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GEFOS meta-analyzes - Replication phase on GENOMOS studies – 3rd teleconference

Date: 20-04-2010 16:30-17:30 h (CET)

Attendees

Present	**Abscent**
ROTTERDAM: Rotterdam: Fernando Rivadeneira, Karol Estrada, Ling Oei	FLOS: Maria Luisa Brandi (Apologies)
FOS: David Karasik, Doug Kiel	AOS: Kim Brixen
APOS: Lynne Hocking	AMISH: Liz Streeten
Ioannina: Vangelis Evangelou	GEVUR: Elza Khusnutdinova
CABRIO: Jose A. Riancho	AROS: Bente Langdahl
GEOS: Francois Rousseau	Carrie Nielson
AMISH: Laura Yerges	LARISSA: Panagoula Kollia
EPIC: Jonathan Reeve , Stephen Kaptoge	CHS: Jane Cauley
BARCOS: Daniel Grinberg, Susana Balcells	SHEFFIELD:Eugene McCloskey
SLO-PREVAL: Simona Mencej	SOF: Steve Cummings
OSTEOS: George Dedoussis	CARLANTINO: Paolo Gasparini
LASA: Natasja van Schoor, Paul Lips	EPOLOS: Marcin Kruk
UFO: Ulrika Pettersson	NEMO: JM Kaufman
DeCode: Unnur Styrkarsdottir	OPERA: Kristina Åkesson
AUSTRIOS: Barbara Obermayer-Pietsch	VIGGOS: Marie-Christine DeVernejoul
AOGC: Matthew Brown, Emma Duncan, David Evans	HUNT: Siri Forsmo
INDIANA: Michael Econs	SOF, MrOS: Eric Orwoll

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MrOS Sweeden: Liesbeth Vandenput	CHS: John Robbins
	CAIFOS: Richard Prince
	EPIC: Alireza Moayyeri
	HKSC: Annie Kung
	CALEX: Sulin Cheng (Apologies)
	CAMOS, MANMC: Brent Richards (Apologies)
	HEALTHABC: Candy Kammerer
	ORCADES: Stuart Ralston (Apologies)
	ERF: Cornelia van Duijn
	FOS: Adrienne Cupples
	INDIANA: Dan Coller

ACTION POINTS:

- **Studies to update information of phenotypes on GEFOS questionnaire (http://www.gefos.org/quest/form.php username: consortium password: cooperation)**
- **Studies to read carefully instructions from KBiosciences on how to send DNA for genotyping. We need 5ng per SNP, considering 100 SNPs, that is 500ng of gDNA (please don't send DNA yet, just prepare your plates) http://www.kbioscience.co.uk/lab%20services/SNP%20Genotyping/genotyping_shipping.html**
- **New proposed deadline to submit DNA is June 1st, 2010.**
- **Studies need to send a signed copy of the GEFOS BMD working group agreement to the e-mail: genomos@erasmusmc.nl , prior genotyping begins.**
- **Rotterdam to send a poll for Biobank option.**

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Participants were welcomed to the 3rd teleconference of GENOMOS genotyping. This strategy was launched by the GEFOS DXA BMD meta-analysis of genome-wide data.

1. Inventory of GENOMOS samples

This inventory will be used to select samples for the GENOMOS replication.

Karol presented an updated report of GENOMOS studies which have uploaded data to the GEFOS questionnaire. The report now includes Total Body DXA. APOSS, NOSOS, EDOS will complete the data collection soon. We currently have 33,000 samples with DNA and fracture information. EPIC will select a subset of samples for replication. We will contact studies that are not listed in the survey. We have budget to include up to 50,000 samples, so we enforce you to invite your partners to be part of this collaboration. Studies that have ultrasound and have not registered the survey will be contacted by Jonathan Reeve. All studies were invited to

1) Update/Insert their numbers to the GEFOS questionnaire, (http://www.gefos.org/quest/form.php username: consortium password: cooperation)

2) Send a signed copy of the GEFOS BMD working group agreement to the e-mail: genomos@erasmusmc.nl.

2. Replication strategy update

It was recommended to create a Biobank so that samples can be used for future GEFOS/GENOMOS projects. One option is to perform whole-genome amplification (WGA). This technique will allow us to amplify from 50ng to 5,000ng sufficiently to type 1,000 markers. The price offered by KBiosciences is 1 euro per sample. This fee would not be sponsored by GEFOS and would be paid for each particular study. Michael Econs from INDIANA mentioned that their institutional review board does not permit assembling a Biobank outside their institution. It was reminded that this effort is targeted to those samples that don't have GWAS data. The working group agreement will be updated considering the BioBank, in this document it will be stated that each study maintains the ownership of their samples and that they can always get their samples back.

Francois Rousseau commented that the genotyping plan for their samples in Montreal. Fernando reminded that the price that KBiosciences is offering is 3.7 euro cents per genotype, and if a particular study decides to their own genotyping, then the study would have to pay the differences in cost. Matthew Brown asked about the stability of the amplified DNA after 6 months. FR mentioned that KBiosciences have optimized their methods in a way that it can be still used in up to 5 years. FR reminded that the main objective right now is doing the genotyping of 100 SNPs (for which we will require 500ng of genomic DNA), but that future research would be greatly benefitted

if DNA is readily available. We will circulate a survey to ask you about your availability for the GENOMOS biobank.

3. Update of GEFOS working groups

DXA BMD working group: Karol gave an update on preliminary results on the meta-analysis in 30,000 population-based samples. Main meta-analysis results in 34 loci (including the 21 known loci) associated with either LS-BMD or FN-BMD after adjusting the meta-analysis for the overall inflation factor. Forty nine additional loci have a P-value between $5x\ 10^{-6}$ and $5x10^{-8}$ in any of the LS of FN BMD meta-analysis and are candidates for replication. We will pursue replication in the complete list of 83 markers and run association analysis for BMD and fracture.

Power estimations using the suggestive hits from GEFOS and replication from GENOMOS gives more than 80% of power to reach a P < 5x10-8 if we add 30,000 samples or more from GENOMOS, this also holds true for association with fractures for variants with OR > 1.2 and MAF > 20%. An excel sheet for detailed phenotype information will be circulated to studies interested in replication. An abstract for preliminary results from GEFOS GWA hits was submitted for ASBMR, but we will wait for GENOMOS studies data for the final paper.

Ultrasound BMD working group: Jonathan Reeve (JR) explained that an abstract to ASBMR was also submitted. An association on region on 7q31 (reported by Korean study in Nat Genet) is observed. The aim is to enlarge the discovery including studies with GWAS before going to replication. JR will encourage people with ultrasound to register via the GEFOS questionnaire. Adding DXA studies of heel improved the significance of hits coming from Ultrasound data alone.

Hip Structural Analysis: David Karasik (DK) summarized the status of this effort. This is applied for people with DXA measurements and analyzed with an algorithm. Right now we have 4,000 women and 4,000 MEN. At the present we have data of 6 studies, meta-analysis after double GC correction shows one hit GWS on chromosome 10 near a cytochrome gene. An abstract was drafted and submitted. Forth additional cohorts are performing analysis as we speak (GOOD, HEALTHABC, INDIANA, HKSC). Replication will be pursued after final meta-analysis of all GWAS studies.

Lean Mass: Doug Kiel, this meta-analyzes has been completed using whole-body DXA or Bioimpedance analysis. An abstract was submitted to ASBMR. We are looking for replication on GENOMOS. Data for Bioimpedance can be entered through the different link sent recently. One GWS hit and several suggestive signals are shown.

4. Other issues

New deadline to send DNAs to KBiosciences: June 1st. 2010 to give more time for the Biobanking proposal. We will share the list of SNPs to be genotyped for those studies going for genotyping in other center (and paying the possible differences in costs).

For the fracture information, we will focus on all types of fractures (excluding high-trauma) with secondary analyzes on fractures occurring after 50 years, non-vertebral, and vertebral fractures (with radiological assessment and possibly morphometry analysis). For the GWAS of vertebral fractures we will definitely use morphometry data. Ling Oei is leading the effort to standardize the vertebral fractures (possibly both Lumbar and Thorasic). Final definition of vertebral fracture will come from vertebral fracture work group.

For those genotyping in house, they should think in returning genotypes 3 weeks after the deadline to send DNAs. (Barbara Obermayer , Francois Rousseau and Unnur from Decode)

5. Next call

We will circulate a doodle link with time options; next call should be within 1 month and prior to the deadline to submit DNAs.