**Agenda (General – Genetics & Epidemiology)**

Confirmed participants: Julie Williams, Sarah Taylor

Apologies: Peter Holmans, Kevin Morgan

1. **Jackson Group new study/collaboration**
2. **Updates from the AAIC conference and PERADES/GERAD annual meeting.**
3. **New conference call schedule**

Every 2 weeks on Monday

1. **Updates from IGAP (Rebecca Sims)**
2. **Polygenic score paper submitted**
3. **Pathway specific risk scores (Cornelia van Duijn)**
4. Any other business

Minutes and **action points** from previous meeting: Document A

Date and time of next conference call (epidemiology): Monday 28th September, 1pm UK time. Agenda items to be sent to Sarah Taylor (taylorsy@Cardiff.ac.uk).

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| **Document A: PERADES/GERAD Annual Meeting Minutes, 2015: Confirmed attendees:** Alfredo Ramirez, Celine Bellenguez, Christian Bannister, Clive Holmes, Cornelia van Duijn, Carlos Cruchaga, Elisa Majounie, Jean-Charles Lambert, Josh Bis, Julie Williams, Julien Chapuis, Rita Louro Guerreiro, Melanie Dunstan, Michelle Lupton, Perminder Sachdev, Peter Schofield, Petroula Proitsi, Rebecca Sims, Sven van der Lee, Sarah Taylor, Shazad Ahmad, Jose Tomas Bras, Valentina Escott-Price, Vincent Chouraki. |

**Minutes**

**Exome Sequencing: Presentation by Rita Guerreiro.**

* Discussion of challenges associated with merging data from different sources (Celine, Julie, Rita).
* Whole genome sequencing (WGS) data does not always corroborate other data (Jean-Charles), & could be combined with other data (eg. CSF or endophenptype data) to improve power (Alfredo).
* **ACTION POINT: Investigate access to ADES & UK10k exome sequencing data (Rita & Beccy).**
* **ACTION POINT: Establish what other data is available in support of WGS (Rita & Jean-Charles).**

**Exome chip replication:** **Presentation by Sven van der Lee.**

* ~30k samples are available = 13k cases & 17k controls (Jean-Charles).
* 3 Sequenom panels designed in descending importance, failed SNPs re-designed for Taqman.
* Sequenom panel 1 was successful in Bonn, including ATP5C1. Preliminary results to be discussed by analysts.
* Sequenom panel 1 at the pre-QC stage in Lille for all 10k samples, completion expected in August.
* **ACTION POINT: Alfredo to have IDs of overlapping samples in Bonn & Lille (Jean-Charles).**
* Alfredo working on Taqman/Open Array, Life Tech need the 128SNP list: NO OBJECTIONS RAISED.
* In future work, available options to be discussed before experiments begin & only one platform used where possible to reduce costs. To be discussed with IGAP.
* **ACTION POINT: Exome chip work to be published urgently. RS to draft & circulate.**

**Polygenic Score:** **Presentation by Valentina Escott-Price.**

* “Take home message” = polygenic score (PS) predicts better than ApoE.
* Scores could be used in combination with other indicators such as plaques.
* Extremes can be used in imaging/clinical trials to predict chance of AD.
* In GERAD the immune response pathway contains the most SNPs.
* **ACTION POINT: Cornelia & Valentina to replicate PS in LOAD using independent datasets.**

**PERADES Epidemiology Update: Presentation by Cornelia van Duijn.**

* **ACTION POINT: Cornelia & Jean-Charles to discuss including additional SNPs for replication from pathway analysis & to investigate the replication hits in pathway results.**
* Important to keep analysis tight & base on the best information possible.
* Ongoing investigations into smoking, future work to include GTEX.
* **ACTION POINT: Evie (Bristol) to present in future on smoking & Mendelian randomisation.**

**Questionnaires & DPUK: Presentation by Elisa Majounie.**

* **ACTION POINT: Elisa to establish whether all questionnaire responders with GWAS data are included in our studies, those not involved are to be invited.**
* **ACTION POINT: Questionnaire to be re-circulated to non-responders.**
* DPUK is a recently begun (& ongoing) UK-wide collection of cohorts to which we can facilitate access for epidemiology/other studies.
* Access is via an online portal which will seamlessly integrate a variety of information sources.

**Genotypic Analysis: Presentation by Christian Bannister.**

* Expressions of interest requested from the group for applying genotypic analysis to other datasets in PERADES. The replication sample could be used to take this forward.
* 8 loci of interest not included in replication will require other datasets for further investigation.
* Concluded that the simplest approach is to use the new IGAP analysis to progress this.
* **ACTION POINT: Genotypic analysis to be taken to IGAP.**

**Pathway Analysis: Presentation by Peter Holmans.**

* The most important pathways appear to be immunity, endocytosis, lipids.
* Rare variant pathway analysis will not work well in ALIGATOR. SKAT-O or similar should be used.

**Other Business:**

**Face-to-face meetings:** with conference call facility suggested every 6 months from now on.

* **ACTION POINT: Jean-Charles to organise the next face-to-face meeting in October/November.**

**US 580 Whole Genome Sequences & 11k Exome Sequences Studies:**

* Samples from GERAD/PERADES may already be included (eg. CHARGE).
* Replication samples are not yet identified but investigations focus on US samples. European samples are not needed therefore our contribution may be limited (for example to rare variant replication). Many samples are available outside the US for replication, but funding is not.
* 600 US WGS are available on DBgap for download. 90% are cases on related individuals.
* **ACTION POINT: Sarah to establish volunteers from each group to identify samples available & those collections that can be intensively expanded for replicating exome sequencing. Samples to be fully prepared for research including MTAs, etc.**
* These samples can also be used to replicate PERADES/GERAD studies.
* The US model of sending out questionnaires, establishing ethics, etc may be of interest, however, in the majority, this stage is completed, access to DNA is outstanding.
* Jean-Charles’ application for a JPDN-funded biobank for 30k cases, 40k controls with DNA available will be of help if successful.
* Cardiff have funding for future replication of some US studies, but decisions are required as to exactly which study, given the price of whole genome sequencing has not reduced as expected.
* Pilot whole genome sequencing could be funded, this would take 18 months. Imputation of cases only would provide a quick paper.
* **ACTION POINT: Cornelia to take forward UK10K imputation of data at Sanger, followed by re-analysis, with Jean-Charles involvement. Suggestion is to perform another GWAS with better information to run in parallel with sequencing.**
* Whole genome sequencing to begin on 200 EOAD as soon as possible.
* Jean-Charles is performing whole genome sequencing on 1k LOAD.

*END*

**Scheduling and Information:**

**Call-in Numbers (Pin Code 592838):** Austria 082040001503 English, 082040001502 German; Belgium 070359945 English, 070359994 Dutch, 070359866 French; France 0821230748 English, 0821230749 French; Germany 01803001178 English, 01803001177 German; Ireland 0818270007; Italy 848390116 English, 848391819 Italian; Netherlands 0870001901 English, 0870001909 Dutch; Spain 902885318 English, 902881200 Spanish; Sweden 09392066300 English, 09392066400 Swedish; UK 08444737373, 87373 mobile; USA 14153630833; Other +448444737373

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