A list of candidate genes to the website (MP)

It was announced that the Genomeutwin members wishing to use the Morgam internal website should contact Kari Kuulasmaa for access. Kari.kuulasmaa@ktl.fi

Next GSG meeting will be held in Amsterdam, June 13th.

LP ended the meeting.

