

Minutes of the First Steering Group Meeting of GENOMEUTWIN, Karolinska Institutet, Stockholm, Sweden September 11th, 2002.

Present:

| Name (hyphen for text) | Affiliation | e-mail |
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The meeting started as scheduled 9.00 AM Swedish time

LP wished all welcome and briefed on the contract status:

- the contract should be signed within a week
- final figure of the budget is still open

It was agreed that MP would prepare the minutes and circulate them among steering group members for comments.

LP started the discussion on inclusion of extra cohorts to GENOMEUTWIN

- this was strongly suggested by the referees
- any extra cost will go from the co-ordinators budget (2nd year)
- we have been contacted by UK, Baltic countries, Malta and Australia.
- non-EU countries OK for Brussels

It was generally agreed that if any additional cohorts would have good strong points they should be considered as potential new members. They should prepare a 3 page, strictly defined, well structured document describing why they want to join, what they have to contribute and what they expect from us. DB volunteered to prepare a form for this (draft attached).

LP gave a introductory talk on the GENOMEUTWIN and genomics (available on the project web site or from MP)

LP described the scientific advisory board, which includes the following persons:

Albert Hoffman
John Bell
John Blangero
Gert vanOmmen
David Evered

Scientific advisory board has yearly meetings where it meets the PIs.

MP gave a talk on the milestones and deliverables

The organisational structure on GENOMEUTWIN was discussed. It was noted, that in the original application the steering group was built from all PIs from P1-P10 and the intellectual core leaders. It was discussed that whether we should have a core steering group, consisting of only the PIs of P1-P10. It was generally agreed that the project should have a flexible structure and the different groups should meet consisting of relevant people, not following a strict structure. However, the steering group should meet at least twice a year. Steering group is mainly responsible for the strategy while the operational group (intellectual core leaders) for the deliverables. It was agreed that we should meet next time in Rome Dec. 2002, a two-day meeting. Next meeting after that would be later in spring 2003 in Helsinki and the one following that in December 2003, possibly in Amsterdam. Workshop I was planned also to be held in Helsinki. A good time for that was thought to be in conjunction (after?) with the meeting "Molecular Epidemiology in the Postgenomic Era II" which is held in Helsinki March 21-23 2003.

TS described the UK twin study, where 1500 DZ twin pairs have genome scan data (700 markers). Not much DNA is left, however.

LP explained that all centers will get the genotypes produced from their own material back to themselves for analysis.

LS suggested that all centers should have a test panel of 5 markers to test for zygosity.

DB and LP emphasized the need for phase information in form of larger sibships and parents. However, TS noted that getting more pairs is a more powerful approach, and more value for money, if possible.

AC gave a talk on SNP genotyping

The cost of SNP genotyping was discussed. It is probable, that it will go down during the GENOMEUTWIN time frame.

Different SNP databases were discussed in general.

AP gave a talk on microsatellite genotyping

It was generally agreed, that the highly informative microsatellite genotyping is an important method for the project.

KC gave a talk on the epidemiological strategy

TS emphasized the importance of environmental covariates, which was agreed upon. JK suggested, that we should not merely study end-point phenotypes, such as "BMI" as such, but also pay attention to intermediate phenotypes such as eating patterns etc. This was agreed to be a good idea, but commented that the approach faces many challenges: varying levels of data collection (LP), selection of

informative families (DB), standardizing (KK). However, LP reminded that this approach was actually the idea for the project; the selected phenotypes are mostly just “umbrella phenotypes” that cover many scientifically interesting intermediate phenotypes.

LS gave a talk on statistical approaches

The role of the statistical core was discussed. The conclusion was that the persons' that are listed to be in the statistical core (and most other intellectual cores) role is more to act as an advisory board, think tank, for the actual performers, NOT do be responsible for the practical day-to-day analyses. A discussion on interim statistical analyses followed. AC emphasized, that any evidence for genotyping errors should be given back to the genotyping centers quickly. JH asked that where would the people employed by the statistical core physically work. LS said that some would work in Leiden, some would be placed in the centers; an important thing would also be that there should be a certain critical mass of people at one place. AP commented that the genotype error detection must be done locally. This was agreed. DB commented that the statistics core would need more twin statisticians. Different programs utilizing twin information were discussed.

NP gave a talk on database issues (note: this is not in the document archive)

The phenotype data will be mostly questionnaire data from centers. The central issue is that how we are going to conceptualise what the db core is/does? Harmonizing the data must be done in co-operation with the epidemiological core.

LP commented that the Database core must provide expertise to centers that nobody would unnecessarily buy expensive equipment. Also, a possibility to build an European datawarehouse exists.

JL described data standards. An example of the guidelines that Swedish twin registry steering group operates under was presented (this is attached).

KK commented that their experience on working 20 years on international datasets (MONICA and MORGAM) is that the easy part are the technical details: formats etc. The hard part is understanding the data: similarity, quality, differences etc.

It was generally agreed that the epidemiological and database intellectual cores must work together. Each center should have a dedicated person to handle db issues. Sample tracking and id are very important issues.

DB commented that a challenge is also multiple data types we will get.

LP commented that no matter the data should be collected in a single database but phenotype and genotype data should be kept separately.

Several comments were made on the challenges that db issues face: A need for a common platform must be clarified (JEH). There are several ways to combine analyses: 1. a common db or 2. data to be obtained from the centers in a format that is easy to combine sequentially (KK): A regular updating of the data is needed (LS). JH saw the need for a centralized db, to check for outliers and other errors.

AE gave a talk on MORGAM (please note: this is not in the document archive)

The MORGAM project (<http://www.ktl.fi/morgam/>) is a continuum of MONICA (<http://www.ktl.fi/monica/>). In Klein conference a decline in coronary events was reported since 1968. MONICA was started in 1983 to MONItor trends in CARDiovascular diseases (CHD event registration is obligatory, stroke optional), and to relate these to risk factor changes in the population over a ten year period. It was set up to explain the diverse trends in cardiovascular disease mortality which were observed from the 1970s onwards. The main results were published in mid-90's. In the mid 80's a genetic component was started in most MONICA cohorts. The most widely known is the ECTIM run by AE and Francois Cambien (Inserm, Paris) that started 1988. Morgam= MONica Risk Genetic Archive Monograph. The genetic component aims to pool the genetic cohorts to get a large number of samples. LP and MP have been involved in MORGAM since mid-90's. In MORGAM experience, the standardising and ethical issues have been quit hard issues. MORGAM is an open network inviting new members which will grow in size. MORGAM joined GENOMEUTWIN during the application process. The two materials complement each other: the results found in twin sample set can be replicated in a prospective epidemiological study. Currently, it is estimated that with the participating centers MORGAM will have approximately 200 coronary heart disease, 1000 stroke and 2000 death endpoints.

JH gave a talk on ethical issues (please note: this is not in the document archive)

A lot has to be done right away. Each center should name a person responsible for ethical issues. Common ethical guidelines should be listed. A monitoring system should be established to keep track of the local processes. Ethics training should be started and develop reearch on LC issues. For this, we would need to apply for new funds.

AE commented that the informed consent form should not be too long. This was agreed. There might be a necessity to re consent people. UK cohort has already done that in certain cases.

Prospective additional cohorts were discussed. A three page application form was suggested to be collected from the prospective cohorts. Funding was seem as an important issue, whether the add-ons would need funding and how much.

Benefits and publication policy were discussed. All contributors should benefit from the project. KOK volunteered to work on publication policy.

RN gave a talk on the EU funding issues

It was emphasized, that we need results by April 2003 to meet the November deadline.

LP ended the meeting and welcomed everyone to Rome.