

Minutes of the 2nd GenomEUtwin meeting; Rome, Italy, December 16.-17th, 2002. Notes taken by Markus Perola, markus.perola@ktl.fi

Attendees:

Steering group:

Dr. Leena Peltonen, KTL, Helsinki, Finland (PI)
Dr. Markus Perola, KTL, Helsinki, Finland
Dr. Antonie Stazi, Institute Superiore di Sanita, Rome, Italy
Dr. Jaakko Kaprio, University of Helsinki, Helsinki, Finland
Dr. Dorret Boomsma, Free University of Amsterdam
Dr. Jennifer Harris, Folkehelseinstituttet, Norway,
Dr. Nancy Pedersen, Karolinska Institutet, Stockholm, Sweden
Dr. Kaare Christensen, University of Southern Denmark, Odense, Denmark
Dr. Aarno Palotie, Finnish Genome Center, Helsinki, Finland
Dr. Alun Evans, University of Belfast, Belfast, UK
Dr. Kirsten Kyvik, University of Southern Denmark, Odense, Denmark
Dr. Kari Kuulasmaa, KTL, Helsinki, Finland
Dr. Ann-Christine Syvänen, University of Uppsala, Uppsala, Sweden
Missing:
Dr. Ulf Gyllensten, University of Uppsala, Uppsala, Sweden

Other participants:

Dr. Kaísa Silander, KTL, Helsinki, Finland
Tiina Aitlahti, Legal Department, University of Helsinki, Finland
Peter McCamom, University of Belfast, Belfast, UK

These minutes do not cover the separate meetings held by the ethical core and genotyping core on December 16th.

Monday 16th, 2003 morning. Meeting of the statistical and epidemiological cores invited by the PI to discuss the analyses of the first phenotype: stature.

Lexis diagrams were presented for participating twin registries

Action item 1: Lexis diagrams to GENOMEUTWIN web site (MP)

Socioeconomic status and its relevance to stature was discussed. KK told about the difficulties in MORGAM to standardising socio-economic status among different countries. This was agreed to be a problem but MORGAM's experience will help.

Birth height is recorded in Netherlands, Norway, Finland. This was agreed to be included in the stature associated phenotypes.

LP described a three stage division of the possible study materials:

1. Genome scan done
2. DNA available
3. "Ideal study"

1 and 2 would consider samples and data that have been already collected and we would have to analyse what there is. However, this approach has been used before with relatively low success.

JK showed the distribution figure of the stature of Finnish twins. The selection of study material for 3, “ideal study” was discussed. It was generally agreed:

1. both discordant and concordant (high-high/low-low; high-high being more interesting) twin pairs should be included.
2. entire sibships (extended families) should be used when easily available
3. parental height should be included in the analyses when possible
 - this would be useful for finding heterozygote parents
 - Netherlands, Finland, Sweden have collected parental height
4. extremely short people might have differing background from tall and this should be realized when selecting the material

LP suggested that a pilot would be started with existing data. After the pilot, a new questionnaire could be sent to selected participants, which could include questions to get “an ideal” phenotype for stature.

The pilot study would include 500 pairs from Finland, 1000 individuals from Norway, 1300 pairs from Netherlands and 500 pairs from UK. These have all genome scan genotype data.

The pilot project will start with genotyping of 1000 Danes. This will help in building up the logistics and co-operation. Parallel to that, the existing genotype data availability (ethical and phenotype existence) will be cleared by the Pis.

ACTION ITEM 2: Denmark sends 1000 Danes to Finnish Genome Center for genotyping (via NPHI).

ACTION ITEM 3: PIs clear whether the genotype data they have is usable for stature.

A series of expert groups was discussed to start working on the phenotyping. It was agreed that such groups should be founded. The members should have front-line knowledge of phenotyping of selected traits (Stature, longevity, migraine, CHD, stroke, BMI). A collection of names was accomplished.

Database issues were discussed.

JEL passed out the database format paper.

MP presented the federated db issue.

Following data was discussed that would be necessary to include in the common db but which could raise some challenges:

- zygosity
- additional sibs

-additional family members

-family members phenotype information
-parental information

It was seen a necessity that epicore and db core work close together.

It was agreed, that db core starts to build up a db for stature

ACTION ITEM 4: db core: pilot db for stature

Db core meets February 10th at Helsinki. The issue of federated db vs. datawarehouse will be discussed the further, when co-operation with IBM clears more.

Statistical issues

LP explained the situation after LS. The Leiden core is still willing and committed to serve as a statistical core unit and has many strengths. However, the knowledge on genetical statistics is thin.

LS had sent letters for OH+Susan Service to invite them to work as statisticians for the project. However, it was not known whether the situation would change now for them.

For now (next 6 months), each center should have their own statistician. Some financial support for that could be obtained from Leiden's share.

Ethical issues

JH described the morning's ethical core meetings main points.

-it was discussed what each center need to do to get the data to the cores
-generally, genotype data should not be given back to participants (MORGAM is an exception)

OECD, EU has recommended that all scientific data should be released to use

A write up of the db system would be necessary for the ethical core to produce applications for ethical reviews.

EC does not generally require reconsenting for studies, however, countries have differing practices.

ACTION ITEM 5: A write up of the db system will be produced by the db core to ethical core.

Epidemiological core

LS presented lexis diagrams for the centers (on the website)

Following points were raised:

- Only full blood siblings would be included as additional family members for the twins.
- also unlike sex twins should be considered for the analyses
- cheek swabs would be an alternative way to collect DNA, however blood is preferred
- genome scanning approach is the primary way of advance, over candidate gene analysis. However, some SNP genotyping in the region of interesting genes and loci would be done early on to build up the logistics.

LP brought up the question of crediting junior scientists. It was generally agreed that the project would produce some “big papers” where the authors would be listed as a consortium etc (this would be discussed the next day), however it was recognized that junior scientists would need credit from their work.

It was agreed that:

1. Any center can analyse their own data
2. Any center can analyse all data (however, at the recognition of db and epi core, also all centers should know when and by whom their data in analysed).

The day ended with a pleasant dinner at the hotel restaurant

Tuesday 17th, 200. Meeting of the steering group. Institute superiore di sanita, Rome, Italy

Dr. Peltonen lit a candle and a moment of silence was held in memory of our statistical core leader, Dr. Lodewijk Sandkuyl

Financial issues, LP

-40% of the TOTAL sum of money has been distributed to the centers. It was pointed out that this should cover for 40% of the entire 4 year period.

-all centers should keep timesheets for the manpower put on the project. The format will be put on the website

ACTION ITEM 6: timesheet (MP)

In October, EU needs to get a fiscal report from all centers. However, the scientific results are separate from this and in practice the results need to be ready in April to meet the October deadline.

ACTION ITEM 7: LP will set up Scientific Advisory Board meeting in January.

Web site, MP

MP presented the new website for the project. A discussion followed:

-the font should be dark on white background

Following information was seen necessary to add to the website:

-Each center should provide short description of the project and their part in it in local language.

-Mx scripts should be put to the website for the participants to use

ACTION ITEM 8: Centers provide the above info.

Reports of the process in subgroups followed

Genotyping (Syvänen)

AC described that the SNP and microsatellites centers have the facilities ongoing and ready for high-throughput genotyping. The limiting step is the cost which is about 0,25c a genotype.

DNA would be used both for genome scans and SNP genotyping

Concentration of DNA needs to be determined by reliable methods. Old stored DNA may have hundred-fold differences in concentration.

A key issue is how to select the markers. This should be considered carefully, especially for SNPs to save money and DNA.

DNA needed for a genotype is 2,5ng. Totally, 10 mikrograms is needed for approximately 500 SNPs and 500 mikrosatellites.

P1 (NPHI) offered the service to extract DNA from freshly drawn blood at the price of chemicals; 13€. Markus.perola@ktl.fi should be contacted for the details.

RNA for expression studies needs to be collected at some point, however currently the price is a limiting factor for large-scale collection.

Epidemiology (Christensen)

It was suggested that each phenotype should have a group of experts who would be responsible to advice in the phenotyping issues. These groups should have a presentation of the phenotype in question in the 1st GENOMEUTWIN workshop, even some analyses done on existing data. The experts should get credit from their work.

Expert and manuscript groups

Stature

- Peter McCarron
- Karri Silventoinen
- Jaakko Kaprio (manuscript leader)
- Leo Beem
- Dorret Boomsma

- Gonneke Willemsen
- Markus Perola (phenotype leader)

BMI

- Kirsten Kyvik
- Kirsi Pietiläinen
- Aila Rissanen
- Gonneke Willemsen
- Rune Frants
- Jennifer Harris (leader)

Longevity

- Kaare Christensen (leader)
- Axel Skytthe
- Simone Siampooli
- Antonie Stazi
- Jaakko Kaprio
- Jennifer Harris

Coronary Heart Disease

- Hugh Tunstall-Pedoe (phenotyping leader)
- Ulf deFaire
- Marco Ferrario
- Markku Koskenvuo
- Gonneke Wilemsen
- Rune Frauts
- Eco de Feus
- Alun Evans (manuscript leader)

Stroke

- Kjell Asplund
- Peter McCamom
- Soren Bak
- Markku Koskenvuo
- Simona Giampaoli
- Leader (from Denmark)

Migraine

- David Gaist
- Elisabeth Waldenlind
- Nicole Vanacope
- Giovanni Ristoni
- Mikko Kallela
- Dorret Boomsma (manuscript leader)
- Elles Mulder (phenotype leader)

Additional manuscript groups:

Legal and ethical issues:

- Jennifer Harris (leader)
- Kaisa Silander
- Tiina Aitlahti

Genotyping, SNP selection

- Chrise Syvänen

Introductory paper:
Leena Peltonen
Dorret Boomsma (statistics)

Issues that the phenotyping groups need to consider:

- what data is on hand
- what would be the “ideal” questionnaire
- what would be the “reasonable” questionnaire

ACTION ITEM 9: KC contacts the leaders to start up the work on phenotypes.

ACTION ITEM 10: Each leader presents the phenotyping issues at GENOMEUTWIN workshop in March.

ACTION ITEM 11: Each manuscript leader prepares a manuscript about the phenotype for Twin Research, deadline in spring. The manuscript should have titles and the list of authors and subheadings ready asap and this should be presented to the publication committee.

Statistics and databases (Peltonen, Litton)

JEL presented the idea of the prototype database which will be formed on the data of 100 twins as a pilot and a testing ground. Generally, the idea of federated database is supported. Discoverylink offers also analysis options which are relevant and interesting.

Important issues are data standards and missing data standards.

EU twin number was discussed.

ACTION ITEM 12: DB core writes up an easy to understand description of the db structure for the web site.

Ethics (Harris)

Data in this project is different and the ethical issues are hard to coordinate. Ethical core deals with both Informed Consent and Data Confidentiality.

All countries need to work to get the ethical consents in order for the samples that will be used for the study.

ACTION ITEM 13: It is recommended that the centers meet with local ethical and data confidentiality boards.

ACTION ITEM 14: Ethical core will produce a prototype IC form.

Ethical core will also eventually produce an ethics manual and ethical guidelines for the study which will be put on the website. Outside experts will be called to take part in the core activities. Also a training manual for ethical issues will be produced. JH is recruiting students to work on the ethical issues for the project. The project offers great resources for ethical studies. Some issues would be:

- Social inequalities in health across Europe
- Factors that affect IC in twin studies

Some data for ethical research could be collected in study questionnaires.

ACTION ITEM 15: AE will produce a format for material transfer agreements.

Publication policies (Kyvik)

Dr. Kyvik presented a review of publication policies from different studies.

It was agreed that a publication committee would be formed, which would go through the planned publications produced from the project and present those to the steering group.

The members of the publication committee:

Kirsten OhmKyvik
Kari Kuulasmaa
Ann-Christine Syvänen

ACTION ITEM 15: publication committee produces a draft of publication rules for the next steering group meeting

ACTION ITEM 16: An example, how the project should be acknowledged in the papers will be put on the website.

Would there be conflicts, they will be settled at the steering group. If this is not successful, the matter will be brought upon for the scientific advisory board.

The subject of additional members (twin cohorts):

LP presented the details of applicant members.

It was agreed that we would have two kind of members:

1. Full partners
2. Associate partners

It was noted, that we have the obligation to share information with the new full partners as well.

There should be strong scientific basis for inclusion of new members for following reasons:

- not too much expansion
- fiscal limits
- time issues

It was agreed that UK and Australia could be invited in as full partners. 100-150k € would be directed to them. UK has genotype data so they would be paid; however Australia would be paid in means of genotyping services and travel costs.

Malta and Lithuania would be called in as associate members. They would get access to the open workshops with some travel support and access to use the cores. Also scientific consultation and training would be given.

A requisite for the above arrangements is that the centers give GENOMEUTWIN data and/or necessary samples for genotyping.

ACTION ITEM 17: LP will draft a letter for the centers, steering group will review it.

GENOMEUTWIN WORKSHOP 1, phenotyping

Will be held in Helsinki, Finland cojoined with the Nordic Molecular Epidemiology meeting in March

Genomeutwin students should be encouraged to participate

Expert groups (above) will produce data for the meeting from project cohorts.

- heritability
- agegroups
- comparisons across countries

Mx Workshop will be held in September/October

Next steering group meeting will be in early April in Amsterdam.

LP ended the meeting