

No.18
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AETIONOMY – CONSORTIUM MONTHLY UPDATE

Message from the Coordinators

Dear AETIONOMY partners,

After a couple of heavy months of updates to the DoW and the Annual Report for everyone, special thanks to Jacqueline and Stephan, the focus for us all turns to the science (please PO don't remind us that there will be revisions coming to both!)

Back to the science. With frenzied efforts overtaking all of the clinical partner's laboratories there are plenty of sample transfer logistics ongoing, thanks to Stephanie at ICM for keeping a handle on this, and soon there will be a glut of data flowing. With these data will come the inevitable challenges, which we rely on the close partnerships between WPs 2, 3 and 5 to help address.

The opportunities and the challenges of these final few months of the project will be the focus of the face to face WP 5/3 organised workshop hosted in the UK at the end of April. We hope that these discussions will spur us on towards the collaborative endpoint for AETIONOMY as we move into the final phase.

Now to some business and reminders, please all take note of the timelines on the final page of the bulletin and for those partners who will be exchanging data and integrating data into the AKB [from May 25th](#) this year, please go back and review Marc Stauch's email from March with your institutions Data Privacy Officers as the GDPR is an important consideration. Last but not least please review the deliverables due to your work package and ensure that we post reports on time.

Thanks

Your PO (Phil, Martin, Jaqueline, Stephan and Tobias)

General Information

Upcoming Meetings

- WP 3-5 Workshop & Datathon – UCB, UK April 26 & 27 2018
- EAN Conference 16-19 June 2018, Lisbon
- ISMB Conference 6-10 July 2018, Chicago
- PO/SC Meeting, Luxembourg 5/6 July 2018
- Final WP3-5 Workshop & Datathon – BBRC, 21 Sept
- Final General Assembly and NDD Symposium on 29th & 30th Nov 2018 – Bonn, Germany

Reminder that all publications need to be submitted to the Project Office **before** submission. Same for Congress abstracts, etc.!

Please review the Project Agreement for more details. Remember to follow the **IMI mandatory** communication guidelines with regards to funding statements and logos.

Did you know that **AETIONOMY** should always be capital letters?

Deliverables due to IMI in 2017 (DoW v5.1, Aug 2017)

- D5.3.2 & D5.3.5 due M48
- D2.5.3.4 due M50
- D3.9.3.1 due M50
- D5.1.6.4 due M52
- D1.4.2 due M55

WP1 – Governance & Coordination

- The annual report for year 4 was successfully submitted to IMI on time. We have had a first set of comments and expect most of them after 9th April.
- The final amendment to the Description of Work, v6.0 of March 2018 was submitted to IMI. Thanks to those that contributed. We will keep you posted on IMI feedback.
- The Final Symposium and last General Assembly date will now be held on the **29th & 30th November 2018**. This will take place in Bonn, Hotel Hilton. We are lining up our speakers and it will be a great meeting. We will communicate further info in the next bulletin. We expect all partners to present at this final conference on neurodegeneration.
- **The PO again would like to ask all WPs to please try to submit the deliverables on time as we are being measured on this!**

WP2 – Knowledge & Data Management

- WP2 continues to work on improving the usability of the AKB. UL is currently working on integrating the [Ada System](#) to the AKB, this will bring new analytical pipelines based on Machine Learning to be described in the D2.4.3.2.
- The new datasets received are being processed or under curation. This includes the UKB AD Inflammation study, KCL and Tuebingen studies, and 14 UCB studies.
- WP2 partners are proceeding on the enrichment of the 3D brain imaging data of the Virtual Dementia Cohort (VDC) to incorporate processed functional and structural information (fMRI and DTI data).

Additionally information of the BEL disease models and Bayesian Networks (BNs) will be analyzed for the incorporation into the 3D brain simulation. A meeting was held to plan this integration of BEL/BN related information via the TVB interface.

WP3 – Knowledge Integration & Mining

At EMC a new event-based modeling approach (EBM) has been developed in the past months, that seems to be more robust and accurate than other published approaches. A property of the new approach is that it is also calculating the disease stage per subject. In the last weeks this modeling was applied on 1.737 ADNI cohort subjects. AD-related non-imaging and imaging biomarkers, including volume measures of hippocampus subparts, were used as events. APOE-epsilon4-related info was used to see the effect on the EBM outcome.

The first finding seems to be that the event order is not influenced by APOE, but that events are becoming abnormal more early (disease staging) in the case of APOE \neq 0.

EBM will applied to other cohort data and further experiments will be done, also using other (different) AD-related genetic info as well as relevant Chromosome 17 SNPs.

- Partners UCB and Fraunhofer are developing and verifying the Bayesian Network approach for patient stratification.
- Another activity of this collaboration is the validation of the ADNI-based AD risk model applied to the AddNeuroMed cohort data.
- Finally, this team is generating a virtual AD patient cohort with a similar feature distribution like in the ADNI cohort.

During the VDC workshop in February the integration of the different approaches for the generation of the VDC ADNI Avatar were discussed and reported in deliverable D2.5.3.3. For more information check the BSCW AETIONOMY workspace under the URL:
<https://bscw-biosc.scai.fraunhofer.de/bscw/bscw.cgi/45405>

- A webinar '*Mining on Bayesian representations of major cohort studies (incl. ADNI and PPMI)*' is planned in April to present the result of these different Bayesian Network approaches.

WP4 – Ethical & Legal Governance

LUH has circulated the finalised data protection supplemental agreement for signing to all partners that will continue to handle patient data in the project after 25 May 2018, when the new EU General Data Protection Regulation (GDPR) takes effect; the cooperation of partners in getting this document signed is much appreciated, as it is designed to ensure that data processing in the project remains compatible with the updated EU data protection regime. Dr Marc Stauch, LUH, has also addressed the GA of AETIONOMY's sister-project, PRECISESADS, in Ascot, UK on compliance issues facing that project too that is a result of the GDPR."

WP5 – Clinical Validation (1/2)

Sarah Bujac, Luc Canard and Ullrich Wuellner have been exploring the PD EFPIA data in the SAS Multi-sponsor Environment. The aim is to demonstrate the utility of the EFPIA data and, in the process, gain insights into the effect of baseline characteristics, such as age and gender, on dopamine agonist response in Early PD.

AETIONOMY sample plan:

90% of the shipping plan will be completed by the end of the month / 1st week of April. The remaining 10% are part of external cohorts' samples that we are currently selecting and preparing for shipment to the different analysis labs. These shipments are summarized below, with an actual update on their status:

From	Samples	To	Status	Actual/Estimated date
KI (Prof. Svenningsson)	105 DNA	ICM	Partially	26 MARCH 18
	150 DNA add. Cohort	ICM	Planned	Extraction ongoing
	32 CSF	UKB (MH)	Planned	3 APR 18
	32 CSF	IDIBAPS	Planned	3 APR 18
UKB (Prof. Wuellner)	94 DNA	ICM	OK	26 FEB 18
	48 DNA	ICM	Planned	28 MARCH 18
	22 CSF	KI	OK	28 MARCH 18
	22 CSF	IDIBAPS	OK	5 MARCH 18
	22 CSF	UKB (MH)	NA	Internal transfer
UKB (Prof. Heneka)	240 DNA add. Cohort	ICM	Planned	Selection ongoing
	220 CSF add. Cohort	KI	OK	20 FEB 18
	220 CSF add. Cohort	IDIBAPS	OK	26 FEB 18
ICM (Prof. Corvol)	47 CSF + 14 add. Cohort	KI	OK	7 MARCH 18
	37 CSF + 9 add. Cohort	UKB (MH)	OK	7 MARCH 18
	47 CSF + 14 add. Cohort	IDIBAPS	OK	7 MARCH 18
	318 DNA + 642 add. Cohort	UKB (UW)	Planned	3 APR 18
IM2A (Prof. Dubois)	7 DNA + 364 add. Cohort	ICM	NA	Internal transfer
	23 CSF add. Cohort	KI	Planned	3 APR 18
	23 CSF add. Cohort	UKB (MH)	Planned	3 APR 18
IDIBAPS (Prof. Sanchez-Valle)	137 CSF add. Cohort	UKB (MH)	OK	6 MARCH 18
	137 CSF add. Cohort	KI (PS)	Planned	3 APR 18

WP5 – Clinical Validation (2/2)

- AETIONOMY sample analysis update:
~350 DNA samples have already been genotyped at ICM, i.e. 35% of the total DNA samples to be analyzed.
- AETIONOMY data management plan:
 - Clinical study data entry into REDCap eCRF is finished at all sites.
 - Queries have been issued, with a rate of 80% being resolved to date.
 - Database lock is planned early April after the listings review meeting. New queries may be issued after that.
- AETIONOMY data validation plan:

We are setting up a Data Review Committee to be held beginning of April to validate the AETIONOMY clinical study dataset.

This dataset that will then be analyzed, by the end of April.

Publications Corner

- Mouton-Liger F *et al.* (ICM):
Parkin deficiency amplifies NLRP3 inflammasome activation by attenuating an A20-dependent negative feedback loop.
GLIA *in press.*

Happy Easter to all



Reference: Wikipedia

Important Timelines to Project End

M49	M50	M51	M52	M52	M53	M54	M55	M56	M57	M58	M59	M60	
31-Jan-18	15-Feb-18	Mar-18	26 or 27 Apr	30-Apr-18	may	june	Jul-18	August	20-21 Sep	3-5 Oct 18	29 & 30 Nov	31-Dec	28-Feb-19
all known samples documented in excel planner	planned shipment date of samples to analysis labs	Data analysis on data sets already available EMIF 1000	final Workshop WP3/5 & datathon? UK	results available	biomarker data analysis	biomarker data analysis	SC mtg / results interpretation UL	Holiday	final Workshop WP3/5 & datathon? BBRC, Barcelona	Granada Genomics Conference / Joint Taxonomy Mtg?	NDD Conference & Final GA	Project ends	Final report due to IMI
	clean	cohort data											
	Draft Agenda for NDD ready												
	Project Plan for analysis due from WP3	Newsletter Identification of new mechanisms for NDD	Determine if amendment is needed / budget shifts			Newsletter - the Virtual Dementia Cohort	02-05/2018 5th July Luxembourg (JC)				Newsletter - The new Taxonomies		

Did you know that all the project deliverables submitted to IMI are available on our BSCW Server?

Check them out at: <https://bscw-biosc.scai.fraunhofer.de/bscw/bscw.cgi/42644>