

## Minutes for the GenomEUtwin steering group (GSG) meeting, Paris January 13-15., 2004

Present:

Leena Peltonen (LP)  
Antonia Stazi (AS)  
Aarno Palotie (AP)  
Kirsten Ohm Kyvik (KOK)  
Kari Kuulasmaa (KK)  
Jaakko Kaprio (JK)  
Alun Evans (AE)  
Kaare Christensen (KC)  
Nancy Pedersen (NP)  
Jennifer Harris (JH)  
Jan-Eric Litton (JEL)  
Nick Martin (NM)  
Tim Spector (TS)  
Jacob Mortensen

Notes taken by Markus Perola

- 13.5.2004: Working dinner: General discussion of the project status and SAB report.

14.5.2004

- LP opened the meeting.

Apologies: Ann-Christine Syvänen

- LP informed GSG of the SAB report progress:

-the report is not yet finalized, but according to Bernard Mulligan, the draft is more or less accepted

-some more details will be requested and some specific suggestions for the data analyses will be expected

- LP informed the GSG that the financial amendment is accepted by Brussels and distributed the letter with attachments for the GSG members.
- LP stressed the importance of preparing for the mid-term review in fall.

**ACTION ITEM 1:** Continuation of the discussion of the still missing SAB report with Brussels (LP)

- LP distributed and presented the letter by TS requesting additional funding (attached).

TS presented his grounds for the request:

- high cost environment in London
- high input from the UK Twin register for the project

The item was discussed and decided that a proposal would be drafted by LP for tomorrow's meeting.

- KC presented the current status of data collection by the database core as well as the results from the efforts of the phenotyping expert groups (attached)

-a general impression at this point was that for stature, height, migraine and CHD the twin registers would provide enough cases for the purposes of the GenomeUtwinn, but for stroke and longevity the number of accessible pairs might be too small.

The minimum data for all twins in the project was suggested to be: Id number, year of birth, year of death, sex, zygosity, diagnosis, diagnosis-level (A-D)

- KC presented the current status and efforts of the Danish Twin Register (attached).
- JK presented the status and efforts of the Finnish Twin Cohort Study (attached)

-the participant has several sub-studies with deeply phenotyped data and this was seen as a possibility for co-operation among participants: the participants should review each others data and consider seriously the possibility of co-operation and data pooling –especially of the genotyped samples.

ACTION ITEM 2: GenomeUtwinn website will establish pages for the descriptions of the sub-studies in each project and/or links to the relevant pages. Also, the phenotype pages will be updated to reflect the current consensus. (MP)

- Antonia Stazi presented the current status and data collection by the Italian Twin Register

-A new possibility has opened to co-operate with the Mendel Institute in Rome for access into their data collected from Italian twins.

-This would significantly increase the number of stroke cases in the Italian study sample.

ACTION ITEM 3: Collaboration with the Mendel Institute is further advanced (AS)

ACTION ITEM 4: Every effort is made to obtain stroke sample from the Italian registry, and an intensive collaboration with Mendel is established (AS)

- JH presented the current status and data collection by the Norwegian Twin Register

-Norway would like to get more concrete advice from the GenomeUtwinn phenotype and statistical cores for harmonization of the data collection

-Norwegian Twin Register will need to re-consent the participants for the new phenotypes studied.

- NP presented the current status and data collection by the Swedish Twin Register

-Sweden is initiating a new sample and phenotype collection in February 2004  
 -Swedes have spent a significant amount of time in harmonizing and building up the database infrastructure for the project.  
 -JEL emphasized the critical importance of the harmonization and coding of the phenotype data across participants.  
 -the migraine phenotype will be used to serve as a model phenotype for building up the project database  
 -the prioritization issues for sample collection were discussed. The consensus was that concordant case pairs for a selected phenotype would have the first priority in sample collection. The discordant pairs would have the second priority.  
 -the source for DNA was discussed. The consensus was that DNA extracted from whole blood would be the golden standard for the project; however blood spots / buccal cells could be collected under special circumstances (for example children). Whole blood is collected from participants whenever possible.

ACTION ITEM 5: The database core will co-ordinate the construction of the project database using migraine phenotype as the model phenotype

- TS presented the current status and data collection by the UK Twin Register (attached).

-UK twin register has a extensive amount of quantitative phenotypes (attached) collected from most of the participants. Genome scan data exist for the majority of UK pairs.  
 -this was generally regarded as a very significant added value for the project that should be utilized to the fullest.

KC suggested that TIA could be used to increase the number of cases in the stroke category.

LP suggested that some kind of cluster analyses should be employed in those centers with deeply phenotyped individuals to reveal potential clustering and new associations among phenotypes. These could be used as more specific phenotypes for the locus mapping efforts.

ACTION ITEM 6: A plan will be formed for the pooled analyses of the intermediate phenotypes (HH)

- NM presented the current status and data collection by the Australian Twin Register (attached).

-Australia has provided the project with two set of material genome scanned and phenotyped for stature and BMI.  
 -Australia is very interested in participating in the analysis process, especially for BMI.

## Lunch

- BD Presented the current status and work progress by the Netherlands Twin Register (attached).

-the Dutch have been very active in providing Mx scripts to GenomEUtwin participants and the whole scientific community.

- JEL presented the current progress, deadlines and milestones for the database core (attached)

-the milestones were seen as very important and the current structure should be set at test as soon as possible

-the working version of the information integrator should be trial tested among the relevant participants

- MP presented the status of the linkage analyses of pooled data on BMI (attached)

-stature results will be distributed in the near future after the careful confirmation and checking of the data. A manuscript is aimed during the spring

-two interesting peaks for BMI were presented

-MP's plan for further analysis was accepted

-Danish data available will be joined in the analyses of pooled data

-pooled data will be analysed by MP with close interactions with HH.

- HH presented the current status work progress by the statistical core (attached).

**ACTION ITEM 7:** Leiden will look into what longitudinal effects are detectable for BMI in the project data before the end of February (HH).

Leiden will arrange a statistical workshop in Leiden in May 2004. LP suggested that the project consultants: Kenneth Lange, Janet Sinsheimer, Eric Sobel and Joe Terwilliger would be invited to this workshop. Several centers expressed their desire to be more closely linked to the statistical analyses. This will be orchestrated by Leiden

The genotyping core will genotype 200 most informative pairs for BMI and stature from each center, selected by the cooperation between centers and the statistical core.

- AE presented the results of the coronary heart disease phenotype group (attached) and proposed a qualitative trait criteria
- AP presented the results of the migraine phenotype group (attached).

The meeting was adjourned for the day.

**Third day, 15.1.2004**

- LP opened the meeting by presenting a suggestion of redistributing a fraction of remaining funds of the Leiden group (statistical core) to strengthen the statistical efforts of participating centers (suggestion attached).

The suggestion was generally accepted and the trimmed figures will be sent for participants for the final review.

ACTION ITEM 8: The redistribution plan will be sent to partners and to Brussels (LP).

- Responsible scientist and partner(s) for each main phenotype were selected. These will have the main responsibility of the advancement of the analyses of the given phenotypes.

BMI+stature: JH, MP

Migraine: DB, NM

CHD (a qualitative phenotype): NP, JK

QTLs related to CHD (hyperlipidemias, hypertension): TS, NM

Stroke: KC, AS

Longevity: KC, AS

- AP explained the planned analyses of the trios for haplotype comparisons across the participating cohorts, put forward by Ann-Christine Syvanen.

A set of trios will be analysed for 100 SNPs from all centers where the samples are available based on the schedule presented by A-C.S.

ACTION ITEM 9: Chromosome 4 migraine region was chosen for the candidate region. It was noted that it being still quite wide, the whole region cannot be included in these analyses but the actual 1 Mb should be carefully chosen by the migraine group and genotyping group. Also, it was emphasized that all available data about the region should be carefully analyzed before selecting the SNPs for genotyping (for example hapmap data on the region).

- JH presented the issues concerning the ethical core (attached)

-ethical core has received funding on a collaborative project through conjunction the Functional Genomics platform administered by the Norwegian Research Council.

- LP presented the international collaboration between GenomeUtwinn and P3G (attached). JH and LP described the CoGene collaboration. These two overlapping collaborations were unanimously supported. More detailed information of them will be provided on the website.

JK presented the guidelines for student exchange (attached). There was no objection for the guidelines and they were accepted.

- GSG meeting schedule was discussed.

The planned Cambridge GSG meeting was cancelled. However, it was noted that most GSG members will be present at Cambridge on Wednesday facilitating some discussion on the urgent issues. It should also be noted that 2-3 students from each center are supported to participate in the Cambridge meeting by the educational funds by 200€, the applications should be sent to JK.

**ACTION ITEM 10:** MP will enquire TS about the abstracts and posters in Cambridge. Students should present a poster mentioning GenomEUtwin.

The next GSG meeting will be in Odense July 5<sup>th</sup>, 2004, in conjunction with the ISTS 2004 meeting. The Sunday afternoon, July 4<sup>th</sup> will be reserved for the GenomEUtwin workshop (KOK)

The discussion about date of the fall GSG meeting was discussed. Ideally the GSG meeting could be arranged in conjunction with one of the following meetings:

IGES Sept 12-13, 2004, The Netherlands

12-th World Congress on Psychiatric Genetics October 9-13, 2004 Dublin

Rome, December, see below

However, since the fall meeting might be necessary to join with the SAB review+mid-term review, the actual date was left for LP to coordinate with Bernard Mulligan.

**ACTION ITEM 11:** LP sets the date for the fall meeting and mid-term review if possible by the end of January.

It was seen necessary to try to get a special session for GenomEUtwin at the International Genetic Epidemiology (IGES) meeting in The Netherlands, Sept 12-13.

It was agreed that each phenotype group will submit an abstract to the IGES. The abstract will be drafted by the responsible scientists (see above)

**ACTION ITEM 12:** Karri Silventoinen will organize the symposium (JK).

- LP proposed that GenomEUtwin should submit a paper on GenomEUtwin on an online journal pLoSL.

The idea was supported by the GSG. The paper should include pooled analyses of the data presented in Twin research issue.

**ACTION ITEM 13:** LP and DB will draft a paper for pLoSL.

- It was suggested the the GenomEUtwin special edition of Twin Research would be released for free access via the website.

ACTION ITEM 14: NM will pursue this with the publisher.

- It was noted, that there is a need to have a policy concerning any outside proposals for analysing project data. The following guidelines were agreed:

-the suggested analyses should be presented as a candidate study for the publication committee

-a collaborator from GSG should be included in the study.

- Kari Kuulasmaa raised the issue about the documentation of the analyses carried out within the project.

ACTION ITEM 15: KK and JEL will be responsible for forming a documentation archive within the database core.

- NM reminded that Twin Research journal strongly encourages submitting project data to the journal.
- The necessity of enhanced interaction between the key scientists should be encouraged. It was decided that GenomEUtwin will organize a GenomEUtwin project event in Rome in December 2004 where 3-4 scientists from each center working in the project would be invited to present their data.
- LP ended the meeting.