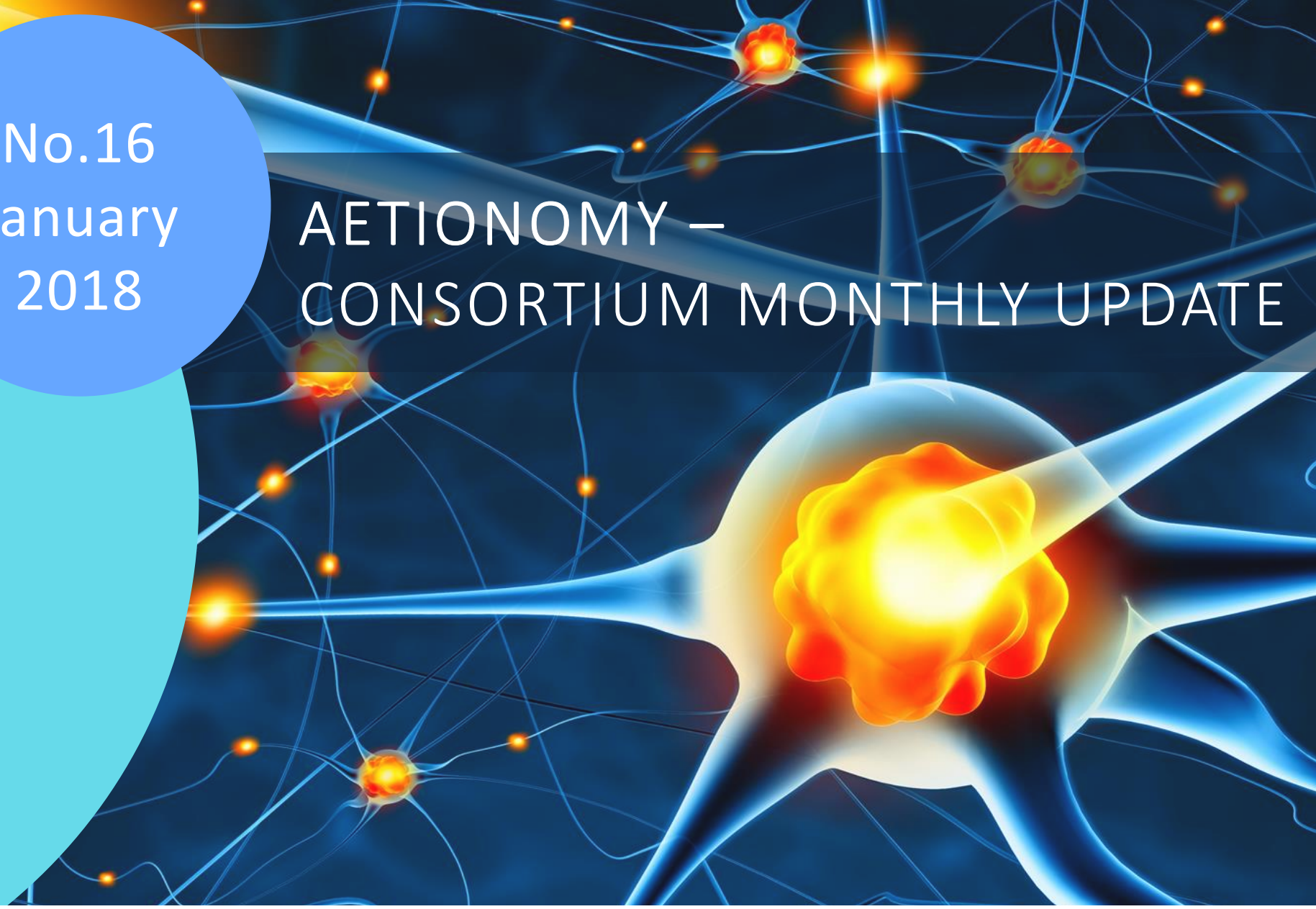
No.16
January
2018

AETIONOMY – CONSORTIUM MONTHLY UPDATE



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AETIONOMY

Message from the Coordinators

Dear AETIONOMY partners,

Happy new year to you all, the Christmas break seems so long ago now but we hope you had a relaxing and rewarding end of year.

At this time of year it is useful to reflect on the undertaking that we collectively agreed to deliver on behalf of our communities, our industry and, most importantly, our patients an ambitious and unprecedented approach to help redefine the outdated standard of medical classification of disease in the challenging NDD space.

As we write this, at the end of January we have 11 months left to realise these challenges and there is clearly still a long way to go, but I hope that we have your full support to stay focused on this goal despite our myriad distractions and full commitment to play your part in helping the community realise these ambitions.

As we stated in the last coordinators' statement we have little time left and we need to focus and prioritise our actions and investments in order to meet this tough timeline, I know we can count on each of you to support us in the actions that we need to take. We have recently agreed on some key timelines that will be being communicated via Work Package leaders, critically the recruitment and sample generation / acquisition phase is complete and we have to ensure that the subsequent steps of data generation are in hand if we are to have a chance with the downstream analytical approaches.

With some difficulty we have agreed on the 30th April 2018 as the drop dead date for the generation of Biomarker data from our accrued samples, this is going to be challenging but the downstream processing of these data and the subsequent analyses from which we will derive the deliverables of the project need to be given a chance to deliver too. The logistics of sample movement and Biomarker data generation will now have to aim to meet these deadlines. In order to facilitate the interpretation of these data we will support a number of WP5/3 workshops (dates on page 4) in which the critical results will be explored ahead of ultimate public delivery of the project's conclusions at joint GA and Final Symposium on 29th/30th November 2018 in Bonn.

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

General Information

Final Recruitment Update					
Site	PD	Controls PD	AD	Controls AD	**PD Total**
ICM	120	40	6	1	**160**
KI	80	25			**105**
UKB	77	16	1	1	**93**
Bordeaux	18	5			**23**
Besancon	6	0			**6**
Toulouse	18	6			**24**
Total:	**319**	**92**	**7**	**2**	**411**

Upcoming Meetings

- WP2 – VDC modelling and implementation workshop AMU, FR 15/16 Feb 2018 – Marseille
- WP3-5 Workshop & Datathon – UCB, UK April 26/27 2018 (tbc with doodle)
- EAN Conference June 2018, Lisbon
- ISMB Conference July 2018, Chicago
- PO/SC Meeting, Luxembourg 5/6 July 2018
- Final WP3-5 Workshop & Datathon – BBRC, 20/21 Sept (tbc with doodle)
- 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)

- D1.2.8 Annual Report due 28 February
- D3.3.5 due M47 (planned M50)
- D5.1.7, D5.3.2 & D5.3.5 due M48
- D1.4.2 due M49
- D2.5.3.3. & D2.5.3.4 due M50
- D3.9.2.1 due M50

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*

WP1 – Governance & Coordination

- The 4th amendment to the DoW has now been officially approved by IMI thus we are working to v5.1 dated 23 August 2017. This is important for all deliverables that are past due. Any doubts, please contact the Project office.
- The Final Symposium and last General Assembly date will now be held on the 29 & 30 November 2018. This will take place in the Bonn area. We will communicate further info in the next bulletin.
- The annual report is due to IMI on the 28th February for all partners to report their scientific and financial contributions to the project. The template has been sent and we will need you to capture all dissemination activities there as well as all task updates via the WP Leaders.
- **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

- UL will start to integrate the Ada System (current NCER-PD report system) in the scope of the AKB. This will add new GUI features to be describe at the D2.4.2.1 and new analytical pipelines based on Machine Leaning to be described on the D2.4.3.2.
- UL will promote the integration of the EMC full imaging datasets (ADNI/ICM) to the BrainMesh interface and release it together with the final interfaces and pipelines at M60.
- AMU has completed the ADNI2 database using the approach of Virtual Brain Technology. 76 patients in ADNI2 have structural MRI data, which were used for virtualization and simulation, complementing the database with simulated functional MRI data. The complete data set is now available to the AETIONOMY consortium.
- WP2 will hold a Workshop on the VDC modeling and implementation strategy, which will be reported in D2.5.3.3. Additionally the outline of a manuscript to publish the VDC approach will be generated (D2.5.3.4).

WP3 – Knowledge Integration & Mining

- AETIONOMY is exploring new ways of stratifying patient subgroups based on OpenBEL graphs which are indicated by mechanism (causal chains) and which include entities that can serve as “biomarkers”. With discrete variables (e.g., SNPs), this seems to be feasible, with continuous variables (like TAU or A-beta 42 concentrations) this is going to be much more challenging. For both the diseases AD and PD “final” graph-based disease models were generated with BEL (see also report D3.6.1).
- An essential activity in AETIONOMY is to generate hypotheses about multiscale mechanisms of neurodegenerative pathophysiology. In the report D3.9.1.2 *Webinar: Implementation of algorithms for mapping and stratification in* ***NeuroMMSig-Server*** Fraunhofer described the realization of this dedicated server. Additionally, through a Bayesian Network Viewer, we can test patient level data for the presence or absence of mechanisms. In 2018 further validations of NeuroMMSig candidate mechanism against available patient cohort data is planned.

Two further reports were submitted to IMI explaining the syndecan (SDCs) based candidate mechanism and how heparan sulfate proteo-glycans (HSPGs) act as key players behind spreading-associated processes in NDD:

- D3.9.2.1 Report on the Generation and calibration of syndecan dependent assays (in vitro) for hypotheses of the clinical study and
- D3.9.2.2 Report on the Identification of new syndecan-ligands and surrogate markers that link syndecan-mediated uptake and signaling mechanisms to clinical variables determined in the clinical study

Our data analyses represents SDCs as a preferred cellular targets for Aβ1-42 to enter cells. Considering the significant overexpression of SDC3 and SDC4 in human AD brains, our SDC dependent cellular uptake assays provide results relevant to human conditions and reveals unknown details of SDC-mediated endocytosis that might be major contributors of neurodegeneration.

- Next: In the planned D3.3.5 Webinar planned in Feb 2018, we will focus again on Bayesian Modelling, especially on expressed feature sets and virtual patient generation.

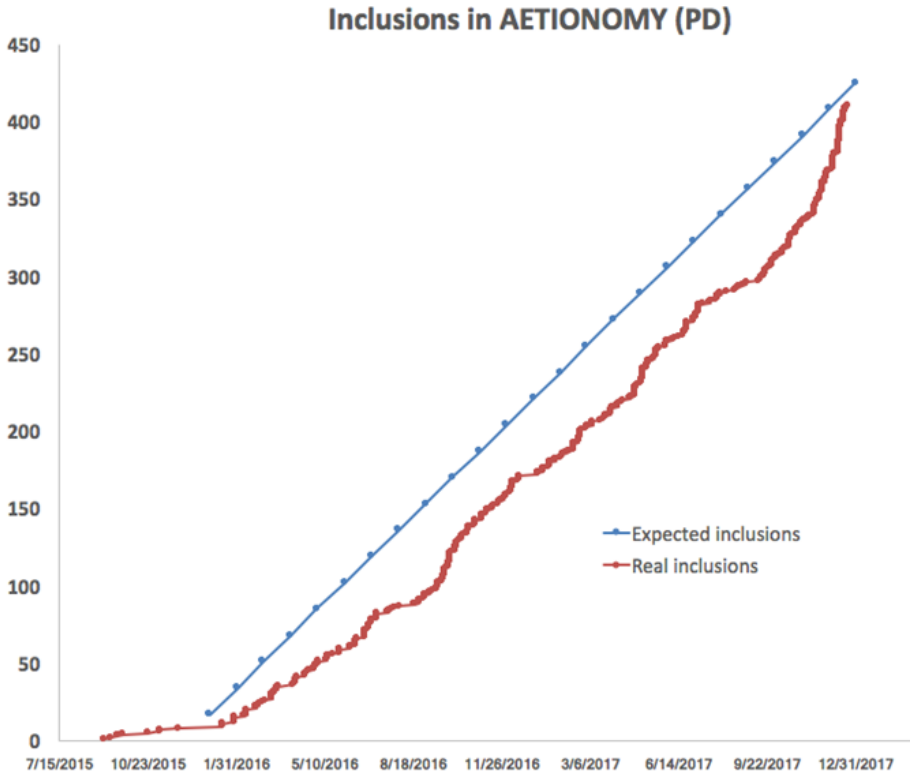
WP4 – Ethical & Legal Governance

- LUH is continuing to analyse and monitor the implications for the project from the impending change to EU data protection law, which will apply from 25 May 2018 when the new General Data Protection Regulation (GDPR) takes effect. As reported in the last monthly bulletin, this was the subject of discussions with the project's external legal and ethics experts at the latest meeting of the AETIONOMY Legal and Ethical Advisory Board, and is examined in detail in the WP4 deliverable D4.5 (submitted to IMI in December 2017).
- LUH has since circulated a draft 'Data Protection Supplemental Agreement' for the attention of all partners who share and use clinical data in the project, which aims to update the existing project data protection framework to be compliant with the GDPR: the relevant partners have been requested to pass this document on for consideration by their legal departments and data protection officers.

WP5 – Clinical Validation

- Recruitment in the AETIONOMY Clinical Study has finished on 31 December 2017. The goal of 400 PD patients recruited has been reached. Congratulations to all centers!
- Congratulations to KI who has recruited 100% of estimated subjects!
- All collected data have to be entered as soon as possible, and at the very latest by the end of February 2018. Thanks to all sites for completing REDCap eCRF in the best terms.
- Next step before moving towards dataset analysis: data cleaning of REDCap database. A substantial work of data management will be handled on the upcoming weeks/months.
- We are preparing a comprehensive list of all available samples from AETIONOMY CS and partners' cohorts, to manage data analysis scheduling.
- King's college has already sent ~100 DNA samples to ICM. Tubingen has also sent a batch of CSF and plasma samples (~100 and 250, respectively) to KI and UKB.
- Regular telcos have been set up between WP3 and WP5 for progressing reports on genomic-based stratification of patients

Clinical Study Recruitment…



Publications Corner

Dissemination Activities

Announcements

After almost 4 years, Adriano is leaving the LCSB. On February 15th, he will start a new position at the Queen Mary University of London (QMUL) as a Rutherford Fellow Research Lecturer in Health Data Research. We wish you well Adriano!

AMU has a course offering on 26th February in Berlin ***full brain network modeling using the open-source neuroinformatics platform 'The Virtual Brain'***: *www.thevirtualbrain.org/node6*

	AETIONOMY CS	PD group				AD group			Total Subjects
		iPD patients	Familial form of PD (FPD)	At risk PD subjects (AR-PD)	Healthy PD controls (HC-PD)	At risk AD subjects (AR-AD)	Prodromal AD subjects (PAD)	Healthy AD controls (HC-AD)	
All centers	Estimated number of subjects	284	55	70	112	40	60	60	681
	Actual number of subjects	255	25	39	92	5	2	2	420