

**Minutes of the III Genomeutwin Steering group meeting 23.3.2003 Biomedicum,
Helsinki, Finland**

Notes taken by: Markus Perola

Present:

Dorret Boomsma (DB)
Kaare Christensen (KC)
Ann-Christine Syvänen (AC)
Alun Evans (AE)
Jennifer Harris (JH)
Hans van Houwelingen (HH)
Jaakko Kaprio (JK)
Kari Kuulasmaa (KK)
Kirsten Ohm Kyvik (KOK)
Aarno Palotie (AP)
Nancy Pedersen (NP)
Leena Peltonen (LP)
Markus Perola (MP)
Tim Spector (TS)
Antonia Stazi (AS)

LP welcomed everybody and gave an update from Brussels:

- Bernard Mulligan been very helpful and active but for personal reasons could not attend this time, but will come for the next meeting
- next meeting of the steering group will be held in Copenhagen (Hilton/Kastrup) on the 8th of May. It will be one day meeting.
- Scientific Advisory Board (SAB) will meet in October, the date is to be decided by EU officials

Hans van Houwelingen and Tim Spector were introduced as new members of the steering group

HH leads the statistical core from Leiden, TS heads the UK Twin Registry

Also, Nick Martin will be a member, as Australian Twin Registry joins Genomeutwin.

Money transfer to the U.K. partner and allocation of genotyping as well as travel funds will be provided for the Australian partner as soon as the contract has been signed.

TS inquired about the future of the funding. LP explained that the Steering group has decided to reserve 300.000€ for inclusion of new members for 2 years. In practise, this will be divided between UK and Australia. Steering group will later decide on the remaining funds reserved for prospective members and everybody is encouraged to apply, alone or together, for more funding. Would the project get more funding or continuation after four years, the situation will naturally improve for all partners.

TS gave a short introductory talk about UK Twin Registry. He emphasized that they are very happy to join but that the level of funding is very low and they can't do a lot with what they got, the salary expenses being extremely high in London. UK Twin Registry wants to be involved in the analysis stage and will apply for more funding. TS also said, that genotypes from already scanned twins in the UK twin registry are available for the traits listed in the Genomeutwin proposal.

Possibilities for funding were reviewed:

- EU 6th framework (2nd round, October 2003) has a special funding opportunity for genotyping large epidemiological samples (LP)
- also, special funding can be obtained from the 6th framework for biobanking (DB)

LP stated that it is clear and was in the scope of the original application that no center has enough funding from Genomeutwin for additional DNA collection

LP stated, that since SAB will meet in October, not May, the so-called "April deadline" will change to September

We will have to prepare a report with milestones and deliverables in September.

Since the sad passing of Dr. Lodevijk Sandkuijl, Dutch and Danish Twin Registries were assigned to handle statistical issues while Leiden was recruiting people for this project. DB gave an update of what was accomplished so far:

-A library of Mx scripts was created for uses of Genomeutwin, this will be demonstrated on Monday

- simulations
- quantitative analyses
- sex differences
- twins/extra sibships
- QTL linkage analyses
- association
- dominance
- combined linkage and association
- uni+multivariate analyses
- longitudinal

Next important thing is to get people to start using the scripts. Some requests still under work, however, when those scripts are included, the responsibility will be redirected to Leiden. The Leiden group will start by analysing which samples would be selected for linkage analyses.

LP gave an overview of the meeting with DB, KC, HH, LP and MP about statistical issues which was held in Helsinki 22.3.2003 (the day before this meeting). HH is committed to take responsibility in statistical core and has recruited two persons for the purposes of this project. However, for the following 12-18 months, the salaries of 6 people will be divided between Leiden, Odense and Amsterdam so that Leiden will get the salaries of three persons, Odense 1,5 and Amsterdam 1. The evaluation of this

arrangement and allocation of the rest of the funding for statistical analyses will be done after this period.

ACTION ITEM 1: Each center lists their experts in statistics and e-mails the list to HH by end of March for the next steering group meeting.

It was agreed that the project should experiment new and novel statistical methods but also a fixed set of statistical methods should be agreed upon.

-Visits between centers are strongly encouraged.

-Statistical experts should meet as a group 2-3 times a year, the next meeting could be scheduled on the 9th of May.

-A database of results will be formed by HH.

-LP emphasized that all graduate students and post-docs should receive some scientific credit (publications) from the project. There will be a few major genomeutwin publications but otherwise publication is encouraged, Genomeutwin should be noted in the acknowledgements. The formulation of this acknowledgement is available on the website.

-DB reminded that there will be a statistical workshop in September 15.-19. in Amsterdam. This is directed to students.

-LP noted that the week before that an advanced linkage analysis (8.-12.9.2003) course will be held in Helsinki, led by Ken Lange and including many distinguished speakers such as Eric Sobel, Janet Sinsheimer, Rita Cantor, Steve Horvath. It was agreed that this workshop could be introduced as a Genomeutwin workshop as well and all centers should have the possibility to get 1-2 participants in the course. These applicants should have fairly advanced knowledge in the genetic statistics.

-TS noted that in April 2004 there will be a Solar QTDT meeting in Cambridge. This will be included also in the Genomeutwin training program.

-all courses in the Genomeutwin training program should give a possibility for each center for 1-2 participants.

Action item 2: DB, KC and HH agree on practicalities on statistical issues.

Action item 3: LP will inform the partners of the deadline for applications to the advanced statistis course in Helsinki.

The training budget was discussed. The total is 90K€ of which the Amsterdam course will take 25K€. This amount of funding for one course is high and potentially the number of courses needs to be cut down.

-An ethics workshop is under planning (JH)

NP gave an update for database core issues:

-a couple of meetings held

-Genomeutwin id no. is decided.

-for ethical issues, it is important to have principles of who has access to the data. It was agreed, that this should be analysis based, steering group will decide who will get access at the data.

-in general, the database data in Genomeutwin should be anonymized at all respects; only the original Participating Centers should have id data.

-the issue of federated database was discussed. It was agreed that this would be suitable for the Genomeutwin purposes and the option shall be pursued by the statistical core.

Action item 4: Db core will explore the federated database structure for the purposes of Genomeutwin.

JH gave an update on the ethical core issues:

- ethical core will prepare an example for informed consent form, also for reconsenting
- reconsenting was seen necessary only in Norway
- the availability and possibility to analyse intermediate phenotypes was discussed – would it require reconsenting? UK would not, Netherlands not, Sweden not, Denmark not Italy would need, Finland was not sure.
- a template for ethical application will be prepared as well.
- a manuscript of ethical issues will be prepared (JH)
- Bertha Maria Knoppers, Mats G. Hansson, Tiina Aitlahti are the external experts in the ethical core.
- it was emphasized by LP that no genetic info should be promised to be given back to participants. This opposes the clear-cut opinion for most ethical guidelines for example those of UNESCO. However, since the genotypes are produced in research laboratories, they do not fulfill the criteria of the diagnostic setting.

Action item 5: a short description of data security issues of databases and the access of the data will be produced by the database and ethical core for the ethical permits (JH+NP)

At this point, LP summarized the discussion:

A: guidelines of how the data is imported to databases will be necessary.

B: We are more favourable for local databases to hold the phenotype data, instead of datawarehouses.

C: Ethical issues:

- steering group decides the rules of the access of the data
- in general, all local scientists will have access to their own data
- Each PI is responsible for permits and data security on their own group

Policies for publication were discussed:

-KOK's presentation at the Rome meeting are listed in the Genomeutwin webpage and the principles set in Rome apply. Working group of the publication rules (chaired by K.O K) will provide their report in the next meeting.

KC gave an overview of the Epicore issues:

- we should set priorities for the phenotypes
- HH prepares selection criteria for the Copenhagen meeting

-a three-step approach should be utilized:

1. epidemiological data is collected
2. The available data is analysed
3. New data is collected

-LP suggested that we would need to update the tables in the original application.

Action item 6: HH Prepares selection criteria for the Copenhagen meeting

Action item 7: MP coordinates data preparation effort for stature.

AC gave an update of the genotyping status

-both multiallelic and SNP genotyping have started

-a lot of effort have been put into quality assesment

-a set of 60 trios (parents+offspring) is genotyped for quality assessment and haplotype and LD predicment.

-a total of 127.000 genotypes have been produced

LP gave an update on database issues

-these slides can be seen at www.genomeutwin.org

MP reviewed the candidate genes and loci for stature

-these slides can be seen at www.genomeutwin.org

MP reviewed the www.genomeutwin.org webside

Action item 8: An update of db issues will be given in Copenhagen

The special issue of Twin Research was discussed.

-Nick Martin requested us to propose a special editor for this issue. Tim Spector agreed to be the one.

-all manuscript groups should contact the external reviewers first to ensure their willingness for the review process. One should be external from the Genomeutwin group.

Each manuscript group gave an update:

Stature: Outline has been distributed (JK)

BMI: Outline has been distributed (JH)

Longevity: Analyses done, going on well (KC)

CHD: in preparation, will be a general review concentrating on specific issues for twins, like Barker hypothesis. Heritabilities of some of the intermediate phenotypes will be collected from the centers (AE).

Stroke: In good condition (KC)

Migraine: In good shape (DB)

Legal and ethical issues: In good shape, outline out

Genotyping: will be a review, concentrating on the genotyping (both SNPs and multiallelics) and SNP selection.

General description of the project (LP) is being prepared

Statistical methods paper is being prepared (DB)

-the manuscripts should have 5-8 printed pages, 30 references and 3000-4000 words.

Action item 9: Manuscripts for the Twin Research special issue will be distributed latest by the Copenhagen meeting

Action item 10: Phenotype groups produce a study plan how to continue pursuing their phenotype in this project.

LP ended the meeting and welcomed everyone for a dinner in restaurant Lehtovaara.