

SyDAD

Synaptic Dysfunction in Alzheimer Disease www.sydad.eu

SyDAD is a European Training Network, sponsored by Horizon 2020 Marie Skłodowska Curie Actions that will support 15 Early Stage Researchers (ESRs, PhD students).

SyDAD network offers an interdisciplinary and innovative PhD programme with cutting edge methodologies, an excellent training programme, international exchanges, and a translational and collaborative orientation.

The aims of SyDAD are

to train 15 Early Stage Researchers to a new generation of researchers with an innovative mindset and full understanding of the requirements of academia and pharmaceutical companies, as well as clinical and societal challenges associated with Alzheimer disease;

to, through a collaborative research programme, elucidate how the different pathways underlying synaptic dysfunction in Alzheimer Disease relate to each other, to identify novel pharmaceutical targets, and to create a drug discovery platform for future implementation of the results.

SyDAD will recruit 15 ESRs. Recruitment starts in September 2015 and will be advertised on EURAXESS <http://ec.europa.eu/euraxess/>. Indicative start date is January-April 2016. For eligibility rules see the last page of this document.

Participating organisations are Karolinska Institutet, Stockholm; University of Bordeaux; University of Milano; Deutsches Zentrum für Neurodegenerative Erkrankungen (DZNE), Bonn; Janssen Pharmaceutica, Beerse; and **Axon Neuroscience, Bratislava**.

Collaborations, secondments, and training will also take place at Gothenburg University, Astra Zeneca Translational Center, AlzeCure Discovery, Serendipity Innovations, and Alzheimer Europe.

Further information of the programme is provided below or by the respective site-responsible scientists:

Karolinska Institutet, Stockholm
University of Bordeaux
University of Milano
DZNE, Bonn
Janssen Pharmaceutica, Beerse
Axon Neuroscience, Bratislava

susanne.frykman@ki.se (SyDAD project manager)
christophe.mulle@u-bordeaux.fr
monica.diluca@unimi.it
eckhard.mandelkow@dzne.de
AEBNETH@its.jnj.com
novak@axon-neuroscience.eu

Summary of the SyDAD European Training Network

There is an urgent need for finding novel approaches to promote drug discovery for Alzheimer Disease (AD). Despite an overwhelming increase of dementia costs and an aging population, there is currently no disease-modifying therapy on the market and we are facing a large number of failed clinical trials and the decisions of several big pharmaceutical companies to discontinue their nervous system R&D programmes. Increased collaboration between academia, providing a huge knowledge base; and the private sector, providing the understanding of the drug discovery value chain, would provide a novel approach to find cures for dementia.

The “*Synaptic Dysfunction in Alzheimer Disease*” (SyDAD) project will significantly contribute to this innovative approach by training a new generation of researchers with experience and full understanding of the requirements of academia, pharmaceutical companies, as well as the clinical and societal challenges associated with AD. These *early-stage researchers* (ESRs) will thus have excellent interdisciplinary career opportunities.

The research programme will focus on *synaptic dysfunction*, the main connection point between pathology and cognitive decline in AD. Given the complementary expertise of SyDAD participants, we will have excellent opportunities to progress in the understanding how the different pathways underlying synaptic dysfunction in AD relate to each other and to identify novel pharmaceutical targets. To enable future implementation of the research findings into clinical trials, we will also utilise the expertise of the companies and the clinics in the network to develop a drug discovery platform.

The ESRs will be trained in this environment, provided with the three sides of the Knowledge Triangle (Education, Research, and Innovation) and with a mind-set for future commercial and clinical utilisation of their research findings. Apart from the innovative and collaborative approach of the research programme, the ESRs will also be provided with a training programme where state-of-the-art methodology, innovation, and transferable skills are the key components.

The trained ESRs, the participating organisations, and their extended networks will have excellent opportunities to provide a solid ground to *tackle one of the major societal challenges of our century: Finding therapies to decrease the suffering and economic burden of AD patients.*

Key assets of the project include:

- World-class complementary expertise in synapse biology (UB, UMIL)¹; pre-clinical AD research including A β (KI, UMIL, UB), Tau (DZNE, AN, JPNV), and mitochondria (KI, DZNE, UB), clinical AD research (KI), drug discovery (JPNV, AN, AZ, AC), and biomarkers (GU, AZ).
- Availability of a diverse array of animal models—including models unique to the network—which will allow delineation of how the different pathways relate to each other.
- Extensive experience in translating basic research findings to innovation and implementation, including clinical trials. Participants include AN (an academic-based SME that has managed to take a basic research finding into clinical trials), SI (a company specialising in refining research-based innovations into ventures) and the KI clinical trial centre for AD.
- Access to the newly established Bordeaux School of Neuroscience, a unique international training laboratory equipped for modern and cutting-edge neuroscience.
- Access to cutting-edge equipment and expertise, including electrophysiology in slices and *in vivo*, optogenetics, cellular imaging (super-resolution microscopy, two photon microscopy, confocal and spinning disk microscopy, Ca²⁺ imaging) and mass spectrometry.
- Close collaboration with the clinics and access to AD patient material, including brain, CSF, and blood samples.

¹ Participating organisations: KI, Karolinska Institutet; UB, University of Bordeaux; UMIL, University of Milano; DZNE, Deutsches Zentrum für Neurodegenerative Erkrankungen; JPNV, Janssen Pharmaceutica NV; AN, Axon Neuroscience; SI, Serendipity Innovations; AE, Alzheimer Europe

SyDAD PhD projects

Karolinska Institutet, Stockholm (Contact person Susanne Frykman, susanne.frykman@ki.se)

1. Synaptic proteome and A β interactome in AD brain and mouse models.
2. Targeting Cholesterol homeostasis and synaptic maturation.
3. Mitochondria stabilisers and synaptic function in AD.
4. EEG as a functional central biomarker in AD.

University of Bordeaux (Contact person Christophe Mulle, christophe.mulle@u-bordeaux.fr)

5. Role of APP in presynaptic mechanisms.
6. Mitochondrial dysfunction in relation to synaptic function in mouse models of Alzheimer's disease.
7. Plasticity of local hippocampal circuits in mouse models of Alzheimer's disease: relation with episodic memory encoding.

University of Milano (Contact person Monica di Luca, monica.diluca@unimi.it)

8. Linking actin-dependent dendritic spine remodelling and ADAM10 activity in AD: the role of CAP2.
9. A spine to nucleus signalling pathway in Alzheimer's disease.
10. Development of cell permeable peptides capable of increasing ADAM10 activity

Deutsches Zentrum für Neurodegenerative Erkrankungen (DZNE), Bonn
(Contact person Eckhard Mandelkow, eckhard.mandelkow@dzne.de)

11. Cascade linking A β and tau-dependent toxicity to synapse loss.
12. Loss-of-function genetic screening using CRISPR/Cas9.
13. Synaptic plasticity and calcium remodeling.

Janssen Pharmaceutica, Beerse (Contact person Andreas Ebneith AEBNETH@its.jnj.com)

14. The roles of physiological and pathophysiological tau in synapse function and morphology.

Axon Neuroscience, Bratislava

(Contact person Michal Novak, novak@axon-neuroscience.eu)

- 15. Rescue of truncated Tau-mediated synaptic dysfunction *in vivo*.**

Marie Skłodowska Curie Actions, European Training Networks Eligibility Criteria

Early Stage Researchers (ESR)

ESR shall, at the time of recruitment by the host organisation, be in the first four years* (full-time equivalent research experience) of their research careers and have not been awarded a doctoral degree.

Duration of appointment: 3 - 36 months (typical appointment: 36 months)

* *counted from the date on which the researcher obtained a degree entitling him/her to embark on a doctoral programme (in the country in which it was obtained or in which s/he is recruited) — even if the doctorate was never started or envisaged*

Mobility rule

The researcher must not have resided or carried out his/her main activity (work, studies, etc.) in the country of his/her host organisation for more than 12 months in the 3 years immediately prior to his/her recruitment. Short stays, such as holidays, are not taken into account.

Estimated salary

The ETN will cover up to 36 months for a maximum of 15 researchers. Note that the estimates might change.

Per researcher-month in Slovakia:

Living allowance: €2565 (including social security costs and tax)

Mobility allowance: €600

Family allowance: €250 (only for ESRs who have a family)