

## **Agenda for the Genomeutwin Steering Group meeting July 5<sup>th</sup>, Odense**

Notes taken by Markus Perola (MP)

Dr. Leena Peltonen, KTL, Helsinki, Finland (LP)  
Dr. Antonia Stazi, Istituto Superiore di Sanita, Rome, Italy (AS)  
Dr. Jaakko Kaprio, University of Helsinki, Helsinki, Finland (JK)  
Dr. Dorret Boomsma, Free University of Amsterdam (DB)  
Dr. Jennifer Harris, Folkehelseinstituttet, Norway (JH)  
Dr. Nancy Pedersen, Karolinska Institutet, Stockholm, Sweden (NP)  
Dr. Kaare Christensen, University of Southern Denmark, Odense, Denmark (KC)  
Dr. Aarno Palotie, Finnish Genome Center, Helsinki, Finland (AP)  
Dr. Alun Evans, University of Belfast, Belfast, UK (AE)  
Dr. Kirsten Kyvik, University of Southern Denmark, Odense, Denmark (KOK)  
Dr. Kari Kuulasmaa, KTL, Helsinki, Finland (KK)  
Dr. Ann-Christine Syvänen, University of Uppsala, Uppsala, Sweden (AC)  
Dr. Juha Muilu, KTL and Finnish Genome Center, Helsinki, Finland (JM)  
Apologies:  
Dr. Jan-Erik Litton, Karolinska Institutet, Stockholm, Sweden

### **Welcome, Apologies (Peltonen)**

Each partner was provided with the amendment from EC for fund transfers for information. The administrators at each Participating Center should react accordingly, i.e. sign his/her personal sheet and send the signature directly to Brussels like indicated in the document. Administration of NPHI has checked the facts and signed the document already (the copy of this signature was enclosed)

JM replaces Jan-Erik for this meeting.

### **Minutes of the last meeting (Perola)**

No comments were given.

### **Update on EC communications and collaboration (Peltonen)**

Deadline for the midstream report is approaching. LP has called BM for details in the reporting.

### **mid-term review (Action Item (AI) 11 from Paris)**

Deadline mid-September for the mid-term report. We start to work on the report early August. First scientific papers should be submitted before SAB meeting, taking place on the 14th-15th of October in Dublin. The joined meeting with the Morgam steering group will probably take place immediately following this. Everybody should be prepared to fly in on the 13<sup>th</sup> for a dinner before the meeting. To have overlap with MMG, people should plan to fly out on the 16th, Saturday morning.

### **“sister projects of EU” (GEHA, EuroClot, EuroHead, P3G)**

Many new projects linked to Genomeutwin or using resources of Genomeutwin have been funded by EU.

GEHA ( Genetics of Healthy Aging) :KC described the project: About 20 centers, KC in the steering group. MP attended the kick-off meeting. KC will try to get MP in the steering committee. The project in itself is a good addition to the aims of Genomeutwin, given that it is targeting longevity. However, they obviously could use additional help in genetics.

**ACTION ITEM 1: KC will start discussions to get MP from Genomeutwin to the GEHA steering group**

EUROHEAD (Molecular background of migraine): AP described the project. Total of 8 participants are working on human and mouse traits associated with migraine. Variants identified in the project will be tested in Genomeutwin cohorts for their population effects.

EUROCLOT (Coronary heart disease and coagulation pathways): TS described the project ( slides attached). 8 participants. Very intense phenotyping in the first 18 months.

DIOGENES ( Genetic and environmental background of diabetes) JK described the project that is collecting significant amount of data of body composition against diet. Helsinki is participating with the FinnTwin 16 cohort. Final budget negotiations ongoing, budget cut from 15M€ to 13.5M€

KOK described an attempt to produce a multiple birth register for Europe, which is initially not meant for genetic studies.

LP described P3G happenings. EC and GenomeCanada met a week ago in Canada for plans of a joint funding process. UK Biobank might be committing more to P3G. Some funding is possible coming for the core functions of P3G. Joint application submitted for the last call of FP6 (CA) and for the first call of FP7 (IP).

JK reported that CDC (USA) wants to organize a meeting in February/March with Genomeutwin to discuss our experience in relation to starting US projects.

DB informed about a meeting on the 20th of September in Brussels for planning the funding of P3G and it's links to FP7. DB and LP will be present

**-Rome meeting in December (Kaprio and Stazi)**

AS presented the tentative plan for Genomeutwin meeting

Sunday 12<sup>th</sup> reception

Monday 13<sup>th</sup> 9-17: 4 sessions of 1.5h

Tuesday 14<sup>th</sup> 9-15 : 4 sessions of 1.5h sections

Sessions could be focused on the 6 phenotypes plus the Lab and Stat methodology, with a main paper for each subject (20 minutes) and at least two 10 minute papers presented by students or young researchers.

JH: young investigators should cross talk at a meeting.

Each group should come up with 3-4 postdocs etc who are really working with Genomeutwin data.

JH: Number of post docs in the projects.

NM&DB: We should request for abstracts and select the best papers for presentations. AS will send an abstract form to centers. Submission before October 10<sup>th</sup> SAB meeting.

**ACTION ITEM 2:** AS sends out requests for abstracts and a form for abstracts.

**ACTION ITEM 3:** NM, DB, AE evaluate the abstracts and select the best ones for presentations.

#### **-collaboration with Mendel institute (Stazi)(AI 3 and 4)**

AS described Mendel Institute's archival data. 27.000 twins born in 1930-1970. Data is hand-written on paper files and hard in practice to get into usable shape. Only 1300 people filed electronically with few data points.

**ACTION ITEM 3:** AS asks an investigator from the Mendel Institute to speak at the Rome meeting.

#### **Reports from the core leaders (10 min + 5 min for discussion each)**

##### **-Epidemiological Core (Christensen)(AI 2)**

KC presented the minimum requirements for data collection (attached). Denmark has sent 200 extremely height discordant/concordant pairs to Finland.

Finland has selected the samples from the existing pairs and a coming collection by the end of this year.

Netherlands is not sure when they can accomplish the 200 pairs.

Australia will collect the samples by the end of the year, and they should be coming for genotyping to Finland early 2005.

Sweden: 150 pairs discordant for CVD available in September. Extracted at Swedish biobank. Other phenotypes should be available by the end of this year.

Norway: Data matching done. New law requires a permission from the participants for samples to be sent out of the country, but these issues are clearing and the samples should be available by the end of this year.

UK: All samples provided and genotyped.

Italy: 20-year age group, 80 discordant pairs for height and BMI should be available by the end of the year.

**ACTION ITEM 4: Discordant pairs for stature and BMI should be ready for genotyping by the end of this year.**

**-Ethical Core (Harris)**

JH presented the status of the ethical core. Presentation attached.

Participation of all centers in the ethical meetings and discussion was seen very important.

IP issues were discussed. It was decided that the IP issues will be discussed among GSG when these matters arise, no special preliminary decisions/agreements will be made by Genomeutwin.

**-Statistical Core (Houwelingen) (AI 6 and 7)**

HP presented the status of the statistical core (attached).

It was seen important to compare the meta-analysis method developed by Houwelingen's group with the existing, published genome scan meta-analysis methods.

Ken Lange is willing to revise Mendel package according to Genomeutwin's needs.

**ACTION ITEM 5:** HH will send an short e-mail requiring special needs of each center for statistical analysis programs This is to be reviewed by the statistical core and sent to Ken Lange as a request. Statistical core will together with MP start to produce a collection of statistical instruments (programs and the manual for them) on the website.

Intermediate phenotypes. HH requests data for analyses of intermediate phenotypes.

**-Database Core (Muilu) (AI 5 and 15)**

JM presented the status and plans for the database core.

The data security issues were discussed.

JM demonstrated the federated database system connected to three Genomeutwin participants, using query interfaces. This system works now between these places. The

rate limiting step is that the centers would get servers to use for their own Genomeutwin data storing. These blue boxes for each center should be ordered through JM, who is negotiating a better price for these servers.

DB: Technical information needed.

**ACTION ITEM 6:** JM will provide precise technical and price information (based on the Genomeutwin quotation from IBM) for the Bluebox server and each center will make an effort to obtain that. Data security issue of the federated database will be especially discussed in the next meeting of the steering group to advance the federated database.

**-Phenotyping core (NP):**

The phenotype groups were discussed with special emphasis on cardiovascular phenotypes.

NP described the on-going work on the qualitative phenotype issues:

Qualitative traits: The sites having old enough twins have contributed to the effort (Finland, Sweden and Denmark). Sweden has budgeted the collection of 1900 pairs of which 500 have coronary end-points for at least one of them. However, for a genome scan effort there are not enough DZ concordant twin pairs. It is important to collect pairs among the three centers for future accumulation of endpoint data.

QTLs related with CVD were discussed. Australia and Netherlands are collaborating and want to publish their data before giving that to the common use in Genomeutwin. No timeframe was provided for this to happen.

TS presented the on-going work on the BP and other CVD related phenotypes. Finns and Danes have small cohorts which were not included and TS presented results based on the UK data. The following sample materials could be pooled for QTL traits:

- Denmark has 350 genomescanned pairs with lipid phenotypes,
  - Finland 300 genome scanned pairs and 300 pairs to be genome scanned.
  - Sweden 1900 being collected will have the phenotype data (not genome scanned).
- By the end of October 500 pairs will be ready and sent to genome scans
- some Dutch pairs will be available for genomescanning with phenotypes soon.
  - 300 Dutch pairs will become available soon with genome scan data

The Dutch and Australian data will become available in 18 months.

There is a need for 1600 genomescans for the project. There is funding available for a less than 1000.

A matching-funds solution for genotyping was suggested.

Italy had looked into the availability of stroke cases. Three pairs was found.

**ACTION ITEM 7:** For qualitative end state diagnosis, systematic data collection ongoing to obtain sufficient number of concordant pairs. Genotyping core will prepare

a proposal facilitating genomescan for 800-1000 pairs during next 12 months. These would greatly contribute to the QTL traits when combined with UK material.

**-Request for additional funding:**

TS presented his case for reallocation of funds, which will run out in six months. LP expressed that redistribution is the only way to get funding directed to UK.

This matter was discussed among GSG. No solution was found to do any more reallocation of funds towards UK. AS and JH will look into their budgets, all others stated that the reallocation is not possible.

**-Migraine:**

DB summarized the migraine status. The final questionnaire and diagnostic criteria have been circulated via e-mail. These will be put on the website.

**ACTION ITEM 8:** MP will put the documents on the website.

AS left the meeting.

DB suggested genotyping SNPs in MZ twins for variability genes.

**ACTION ITEM 9:** DB requests what numbers of MZ twins would be needed for variability studies. Preference would be for the ones with repeated measurements. First candidate region would be the original chromosome 4 locus from Kåre Berg's studies. DB also contacts HH for power calculation issues for this project.

Lunch

DB, NM, NP left the meeting.

**Training issues:**

JK described the three courses to be held this fall (Oslo, Helsinki, Amstradam).

Three applicants for training exchange were presented:

	Visit	Requested sum
Christel Middeldorp	Amsterdam->Australia	3100
Cheryl McFarlane	Belfast->Paris	6 mo
Corrado Fagnani	Italy->Amsterdam	3000

These applications were accepted with the exception that Dr. McFarlane visit was limited to three months, after which she could apply for more funding if that is necessary.

The project should be a project specifically targeted for Genomeutwin and the work accomplished should be reported in the Genomeutwin meeting in Rome or later.

**ACTION ITEM 10:** JK reports the decision and the above requirements to the applicants.

**-Publication plan:**

KK presented the MORGAM publication plan. It was discussed that this project does not need such structure at this point but each phenotype leader represents Morgam's publication leader. It was agreed that generally the phenotype leaders make a publication proposal for the GSG.

**ACTION ITEM 11:** A form will be produced for the publication report of the joint analyses for Genomeutwin (MP). These will typically include several cohorts. The publication report forms will be sent to KOK and CC:d to LP.

**-Genotyping:**

A special plan will be produced for the remaining, needed genomescreens ( see above) . SNP genotyping: Different projects for SNP genotyping were considered, which SNPs and which study populations?

1. Migraine candidate SNPs on chr 4.

Decision: Genomeutwin trios, SNPs will be selected by AC and AP

2. SHOX gene (stature)

Danish extreme samples and Danish normal population, 25 SNPs already selected by AC

3. Chromosome 6 and/or 8 for height.

A linked subcohort, with SNPs in relevant genes. This will be decided by MP and AC

4. SNP blood pressure

1200 UK pairs, genes to be selected. Genotyping people (AC, TS) decide on the strategy: microsatellites might be necessary.

**ACTION ITEM 12:** Uppsala starts genotyping SHOX gene SNPs in Danish samples and migraine SNP in Genomeutwin trios. Items (2) and for need further clarification but should progress to genotyping stage before the fall meeting.

KK presented the Genomeutwin documentation plan (attached). Current documentation was seen generally adequate. However, it was agreed that Helsinki and Leiden collaborate in forming a website where a updated list of programs and tools would be listed.

**ACTION ITEM 13:** Shadow website is reviewed by MP and HP/HH and released asap.

**ACTION ITEM 14:** Height and BMI papers will be submitted in September (MP)

Other papers soon to be submitted, latest by the SAB meeting:

Blood pressure (TS)

SHOX (AC)

CHD and height (JK)

Methodology (Jeremie Lebrech)

Morgam paper in press (AE)

Longevity (KC)

**ACTION ITEM 15:** All centers update the status of the blood collection data in September (AP)

**ACTION ITEM 16:** Material about SAB meeting will be circulated in August (MP)

The meeting was adjourned.