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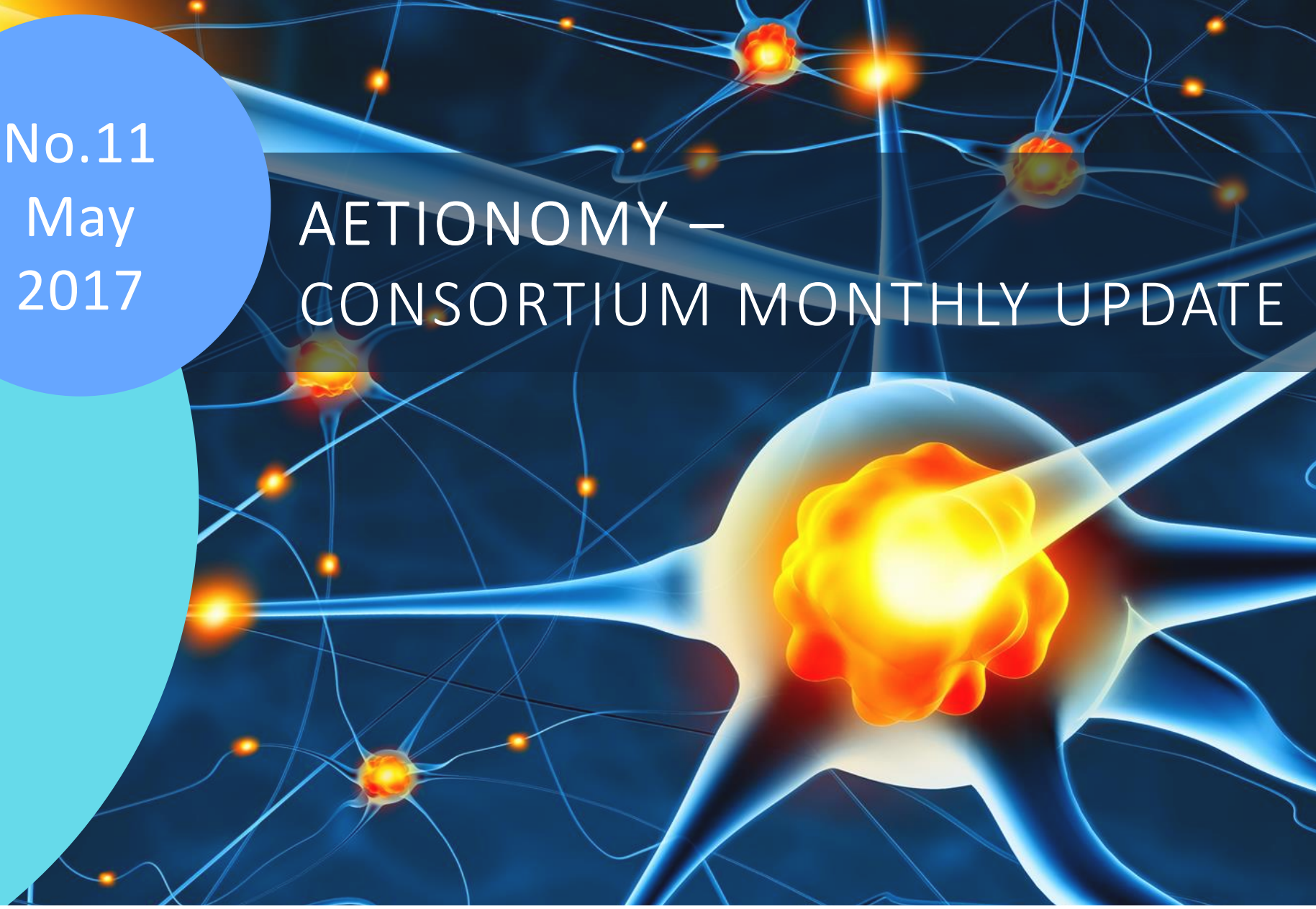
AETIONOMY – CONSORTIUM MONTHLY UPDATE



ucb Fraunhofer SCAI efpia imi innovative medicines initiative AETIONOMY

Message from the Coordinators

During the last month we have all worked hard to pull together information to support the annual report, the responses to the reviewers comments from the Interim review and the definition of the new DoW to take us forward into the next and final phase of the project - a herculean task to which we should recognise the value that Jaqueline and Stephan have brought in coordinating the range of contributions and Tobias in updating all financial data.

We have also taken some strong and hard decisions as to the future make of up the consortium, its leadership and the directions that we need to take to ensure our success in the remaining time, there is still a lot of work to do and some considerable milestones to overcome but we believe in the fortitude of the members and their renewed commitment to the goals of the project.

Kindest regards,

Phil and Martin

Biomarker Lounge of candidate mechanisms:

https://bscw-biosc.scai.fraunhofer.de/bscw/bscw.cgi/45602

General Information

Recruitment Update				
Site	**PD**	**AD**	**Controls**	**Total**
ICM	84	0	37	121
KI	55	0	16	71
UKB	51	0	12	63
Total:	**190**	**0**	**65**	**255**
EPAD	x	x	82 BBRC	237 Global

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.

Upcoming Meetings

- WP3/WP5 Mtg 22 June at ICM, in Paris with SC Meeting & working dinner on the 21st in Paris
- Virtual Dementia Cohort strategy workshop 6-7th July at AMU, Marseille
- Workshop on Computational Neuroscience in Marseille, 12-13th July (https://amidexcompneuro.net/)
- AAIC Conference 16-20 July 2017 in London
- General Assembly IV at Novartis, in Basel on 30th Nov & 1st Dec 2017

Deliverables due to IMI in 2016 & 2017 (late)

- D3.3.3 & D3.3.4 Webinar and report to review the pathophysiology graphs and potential hypotheses to be tested (M34 & M38)
- D2.2.3 Examination of data together with users for inconsistences (M36)
- D3.6 Generation of specific hypotheses about disease sub-groups (M36)
- D2.4.2 User documentation for querying interface (M37)
- D3.8 Data analysis work plan for the WP5 clinical study (M40)
- D5.1.3.8 To confirm choice of biomarkers for final protocol (M40)

WP1 – Governance & Coordination

- The **Annual Report (AR)** for IMI on both scientific and financials has been re-submitted to IMI. Payments are stopped until IMI is satisfied with our responses. We will notify you as soon as we hear back from them.
- The **Interim Review** formal response together with the final **DoW amendment** is due to IMI by 7th June. We have had some feedback but *we do request all partners* to review their contributions as this is the last time we will amend as the project ends in 20 months.
- We are still planning on using the **EAN congress in June 2018 in Lisbon** as our final congress presenting all AETIONOMY results. AE has been very helpful in obtaining information on costs and methods and is currently helping us draft a general info poster.
- We are still working on getting access to the Tuebingen samples for use in validating our hypotheses. Legal agreements are currently being drafted.

WP2 – Knowledge & Data Management

- The **Clinical datasets from IDIBAPS** - Screening, Validation and AD Dementia cohorts have been updated and loaded. They are now available provided the agreements are in place. Please visit the ticketing system to request access.
- WP2 is currently working on **Extraction of major trajectories and distributions** from curated ADNI and PPMI data. Partner Fraunhofer has made progress in extracting trajectories from ADNI datasets. Moreover, we have obtained a pre-processed PPMI dataset that will allow us to extract major PD trajectories.
- Partner AMU, now has access to the **ADNI imaging data processed at EMC** with their imaging pipelines, to aid with the Task 2.5 Virtual Dementia Cohort.
- Reinhard Schneider delivered a keynote , *"Big Data and Computation Platform for the Detection of Biomarker"* , at Digital Future Berlin 2017. May 12 and 13th.
  For more information visit : https://science-match.tagesspiegel.de/digital-future/digital-science
- Current goals of the final amendment of the DoW are to implement additional efforts to **increase usability** of the Knowledge base and to extend the contributions to **generate the Virtual Dementia Cohort**.

WP3 – Knowledge Integration & Mining

- We are now looking forward to the validation against patient-level data. The WP3 members agreed on a **validation strategy** which will be realized during the next months. WP3 is currently in preparations of the following action items:

  i. We will execute a **webinar on Bayesian modeling** and their contribution for the validation of our in silico candidate mechanisms. The recording will be offered as a training of this approach. A report will be soon available which represents D3.3.3.

  ii. As a follow up another webinar is planned describing **first validation results** of the Bayesian modeling and further approaches, like Event Based Modeling. A recording and a report D3.3.4 will be afterwards available.

  iii. We are in contact with Simon Lovestone's team - **Univ. Oxford** and Klaus Romero – **C-Path institute** to get access to further patient data for our planned candidate mechanisms validations. Additionally, a Fraunhofer Team will visit partner **Karolinska** in Stockholm in August.

URL of the Validation Strategy Concept:
https://bscw-biosc.scai.fraunhofer.de/bscw/bscw.cgi/66713

- Deliverables **D3.6 and D3.8** are drafted and will be soon submitted.

- WP3 provided all candidate mechanisms incl. available evidences in their **Biomarker Lounge** under the URL:
https://bscw-biosc.scai.fraunhofer.de/bscw/bscw.cgi/45602

WP4 – Ethical & Legal Governance

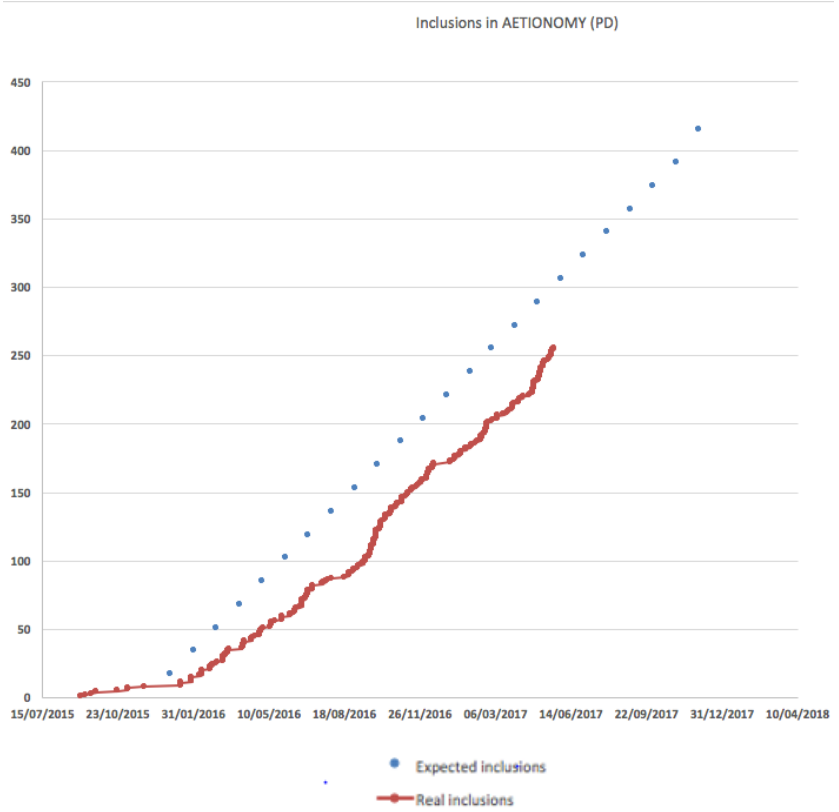
- Following last month's successful **joint legal and ethics meeting with PRECISESADS** in Berlin, WP4 has compiled a detailed report of the presentations and discussions that occurred; this will be submitted to IMI as AETIONOMY deliverable **D4.3.2**.
- WP4 is also playing an active part in initiatives to gain access to two sets of **bio-samples for analysis in AETIONOMY**, from the University of Tuebingen and King's College London, respectively. To this end LUH has supplied a draft framework agreement for facilitating the transfer in one case, as well as providing advice on relevant documentation and consent requirements.

WP5 – Clinical Validation

- The amendment for the AETIONOMY protocol has been approved by Regulatory Authorities on the 5th of May (EC approval pending).
- The 3 new clinical centres will be opened in June in France (Besancon, Bordeaux and Toulouse) for the PD group recruitment.
- The first AD subject will be included on June 6 at the ICM clinical centre. We hope UKB will also start to recruit.
- An amendment have been submitted on May 16th to EC in Sweden to increase the number of PD subjects to be recruited at this clinical center.
- Pharmacoidea partner will now be part of WP3 due to its close collaboration with Fraunhofer.
- Reminder that the WP3/WP5 F2F meeting will be organized at ICM on the 22nd of June to finalize the analysis plan and to select additional mechanistic hypotheses that could be tested in AETIONOMY clinical study.

Clinical Study Recruitment

- Regarding PD recruitment the following graphic shows our inclusions.



- Regarding AD recruitment at BBRC, the number of inclusions is 82.

In total EPAD LCS enrolled 221 participants.

Publications Corner

Updates on submitted/accepted publications:

- Daniel Domingo-Fernández, Alpha Tom Kodamullil, Anandhi Iyappan, Mufassra Naz, Mohammad Asif Emon, Tamara Raschka, Reagon Karki, Stephan Springstubbe, Christian Ebeling, Martin Hofmann-Apitius: ***Multimodal Mechanistic Signatures for Neurodegenerative Diseases (NeuroMMSig): a web server for mechanism enrichment***. Bioinformatics. (in revision)

- Mufassra Naz, et al.: ***Reasoning over genetic variance information in cause-and-effect models of neurodegenerative diseases***. Briefings in bioinformatics 17.3: 505-516.

- Kodamullil, A.T., et al.: ***Computable cause-and-effect models of healthy and Alzheimer's disease states and their mechanistic differential analysis***. Alzheimer's & Dementia 11.11: 1329-1339.

- Iyappan, A. et al.: ***Towards a Pathway Inventory of the Human Brain for Modeling Disease Mechanisms Underlying Neurodegeneration***. Journal of Alzheimer's Disease 52.4: 1343-1360.

- Alpha Tom Kodamullil, Firas Zekri, Meemansa Sood, Bastian Hengerer, Luc Canard, Duncan McHale, Martin Hofmann-Apitius: ***Tracing the money for development of AD drugs: mapping investment to opportunities and possible drug target mechanisms*** *(Nature Reviews Drug Discovery, in revision)*

- Alpha Tom Kodamullil, Erfan Younesi, Anandhi Iyappan, Reagon Karki, Sumit Madan, Martin Hofmann-Apitius: ***Of mice and men: comparative analysis of neuro-inflammatory mechanisms in human and mouse using cause-and-effect models*** *(Journal of Alzheimer´s Disease, in revision)*

- Reagon Karki, Alpha Tom Kodamullil, Mufassra Naz, Martin Hofmann-Apitius: ***Comorbidity analysis between Alzheimer's disease and Type 2 Diabetes Mellitus based on disease network models and the role of T2DM drugs***. *(Journal of Alzheimer´s Disease, submitted)*

- Emon MA, Kodamullil AT, Karki R, Younesi E, Hofmann-Apitius M: ***Using Drugs as Molecular Probes: A Computational Chemical Biology Approach in Neurodegenerative Diseases***. Journal of Alzheimer's Disease, 56(2), 677-686.