EEA and Norway Grants 2009-2014
Programme LV05
"Research and Scholarship Programme"

RESEARCH ACTIVITY

INTERIM REPORT NO. / FINAL REPORT
REPORTING PERIOD 01.01.2017. –30.04.2017.

Contract No.	**NFI/R/2014/023**

Title of the Project:

Benefits and detrimental effects of sequence variants of Amyloid-β: towards the use of small peptides for aggregate dissolution therapy in dementia

Submitted by *the Organic Synthesis Institute of Latvia (OSI)*

In consortium with: *Latvijas Universitāte (LU), University of Oslo (UiO)*

Type of research	☒ basic
Thematic area	☒ health
Sub-field	P351 Structural Chemistry B210 Histology, Histochemistry, Tissue Culture B520 General Pathology B740 Pharmacological Sciences B650 Psychiatry

II. Implementation progress

2.1. INDICATORS.

Mandatory outcomes and outputs generated by the Project

Outcome 1: Increased research cooperation between Norway and the Beneficiary State	*Outcome indicator:* Number of joint publications authored by project participants from both BS and DS (published or accepted for publication) **Target total: 4** **Actual Interim Report 1: 0** **Actual Interim Report 2: 0** **Actual Interim Report 3: 0** **Actual Final Report: 4** **ACTUAL TOTAL ALL REPORTS: 4**
	Output 1: Institutional cooperation at the level of higher education and science between Latvia and Norway *Output 1 indicator:* Number of cooperating research institutions within the programme **Target total: 3** **Actual Interim Report 1: 3** **Actual Interim Report 2: 3** **Actual Interim Report 3: 3**

	Actual Final Report: 3 **ACTUAL TOTAL ALL REPORTS: 3**
Outcome 2: Strengthened research capacity in the Beneficiary State and increased application of research results through research cooperation between Norway and the Beneficiary State	*Outcome indicator:* Number of published international peer-reviewed publications **Target total: 4** **Actual Interim Report 1: 0** **Actual Interim Report 2: 1** **Actual Interim Report 3: 6** **Actual Final Report: 2** **ACTUAL TOTAL ALL REPORTS: 9**
	Output 1: Increased application and dissemination of research results internationally *Output 1 indicator:* Number of international publications in preparation **Target total: 4** **Actual Interim Report 1: 2** **Actual Interim Report 2: 2** **Actual Interim Report 3: 4** **Actual Final Report: 3** **ACTUAL TOTAL ALL REPORTS: 11**
	Output 2: Increased training of early stage researchers *Output 2 indicators:* 2.1.Number of PhD students and Postdocs trained within the projects **Target total: 8** **Actual Interim Report 1: 1 (Jolanta Upīte)** **Actual Interim Report 2: 9 (Jolanta Upīte, Vladimirs Piļipenko, Ulrika Beitnere + 6 students)** **Actual Interim Report 3: 2 (Vladimirs Piļipenko, Jolanta Upīte)** **Actual Final Report: not applicable** **ACTUAL TOTAL ALL REPORTS: 12** 2.2.Percentage of female PhD students and postdocs trained within the projects **Target total 50%** **Actual Interim Report 1: 100%** **Actual Interim Report 2: 85%** **Actual Interim Report 3: 50%** **Actual Final Report: not applicable** **ACTUAL TOTAL ALL REPORTS: >50%** **One should keep an eye on gender equality also for men esp in Latvias science!**
	Output 3: Number of scientific publications (published or approved publication) Output 3 indicator: Number of scientific publications: **Target total: 4** **Actual Interim Report 1: 0** **Actual Interim Report 2: 1** **Actual Interim Report 3: 6** **Actual Final Report: 3** **ACTUAL TOTAL ALL REPORTS: 10**

Optional project outcomes and outputs

Outcome 1: Strengthened research capacity in Beneficiary States and increased application of research between Norway and the Beneficiary	Output 1.4.: PhD student exchange Output 1.4. indicator: indicator: Number of students exchanged between the countries **Target total:8** **Actual Interim Report 1:1** **Actual Interim Report 2:8**

States.	**Actual Interim Report 3:2** **Actual Final Report: 0** **ACTUAL TOTAL ALL REPORTS: 12**

2.2. DESCRIPTION OF PROJECT ACTIVITIES

Work package No.1: Definition of aggregation properties between different Aβ species *in vitro*

Progress reached so far in %: **100** (*Please assess the overall progress of the Work package up to date in %*)

Description (*work performed during the reporting period*):

In case of any derogations from the scheduled provisions, including the time schedule, please provide an explanation)

The overall goal of this project was to develop the new strategy for the treatment of the Alzheimer's disease (AD). As stated in the previous reports, the OSI researchers have constructed a new expression system for over-expression of Aβ, far superior previous published protocols in terms of yields. The new Aβ construct, where we take advantage of a solubility tag from dragline spider silk (hereafter denoted NT*) have been optimized in terms of production and purification. This new construct has been used as a template for new clones such as $hA\beta_{40}$, $hA\beta_{42}$, $hA\beta_{2\text{-}40}$, $hA\beta_{2\text{-}42}$, $hA\beta_{40}A2V$, $hA\beta_{42}A2V$, $hA\beta_{1\text{-}16}$, $hA\beta_{1\text{-}16}A2V$. We have also taken advantage of the NT* tag to prevent Aβ from aggregating and have been expressed and purified $NT^*A\beta_{42}WT$ and $NT^*A\beta_{42}A2V$ fusion constructs that will be used in Work package 2. Techniques used for molecular cloning includes PCR, agarose gels, gel extraction kit etc. All new constructs are sent for sequencing to ensure correct nucleotide sequence. We have further on optimized purification protocols for $hA\beta_{40}$, $A\beta_{42}$, $A\beta_{40}A2V$ and $A\beta_{42}A2V$ peptides from LB and M9 medium, as they show different propensities to aggregate during the purification. Based on the optimized protocol, ^{15}N labelled $A\beta_{40}A2V$ was produced and 2D ^{15}N HSQC, 3D-^{15}N edited NOESY and TOCSY spectra were acquired to assign the ^{15}N and ^{1}H chemical shifts of the peptide, which will be necessary to characterize the peptide dynamics and probe the conformation of high molecular, NMR invisible species. Based on these assignments, we have confirmed previously Thioflavin T measurements with NMR spectroscopy. We have also used solid state NMR to study fibril morphology of $A\beta_{40}$ A2V. Although, so far, these experiments have not yet been successful due to polydisperse samples and optimization is ongoing. Moreover, we have been working with ITC experiments to determine the $A\beta_{40}$ peptide affinity for Cu^{2+} ions.

One manuscript is in preparation with data from the new constructs, one article is published describing the NT* solubility tag and we have also submitted a review article about Aβ and Alzheimer's disease.

Key expert: Dr. Henrik Biverstål

Other experts involved: Rihards Aleksis, Dr Kristaps Jaudzems

Equipment: (not applicable, all needed equipment available)

Other: (not applicable)

Output No. 1.1.: 2 value reached: 2; Month: 24
Output No. 1.2.: 2 value reached: 2; Month: 24
Output No. 1.3.: 2 value reached: 2; Month: 24
Output No. 1.4.: 1 value reached: 0; Month: 6
Output No. 1.4.: 1 value reached: 0; Month: 18

Work package No. 2: Effectivity of the new Aβ peptide species *in vivo* and *in vitro*

Progress reached so far in %: **100** (*Please assess the overall progress of the Work package up to date in %*)

Description (*work performed during the reporting period*):

In case of any derogations from the scheduled provisions, including the time schedule, please provide an explanation)

As we stated in the previous report, the aim of the collaboration between three institutions (LU, OSI and UiO) is to create a novel approach in the area of AD therapy. This approach is based on the possibility of dissolving beta-amyloid aggregates in the central nervous system and providing their elimination from the brain through blood circulation. There were regular monthly based *Skype* discussions between Norwegian partner Prof. J. Pahnke and University of Latvia partner Prof. B. Jansone about work progression regarding Work package 2. Also, we have had extra project meeting at the TransportDEMENTA1 and 2 meetings in December 2015 in Oslo and September 2016 on Hurtigruten. The final project meeting will be helt at the TransportDementia3 meeting in Sept 2017 in Svolvær.

The LU partner has purchased lab animals (ABCB1-hmAG etc mice) and Alzet pumps for the mouse surgery in 2015/2016. During this period, LU researchers have continued to perform *in vivo* models using behavioural tests (like water-maze etc) and *ex vivo* methods (Western blot test and immunohistochemistry). Methodology has been established and reference compounds are being tested and obtained were introduced into the manuscripts that are going to be published. Research project is performed in synergy with the Scholarship Activity 'Enhancing human capital and knowledge in health science by institutional cooperation and mobility between the University of Latvia and three Norwegian universities' No. EEZ/NFI/S/2015/019.

In the first half of the 2016, 6 students from the University of Latvia Faculty of Medicine, 2 PhD students exchanged to the University of Oslo, Department of Neuro-/-Pathology (PAT) Translational Neurodegeneration and Neuropathology Lab has been done in order to obtain skills high quality skills in animal database acquisition, surgery with Alzet pumps on mice and method validation. Staff mobility from University of Latvia to University of Oslo was carried out: a) postdoctoral researcher Ulrika Beitnere, PhD, joined Prof. Pahnkes lab for 5 weeks to learn about mouse housing and breedings, participate and conduct stereotactic mouse surgery, infusions and ex vivo analyses: IHC, ELISA, to learn new protocols and approaches, to participate in seminars organized at the UiO. Project leader from the University of Latvia prof. Baiba Jansone was visiting prof. J. Pahnke lab to evaluation of the progress and future work plan of the research project and to work on the future collaborations plans between UL and UiO about the participation in research calls, for example, ERA-NET Neuron and others. The main purpose for this moblity was to enhance human capital and knowledge base at the Faculty of Medicine, University of Latvia (UL) and increasing the institutional cooperation with the University of Oslo (UiO) Department of Neuro-/Pathology (PAT), Translational Neurodegeneration and Neuropathology Lab (Head of the Department: Prof. J. Pahnke).

In the laboratory of the Norwegian partner Prof. Pahnke, the *in vivo* experiments have been performed. Jolanta Upite, a PhD student from University of Latvia spent in total 9 months at the UiO (2016-2017) in the frame of the mobility agreement between the two institutions to perform operations.

Different experimental setups were defined: *i)* early-long group, *ii)* late-long group. In case of the early-long group, 6 different beta-amyloid peptides (wild type human hAβ(WT)1-6, A to T mutated human hAβ(A2T)1-6, A to V mutated human hAβ(A2V)1-6, wild type mouse mAβ(WT)1-6, A to T mutated mouse mAβ(A2T)1-6 and A to V mutated mouse mAβ(A2V)1-6) were dissolved in artificial cerebrospinal fluid (aCSF) and loaded into Alzet pumps (model 2006), 2 pumps/peptide. These pumps- using the new method to fix the cannula- were implanted into 50 days old male APP/PS1 +/0 mice by stereotactic surgery. In case of the late-long group, the 6 different beta-amyloid peptides were loaded into model 2004 Alzet pumps and implanted into 75 days old male APP/PS1 +/0 mice by stereotactic surgery. After the surgery, the animals were placed into separated cages and were monitored for 50 days (early-long group) or 25 days (late-long group). Animals showed normal behavioural without any sign of pain/discomfort caused by carrying the implanted pump. At the age of 100 days, mice were sacrificed and brains were collected and stored in buffered 4% PFA solution for 3 days and then in 1x PBS – 0.01% Na-azide solution for paraffin embedding and immunohistochemistry. Processing of the brains cutting and staining with 4G8 antibody was performed. Statistical analyses were performed to reveal the effect of the different peptides on the amount of plaques. In parallel, full-length (42 amino acids) beta amyloid peptides (wild type and A2V mutant) tagged with spider-silk protein have been expressed and purified by the OSI partner Dr. Henrik Biverstål. These peptides were loaded into Alzet pumps (model 2006 and 2004) and implanted into 50-days-old and 75-days-old male APP/PS1 +/0 mice, respectively. Brains will be collected and processed as described above.

At the University of Latvia (Faculty of University, Department of Pharmacology) stereotactic mouse surgery

and miniosmotic pump implantation with later *in vivo* tests in rodents have done to evaluate cognition and memory performance in water-maze test, that followed by the evaluation of brain biomarkers (for the neuroinflammation, brain plasticity etc.) by immunohistochemical analysis, polymerase chain reaction (PCR) and Western blot method.

Key expert: Prof. Dr. med. Dr. rer. nat. Jenss Pānke (Jens Pahnke), E.F.N.

Key expert: Prof. Baiba Jansone

Other experts involved: Prof. Vija Kluša

Equipment: (not applicable, all needed equipment is available)

Other: (not applicable)

Output No. 1.1.: 2 value reached: 4; Month: 24
Output No. 1.2.: 2 value reached: 2; Month: 24
Output No. 1.3.: 2 value reached: 4; Month: 24

Output No. 1.4.: 2 value reached: 1; Month: 6 (1 student)
Output No. 1.4.: 2 value reached: 8; Month: 12 (8 students)
Output No. 1.4.: 2 value reached: 2; Month: 18 (2 students)

2.3. SUMMARY OF PROJECT ACTIVITIES (*work performed during reporting period*) – PUBLISHABLE PART

Alzheimer's disease (AD) is a widespread neurodegenerative disease. Around 2040 the number of patients suffering from AD will be about 80 million. Up to now a specific therapy for AD is not available and stands as a major challenge for the researchers. The most intensively studied pathological hallmark of AD is extracellular aggregated beta-amyloid peptide senile plaques. Progressive deponation of mentioned pathologically folded proteins and their accumulation in the brain tissues causes a massive neural dysfunction that leads to the dramatic decrease in overall functioning of the central nervous system. The aim of the collaboration between three institutions (LU, OSI and UiO) is to create a novel approach in the area of AD therapy. This approach is based on the possibility of dissolving beta-amyloid aggregates in the central nervous system and providing their elimination from the brain through blood circulation. OSI researchers performed *in vitro* assays (mainly NMR and Thioflavin T) for interaction studies between hAβ and Aβ fragments (hA$\beta_{1\text{-}6}$, hA$\beta_{1\text{-}6}$A2V, hA$\beta_{1\text{-}6}$A2T, hAβ_{40}A2V, hAβ_{42}A2V, mAβ_{42}, hAβ_{42}R5G, hAβ_{42}Y10F and hAβ_{42}H13R have been tested). We have also made two constructs based on Aβ(A2V)$_{1\text{-}6}$ with two different cell penetrating peptides tags to assist passage over the blood brain barrier, TAT-Aβ(A2V)$_{1\text{-}6}$ and AntP-Aβ(A2V)$_{1\text{-}6}$. A new method for overexpression of Aβ and variants thereof has also been established where we make use of a solubility tag from spider-silk protein. Results obtained during the project have been compiled into one published article, one manuscript and one submitted review article from OSI.

LU researchers are investigating the short sequence peptides using *in vivo* models (by implementing behavioural and cognitive methods) and *ex vivo* methods (immunohistochemical staining and western blotting) in tight collaboration with both other partners: Organic Synthesis Institute of Latvia and University of Oslo. To reveal the positive effects of different mutated amyloid beta peptides, *in vivo* experiments (surgical implantation of Alzet pumps carrying different amyloid beta peptides) are taking place in the laboratory of the Norwegian partner Prof. Jens Pahnke. Western blot method validation for the assessment of the toxic amyloid beta 42 and 40 in the transgenic mice brain with 6E10 antibody that recognizes both: APP protein (~100 kDa) and amyloid beta 42 and 40 (~4 kDa) has been performed. Research project is being performed in synergy with the Scholarship Activity 'Enhancing human capital and knowledge in health science by institutional cooperation and mobility between the University of Latvia and three Norwegian universities' No. EEZ/NFI/S/2015/019.

Staff mobility (2 PhD students and 1 postdoctoral researcher exchange to the University of Oslo, Department of Neuro-/-Pathology (PAT) Translational Neurodegeneration and Neuropathology Lab) has been done in order to perform project experiments.

2.4. TIME SCHEDULE (*actual*)

No	Title of Work package	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4
		1st REPORT								2nd REPORT							3rd REPORT						FINAL REP.			
1	Definition of aggregation properties between different Aβ species in vitro	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
2	Effectivity of the new Aβ peptide species in vivo and in vitro	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

2.5. DISSEMINATION ACTIVITIES of RESEARCH RESULTS

No	Activity	Description (topic, aim, communication tools)	Target groups	Time-frame	Venue	Organiser	Partners/parties involved	Contact person	Assessment of the activities
1	Meeting of The Latvian Academy of Sciences	Agenda of the meeting, presentation	Researchers, students, academics, general public	June 15, 2017	Building of the Latvian Academy of Sciences	The Latvian Academy of Sciences, section	LU, OSI, UIO	Baiba Jansone	http://85.254.195.100/index.php?option=com_content&task=view&id=3814&Itemid=71
2	Meeting of the Latvian Society of Pharmacology	Agenda of the meeting, Presentation	Researchers, students, academics	May 10, 2017	LU DAC, Riga	Latvian Society of Pharmacology	LU, OSI, UIO	Baiba Jansone	Jolanta Upīte's Presentation
3	„The EEA Scholarships Programme – a Plus in Education"	Agenda of the meeting, Presentation	general public/ researchers/ students/ academics	March 24, 2017	Bucharest, conference hall in the Hotel Sheraton.	IZM and VIAA	LU, OSI, UIO	Baiba Jansone	Jolanta Upīte's Presentation
4	2nd meeting of Baltic Physiological Societies	Presentation, Abstract	Researchers, students, academics	March 24, 2017	University of Kaunas	Baltic Physiological Societies	LU	Baiba Jansone	Presentation, Abstract
5	75th Annual Conference of the University of Latvia	Presentation, Abstract	Researchers, students, academics	February 24, 2017	LU DAC, Riga	University of Latvia	LU, OSI, UIO	Baiba Jansone	Jolanta Upīte's Presentation
6	Conference: AD/PD™ 2017	Abstract	Researchers, students, academics	March 29-April 2, 2017	Vienna, Austria	AD/PD™ 2017, Committees	LU	Baiba Jansone	Abstract
7	TransportDEMENTIA1 meeting	presentations	Researchers, students, academics	Dec 2015	Oslo, Holmenkollen hotel	Jens Pahnke	OUS, UiO, NFR	Jens Pahnke	http://pahnkelab.eu/transportdementia-meetings/
8	TransportDEMENTIA2 meeting	Presentations	Researchers, students, academics	Sep 2016	Tromsø - Kirkenes, Hurtigruten boat	Jens Pahnke	OUS, UiO, NFR	Jens Pahnke	http://pahnkelab.eu/transportdementia-meetings/

9	TransportDEMENTIA3 meeting	presentations	Researchers, students, academics	Sep 2017	Svolvær, Lofoten	Jens Pahnke	OUS, UiO, NFR	Jens Pahnke	http://pahnkelab.eu/transportdementia-meetings/

2.6. PUBLICITY MEASURES

No	Activity	Description (topic, aim, communication tools)	Target groups	Date and place	Organiser	Partners/parties involved	Contact person	Assessment of the activities
1	results publication (activity Nr.1.0, 5.0)	Project activities, results, online	general public/ researchers / students	January – April 2017	OSI	researchers	Henrik Biverstål	access to the OSI homepage: http://www.osi.lv/projekti/projekts-nr-nfir2014023-dazadu-beta-amiloida-peptidu-sekvencu-efekti-fokuss-uz-iso-peptidu-pielietojuma-iespejam-demences-terapija/
2	Press release about collaboration and meeting in Bucharest (activity Nr.3.0)	Project activities, partners collaboration, results, online	general public/ researchers /academics / students	March 23-24, 2017	LU	general public/ researchers	Baiba Jansone	http://www.mf.lu.lv/zinas/t/44203/ LU un MF Facebook, Twitter
3	results publication (activity Nr. 5.0)	Project activities, partners collaboration, results, online	general public/ researchers / students	April 28, 2017	LU	researchers	Baiba Jansone	access to the LU homepage: http://www.lu.lv/par/projekti/eez-norvegija/petnieciba/peptidi/
4	Seminar (activity Nr. 4.0)	Project activities, partners collaboration, results, online	researchers / students / academics	March 17, 2017	LU	Researchers, students, academics	Baiba Jansone	Protocol of the seminar

2.7. SCIENTIFIC PUBLICATIONS

No	Title	Authors	Name of journal	Citation index	Submitted/ Accepted/ Published	Link (if relevant)
1	Atypical 1,4-dihydropyridine derivatives, an approach to neuroprotection and memory	Vija Klusa	Pharmacological Research 2016	4.408	Published	http://www.sciencedirect.com/scie

	enhancement (1.1.and 1.3.)					nce?_ob=ArticleListURL&_method=list&_ArticleListID=-1007516255&_sort=r&_st=13&view=c&md5=30d6107501f53bf9ae25b5bf43475ed5&searchtype=a
2	*Sideritis spp.* Extracts Enhance Memory and Learning in Alzheimer's β-Amyloidosis Mouse Models and aged C57Bl/6 Mice (1.1. and 1.3.)	Hofrichter J *et al.*	J Alzheimers Dis 2016	3.920	Published	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4981905/
3	The choroid plexus in health and in disease: dialogues into and out of the brain (1.1. and 1.3.)	Marques F *et al.*	Neurobiol Dis 2016	4.856	Published	http://www.sciencedirect.com/science/article/pii/S0969996116302030
4	Revisiting rodent models: *Octodon degus* as Alzheimer's disease model? (1.1. and 1.3.)	Steffen J *et al.*	Acta Neuropathol Commun 2016	11.360	Published	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5002178/
5	Lunasin is a redox sensitive intrinsically disordered peptide with two transiently populated α-helical regions. (1.1. and 1.3.)	Aleksis R *et al.*	Peptides 2016	2.535	Published	http://www.sciencedirect.com/science/article/pii/S0196978116301838
6	Memory-enhancing and brain protein expression-stimulating effects of novel calcium antagonist in Alzheimer's disease transgenic female mice (1.1. and 1.3.)	Jansone B *et al.*	Pharmacol Res 2016	4.816	Published	http://www.sciencedirect.com/science/article/pii/S1043661816302730
7	Dementia-related Bri2 BRICHOS is a versatile molecular chaperone that efficiently inhibits Aβ42 toxicity in Drosophila (1.1. and 1.3.)	Poska H *et al*	Biochemical J	3.562	Published	https://www.ncbi.nlm.nih.gov/pubmed/27514716 or http://www.biochemj.org/content/473/20/3683
8	Three activities from one	Chen G *et*	Nat Struct Mol	12.595	Submitted	

	chaperone domain: client specificity of Bri2 BRICHOS is governed by quaternary structure (1.1. and 1.3.)	*al.*	Biol 2017			
9	Expression of endogenous mouse APP modulates β-amyloid deposition in hAPP transgenic mice (1.1., 1.2. and 1.3.)	Steffen J *et al.*	Acta Neuropathol Com 2017	11.360	published	https://actaneurocomms.biomedcentral.com/articles/10.1186/s40478-017-0448-2
10	Improved method for cannula fixation for long-term intracerebral brain infusion (1.1., 1.2. and 1.3.)	Sike A. *et al.*	Journal of Neurosci Methods 2017	2.554	Submitted (under revision)	
11	Alcheimers slimības izpētes aktualitates (1.2. and 1.3.)	Jansone B *et al.*	Latvijas Ārsts 2017	none	published	See attachment
12	Efficient protein production inspired by how spiders make silk (1.1. and 1.3.)	Kronqvist N *et al.*	Nature Com 2017	12.124	published	https://www.nature.com/articles/ncomms15504
13	Structural studies of amyloid-β peptides: unlocking the mechanism of aggregation and the associated toxicity (1.1., 1.2. and 1.3.)	Aleksis *R et al.*	Biochimie 2017	3.112	Submitted (under revision)	

2.8. SYNERGY MEASURES (detailed description including measurable indicators)

Research project is performed in synergy with the Scholarship Activity 'Enhancing human capital and knowledge in health science by institutional cooperation and mobility between the University of Latvia and three Norwegian universities' No. EEZ/NFI/S/2015/019; host lab in Norway: Prof. Jens Pahnke lab at the University of Oslo:

1) PhD student exchange: Jolanta Upīte. Duration of her scholarship is 9 months (period from November 2015 till August 2016, and Jan-Mar 2017);
2) PhD student exchange: Vladimirs Piļipenko. Duration of his scholarship is 4 months (January – February 2016, June 1 – July 31, 2016).
3) 5 Master students from the LU Faculty of Medicine (April, 2016)
4) 1 Bachelor student from the LU Faculty of Medicine (April, 2016)
5) Ulrika Beitnere (Post doc.) for 1 months (April 14 –May 22, 2017)
6) Baiba Jansone (Academic) for 1 week (May, 2017)

Student's mobility continued after Scholarship Activity 'Enhancing human capital and knowledge in health science by institutional cooperation and mobility between the University of Latvia and three Norwegian universities' between University of Latvia and University of Oslo:

7) PhD student exchange: Jolanta Upīte. Duration one week (period Sept 2016).
8) PhD student exchange: Jolanta Upīte. Duration app. 1.5 months (period January-February, 2017)
9) PhD student planned exchange: Jolanta Upīte. Duration app. 1.5 months (period August-September, 2017)

2.9. HORIZONTAL PRIORITIES

The project involves researchers of both genders, so the project has positive direct impact on gender equality, however, Latvian scientific institution in general are missing male researchers from Latvia. It could be taken into consideration to support more male researchers in future NFI programs.

Taking into account the created work places, project also has a positive indirect impact on economic and social sustainability.

2.10. STUDENTS and POST-DOCS

Names of students and Postdocs trained	Activities carried out *(incl. reference to work package and bachelor/master/PhD theses drafted based on research results)*
1. Jolanta Upīte ſ (PhD student) 2. Vladimirs Piļipenko (PhD student) 3. Ulrika Beitnere (Post doc.) 4. Baiba Jansone (academic) 5. 5 Master students (students) 6. 1 Bacholor student (student)	Work package No. 2: at the Pahnke lab / UiO 1. animal models, PCR methodology. 2. Alzet pump implantation in rodents 3. Western blotting method 4. *In vivo* infusion techniques and *Open field* test. 5. *In vivo* infusion techniques and M*orris water maze* test.

2.11. RISKS IDENTIFIED

Outcome	Outcome	Description of risk	Impact Assessment	Risk mitigation plan
1	-	-	-	-

2.12. SUSTAINABILITY PLAN (*applicable to Final report*) (*please provide detailed steps (measurable indicators) to be taken to ensure sustainability of project results and maintain long-term collaboration with Norwegian partner in high quality research). In case of any derogations from the scheduled provisions, please provide an explanation.*

Long-term collaboration will be maintained through the personal collaboration developed during the project and by targeting future funding opportunities for joint research applications under Horizon 2020 and other international programs. One successful collaboration is currently running between Henrik Biverstål and Jens Pahnke (JPND, PROP-AD, funded since Jan 2017) and two applications submitted by Jens Pahnke and Baiba Jansone is currently under revision (ERARE TreatNCL and ERA Neuron JTC2017 UltraABC).
Sustainability of the achieved results have been and will further be ensured by publication of the generated knowledge in well-established, peer-reviewed journals.
The project web pages will be available after the end of the project and will be further developed as platform for the groups.
The synergy activity between research project NFI/R/2014/023 "Benefits and detrimental effects of sequence variants of Amyloid-p: towards the use of small peptides for aggregate dissolution therapy in dementia" and Scholarship Activity project Nr. EEZ1NFI1S12015/019 "Enhancing human capital and knowledge in health science by institutional cooperation and mobility between the University of Latvia and three Norwegian universities" provided with the excellent opportunity to exchange the students (5 Master students and 1 Bachelor student, two PhD students (Jolanta Upīte and Vladimirs Piļipenko) and, as well as perform the academic staff mobility Postdoc Ulrika Beitnere) and Prof. Baiba Jansone to additionally strengthen the collaboration between the universities. Even more, PhD students Jolanta Upīte was continuing her research work at University of Oslo at Prof. Jens Pahnke lab after the ending of this mobility program. On January and February in 2017, she was working on experiments in connection with ongoing research project between universities and her PhD thesis work in Oslo University. Sustainability regarding the students exchange between universities will be maintained in the nearest further, for example, PhD student Jolanta Upīte will continue her research work at Prof. Jens Pahnke lab in autumn 2017.

III. FINANCIAL SUMMARY *(attached in Excel file)*

Herewith I confirm that the information given in the report is true and corresponds to the actual work done within the Project and the copies added correspond the originals.

Principal Investigator:

Name	Henrik Biverstål
Signature	
Date	5/7/2017

Legal representative of the Project Promoter:

Name	Osvalds Pugovičs
Signature	Latvijas Organiskās sintēzes institūta direktora vietniece D.Kārkle
Date	06.07.2017