CONSORTIUM MONTHLY UPDATE No. 1 – April 2016

WP1 – Governance & Coordination

- 2nd Periodic Report has been submitted to IMI. All form Cs have now been received and we await feedback on both the financial & scientific portions
- Version 3.0 of the Description of Work has been submitted to IMI and we are awaiting final approval of v3.2_17 Feb 2016.
- Interim Review Responses – no feedback yet from IMI.
- Proposal for new members to be added to the Consortium will be discussed at next SC and then proposed to the GA. Stay tuned.

Publications Update

Reminder to use the mandatory IMI funding statement and send all papers to the PO prior to submission as per the Project Agreement

WP2 – Knowledge & Data Management

- F2F meeting at SCAI on 15th March: Extensive discussion on technical details for the integration of tools
  a) Web semantics: apiNAMOTY as query builder for tranSMART
  b) Data visualization : BEL sub-networks in apiNATOMY tiles representing brain regions
  c) Circuit board : Connectivity map(connecting tiles via shared genes present in contextual BEL subnetworks)
- Follow up developers TELCO on integration of tools for AETIONOMY was held on the 23rd and another developer meeting suggested for end of April and follow up documents uploaded to BSCW.
- Backup frequency for RedCap and ticketing system increased to daily.
- tranSMART backup set to weekly(Sun) and to be done manually after changes earlier during the week.

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WP3 – Knowledge Integration & Mining

- EMC & UCL are focusing on the extraction of connectome data from ADNI & PPMI radiology data;
- Sanofi, KI & UCL are following up on the principal component analysis of PPMI clinical data presented in Bonn last month;
- Christine Girges starts full-time on AETIONOMY at UCL on April 4th to co-ordinate the neuroanatomical map of clinical indices;
- Sanofi, UCB & KI continue to analyse PPMI data stratification linking SNPs with clinical and radiological aggregate data;
- SCAI will share a neuroMMSIG list of 10 AD and 10 PD mechanisms on April 15th, ahead of the WP2-WP3 hackathon at KI on April 25th.

WP4 – Ethical & Legal Governance

(WP4) is continuing to monitor and manage the requirements for data sharing in the project.
It is also liaising with the EPAD project over securing future access to the data and samples that will be collected there in order to carry out analysis for AETIONOMY purposes. In addition, on the data security side, it is participating in ongoing discussions with the EFPIA partners on coordinating the required AETIONOMY database security audit.
The WP4 partners LUH and Alzheimer Europe continue to cooperate closely on the ethical issues surrounding the collection of prospective data and samples in the WP5 observational study, and are planning a joint dissemination article in the area for submission to a peer-reviewed medical ethics journal."

WP5 – Clinical Validation

- EPAD collaboration to recruit AD subjects' group is moving forward. A data and samples sharing agreement needs to be set up between both consortia.
- WP3 & 5 met on 15th March in Fraunhofer to discuss hypothesis generation with the clinicians. Minutes to be available soon.
- An amendment of the AETIONOMY protocol is currently prepared in order to align both protocol regarding clinical and neuropsychological assessments

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Recruitment Update				
Site	**PD**	**AD**	**Controls**	**Screening**
ICM	22	0	2	0
KI	7	0	2	0
UKB	0	0	0	Not started
Neurorad	0	4	8	16
Oxford	0	0	0	Not started
EPAD	0	0	0	Not started
TOTAL	**29**	**4**	**12**	**16**

Upcoming Meetings

- SC Teleco - 15th April 2016 from 11 to 12h00
- WP 2 & 3 – at KI in Stockholm – 25th April 2016
- WP 3 & 5 – at ICM in Paris – 23 May 2016
- WP 3 & 5 – at TBC – October 2016
- 3rd General Assembly – at Sanofi, Paris on 1 & 2 Dec 2016
- AD/PD – Vienna, - March 29 – April 2 2017

The AETIONOMY Family grows!

Congratulations to Matt Page (UCB)!
We wish Cecile Gaudebout (ICM) and Shweta Bagewadi (Fraunhofer) good luck for their imminent arrivals.

Deliverables due to IMI in April 2016 (or outstanding)

- D5.2.4 : At least one patient has been recruited in each clinical centres (M25)
- D5.1.3 : Minutes from the choice of biomarker for final protocol meeting (M27)

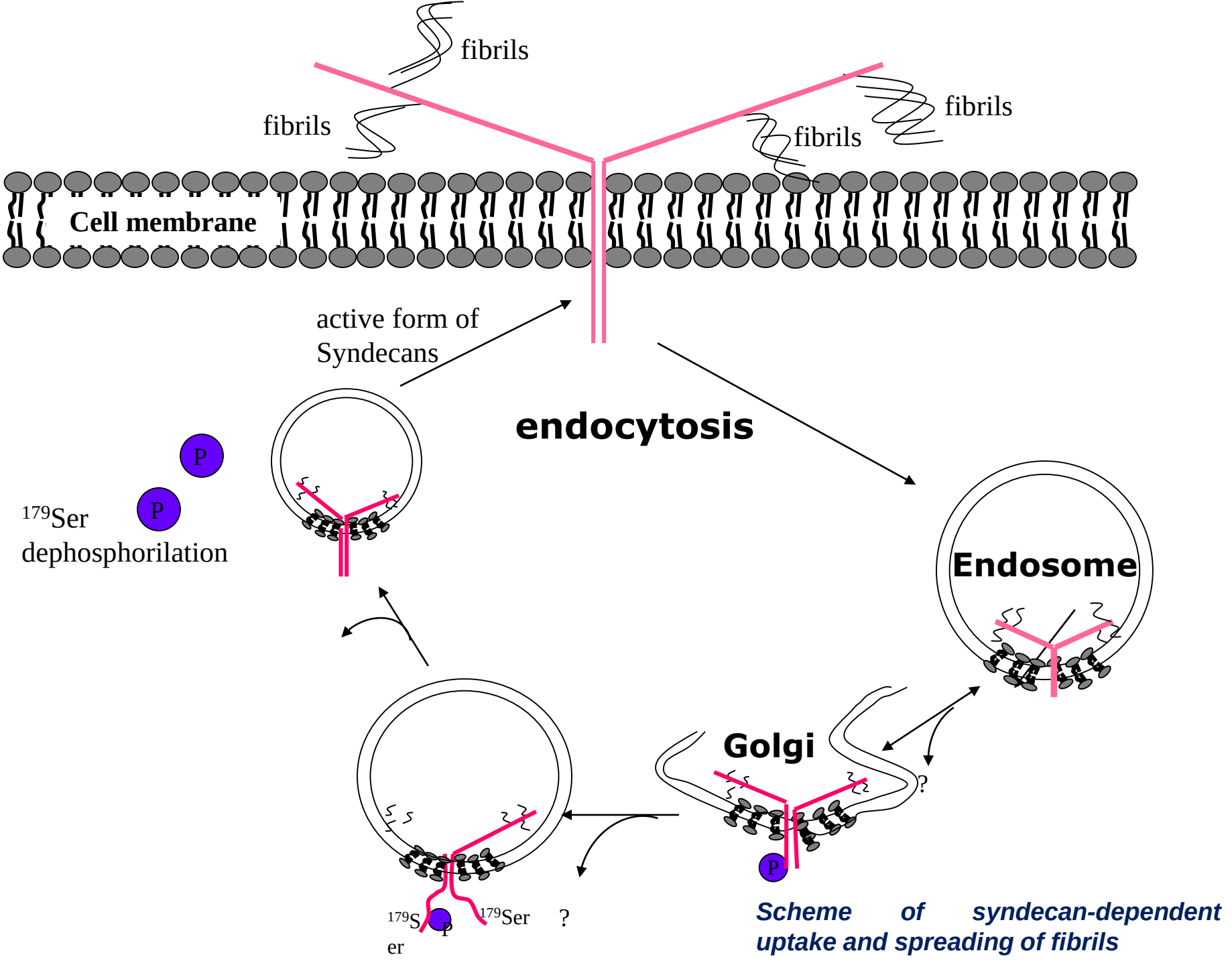
WP5.4
PHI update – the 2nd hypothesis

Tamás Letoha
Pharmacoidea Ltd.

New hypothesis: syndecan-dependent spreading of aggregates

- **Background:** Recent evidence suggests that aggregates of misfolded proteins such as tau and α-synuclein (α-syn), have the capacity to spread from one cell to another and thereby induce neurodegeneration. A thorough understanding of the molecular and cellular mechanisms underlying propagation and prion-like spreading of oligomeric and/or fibrillar aggregates is likely to be a rich source of innovative targets for the development of novel disease modifying therapies.

- **Hypothesis:** Considering the evidence for heparan sulfate proteoglycans (HSPGs) mediated the spreading and intracellular transport of misfolded proteins (including ß-amyloid, α-synuclein and tau, Funk et al., J Biol Chem. 2015), PHI proposes that the syndecan family of proteoglycans as key targets in the seeding/spreading mechanism of aggregates. Several aspects of HSPG dependent cellular uptake will be assessed, including: i) membrane attachment and interaction with HSPGs, ii) internalization and related signaling pathways, iii) intracellular transport, iv) endosomal sorting & release. Uptake assays will be first studied in cell lines specific/expressing the certain HSPG or its mutant variants, later more general and patient derived cell lines will be utilized. To test these hypothesis, PHI made the following preparatory steps:
  - Cloned a GFP tagged tau to be expressed in various cell lines
  - Began cloning human α-synuclein
  - Developed several syndecan overexpressing and mutant cell lines



Scheme of syndecan-dependent uptake and spreading of fibrils

PHARMACOIDEA

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