

Questionnaire

Summary of the main activities of a research institute of the Slovak Academy of Sciences

Period: January 1, 2016 - December 31, 2021

1. Basic information on the institute:

1.1. Legal name and address

Institute of Neuroimmunology SAS (NIU SAS)
Dubravská cesta 9
845 10 Bratislava

1.2. URL of the institute web site

<http://www.niu.sav.sk>

1.3. Executive body of the institute and its composition

Directoriat	Name	Year of birth	Years in the position, from - to
Director	prof. Michal Novak, DVM, PhD, DSc, Dr.h.c.	1947	25, 1996 - 2020
Director	assoc. prof. DVM. Norbert Zilka, DSc	1973	1, 2020 - 2024
Deputy director	prof. RNDr. Eva Kontsekova, DSc	1959	1, 2020 -
Deputy director	RNDr. Rostislav Skrabana, PhD	1965	11, 2010 - 2020
Scientific secretary	RNDr. Monika Zilkova, PhD	1973	12, 2010 -

1.4. Head of the Scientific Board

Assoc. Prof. RNDr. Peter Filipcik, PhD

1.4.1. Composition of the International Advisory Board

International advisory board of NIU SAS includes researchers from several countries. Members of the board are internationally recognized scientists, authors of ground breaking discoveries in the field of neurodegeneration:

Prof. Khalid Iqbal, Ph.D.,
Department of Neurochemistry
New York State Institute for Basic Research
Inge Grundke-Iqbal Research Floor
1050 Forest Hill Road
Staten Island, NY 10314

H-index: 120
Citations: 59 925
Publications: 656
Source: WoS/June 2022

Prof. Bengt Winblad, MD, Ph.D.
H1 department fo Neurobiology,
Care Sciences and Society
Karolinska Istitutet
171 77 Stockholm
Sweden

H-index: 116
Citations: 60 277
Publications: 825
Source: WoS/June 2022

Assoc. prof. MUDr. Jakub Hort, M.D., Ph.D.
Department of Neurology
Second Faculty of Medicine
Charles University
V Úvalu 84
150 06 Praque 5
Czech Republic

H-index: 29
Citations: 3 242
Publications: 235
Source: WoS/June 2022

Prof. MUDr. Irena Rektorova, Ph.D.
Research Group Leader senior
Masaryk University
Kamenice 753/5
625 00 Brno

H-index: 26
Citations: 2 322
Publications: 148
Source: WoS/June 2022

1.5. Basic information on the research personnel

1.5.1. Fulltime equivalent work capacity of all employees (FTE all), FTE of employees with university degrees engaged in research projects (FTE researchers)

2016		2017		2018		2019		2020		2021		2016-2021	
FTE all	FTE researchers	FTE all	FTE researchers	FTE all	FTE researchers	FTE all	FTE researchers	FTE all	FTE researchers	FTE all	FTE researchers	average FTE all per year	average FTE researchers per year
38,74	22,82	47,60	26,65	49,47	28,08	48,33	27,03	47,25	26,32	47,83	25,26	46,54	26,03

1.5.2. If applicable, add also a short information on the merger of the institute in the evaluation period. You can also add rows in the above table corresponding to the founding institutes

1.6. Basic information on the funding of the institute

1.6.1. Institutional salary budget, other salary budget¹, non-salary budget²

Salary budget	2016	2017	2018	2019	2020	2021	average
Institutional salary budget <i>[millions of EUR]</i>	0,426	0,506	0,538	0,673	0,791	0,782	0,619
Other salary budget <i>[millions of EUR]</i>	0,334	0,385	0,449	0,467	0,356	0,482	0,412
Total salary budget <i>[millions of EUR]</i>	0,761	0,891	0,987	1,140	1,147	1,264	1,032
Non-salary budget <i>[millions of EUR]</i>	0,534	0,561	0,673	0,865	0,724	0,790	0,691

1.7. Mission Statement of the Institute as presented in the Foundation Charter indicating the years when it was adopted and revised

The Institute's Foundation Charter was issued by the Presidium of SAS on August 13th 2008.

The Institute conducts scientific and research activities in the fields of medical, veterinary, and biological sciences, with the emphasis on neuroscience, neuro-proteomics, immunology, molecular biology, structural biology, genetics, and bioinformatics. Institute's activities focus on the basic research of physiological and pathological processes in the central nervous and immune systems. The Institute explores causes and mechanisms modifying the function and mutual communication of these two systems, especially in the context of neurodegenerative disorders.

The Institute provides consulting and expert services based on its principal activities.

The Institute offers PhD studies in accordance with generally binding legal acts.

The Institute also publishes the results of its research activity by means of periodical and non-periodical press.

In 2016, the Foundation Charter was revised and three Addenda were adopted that changed the Institute accounting type from a budgetary institution to a contributory institution, changed the organization structure of the Institute by including a detached laboratory in Kosice and detached offices in Bratislava, and allowed the Institute to perform business activities in the following areas:

- DNA diagnostics, gene expression analysis by quantitative PCR, preparation of expression vectors and production of recombinant proteins in eukaryotic and prokaryotic cells;
- Preparation of monoclonal and polyclonal antibodies, preparation of recombinant proteins, labelling of proteins and development of diagnostic tests based on antibodies and their diagnostic use, analysis of surface markers by flow cytometry;
- Characterisation and quantification of proteins by mass spectrometry, analysis of the protein structure, quantification of metabolites in body fluids.

As of **January 1st 2022**, pursuant to Section 21aa (1) of the Academy Act, as amended by the Act No. 347/2021 Coll. (that entered into force on Oct 5, 2021), organisations of the Slovak Academy of

¹ Salary budget originating outside the regular budgetary resources of the organization, e.g. from the project funding.

² Includes Goods and Services and PhD fellowships

Sciences changed their legal form to public research institutions. Accordingly, the legal form of the Institute of Neuroimmunology of the Slovak Academy of Sciences changed from a state to a **public research institution** and the institute foundation charter was updated accordingly.

The primary activity of the Institute is research in the following fields of science and technology (as defined by the Directive 27/2006-R of the Ministry of Education, Science, Research, and Sport of the Slovak Republic):

- a) Biological sciences (010600)
- b) Medical sciences (030000)
- c) Veterinary sciences (040300)
- d) Biotechnologies in agriculture (040400)
- e) Psychological sciences (050100), mainly Clinical psychology (050102)
- f) Logopaedics (050303)
- g) Bioinformatics (010202)
- h) Biophysics (010303)
- i) Chemical sciences (010400)
- j) Industrial biotechnology (021000)

Further activities include:

- a) management of the research and development infrastructure owned by the Institute,
- b) acquisition, processing, and dissemination of information from the fields of science of technology and knowledge acquired through the Institute's own research and developmental activities,
- c) collaborations with universities on PhD programs (third-level university education) in the field of Biology,
- d) collaboration in the fields of science and technology with universities and other legal entities performing research and development, and with entrepreneurs, in the Institute's research fields.

Activities of the organization are defined in agreement with Section 2 (1) of Act No. 243/2017 Coll. on Public Research Institutions.

1.8. Summary of R&D activity pursued by the institute during the evaluation period in both national and international contexts. Describe the scientific importance and societal impact of each important result/discovery. Explain on general level – the information should be understandable for a non-specialist (recommended 5 pages, max. 10 pages for larger institutes with more than 50 average FTE researchers per year as per Table 1.5.1.)

THE FOUNDER OF THE INSTITUTE – PROF. MICHAL NOVAK

Prof. MVDr. Michal Novak, DrSc., the founder and the first director of the Institute, is a world renowned Alzheimer's disease researcher. He was awarded the 2016 Prize for Research in Health Care for the Elderly and in Health Promotion by the World Health Organization in Geneva, Switzerland, and the prestigious AAIC Khalid Iqbal Lifetime Achievement Award in 2021. (Denver, USA).

Prof. Novak has worked in the Laboratory of Molecular Biology, MRC Cambridge for 10 years in close collaboration with three Nobel Prize laureates – Sir Aaron Klug, John Walker, and César Milstein. César Milstein, who was awarded the Nobel Prize (1984) for the discovery of the principle for production of monoclonal antibodies, supported the foundation of the Institute.

R&D ACTIVITIES

The Institute of Neuroimmunology is a leading research centre in the field of basic and applied neuroscience and immunology in Slovakia. The research in the institute deals with a broad range of interests, starting from molecular pathways, through cellular signalling, and molecular communication between brain networks, to the cognition, movement, and behaviour.

Our overarching scientific aims are to address major knowledge gaps in physiology and pathology of human brain and spinal cord, with special emphasis on **neurodegenerative disorders** (Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis etc.), **brain infection diseases** (Lyme disease, tularemia, West Nile fever etc.), and **traumatic brain and spinal cord injuries**.

To achieve these objectives the institute employs state-of-the-art genomic, transcriptomic, proteomic, metabolomic, molecular, and cell biology techniques to investigate problem-oriented basic and applied research. In addition, it hosts doctoral studies in a) neuroscience, b) immunology and c) molecular biology, in collaborations with universities across the country as well as at international level. In order to coordinate the neuroscience research with university partners, **Centre of Biomedical Microbiology and Immunology** (CBMI) was set up as a joint laboratory based on the campus of the University of Veterinary Medicine and Pharmacy in Košice.

The institute has become the scientific representative of the Slovak Republic in the EU **Joint Programming - Neurodegenerative Disease research** (JPND), the largest global research initiative aimed at tackling the challenge of neurodegenerative diseases. JPND aims to increase coordinated investment between participating countries in research aimed at finding causes, developing cures, and identifying innovative ways to care for those with neurodegenerative diseases.

Institute of Neuroimmunology represents the National Scientific Centre of Slovak Republic in the **International Centre for Genetic Engineering and Biotechnology** (ICGEB). ICGEB is a unique

intergovernmental organisation, which forms a highly interactive network with almost 70 member states.

The mission of the Institute is to deliver the results of the research from the bench directly to the patients suffering from neurodegenerative disorders, and consequently translate the scientific knowledge into the improvement of their everyday life. To achieve this goal, the Institute established the first Alzheimer's Diagnostic Centre in Slovakia, the Centre MEMORY, a specialized preventive diagnostic and educational daily care facility for elderly people and people with memory disorders, especially for patients with Alzheimer's disease.

The purpose of the institute is to increase awareness about brain diseases, provide education, and disseminate the current knowledge on these disorders throughout the country. In collaboration with Slovak Alzheimer's Society and Slovak Society for Neuroscience we organise regular conferences for clinicians, scientists, and caregivers.

The commitment of the institute is to improve the diagnostics strategy in the Slovak republic by bringing cutting-edge innovative technologies into clinical practice. The Institute is the leading force in the molecular biomarker screening for several fatal human brain disorders.

ALZHEIMER'S DISEASE RESEARCH

Precise control of the brain microenvironment is important for the brain's function. The exchange of substances between the periphery and the brain is highly regulated by a functional entity called the neurovascular unit (NVU). **Andrej Kovac's** research team belongs to the pioneers in the NVU research in Alzheimer's disease and related human tauopathies. They have collaborated with the giants from the field like William Banks (University of Washington, Seattle, USA) or Maria Deli (Biological Research Centre of the Hungarian Academy of Sciences, Szeged, Hungary). Tauopathies represent a heterogeneous group of neurodegenerative diseases characterized by abnormal deposition of tau protein in various nervous system cell types. The team demonstrated that NVU disruption – driven by chronic neuroinflammation, was characterised by production of pro-inflammatory signaling molecules such as cytokines, chemokines, and adhesion molecules by glial cells, neurons, and endothelial cells (*Majerova et al., 2018, J Neural Transm; Michalicova et al., 2020, Front Mol Neurosci*). These changes can modify the integrity of the barrier and migration of immune cells into the brain, which may finally lead to structural changes in capillaries (*Deli and Kovac, 2020, Curr Pharm Des; Majerova et al., 2019, PLOS One*). The NVU represents a major bottleneck in successful therapy of various brain disorders. Using state-of-the-art molecular biology techniques, they discovered novel brain delivery vectors that can transport large molecules into the brain (*Majerova et al., 2020*).

Tomas Smolek's research team has studied the mechanism of spreading of tau pathology by using transgenic rat model for tauopathy (*H2020/JPND – Pathway complexities of protein misfolding in neurodegenerative diseases: a novel approach to risks evaluation and model development*,

2016-2019). Their study was the first to demonstrate that human AD tau can spread in the rat brain (Smolek et al., 2019, *Mol Neurobiol.*) in a similar way as was described in mouse models. In addition, they showed that the immune response modulating genetic variability is one of the factors influencing the propagation of tau neurofibrillary pathology (Smolek et al., 2019, *Front Aging Neurosci.*).

Systems neuroscience group of Tomas Hromadka focuses on the main question of how changes in the activity of neural circuits lead to specific changes in behaviour. The team developed animal models of tauopathies based on AAV vectors (Vogels et al. 2020, *J Alzheimer Dis*) and studied changes in activity and morphology of pyramidal cells, inhibitory interneurons, and microglia in vivo during early stages of Alzheimer's disease.

Research team of **Rostislav Skrabana** investigated the structural pathways leading to pathological switching of disordered tau protein molecule into toxic, disease-associated oligomers and polymers (Skrabana et al., 2017, *J Alzheimer Dis.*), highlighting the role of conformational rearrangement upon molecular truncation (Novak et al., 2018, *J Alzheimer Dis.*).

BIOMARKERS FOR TRAUMATIC BRAIN INJURY

The mechanism and biomarkers of traumatic brain injury (TBI) represent one of the leading research topics at the Institute. The research team of **Peter Filipcik** has actively participated in two international projects on TBI (***ERANET – Repetitive Subconcussive Head Impacts -Brain Alterations and Clinical Consequences, 2017-2019; ERANET – Neurovascular damage determines disease pathophysiology in pediatric mild traumatic brain injury: source of new biomarkers, 2020-2022***).

Peter Filipcik's group continues its research activities focused on TBI with several partners from Slovak and foreign universities. Their research is performed at of three complementary levels: in vitro analysis and experimental manipulation of human cells, animal models, and human experiments in collaboration with the Comenius University. The team has focused on developing a microRNA (miRNA) and long-noncoding RNA (lncRNA) based biomarker profile in the peripheral fluids which may reflect brain deterioration. They have explored the short-term effects of accidental head impacts and repetitive headers on circulating microRNAs, accounting for the effects of high-intensity exercise alone. The analysis of blood samples from professional soccer players was performed at rest and after three conditions: accidental head impacts in a match, repetitive headers during training, and high-intensity exercise. The samples were screened to detect microRNAs expressed after each exposure. Identified microRNAs were then validated to determine consistently deregulated microRNAs. Deregulated microRNAs were further explored using bioinformatics to identify target genes and characterize their involvement in biological pathways. The results of their work suggest that accidental head impacts led to deregulation of eight microRNAs that were unaffected by high-intensity exercise; target genes were linked to 12 specific signalling pathways, primarily regulating chromatin organization, Hedgehog and Wnt signalling. Repetitive headers led to

deregulation of six microRNAs that were unaffected by high-intensity exercise; target genes were linked to one specific signalling pathway (TGF- β). High-intensity exercise led to deregulation of seven microRNAs; target genes were linked to 31 specific signalling pathways. The identified microRNAs specific to accidental head impacts and repetitive headers in soccer can be potentially useful as brain injury biomarkers.

Interestingly, the neurofilament light protein and tau protein in serum were unaffected by head impacts in soccer. However, tau levels seemed to rise in response to exercise (*Sandmo et al., 2020, Brain Inj*). They also performed extensive research of circulating miRNA following head traumas in soccer players.

More than 20 articles were published or accepted for publication by the research team of Peter Filipcik (including papers in collaboration) during the assessment period. One of the projects granted to the group by APVV was evaluated among the best projects and was included in “Excellent projects – 2018” publication, issued by APVV agency. Specific results gained a broad attention: <https://www.genengnews.com/topics/omics/rna/mirna/blood-mirna-changes-in-soccer-players-could-represent-biomarkers-of-brain-injury/>.

PARKINSON’S DISEASE RESEARCH

Recently, the Institute established new research group focused on Parkinson’s disease pathology lead by two internationally recognized researchers **Dominika Fricova** and **Alzbeta Kralova Trancikova**, who were both awarded a competitive L’OREAL-UNESCO Prize for Women in Science (2020 Dominika Fricova, 2021 Alzbeta Kralova Trancikova).

The team working under the supervision of **Dominika Fricova** is focused on the role of senescence in Parkinson’s disease (PD). The project is funded by Marie Skłodowska-Curie Cofund project (SASPRO 2) and represents an innovative strategy for identification of new potential targets in Parkinson’s disease treatment. Additionally, Dominika Fricova published an article underlining the potential role of mesenchymal stem cells and extracellular vesicles in Parkinson’s disease treatment in a highly respected journal (*Fricova et al., 2020, Nature Regenerative Medicine*).

Alzbeta Kralova Trancikova studies the alpha-synuclein associated pathology within the gastrointestinal tract organs and its spreading to the CNS structures in mouse models of PD as well as samples from patients suffering from PD at different stages of the disease (Detection of early stages of Parkinson's disease by fluorescence multiphoton microscopy and FLIM analysis 2018-2020, Spread of alpha-Synuclein-associated pathology across gastrointestinal organs in a mouse model and patients with Parkinson's disease 2021-2024). Early diagnosis of PD is still insufficient and neurodegenerative diseases are currently one of the main challenges of medicine and medical research. Therefore, her work is also focused on the development and optimization of potential diagnostic methods from readily available, non-invasive biological material for the patient (advanced microscopic methods - FLIM and confocal microscopy from whole mount tissue micro biopsies or

RT-QuIC analysis from body fluids) (*Harsanyiova et al., 2020, Front Neurosci; Fricova et al., 2020, Int J Mol Sci; Pokusa et al., 2018, Physiol Res*)

Their collaborative efforts are demonstrated by their publication concluding the potential of alpha-synuclein as a biomarker for early detection of Parkinson's disease (*Fricova et al, 2020, Int J Mol Sci*) and an exciting collaboration with the Centre for rare movement disorders at Department of Neurology, Pavol Jozef Safarik University in Kosice, Slovakia, supporting their studies with Parkinson's disease patients' samples.

STEM CELL THERAPY FOR SPINAL CORD INJURY

The main focus of the research team of **Dasa Cizkova** is on the stem cell therapy of the spinal cord injury (***ERANET – Spinal cord repair: releasing the neuron-intrinsic brake on axon regeneration, 2017- 2019; V4 – Bridging the gap between science, education and enterprise in regenerative medicine, 2020-2022***). The team provided a comprehensive proteomic study of canine bone marrow-derived mesenchymal stem cells and conditioned media isolated from healthy adult dogs of different breeds. Using proteome profiling they identified for the first time the dynamic release of various bioactive molecules, such as transcription and translation factors and osteogenic, growth, angiogenic, and neurotrophic factors from canine stem cell conditioned medium (*Humenik et al., 2019, Mol Cell Proteomics*). The conditioned medium was used for further therapy of dogs with spinal cord injury. The treatment did not show any adverse effects or complications, and in combination with comprehensive physiotherapy it demonstrated clinical benefits (*Vikartovska et al., 2019, Int J Mol Sci*). In addition, they showed that the conditioned medium of mesenchymal stem cells improved motor function recovery and attenuated inflammation in a rat model of spinal cord injury (*Cizkova et al., 2019, Int J Mol Sci*).

THE MECHANISM OF TRANSLOCATION OF PATHOGENS ACROSS THE BLOOD BRAIN BARRIER

The research team of **Mangesh Bhide** identified multiple mechanisms of how dangerous bacterial (*Borrelia garinii*, *Neisseria meningitidis*) or viral pathogens (West Nile virus) are translocated across the blood-brain barrier (BBB) and cause meningo-encephalitis. The team described the protein-protein interactions between pathogen surface proteins and receptors on the brain microvascular endothelial cells (*Kanova et al., 2018, Front Microbiol; Tkacova et al., 2020, Ticks Tick Borne Dis*). The authors used a variety of approaches to reveal ligand-receptor interface combined with state-of-the-art bioinformatic tools, which may generate a large dataset allowing to identify multiple interaction partners (*Bencurova et al., 2018, Mol Omics; Hortvatic et al., 2018, Methods Mol Biol; Mertinkova et al., 2020, Sci Report*). The team also created several peptide candidates or single domain antibodies for the development of novel antiviral therapeutics against West Nile Virus (*Mertinkova et al., 2021, Sci Report; Hruskovicova et al., 2022, Front Microbiol*). The developed peptides and antibodies are being used to generate novel drug delivery system (DDs) made of either

amphiphilic dendrimers or polymeric nanoparticles (***EuroNanoMed2018-049 Nanosystems conjugated with antibody fragments for treating brain infections, EuroNanoMed2021 Developing novel nanopharmaceutics against bacterial infections at center nervous system***).

ANTI-VIRAL PEPTIDES FOR THERAPY OF COVID-19

Contributing to global efforts to contain the COVID-19 pandemic, the research team of **Mangesh Bhide** has developed single domain antibodies and anti-viral peptides targeting the receptor binding domain of spike protein (***APVV PP-COVID-2020 Development of therapeutic biomolecules to block SARS-CoV-2 infection***). Both biomolecules can neutralize SARS-CoV-2 virus-like particles carrying the spike protein of delta variant B.1.617 and original D614 genotype.

STRUCTURE OF NON-GLOBULAR PROTEINS

The Institute has long-standing tradition in structural analyses of non-globular proteins (NGPs). NGPs encompass different molecular phenomena that defy the traditional sequence-structure-function paradigm. NGPs include intrinsically disordered regions, tandem repeats, aggregating domains, low-complexity sequences, and transmembrane domains. Although growing evidence suggests that NGPs are central to many human diseases, their functional annotation is very limited. The research team of **Rostislav Skrabana** has participated in a pan-European COST project (***COST, Non-globular proteins - from sequence to structure, function and application in molecular physiopathology, 2015 – 2019***). One of the outputs of the project was the standardization of the design of aggregation experiments used in the research of NGP role in proteinopathies (*Martins et al., 2020, Front Mol Neurosci.*) Analysing the results of nuclear magnetic resonance spectroscopy (NMR), the authors demonstrated that subtle differences in transient structural motifs of homologous tau and MAP2c proteins are linked to their contrasting properties, manifested by specific interactions and function. Their interactions are further regulated by post-translational modifications, particularly phosphorylation (*Melkova et al., 2019, Biomolecules; Kitoka et al., 2021, Front Mol Biosci.*). Another focus of the team is the investigation of small local structures in non-globular proteins, which can determine their physiological and pathological fate (*Cehlar et al., 2021, Gen Phys Biophys.*).

CANINE DEMENTIA

Norbert Zilka's research team has become the leading force in the study of molecular mechanism of canine dementia. In 2017, we published the book "Canine and feline dementia" (*Springer, editors Gary Landsberg, Aladar Madari, Norbert Zilka*) which deeply focused on the epidemiology, diagnostics, therapy, and molecular basis of canine and feline dementia or cognitive dysfunction syndrome. We described the risk factors for canine cognitive dysfunction syndrome in Slovakia (*Katina et al., 2016, Acta Vet Scand*), synaptic impairment and neuroinflammation associated with canine cognitive impairment (*Smolek et al., 2016, J Comp Neurol.*). Furthermore, we demonstrated

that a brain injury biomarker (neurofilament light chain) and biochemical parameters (ALT, AST, Na, and Cl) in blood serum may predict canine cognitive impairment in aged dogs (*Vikartovska et al., 2021, Front Vet Sci*).

APPLIED RESEARCH

IMMUNOLOGY AND IMMUNOTHERAPY FOR NEURODEGENERATIVE DISEASES

The institute has participated in the development of new biological therapeutics for Alzheimer's disease, supported by targeted research grants from a biotech company AXON Neuroscience SE. The developed active tau vaccine AADvac1, a first-in-man, first-in-kind tau vaccine for this fatal neurodegenerative disorder (*Kontsekova et al., Alz Res Ther, 2014a, b*), was demonstrated to be safe, well tolerated, stimulated high levels of antibodies, slowed down neurodegeneration in the brain, and reduced cognitive impairment (*Novak et al., 2018, Front. Neurosci.; Novak et al., 2021, Nature Aging*).

Within this project, the team of **Eva Kontsekova** investigated the molecular mechanisms of spreading of neurofibrillary pathology of tau across the brain, namely how neurons take up pathological tau proteins ("AD-tau seeds") from the extracellular space. These seeds then corrupt normal neuronal tau proteins, cause them to aggregate, and further spread the pathology. The team has shown that a novel therapeutic monoclonal antibody DC8E8 can efficiently prevent the neuronal internalization of extracellular AD tau species by masking the regions of tau essential for the interaction with Heparan Sulfate Proteoglycans (HSPGs) on neuronal surface (*Weissova et al., 2019, Acta Neuropathol. Comm.*). The group also showed that human primary microglia, isolated from the brains of deceased Alzheimer's patients, can be promoted by suitable monoclonal anti-tau antibodies to effectively eliminate extracellular pathologic tau proteins (*Zilkova et al., 2020, Acta Neuropathol. Comm.*). This work is a result of a collaboration with Dr. Hoozemans from Amsterdam UMC of Vrije Universiteit Amsterdam and Department of Pathology of Amsterdam Neuroscience (The Netherlands).

SLOVAK ALZHEIMER'S DISEASE COHORT

The Institute has become the driving force behind innovative approaches to improve diagnosis of Alzheimer's disease and care for the patients with dementia and their caregivers in the Slovak republic. The institute (supervised by **Petr Novak**) in collaboration with Centre MEMORY were engaged in an international project which aimed to bring new understanding of which aspects are most important to patients and caregivers to preserve and improve their autonomy, dignity, and quality of life (*H2020/JPND – Alzheimer's disease data-driven insights on individual outcomes of importance, 2019 -2022*). We created the very first Slovak database of well-defined Alzheimer's disease cohort, and set up new diagnostic algorithm for the diagnosis of Alzheimer's disease in the MEMORY Centre.

THERAPEUTIC ANTIBODIES AGAINST COVID-19

NIU SAS has also been actively involved in the COVID-19 program in Slovakia. In collaboration with the Biomedical Research Centre of the Slovak Academy of Sciences, we have created an academy-wide screening network to monitor SARS-CoV-2 positive cases. In collaboration with COVIDAX, the research team of **Eva Kontsekova** developed several assays for antibody and cell responses which were used to monitor immune response to COVID-19 infection and vaccination. Moreover, the Institute took part in the development of therapeutic antibodies against COVID-19. The antibodies, developed by hybridoma technology, displayed high affinity to all variants of concern (*Kovacech et al., 2022, EBioMedicine by Lancet*).

EUROPEAN RESEARCH POLICY

Since its establishment, the Institute of Neuroimmunology has been the official representative of the Slovak republic in the EU Joint programming - Neurodegenerative disease research (JPND), the largest global initiative in neurodegeneration research. The ultimate goal of JPND is to find cures for neurodegenerative diseases and to enable early diagnosis for early targeted treatments.

Since its foundation, NIU SAS has also been actively participating in the European research strategy through the Joint programming initiative. Under the umbrella of an international project (***H2020/JPND – Coordination Action in support of the sustainability and globalisation of the Joint Programming Initiative on Neurodegenerative Diseases, 2015 – 2021***) we aimed to support the development of JPND capacities by creating a dedicated structure responsible for the long term JPND management and implementation, and the global extension of these capacities especially to non-participating EU Member States .

SUMMARY

The Institute of Neuroimmunology SAS remains a leader in the research of human brain and spinal cord disorders in the Slovak national scientific milieu, supported by strong international collaborations. We have actively participated in a variety of international projects (H2020, JPND, ERA-NET, COST) which have covered multiple aspects of basic and applied neuroscience research:

- Alzheimer's and Parkinson's diseases – mechanisms leading to neurodegeneration and their biomarkers
- Blood brain barrier damage in human tauopathies
- Astrocytes and microglia - modulators of neurodegenerative processes
- Traumatic brain injury – molecular pathways and biomarkers
- Stem cell therapy for spinal cord injury
- Interaction of pathogens with brain microvascular endothelial cells
- Structure of non-globular proteins
- Canine dementia – pathogenesis and biomarkers

The institute has also been involved in Alzheimer's disease drug development and the COVID-19 program in Slovakia, demonstrating high translation potential of its research.

2. Partial indicators of main activities:

2.1. Research output

2.1.1. Principal types of research output of the institute: basic research/applied research, international/regional (in percentage)

basic research/applied research: 80 % / 20%

international research/regional research: 90% / 10%

2.1.2. List of selected publications documenting the most important results of basic research. The total number of publications should not exceed the number of average FTE researchers per year. The principal research outputs (max. 10% of the total number of selected publications, including Digital Object Identifier – DOI if available) should be underlined. Authors from the evaluated organizations should be underlined.

1. TOKAR, T. - PASTRELLO, C. - ROSSOS, A.E.M. - ABOVSKY, M. - HAUSCHILD, A.C. - TSAY, M. - LU, R. - JURIŠICA, Igor**. mirDIP 4.1-integrative database of human microRNA target predictions. In *Nucleic acids research*, 2018, vol. 46, iss. D1, p. D360-D370. (2017: 11.561 - IF, Q1 - JCR, 9.025 - SJR, Q1 - SJR, Current Contents - CCC). (2018 - Current Contents). ISSN 0305-1048. Available at: <https://doi.org/10.1093/nar/gkx1144>
2. POTOČNÁKOVÁ, L. - BHIDE, Mangesh - BORSZEKOVÁ PULZOVÁ, Lucia. An Introduction to B-Cell Epitope Mapping and In Silico Epitope Prediction. In *Journal of immunology research : an open access journal*, 2016, vol. 2016, article number 6760830, 11 p. (2015: 2.812 - IF, Q3 - JCR, 1.467 - SJR, Q1 - SJR). ISSN 2314-8861. Available at: <https://doi.org/10.1155/2016/6760830>
3. JADHAV, Santosh - AVILA, J. - SCHOLL, M. - KOVACS, G.G. - KOVARI, E. - ŠKRABANA, Rostislav - EVANS, L.D. - KONTSEKOVÁ, Eva - MALAWSKA, B. - DE SILVA, R. - BUEE, L.** - ŽILKA, Norbert**. A walk through tau therapeutic strategies. In *Acta Neuropathologica Communications*, 2019, vol. 7, no.1, art. no. 22. (2018: 5.883 - IF, Q1 - JCR, 3.279 - SJR, Q1 - SJR). ISSN 2051-5960. Available at: <https://doi.org/10.1186/s40478-019-0664-z>
4. SHI, M. - KOVÁČ, Andrej - KORFF, A. - COOK, T.J. - GINGHINA, C. - BULLOCK, K.M. - YANG, L. - STEWART, T. - ZHENG, D. - ARO, P. - ATIK, A. - KERR, K.F. - ZABETIAN, C.P. - PESKIND, E.R. - HU, S.C. - QUINN, J.F. - GALASKO, D.R. - MONTINE, T.J. - BANKS, William A. - ZHANG, J. CNS tau efflux via exosomes is likely increased in Parkinson's disease but not in Alzheimer's disease. In *Alzheimer's & Dementia*, 2016, vol. 12, p. 1125-1131. (2015: 11.619 - IF, Q1 - JCR, 4.581 - SJR, Q1 - SJR, Current Contents - CCC). (2016 - Current Contents). ISSN 1552-5260. Available at: <https://doi.org/10.1016/j.jalz.2016.04.003>
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Canine and Feline Dementia. Editors: Landsberg, Gary, Mađari, Aladár, Žilka, Norbert. Heidelberg, Nemecko : Springer International Publishing, 2017. 159 s. Dostupné na: <https://doi.org/10.1007/978-3-319-53219-6>. ISBN 978-3-319-53218-9

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JAMPÍLEK, Josef - KRALOVA, K. - NOVÁK, Petr - NOVÁK, Michal. Nanobiotechnology in Neurodegenerative Diseases. In *Nanobiotechnology in Neurodegenerative Diseases*. - Cham : Springer Nature Switzerland, 2019, p. 65-138. ISBN 978-3-030-30929-9. Dostupné na: https://doi.org/10.1007/978-3-030-30930-5_4

JAMPÍLEK, Josef** - KRÁLOVÁ, Katarína. Nanoweapons against tuberculosis. In *Nanoformulations in human health : Challenges and Approaches*. - Switzerland : Springer Nature Switzerland AG, 2020, chapter 21, P. 469 - 502. ISBN 978-3-030-41857-1.

2.1.4. List of monographs/books published in Slovakia

ŽILKA, Norbert. *ALZHEIMER - malý sprievodca Alzheimerovou chorobou*. Bratislava : Marenčin PT, spol. s r.o., 2021. 224 s. ISBN 978-80-569-0859-4

2.1.5. List of other scientific outputs specifically important for the institute, max. 10 items for institute with less than 50 average FTE researchers per year, 20 for institutes with 50 – 100 average FTE researchers per year and so on

ČÍŽKOVÁ, Dáša - MURGOČI, Adriana-Natalia - KRESAKOVA, Lenka - VDOVIAKOVA, Katarina - CIZEK, Milan - SMOLEK, Tomáš - CUBÍNKOVÁ, Veronika - QUANICO, Jusal - FOURNIER, Isabelle - SALZET, M. Understanding Molecular Pathology along Injured Spinal Cord Axis: Moving Frontiers toward Effective Neuroprotection and Regeneration. In *Essentials of Spinal Cord Injury Medicine*. - Rijeka : IntechOpen, 2018, p. 1-21. ISBN 978-1-78923-249-3. Available at: <https://doi.org/10.5772/intechopen.72118>

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MAJEROVÁ, Petra - KOVÁČ, Andrej. Pathophysiology of the Blood-Brain Barrier in Neuroinflammatory Diseases. In *The Blood Brain Barrier and Inflammation*. - Cham : Springer International Publishing, 2017, p. 61-79. ISBN 978-3-319-45514-3. Available at: https://doi.org/10.1007/978-3-319-45514-3_4

RAHMATI, S. - PASTRELLO, C. - ROSSOS, A. - JURIŠICA, Igor. Two Decades of Biological Pathway Databases: Results and Challenges. In *Encyclopedia of Bioinformatics and Computational Biology : ABC of Bioinformatics*. Vol. 1. - Oxford : Elsevier, 2019, p. 1071-1084. ISBN 978-0-1281-1432-2. Available at: <https://doi.org/10.1016/B978-0-12-809633-8.20496-2>

2.1.6. List of patents, patent applications, and other intellectual property rights registered abroad

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2.1.7. List of patents, patent applications, and other intellectual property rights registered in Slovakia

Patent application: PP 24-2019 “New peptide-based system for transporting the drugs into the brain”
Authors of the patent: Majerova Petra, Kovac Andrej, Olesova Dominika

2.1.8. Narrative on the most important research outputs of the institute – especially focused on their importance for society (3-5 pages)

Societal contribution in Slovakia - ADDITION

The planned societal contribution of the ADDITION project for the European community is based on modelling the possible trajectories of Alzheimer’s disease. By researching these trajectories, it becomes possible to predict when important disease milestones will be reached by individual patients – for example the expected loss of self-sufficiency or the expected caregiving burden. Connected to these models is the possibility to research factors that influence said trajectories, evaluate cost-effectiveness, or assess the expected economic and societal impacts of interventions.

Participation in the project had immediate positive societal impacts for Slovakia that exceeded the abovementioned project goals. These include for example the preparation of Slovak versions of several neuropsychological and clinical assessments that were previously absent in the arsenal of Slovak neuropsychologists and other clinical workers, e.g., tools for the assessment of instrumental activities of daily living in patients with mild cognitive impairment and mild dementia, or scales for the assessment of quality of life, dignity, and dependency/self-sufficiency of patients.

The utility of these tools was confirmed in clinical practice in cooperation with the MEMORY Centre, thus expanding the arsenal of tools available to dementia care professionals in Slovakia.

Concurrently, the project served as a feasibility study at the MEMORY Centre, evaluating the possibility of establishing a European standard of dementia diagnosis, with encouraging results.

Over the course of the project, approximately 120 subjects with mild cognitive impairment or Alzheimer’s dementia (AD) received diagnosis and detailed clinical and neuropsychological evaluation, including the confirmation or refutation of the diagnosis of AD. The diagnosis allowed the indication of suitable pharmacological and non-pharmacological treatment. The detailed assessment allowed the tailoring of interventions to the specific phenotype of cognitive impairment seen in individual patients. Meanwhile, refutation of diagnosis usually leads to relief and improvement of the patient’s well-being, emotional state, and quality of life. Regardless of the outcome of the diagnostic process, for these patients, the diagnostic pathway and time from symptoms to diagnosis to treatment was reduced, positively impacting both the patient and healthcare professionals. The longitudinal observation of patients served to detect changes in the patient’s status (such as cognitive decline), which allowed e.g., timely changes in therapy.

These results also indicate that it is possible to implement this diagnostic standard (or one of a similar extent and complexity) at specialised dementia centres in Slovakia. They furthermore constitute an important step towards the integration of diagnostic and therapeutic modalities; the project thus contributed to the interconnection between diagnostic and therapeutic components of dementia patient care.

The project is ongoing, with the main results expected in 2022. Summarily, so far, the project had a positive impact on the lives of the involved patients, their caregivers and families, and Slovak healthcare professionals.

Societal contribution in Slovakia – LANCRE-AD

The LANCRE-AD project seeks to establish a Slovak Alzheimer's disease patient cohort, with harmonised clinical, cognitive, imaging, and biomarker assessment at key Alzheimer's disease care facilities in Slovakia. Via such harmonisation, it will be possible to deliver European-standard neuropsychological assessment and diagnosis to subjects throughout the country. The resulting cohort will inform dementia researchers about the status and idiosyncrasies of AD patients in Slovakia, while the resulting infrastructure will facilitate researcher cooperation, patient participation in research, and early access to experimental therapies.

As the project is in its initial stage, presently the societal impacts have manifested mostly at the level of support for dementia healthcare professionals. In the scope of the project, the consensus Clinician's Uniform Dataset (cUDS) neuropsychological assessment standard recommended by leading European authorities on AD has been implemented in Slovakia, with translations and adaptations of neuropsychological tests that were previously unavailable to professionals. Thusly, the diagnostic tool repertoire especially for the earlier stages of AD dementia was considerably expanded and brought to European standard, allowing both more accurate and early diagnosis, as well as facilitating comparability between European research institutions. Furthermore, said repertoire was also expanded by providing Slovak versions of other cognitive assessment tools above and beyond the scope of the cUDS. These novel and improved tools will improve the quality and accuracy of assessment, as well as early detection of cognitive impairment, allowing earlier intervention.

Even in these early stages of the project, an increase in cooperation between the individual involved sites is becoming apparent; ultimately, this cooperation will result in an increase in information and resource sharing, improvement in accessibility and quality of diagnosis and care, and increase in compatibility of Slovak dementia care structures with their European partners.

Development of therapeutic biomolecules blocking SARS-COV-2 infection (APVV PP-COVID-20-0044)

SARS-CoV-2, the causative agent of the current global pandemic of COVID-19, has resulted in 6.3 million deaths worldwide. Although vaccines administered against SARS-CoV-2 have dampened the severity of the pandemic, sporadic infections in immunized individuals especially by mutants of parental virus are being reported. Therefore, it is important to have therapeutic options besides vaccinations to treat re-occurring SARS-CoV-2 infections. Various monoclonal antibodies (mAbs) have been isolated from memory B cells of recovered patients. Nevertheless, screening for neutralizing mAbs from human memory B cells is a time consuming and laborious process. It is particularly not ideal when a worldwide health emergency needs to be addressed quickly.

Derivatives of heavy chain-only antibodies from camelids known also as nanobodies or Variable Heavy-chain domains of Heavy-chain antibodies (VHHs) pose multiple advantages over conventional mAbs. Nanobodies are scalable in prokaryotic systems, possess low antigenicity, and can be formulated for topical delivery directly to the airways of infected patients through aerosolization.

We have developed nanobodies targeting receptor binding domain (RBD) of spike protein of SARS-CoV-2 that could neutralize the SARS-CoV-2 pseudovirus *in vitro*. The newly developed nanobodies are ready for animal trials and confirmation of virus neutralization and pharmacological safety in *in vivo* conditions.

Newer SARS-Cov-2 variants of concern have been replacing older variants in circulation during the pandemic. Recently, Delta, Omicron, sub lineages of Omicron - BA.1, BA.2, BA.3, BA.4, BA.5, and a recombinant form of Omicron sub lineages -XE are the dominant variants circulating worldwide. Hence, serum antibody activity of vaccinated population will no longer be effective against these new variants. As Omicron strains seem to be causing milder symptoms, however, new vaccine formulations might not be essential and might even represent a more expensive prophylactic option.

Our newly developed nanobodies - VHH_{E12}, VHH_{F8} are capable of neutralizing the Delta variant and can be redesigned in a much more economical way should they fail to neutralize any of the new variants.

2.1.9. Table of research outputs

Papers from international collaborations in large-scale scientific projects (Dwarf team, ALICE Collaboration, ATLAS collaboration, CD Collaboration, H1 Collaboration, HADES Collaboration, and STAR Collaboration) have to be listed separately

Scientific publications	2016			2017			2018			2019			2020			2021			total			
	number	No. / FTE researches	No. / one million total salary budget	number	No. / FTE researches	No. / one million total salary budget	number	No. / FTE researches	No. / one million total salary budget	number	No. / FTE researches	No. / one million total salary budget	number	No. / FTE researches	No. / one million total salary budget	number	No. / FTE researches	No. / one million total salary budget	number	averaged number per year	av. No. / FTE researches	av. No. / one million total salary budget
Scientific monographs and monographic studies in journals and proceedings published abroad (AAA, ABA)	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	2	0,074	1,755	1	0,038	0,872	0	0,000	0,000	3	0,500	0,019	0,485
Scientific monographs and monographic studies in journals and proceedings published in Slovakia (AAB, ABB)	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0,000
Chapters in scientific monographs published abroad (ABC)	0	0,000	0,000	4	0,150	4,490	1	0,036	1,013	3	0,111	2,632	0	0,000	0,000	0	0,000	0,000	8	1,333	0,051	1,293
Chapters in scientific monographs published in Slovakia (ABD)	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0,000
Scientific papers published in journals registered in Current Contents Connect (ADCA, ADCB, ADDA, ADEB)	16	0,701	21,030	20	0,750	22,452	24	0,855	24,324	17	0,629	14,914	40	1,520	34,868	40	1,584	31,653	157	26,167	1,005	25,367
Scientific papers published in journals registered in Web of Science Core Collection and SCOPUS not listed above (ADMA, ADMB, ADNA, ADNAB)	2	0,088	2,629	9	0,338	10,103	12	0,427	12,162	12	0,444	10,528	9	0,342	7,845	14	0,554	11,079	58	9,667	0,371	9,371
Scientific papers published in other foreign journals (not listed above) (ADEA, ADEB)	0	0,000	0,000	0	0,000	0,000	1	0,036	1,013	0	0,000	0,000	1	0,038	0,872	2	0,079	1,583	4	0,667	0,026	0,646
Scientific papers published in other domestic journals (not listed above) (ADFA, ADFB)	0	0,000	0,000	1	0,038	1,123	4	0,142	4,054	0	0,000	0,000	3	0,114	2,615	0	0,000	0,000	8	1,333	0,051	1,293
Scientific papers published in foreign peer-reviewed proceedings (AECA)	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0,000
Scientific papers published in domestic peer-reviewed proceedings (AEDA)	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0,000
Published papers (full text) from foreign scientific conferences (AFA, AFC)	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0	0,000	0,000	0,000
Published papers (full text) from domestic scientific conferences (AFB, AFD)	5	0,219	6,572	1	0,038	1,123	0	0,000	0,000	1	0,037	0,877	1	0,038	0,872	2	0,079	1,583	10	1,667	0,064	1,616

2.2. Measures of research outputs (citations, etc.)

2.2.1. Table with citations per annum (without self-citations)

Citations of papers from international collaborations in large-scale scientific projects (Dwarf team, ALICE Collaboration, ATLAS collaboration, CD Collaboration, H1 Collaboration, HADES Collaboration, and STAR Collaboration) are listed separately

Citations, reviews	2015		2016		2017		2018		2019		2020		total		
	number	No. / FTE researchers	number	No. / FTE researchers	number	No. / FTE researchers	number	No. / FTE researchers	number	No. / FTE researchers	number	No. / FTE researchers	number	averaged number per year	av. No. / FTE researchers
Citations in Web of Science Core Collection (1.1, 2.1)	360	15,78	396	14,86	452	16,10	544	20,13	682	25,91	980	38,80	3 414	569,00	21,86
Citations in SCOPUS (1.2, 2.2) if not listed above	13	0,57	13	0,49	7	0,25	44	1,63	63	2,39	17	0,67	157	26,17	1,01
Citations in other citation indexes and databases (not listed above) (3.2,4.2)	0	0,00	0	0,00	0	0,00	0	0,00	0	0,00	0	0,00	0	0,00	0,00
Other citations (not listed above) (3.1, 4.1)	0	0,00	0	0,00	0	0,00	0	0,00	0	0,00	0	0,00	0	0,00	0,00
Reviews (5,6)	0	0,00	0	0,00	0	0,00	0	0,00	0	0,00	0	0,00	0	0,00	0,00

2.2.2. List of 10 most-cited publications published any time with the address of the institute, with number of citations in the assessment period (2015 – 2020)

1. ALONSO, A. - ZAIDI, T. - NOVÁK, Michal - GRUNDKE-IQBAL, I. - IQBAL, K. Hyperphosphorylation induces self-assembly of tau into tangles of paired helical filaments/straight filaments. In *Proceedings of the National Academy of Sciences of the United States of America*, 2001, vol. 98, p. 6923 - 6928. Available at: <https://doi.org/10.1073/pnas.121119298>
Citations: **214**
2. MADER, Simone - GRENDLER, Viktoria - SCHANDA, Kathrin - ROSTASY, Kevin - DUJMOVIC, Irena - PFALLER, Kristian - LUTTEROTTI, Andreas - JARIUS, Sven - DI PAULI, Franziska - KUENZ, Bettina - EHLING, Rainer - HEGEN, Harald - DEISENHAMMER, Florian - ABOUL-ENEIN, Fahmy - STORCH, Maria K. - KOSOŇ, Peter - DRULOVIC, Jelena - KRISTOFERITSCH, Wolfgang - BERGER, Thomas - REINDL, Markus. Complement activating antibodies to myelin oligodendrocyte glycoprotein in neuromyelitis optica and related disorders. In *Journal of Neuroinflammation*, 2011, vol. 8, p.184. (2010: 5.785 - IF, Q1 - JCR, 2.423 - SJR, Q1 - SJR, karentované - CCC). (2011 - Current Contents). ISSN 1742-2094. Available at: <https://doi.org/10.1186/1742-2094-8-184>
Citations: **149**
3. TOKAR, T. - PASTRELLO, C. - ROSSOS, A.E.M. - ABOVSKY, M. - HAUSCHILD, A.C. - TSAY, M. - LU, R. - JURIŠICA, Igor**. mirDIP 4.1-integrative database of human microRNA target predictions. In *Nucleic acids research*, 2018, vol. 46, iss. D1, p. D360-D370. (2017: 11.561 - IF, Q1 - JCR, 9.025 - SJR, Q1 - SJR, karentované - CCC). (2018 - Current Contents). ISSN 0305-1048. Available at: <https://doi.org/10.1093/nar/gkx1144>
Citations: **103**
4. KONTSEKOVÁ, Eva - ŽILKA, Norbert - KOVÁČECH, Branislav - NOVÁK, Petr - NOVÁK, Michal. First-in-man tau vaccine targeting structural determinants essential for pathological tau-tau interaction reduces tau oligomerisation and neurofibrillary degeneration in an Alzheimer's disease model. In *Alzheimer's Research & Therapy*, 2014, vol.6, 44. (2013: 3.500 - IF, Q1 - JCR, 1.414 - SJR, karentované - CCC). (2014 - Current Contents). ISSN 1758-9193. Available at: <https://doi.org/10.1186/alzrt278>
Citations: **89**
5. KOVÁČ, Andrej - ERICKSON, Michelle A. - BANKS, William A. Brain microvascular pericytes are immunoactive in culture: cytokine, chemokine, nitric oxide, and LRP-1 expression in response to lipopolysaccharide. In *Journal of Neuroinflammation*, 2011, vol. 8, p. 139. (2010: 5.785 - IF, Q1 - JCR, 2.423 - SJR, Q1 - SJR, karentované - CCC). (2011 - Current Contents). ISSN 1742-2094. Available at: <https://doi.org/10.1186/1742-2094-8-139>
Citations: **77**
6. POTOČŇÁKOVÁ, L. - BHIDE, Mangesh - BORSZEKOVÁ PULZOVÁ, Lucia. An Introduction to B-Cell Epitope Mapping and In Silico Epitope Prediction. In *Journal of immunology research : an open access journal*, 2016, vol. 2016, article number 6760830, 11 p. (2015: 2.812 - IF, Q3 - JCR, 1.467 - SJR, Q1 - SJR). ISSN 2314-8861. Available at: <https://doi.org/10.1155/2016/6760830>
Citations: **74**
7. ALONSO, A. - MEDERLYOVÁ, Anna - NOVÁK, Michal - GRUNDKE-IQBAL, I. - IQBAL, K. Promotion of Hyperphosphorylation by Frontotemporal Dementia Tau Mutations. In

Journal of Biological Chemistry, 2004, vol. 279, no. 33, p. 34873-34881. (2003: 6.482 - IF, karentované - CCC). (2004 - Current Contents). ISSN 0021-9258.
Citations: **73**

8. SENGUPTA, A. - KABÁT, Juraj - NOVÁK, Michal - WU, Q.L. - GRUNDKE-IQBAL, I. - IQBAL, K. Phosphorylation of tau at both Thr 231 and Ser 262 is required for maximal inhibition of its binding to microtubules. In *Archives of Biochemistry and Biophysics*, 1998, vol.357, p.299-309. (1997: 2.649 - IF, karentované - CCC). (1998 - Current Contents). ISSN 0003-9861.
Citations: **69**
9. EBRINGER, L. - FERENČÍK, Miroslav - KRAJČOVIČ, J. Beneficial health effects of milk and fermented dairy products. In *Folia microbiologica*, 2008, vol.53, p.378-394. (2007: 0.989 - IF, Q4 - JCR, 0.365 - SJR, Q2 - SJR, karentované - CCC). (2008 - Current Contents). ISSN 0015-5632.
Citations: **68**
10. JADHAV, Santosh - AVILA, J. - SCHOLL, M. - KOVACS, G.G. - KOVARI, E. - ŠKRABANA, Rostislav - EVANS, L.D. - KONTSEKOVÁ, Eva - MALAWSKA, B. - DE SILVA, R. - BUEE, L.** - ŽILKA, Norbert**. A walk through tau therapeutic strategies. In *Acta Neuropathologica Communications*, 2019, vol. 7, no.1, art. no. 22. (2018: 5.883 - IF, Q1 - JCR, 3.279 - SJR, Q1 - SJR). ISSN 2051-5960. Available at: <https://doi.org/10.1186/s40478-019-0664-z>
Citations: **63**

2.2.3. List of 10 most-cited publications published any time with the address of the institute, with number of citations obtained until 2020

1. ALONSO, A. - ZAIDI, T. - NOVÁK, Michal - GRUNDKE-IQBAL, I. - IQBAL, K. Hyperphosphorylation induces self-assembly of tau into tangles of paired helical filaments/straight filaments. In *Proceedings of the National Academy of Sciences of the United States of America*, 2001, vol. 98, p. 6923 - 6928. Available at: <https://doi.org/10.1073/pnas.121119298>
Citations: **532**
2. MADER, Simone - GRENDLER, Viktoria - SCHANDA, Kathrin - ROSTASY, Kevin - DUJMOVIC, Irena - PFALLER, Kristian - LUTTEROTTI, Andreas - JARIUS, Sven - DI PAULI, Franziska - KUENZ, Bettina - EHLING, Rainer - HEGEN, Harald - DEISENHAMMER, Florian - ABOUL-ENEIN, Fahmy - STORCH, Maria K. - KOSOŇ, Peter - DRULOVIC, Jelena - KRISTOFERITSCH, Wolfgang - BERGER, Thomas - REINDL, Markus. Complement activating antibodies to myelin oligodendrocyte glycoprotein in neuromyelitis optica and related disorders. In *Journal of Neuroinflammation*, 2011, vol. 8, p.184. (2010: 5.785 - IF, Q1 - JCR, 2.423 - SJR, Q1 - SJR, Current Contents - CCC). (2011 - Current Contents). ISSN 1742-2094. Available at: <https://doi.org/10.1186/1742-2094-8-184>
Citations: **187**
3. CANU, N. - DUS, L. - BARBATO, C. - CIOTTI, M. - BRANCOLINI, C. - RINALDI, A.W. - NOVÁK, Michal - CATTANEO, A. - BRADBURY, A. - CALISSANO, P. Tau cleavage and dephosphorylation in cerebellar granule neurons undergoing apoptosis. In *Journal of Neuroscience*, 1998, vol. 18, p.7061-7074. (1998 - Current Contents). ISSN 0270-6474.
Citations: **180**
4. SENGUPTA, A. - KABÁT, Juraj - NOVÁK, Michal - WU, Q.L. - GRUNDKE-IQBAL, I. - IQBAL, K. Phosphorylation of tau at both Thr 231 and Ser 262 is required for maximal

inhibition of its binding to microtubules. In *Archives of Biochemistry and Biophysics*, 1998, vol.357, p.299-309. (1997: 2.649 - IF, Current Contents - CCC). (1998 - Current Contents). ISSN 0003-9861.

Citations: **177**

5. ALONSO, A. - MEDERLYOVÁ, Anna - NOVÁK, Michal - GRUNDKE-IQBAL, I. - IQBAL, K. Promotion of Hyperphosphorylation by Frontotemporal Dementia Tau Mutations. In *Journal of Biological Chemistry*, 2004, vol. 279, no. 33, p. 34873-34881. (2003: 6.482 - IF, Current Contents - CCC). (2004 - Current Contents). ISSN 0021-9258.
Citations: **167**

6. FASULO, L. - UGOLINI, G. - VISINTIN, M. - BRADBURY, A. - BRANCOLINI, C. - VERZILLO, V. - NOVÁK, Michal. The neuronal microtubule-associated protein tau is a substrate for caspase-3 and an effector of apoptosis. In *Journal of Neurochemistry*, 2000, vol. 75, no. 2, p. 1-10. ISSN 0022-3042.
Citations: **146**

7. ŽILKA, Norbert - FILIPČÍK, Peter - KOSOŇ, Peter - FIALOVÁ, Ľubica - ŠKRABANA, Rostislav - ŽILKOVÁ, Monika - ROLKOVÁ, Gabriela - KONTSEKOVÁ, Eva - NOVÁK, Michal. Truncated tau from sporadic Alzheimers disease suffices to drive neurofibrillary degeneration in vivo. In *FEBS Letters : Federation of European Biochemical Societies Letters for the Rapid Publication of Short Reports in Biochemistry, Biophysics and Molecular Biology*. - Amsterdam : Elsevier Science Publishers, 2006, vol.580, p.3582-3588. (2005: 3.415 - IF, Q2 - JCR, 2.159 - SJR, Q1 - SJR). ISSN 1873-3468.
Citations: **133**

8. ŠVASTOVÁ, Eliška - ŽILKA, Norbert - ZAŤOVIČOVÁ, Miriam - GIBADULINOVÁ, Adriana - ČIAMPOR, Fedor - PASTOREK, Jaromír - PASTOREKOVÁ, Silvia. Carbonic anhydrase IX reduces E-cadherin-mediated adhesion of MDCK cells via interaction with beta-catenin. In *Experimental Cell Research*, 2003, vol. 290, p. 332-345. (2002: 4.712 - IF). Available at: [https://doi.org/10.1016/S0014-4827\(03\)00351-3](https://doi.org/10.1016/S0014-4827(03)00351-3)
Citations: **133**

9. EBRINGER, L. - FERENČÍK, Miroslav - KRAJČOVIČ, J. Beneficial health effects of milk and fermented dairy products. In *Folia microbiologica*, 2008, vol.53, p.378-394. (2007: 0.989 - IF, Q4 - JCR, 0.365 - SJR, Q2 - SJR, Current Contents - CCC). (2008 - Current Contents). ISSN 0015-5632.
Citations: **121**

10. TOKAR, T. - PASTRELLO, C. - ROSSOS, A.E.M. - ABOVSKY, M. - HAUSCHILD, A.C. - TSAY, M. - LU, R. - JURIŠICA, Igor**. mirDIP 4.1-integrative database of human microRNA target predictions. In *Nucleic acids research*, 2018, vol. 46, iss. D1, p. D360-D370. (2017: 11.561 - IF, Q1 - JCR, 9.025 - SJR, Q1 - SJR, Current Contents - CCC). (2018 - Current Contents). ISSN 0305-1048. Available at: <https://doi.org/10.1093/nar/gkx1144>
Citations: **103**

2.2.4. List of 10 most-cited publications published during the evaluation period (2016-2021) with the address of the Institute, with number of citations obtained until 2021

1. TOKAR, T. - PASTRELLO, C. - ROSSOS, A.E.M. - ABOVSKY, M. - HAUSCHILD, A.C. - TSAY, M. - LU, R. - JURIŠICA, Igor**. mirDIP 4.1-integrative database of human microRNA target predictions. In *Nucleic acids research*, 2018, vol. 46, iss. D1, p. D360-D370. (2017: 11.561 - IF, Q1 - JCR, 9.025 - SJR, Q1 - SJR, Current Contents - CCC).

(2018 - Current Contents). ISSN 0305-1048. Available at:
<https://doi.org/10.1093/nar/gkx1144>
 Citations: **159**

2. POTOČNÁKOVÁ, L. - BHIDE, Mangesh - BORSZEKOVÁ PULZOVÁ, Lucia. An Introduction to B-Cell Epitope Mapping and In Silico Epitope Prediction. In *Journal of immunology research : an open access journal*, 2016, vol. 2016, article number 6760830, 11 p. (2015: 2.812 - IF, Q3 - JCR, 1.467 - SJR, Q1 - SJR). ISSN 2314-8861. Available at: <https://doi.org/10.1155/2016/6760830>
 Citations: **107**

3. JADHAV, Santosh - AVILA, J. - SCHOLL, M. - KOVACS, G.G. - KOVARI, E. - ŠKRABANA, Rostislav - EVANS, L.D. - KONTSEKOVÁ, Eva - MALAWSKA, B. - DE SILVA, R. - BUEE, L.** - ŽILKA, Norbert**. A walk through tau therapeutic strategies. In *Acta Neuropathologica Communications*, 2019, vol. 7, no.1, art. no. 22. (2018: 5.883 - IF, Q1 - JCR, 3.279 - SJR, Q1 - SJR). ISSN 2051-5960. Available at: <https://doi.org/10.1186/s40478-019-0664-z>
 Citations: **96**

4. SHI, M. - KOVÁČ, Andrej - KORFF, A. - COOK, T.J. - GINGHINA, C. - BULLOCK, K.M. - YANG, L. - STEWART, T. - ZHENG, D. - ARO, P. - ATIK, A. - KERR, K.F. - ZABETIAN, C.P. - PESKIND, E.R. - HU, S.C. - QUINN, J.F. - GALASKO, D.R. - MONTINE, T.J. - BANKS, William A. - ZHANG, J. CNS tau efflux via exosomes is likely increased in Parkinson's disease but not in Alzheimer's disease. In *Alzheimer's & Dementia*, 2016, vol. 12, p. 1125-1131. (2015: 11.619 - IF, Q1 - JCR, 4.581 - SJR, Q1 - SJR, Current Contents - CCC). (2016 - Current Contents). ISSN 1552-5260. Available at: <https://doi.org/10.1016/j.jalz.2016.04.003>
 Citations: **74**

5. GALAN, A. - COMOR, L. - HORVATIC, A. - KULES, J. - GUILLEMIN, N. - MRLJAK, V. - BHIDE, Mangesh. Library-based display technologies: where do we stand? In *Molecular Biosystems*, 2016, vol. 12, no. 8, p. 2342-2358. (2015: 2.829 - IF, Q2 - JCR, 1.260 - SJR, Q1 - SJR, Current Contents - CCC). (2016 - Current Contents). ISSN 1742-206X. Available at: <https://doi.org/10.1039/c6mb00219f>
 Citations: **58**

6. POSFAI, E. - PETROPOULOS, S. - DEBARROS, F.R.O. - SCHELL, J.P. - JURIŠICA, Igor - SANDBERG, R. - LANNER, F. - ROSSANT, J. Position- and Hippo signaling-dependent plasticity during lineage segregation in the early mouse embryo. In *eLife*, 2017, vol. 6, art. no. e22906. (2016: 7.725 - IF, Q1 - JCR, 7.296 - SJR, Q1 - SJR). ISSN 2050-084X. Available at: <https://doi.org/10.7554/eLife.22906>
 Citations: **49**

7. YAO, Z. - DAROWSKI, K. - ST-DENIS, N. - WONG, V. - OFFENSPERGER, F. - VILLEDIEU, A. - AMIN, S. - MALTY, R. - AOKI, H. - GUO, H. - XU, Y. - IORIO, C. - KOTLYAR, M. - EMILI, A. - JURIŠICA, Igor - NEEL, B.G. - BABU, M. - GINGRAS, A.C. - STAGLJAR, I. A Global Analysis of the Receptor Tyrosine Kinase-Protein Phosphatase Interactome. In *Molecular Cell*, 2017, vol. 65, no. 2, p. 347-360. (2016: 14.714 - IF, Q1 - JCR, 13.619 - SJR, Q1 - SJR, Current Contents - CCC). (2017 - Current Contents). ISSN 1097-2765. Available at: <https://doi.org/10.1016/j.molcel.2016.12.004>
 Citations: **49**

8. KOTLYAR, Max - PASTRELLO, Chiara - MALIK, Zara - JURIŠICA, Igor**. IID 2018 update: context-specific physical protein-protein interactions in human, model organisms and domesticated species. In *Nucleic acids research*, 2019, vol. 47, p. D581-D589. (2018: 11.147 - IF, Q1 - JCR, 8.636 - SJR, Q1 - SJR, Current Contents - CCC). (2019 - Current Contents). ISSN 0305-1048. Available at: <https://doi.org/10.1093/nar/gky1037>
 Citations: **48**

9. NOVÁK, Petr - KONTSEKOVÁ, Eva - ŽILKA, Norbert - NOVÁK, Michal**. Ten Years of Tau-Targeted Immunotherapy: The Path Walked and the Roads Ahead. In *Frontiers in Neuroscience*, 2018, vol. 12, article number 798. (2017: 3.877 - IF, Q2 - JCR, 1.769 - SJR, Q1 - SJR, Current Contents - CCC). (2018 - Current Contents). ISSN 1662-453X. Available at: <https://doi.org/10.3389/fnins.2018.00798>
Citations: **39**
10. ENDISHA, H. - ROCKEL, J. - JURIŠICA, Igor - KAPOOR, M.**. The complex landscape of microRNAs in articular cartilage: biology, pathology, and therapeutic targets. In *JCI Insight*, 2018, vol. 3, no. 17, p. e121630. (2018 - Current Contents). ISSN 2379-3708. Available at: <https://doi.org/10.1172/jci.insight.121630>
Citations: **38**

2.2.5. List of most-cited authors from the Institute (at most 10 % of average FTE researchers per year) and their number of citations in the assessment period (2015– 2020). The cited papers must bear the address of the institute

Novak Michal
Citations: 1638

Zilka Norbert
Citations: 996

Kovac Andrej
Citations: 509

2.2.6. List of most-cited authors from the Institute (at most 10 % of average FTE researchers per year) and their number of citations obtained until 2020. The cited papers must bear the address of the Institute

Novak Michal
Citations: 3295

Zilka Norbert
Citations: 1428

Filipcik Peter
Citations: 669

2.2.7. List of most-cited authors from the Institute (at most 10 % of average FTE researchers per year) and their number of citations obtained until 2021 of their papers published during the evaluation period (2016– 2021). The cited papers must bear the address of the Institute

Jurisica Igor

Citations: 559

Kovac Andrej

Citations: 332

Bhide Mangesh

Citations: 265

2.3. Research status of the institute in international and national context

- **International/European position of the institute**

2.3.1. List of the most important research activities demonstrating the international relevance of the research performed by the institute, incl. major projects (details of projects should be supplied under Indicator 2.4). Max. 10 items for institute with less than 50 average FTE researchers per year, max. 20 for institutes with 50 – 100 average FTE researchers per year and so on

RESEARCH AREA: NEURODEGENERATIVE DISEASES

Topic/Project name: Coordination Action in support of the sustainability and globalisation of the Joint Programming Initiative on Neurodegenerative Diseases (H2020 – JPND - 681043)

Brief description: The aim was to create a dedicated structure responsible for long-term JPND management and implementation, and extension of JPND membership to EU Member States and other countries and initiatives not yet participating.

Duration: 01.11.2015 – 31.10.2021

RESEARCH AREA: ALZHEIMER'S DISEASE

Topic/Project name: Pathway complexities of protein misfolding in neurodegenerative diseases: a novel approach to risks evaluation and model development (H2020 – JPND - FP-829-085)

Brief description: The aim was to understand the molecular bases of the heterogeneity of human neurodegenerative diseases with potential diagnostic and therapeutic implications.

Duration: 01.5.2016 – 31.12.2019

Topic/Project name: Alzheimer's disease data-driven insights on individual outcomes of importance (HESOCARE-329-074 (H2020/JPND) – ADDITION)

Brief description: The project aimed to bring new understanding of which aspects are the most important to patients suffering from dementia and caregivers to preserve and improve their autonomy, dignity, and quality of life.

Duration: 1.5.2019 - 30.09.2023

Topic/Project name: The tryptophan kynurenine pathway - therapeutic strategy for neuroprotection in tauopathies (CRP/SVK18-01 - ICGEB)

Brief description: The main aim of the project was to analyze how administration of a synthetic analog of kynurenic acid would affect the metabolism of tryptophan and thus modify the process of neurodegeneration in animal model of tauopathies.

Duration: 1.1.2019 - 31.12.2021

RESEARCH AREA: REGENERATIVE MEDICINE

Topic/Project name: Bridging the gap between science, education and enterprise in regenerative medicine (22020272 - Visegrad Fund)

Brief description: The aim was to share experience and exchange information within V4U scientific, educational, and business organizations to improve the visibility and competitiveness of V4U organizations and join the opinion leader positions in the expanding regenerative medicine field.

Duration: 1.10.2020 - 20.3.2022

RESEARCH AREA: STRUCTURAL BIOLOGY

Topic/Project name: Non-globular proteins - from sequence to structure, function and application in molecular physiopathology (NGP-NET)

Brief description: The aim was to create a pan-European scientific network of groups that work on non-globular proteins to strengthen, focus, and coordinate research in this field.

Duration: 31.5.2015 - 25.3.2019

2.3.2. List of international conferences (co)organised by the institute

No	Year	Conference	Place
1.	2016	Neuropsychiatric disorders – From Basic Systems to Clinical Applications: Czech and Slovak Neuroscience Alumni Workshop	Praque
2.	2016	8th international scientific conference "Senior's training and nonpharmacological intervention for Alzheimer's disease Alzheimerovej choroby"	Bratislava
3.	2016	Alzheimer's disease - the epidemic of Third Millenium. Are we ready to face it?	Bratislava
4.	2017	3 rd NGP-Net SYMPOSIUM ON NON-GLOBULAR PROTEINS	Kosice
5.	2017	IVBM Slovakia 2017: International Veterinary Behaviour Meeting	Samorin
6.	2017	9th th international scientific conference "Senior's training and nonpharmacological intervention for Alzheimer's disease"	Bratislava

No	Year	Conference	Place
7.	2018	10th th international scientific conference "Senior's training and nonpharmacological intervention for Alzheimer's disease	Bratislava
8.	2019	11th international scientific conference "Senior's training and nonpharmacological intervention for Alzheimer's disease	Bratislava
9.	2019	4th meeting of Middle-European Societies for Immunology and Allergology - MESIA	Samorin
10.	2021	12th international scientific conference Alzheimerforum 2021	Bratislava/online

2.3.3. List of edited proceedings from international scientific conferences

No	Year	Proceeding
1.	2017	Book of Abstracts - 3 rd NGP-Net symposium on non-globular proteins

2.3.4. List of journals edited/published by the institute and information on their indexing in WOS, SCOPUS, other database or no database, incl. impact factor and other metrics of journals in each year of the assessment period

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- **National position of the institute**

2.3.5. List of selected activities of national importance

We have multiple collaborations with academic institutions at the national and international levels.

We have created a network of institutions focusing on a new diagnostic concept for Alzheimer's disease, which include 1st and 2nd Departments of Neurology of the Faculty of Medicine, Comenius university in Bratislava, and Department of Neurology, Pavol Jozef Safarik University and University Hospital in Kosice.

In collaboration with prof. Daniela Ostatnikova from the Faculty of Medicine, Comenius University in Bratislava we are running several projects on the proteome and metabolome in autistic children.

We have several collaborative projects on Parkinson's disease with the Jessenius Faculty of Medicine in Martin and Department of Neurology, Pavol Jozef Safarik University and University Hospital in Kosice.

In collaboration with the National Institute of Children Diseases we have investigated the immune response against SARS-CoV-2 in children suffering from immunological disorders.

A fruitful collaboration arose with dr. Vladimir Leksa group at the Institute of Molecular Biology, SAS and Medical University of Vienna, Austria, and dr. Peter Barath at the Institute of Chemistry, SAS, on the role of the innate immune response protein lactoferrin in the regulation of fibrinolysis, as well as coronavirus infection.

We initiated a new collaborative project with the group of dr. Milos Hricovini at the Institute of Chemistry, SAS on the computational and spectroscopic characterization of fundamental structural principles of non-globular disordered proteins, with implications for neurodegenerative diseases.

In collaboration with prof. Peter Mikus from the Faculty of Pharmacy, Comenius University in Bratislava we are running several projects on the analysis of endogenous metabolites and pharmaceuticals in body fluids and tissues.

In collaboration with the Faculty of Physical Education and Sport, Comenius University in Bratislava we investigate the molecular pathways associated with head impacts in soccer players.

We have several collaborative projects with Trnava University in Trnava and the Faculty of Physical Education and Sport, Comenius University in Bratislava oriented on the research of cognitive consequences of sport-related traumatic brain injuries in adolescents in the Slovak Republic.

RESEARCH AREA: ALZHEIMER'S DISEASE

Topic/Project name: The model of the neuroimmune crosstalk in Alzheimer's disease (APVV-14-0872)

Brief description: The project had an ambition to unravel disease modification of neuroimmune crosstalk leading to dementia. Using in vivo imaging tools we were able to monitor in situ behaviour and properties of microglia cells located in the vicinity of tangle-bearing neurons.

Duration: 01.07.2015 – 30.06.2018

Topic/Project name: Use of animal models for tauopathies for identification of molecular pathways involved in the etiology of neurofibrillary degeneration (APVV-16-0531)

Brief description: We identified tau interaction partners playing a role in physiological cellular pathways that were either activated in neurons to protect themselves and eliminate pathological proteins, or are inappropriately activated, thus promoting neurofibrillary pathology.

Duration: 01.07.2017 – 30.10.2020

Topic/Project name: 3D In vitro Modelling of Alzheimer's Disease using Astrocytes derived from Induced Pluripotent Stem Cells (APVV-17-0642)
Brief description: We identified inherent differences in global gene expression and protein secretion between healthy and diseased patient iPSC.
Duration: 01.08.2018 – 31.12.2021

Topic/Project name: Inhibitory cortical circuits mediating cognitive dysfunction in Alzheimer's disease (APVV-19-0585)
Brief description: We determined the impact of neurodegeneration on activity of well-defined classes of cortical interneurons and their neuronal circuits in sensory and association areas.
Duration: 01.07.2020 – 30.06.2023

Topic/Project name: Longitudinal Assessment of Neurodegeneration and the Correlates of Relevant Endpoints in AD (APVV-20-0447)
Brief description: We established cohorts for measuring several types of outcomes in the same patients, to establish predictors of disease progression speed, and of the maintenance/loss of the capability to perform activity of daily living.
Duration: 01.07.2021 – 30.06.2024

Topic/Project name: Neuro-glia cell-based model for inter-neuronal spread of tau pathology (APVV-20-0585)
Brief description: We will develop a human multi-glia model system that will allow us to determine the role of glial cells and their activation status under stimulated neuroinflammation on tau spreading mechanism and cell specific distribution.
Duration: 01.07.2021 – 30.06.2025

RESEARCH AREA: THERAPY FOR CNS DISORDERS

Topic/Project name: Development of novel peptide-based system for delivery of therapeutics into the brain (APVV-14-0547)
Brief description: Our project focused on development of novel peptide based transporting vectors for neuropharmaceuticals.
Duration: 01.07.2015 – 30.06.2018

Topic/Project name: Study of functional bio-implants and stem cells for CNS regeneration (APVV-15-0613)

Brief description: We clarified the specific mechanisms of action of bio-implants and MSC in order to: i) reduce pro-inflammatory cytokines released from microglia/macrophages in injured nerve tissue, and ii) enhance the regrowth of nerve fibers.

Duration: 01.07.2016 – 12.06.2020

RESEARCH AREA: **COVID-19**

Topic/Project name: Development of therapeutic biomolecules blocking SARS-COV-2 infection (PP-COVID-20-0044)

Brief description: We validated receptor-binding site on spike protein with advanced proteomics tools (limited proteolysis coupled with mass spectrometry followed by protein array and advanced bioinformatic tools) and developed an agent to block the binding of spike protein to ACE2 and thus host cells.

Duration: 16.09.2020 – 31.12.2021

RESEARCH AREA: **TRAUMATIC BRAIN INJURY**

Topic/Project name: Molecular pathways induced by traumatic brain injury: novel biomarkers and prediction of new therapeutic targets for neurodegeneration (APVV-20-0615)

Brief description: We aimed our research on detailed investigation of miRNAs in peripheral blood of head impact sufferers.

Duration: 01.07.2021 – 30.06.2024

RESEARCH AREA: **PARKINSON'S DISEASE**

Topic/Project name: Spread of alpha-Synuclein-associated pathology across gastrointestinal organs in a mouse model and patients with Parkinson's disease (APVV-20-0331)

Brief description: The main goal of our project is to focus on a more comprehensive analysis of individual GIT tissues, obtained from appropriate animal models and biopsies from patients both in the pre-motor stage and after the onset of motor symptoms of the disease.

Duration: 01.07.2021 – 30.06.2024

2.3.6. List of journals (published only in the Slovak language) edited/published by the institute and information on their indexing in WOS, SCOPUS, other database or no database, incl. impact factor and other metrics of journals in each year of the assessment period

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- **Position of individual researchers in the international context**

2.3.7. List of invited/keynote presentations at international conferences, as documented by programme or invitation letter

2016

Hromadka, T. „From molecules to cognition: Understanding Alzheimer's disease“, Neuropsychiatric disorders – From Basic Systems to Clinical Applications: Czech and Slovak Neuroscience Alumni Workshop, Praha, Czech republic, June 24.–25, 2016

Hromadka, T. Od molekúl k poznaniu: Čo je potrebné k pochopeniu Alzheimerovej choroby? VIII. medzinárodná vedecká konferencia: Aktivizácia seniorov a nefarmakologické prístupy v liečbe Alzheimerovej choroby, Garni*G Hotel Bratislava, Slovakia, September 22-23, 2016

Kovac, A. Biofarmaceutiká – skúsenosti z oblasti neurodegenerácie, VIZE 2016, Brno, Czech Republic, November 22. 2016

Novak, P. Pharmacological and non-pharmacological strategies in the maze of Alzheimer's disease pathophysiology: Is there a road to treatment and prevention? SK EU2016, Alzheimer's disease – epidemic of the third millennium, Bratislava, Slovakia, November 28-29, 2016

Novak, M. Slovak National Program to Combat Alzheimer's disease and Other Dementia. The Netherlands EU Presidency 2016, Conference "Living well with(out) dementia", Amsterdam, Netherlands, May 9-10, 2016

Novak, M. The first tau vaccine for therapy of Alzheimer's disease and FTDL: from tau structure to human clinical trials, The Alzheimer's Association International Conference 2016 AAIC, Toronto, Canada, June 24-28, 2016

Novak, M. Immunotherapy of Alzheimer's disease research & development, Meeting of the EU Research Working Party during Slovak EU Presidency, Brussel, Belgium, September 29, 2016

Novak, M. Slovak national plan to conquer Alzheimer's disease and other forms of dementia, SK EU2016, Alzheimer's disease – epidemic of the third millennium, Bratislava, Slovakia, November 28-29, 2016

Novak, M. Message towards the EU society, SK EU2016, Alzheimer's disease – epidemic of the third millennium, Bratislava, Slovakia, November 28-29, 2016

Prcina, M. What we know about immunosenescence, 3rd Meeting of Middle -European Societies for Immunology and Allergology. Budapest, Hungary, december 1-3, 2016

Zilkova, M. Model for interaction of immune and neuronal systems in neurodegeneration, 3rd Meeting of Middle -European Societies for Immunology and Allergology. Budapest, Hungary, december 1-3, 2016

2017

Hromadka, T. Two photon microscopy ... a solution to all misery, Synapse Methodology Course, Bordeaux, 18.-26. januára 2017

Novak, M. The driver and the others: Monitoring of human AD tau spreading in vivo, 1st EuroTau Meeting 2017, 27. - 28. 4 2017, Lille, France

2018

Kontsekova, Eva. Alzheimerova choroba a imunoterapia, XXI. ČASOMIL, BESKYDY, Bzove, Česká republika, 30.5-1.6.2018.

Novak, Michal - Smolek, Tomas. Humanized Rat Tau Model For AD. 2nd EuroTau Meeting 2018. Lille, France, 26-27, April, 2018.

Smolek, Tomas. How we can modulate tau spreading in vivo. JPnD Meeting 2018. Trieste, Italy, March, 14-16, 2018.

2019

Bhide, Mangesh. Borrelia and complement system: an example of perfect anti-immunology. 4th Meeting of Middle - European Societies for Immunology and Allergology, MESIA 2019, Samorín, Slovakia, November 28-30, 2019

Cizkova, Dasa - Cubinkova, Veronika - Smolek, Tomas. Result report. Eranet Neuron Meeting Bonn, Bonn, Germany, 10-11 oktober 2019

Cizkova, Dasa. Immune profile following acute spinal cord injury. 4th Meeting of Middle - European Societies for Immunology and Allergology, MESIA 2019, Šamorín, Slovakia, November 28-30, 2019.

Filipcik P, Cente M, Toth I, Jurisica I. On the way to non-pharmacological treatment of traumatic brain injury. In "XI. medzinárodná vedecká konferencia: Aktivácia seniorov a nefarmakologické prístupy v liečbe Alzheimerovej choroby. Bratislava, Slovakia, 19. september 2019.

Kovac, Andrej - Majerova, Petra - Michalicova, Alena – Kovacech, Branislav – Novak, Michal. Blood-brain barrier changes induced by intrinsically disordered proteins. 1st Mini-symposium on the blood-brain barrier from basic to clinical research, Nagasaki, Japan, March 7, 2019

Mihaljevic, Sandra - Majerova, Petra – Kovac, Andrej. Changes of the choroid plexus barrier in tauopathies. 4th Meeting of Middle- European Societies for Immunology and Allergology, MESIA 2019, Samorín, Slovakia, November 28-30, 2019.

Novak P, Novak M. Active immunotherapy for Alzheimer's disease – targeting the altered biochemistry of tau protein to halt neurodegeneration. European ICGB - CEI - JRC-EC - UCM Workshop "Trends and prospects of Med/Pharma Biotechnologies in Europe: Towards Strengthening Regional Cooperation Including CEE Countries", Bratislava, Slovakia, June 4, 2019.

Novakova M. Become the sculptor of your brain! In "XI. medzinárodná vedecká konferencia: Aktivácia seniorov a nefarmakologické prístupy v liečbe Alzheimerovej choroby. Bratislava, Slovakia, 19. september 2019.

Sykova, E. Astrocytes and stem cells in pathophysiology of neurodegenerative diseases. Conference The other brain. Ljubljana, Slovenia, November 7-8, 2019.

Sykova, E. M. – Forostyak, S. – Kwok, J.C. – Romanyuk, N. – Rehorova, M. - Raha-Chowdhury, R.- Jendelova, P. – Fawcett, J.W. mesenchymal stem cells and neural precursors derived from induced pluripotent cells preserve perineuronal nets and stimulate neural plasticity in ALS rats. Society for Neuroscience, Chicago, USA October 19-24, 2019. Electronic abstracts no 356.01

Sykova, E. Astrocytes and stem cells in pathophysiology of ageing and neurodegenerative diseases. International conference Functions on Neuroglia, Tbilisi, Georgia, September 26-28, 2019, p. 20

Sykova, E. Astrocytes and stem cells in pathophysiology of neurodegenerative diseases. 4th Meeting of Middle – European Societies for Immunology and Allergology, Samorin, Slovakia, November 28-30, 2019, p. 69

Zilka, Norbert. The importance of being Earnest: the conversation of the brain immune system and degeneration. 4th Meeting of Middle - European Societies for Immunology and Allergology, MESIA 2019, Samorín, Slovakia, November 28-30, 2019.

2020

Majerova Petra, Olesova Dominika, Kovac Andrej. Choroid plexus and its role in tauopathies. 2nd Mini-Symposium on the Blood-brain Barrier from Basic to Clinical Research. March 6.-7. 2020. Fukuoka, Japan

2021

Fricova D. What can we learn from Parkinson's disease related mutations? 'Seminar Speaker Series' of project

StruBioMol, Interreg Slovakia-Austria, European regional development fund, November 23 2021 Nov 23, Bratislava, Slovakia.

Jampilek, Josef. Nanomaterials Suitable to Manage Fungal Diseases. 2021 International Conference on Nanotechnology and Applications (ICNA2021), Online, Guilin, China, July 23-25, 2021

Jampilek, Josef. Application of Carbon-Based Nanomaterials as Drug Delivery Systems. The 3rd International Conference on Graphene and Novel Nanomaterials (GNN 2021), Online, Macau SAR, China, August 16-19, 2021

Kovac Andrej, Olesova Dominika, Michalicova Alena, Majerova Petra. The tryptophan kynurenine pathway as a therapeutic strategy for neuroprotection in tauopathies. 3rd Mini symposium on the blood brain barrier: From basic to clinical research. Online, March 26 - 27. 2021, Izumo, Shimane Japan

Olesova, Dominika - Majerova, Petra - Dobesova, Dana - Brumarova, Radana - Friedecky, David - Kovac, Andrej. Lipid accumulation in brain tissue and CSF correlates with neurofibrillary pathology in a transgenic rat model for tauopathy. In Mini symposium on the blood brain barrier. 3rd Mini symposium on the blood brain barrier. Online, March 26 - 27, 2021, Izumo, Shimane Japan

Sykova E. Stem cells and biomaterial for treatment of spinal cord injury and ALS. COST symposium: Emerging biomaterials and regenerative cardiology and neurology, Prague, Czech Republic, July 27- 29, 2021.

Zilka N., Kovacech B., Kontsekova E. TAUizmus modernej diagnostiky a terapie Alzheimerovej choroby. Pražské gerontologické dny 2021, October 6 - 7, 2021, Praha, Czech Republic

Zilka N. Výsledky fázy II a budovanie slovenskej kohorty pacientov s demenciou. Kognitivní poruchy a demence XVIII, October 14 15 2021, Brno, Czech Republic

2.3.8. List of researchers who served as members of the organising and/or programme committees

No	Name	Year	Conference	Committee	Place
1.	Bhide Mangesh Ramesh	2017	The 11th Central and Eastern European Proteomic Conference	programme & organising	Kosice
2.	Brandoburová Petra	2018	10th international conference on Activation of the elderly and non-pharmacological approaches in the treatment of Alzheimer's disease c	programme & organising	Bratislava
3.	Cehlár Ondrej	2017	3 rd NGP-Net SYMPOSIUM ON NON-GLOBULAR PROTEINS	organising	Kosice
4.	Čunderlíková Mária	2018	10th international conference on Activation of the elderly and non-pharmacological approaches in the treatment of Alzheimer's disease c	programme & organising	Bratislava

No	Name	Year	Conference	Committee	Place
5.	Hromadka Tomas	2021	TENSS, Transylvanian Experimental Neuroscience Summer School	programme	Romania/online
		2021	COSYNE	organising	online
		2019	EBBS 2019	organising	Praque
		2019	TENSS, Transylvanian Experimental Neuroscience Summer School	programme & organising	Romania
		2018	10th international conference on Activation of the elderly and non-pharmacological approaches in the treatment of Alzheimer's disease c	programme	Bratislava
		2016	Neuropsychiatric disorders – From Basic Systems to Clinical Applications: Czech and Slovak Neuroscience Alumni Workshop	programme & organising	Praha
6.	Jampilek Josef	2021	2021 International Conference on Nanotechnology and Applications	programme	online
		2021	25th International Electronic Conference on Synthetic Organic Chemistry	programme	online
		2021	7th Nanomaterials and Nanotechnology Meeting	programme	online
		2020	The 24th International Electronic Conference on Synthetic Organic Chemistry (ECSOC–24)	programme	online
		2019	23rd International Electronic Conference on Synthetic Organic Chemistry (ECSOC-23)	programme	
		2019	8th World Conference on Physico-Chemical Methods in Drug Discovery and Development	programme	Croatia
		2019	Nanomaterials and Nanotechnology Meeting (NanoOstrava 2019)	programme	Ostrava
7.	Kontsekova Eva	2019	MESIA, 4th Meeting of Middle -European Societes for Immunology and Allergology	programme & organising	Samorin
		2016	3rd Meeting of Middle - European Societies for Immunology and Allergology	programme & organising	Budapest
8.	Kovac Andrej	2021	3rd Mini-Symposium on the Blood-Brain Barrier from Basic to Clinical Research	programme	Japan/online
9.	Krakovska Simona	2018	10th international conference on Activation of the elderly and non-pharmacological approaches in the treatment of Alzheimer's disease c	programme & organising	Bratislava
10.	Novak Michal	2019	MESIA, 4th Meeting of Middle -European Societes for Immunology and Allergology	programme & organising	Samorin
		2017	8th International Symposium on Experimental and Clinical Neurobiology	programme	Kosice
		2016	3rd Meeting of Middle - European Societies for Immunology and Allergology	programme & organising	Budapest
		2016	31st International Conference of Alzheimer's Disease International	programme & organising	Budapest
11.	Novak Petr	2018	10th international conference on Activation of the elderly and non-pharmacological approaches in the treatment of Alzheimer's disease c	programme	Bratislava
12.	Skrabana Rostislav	2017	3 rd NGP-Net SYMPOSIUM ON NON-GLOBULAR PROTEINS	organising	Kosice

No	Name	Year	Conference	Committee	Place
13.	Smolek Tomas	2017	2017 Canine Conference - Cognition, Behaviour and Aging in Dogs and Cat	programme	Ontario
14.	Zilka Norbert	2017	IVBM Slovakia 2017: International Veterinary Behaviour Meeting	programme & organising	Samorin
15.	Zilkova Monika	2019	MESIA, 4th Meeting of Middle -European Societes for Immunology and Allergology	programme & organising	Samorin

2.3.9. List of researchers who received an international scientific award

No.	Name	Year	Award	Bestower
1.	Jampilek Josef	2021	Best Paper Award	6th World Congress on Recent Advances in Nanotechnology
2.	Novak Michal	2021	Lifetime Archievement Award	Alzheimer's Association
	Novak Michal	2016	Prize for research in Health Care for the Elderly and in Health Promotion	World Health Organization WHO
3.	Zilka Norbert	2021	Award of Eliska and Zdenek Strmiska	Endowment fund Alzheimer

• Position of individual researchers in the national context

2.3.10. List of invited/keynote presentations at national conferences, as documented by programme or invitation letter

2016

Novak, M. Alzheimer's disease – The story of Slovak Alzheimer's disease research network, National Program to Conquer Alzheimer's disease and Other Forms of Dementia, Smolenice, May 18-20, 2016,

Novak, M. The concept of the national program, National Program to Conquer Alzheimer's disease and Other Forms of Dementia, Smolenice, May 18-20, 2016,

Novak, P. Immunotherapy of Alzheimer's disease, National Program to Conquer Alzheimer's disease and Other Forms of Dementia, Smolenice, May 18-20, 2016,

Kovacech, B. CSF biomarkers for early stages of Alzheimer's disease, National Program to Conquer Alzheimer's disease and Other Forms of Dementia, Smolenice, May 18-20, 2016,

Kovac, A. Behind the horizon of biomarker discovery for AD diagnostics, National Program to Conquer Alzheimer's disease and Other Forms of Dementia, Smolenice, May 18-20, 2016,

Filipcik, P. Nucleic acids as biologics for neurodegeneration? National Program to Conquer Alzheimer's disease and Other Forms of Dementia, Smolenice, May 18-20, 2016,

Zilka, N. Slovak Alzheimer's disease activities – National-international nexus in neuroscience, National Program to Conquer Alzheimer's disease and Other Forms of Dementia, Smolenice, May 18-20, 2016

Prcina, M. Môže byť vakcinácia vo vyššom veku účinná? Biologická liečba v teórii a praxi, Bratislava, September 8, 2016

Cente, M. miRNA ako biomarkery neurodegeneračných ochorení, Biologická liečba v teórii a praxi, Bratislava, September 8, 2016

2017

Novak, M. How to conquer Alzheimer's disease in Slovakia, In Institute of Neuroimmunology – Annual Meeting, Current Status of Experimental Neuroimmunology in Slovakia, May 24-26, 2017, Smolenice, SR

Brandoburova, P. - Krakovska, S. Neuropsychology as the part of dementia diagnostic in Slovakia. Current Status of Experimental Neuroimmunology in Slovakia, May 24-26, 2017, Smolenice, SR

Cehlar, O. - Skrabana, R. - Filipcik, P. – Novak, M.: Tau oligomers toxicity and neuronal spreading: preparation, fluorescence labelling and cell culture study. In 8th International Symposium on Experimental and Clinical Neurobiology, June 18-21, 2017, Kosice, SR

Cehlar, O. - Skrabana, R. - Filipcik, P. – Novak, M.: Tau oligomers toxicity and neuronal spreading: preparation, fluorescence labelling and cell culture study. In Institute of Neuroimmunology – Annual Meeting, Current Status of Experimental Neuroimmunology in Slovakia May 24-26, 2017, Smolenice, SR

Cente, M. - Kosikova, N. - Novak, M. - Filipcik, P. Non-coding RNAs in pathogenesis of neurofibrillary degeneration. Current Status of Experimental Neuroimmunology in Slovakia, May 24-26, 2017, Smolenice, SR

Cížkova, D. - Murgoci, A. N. - Cízek, M. - Cubinkova, V. - Smolek, T. - Petrovova, E. - Kafka, J. - Maloveska, M. - Quanicco, J. P. - Fournier, I. - Salzert, M. Proteomic analyses along injured spinal cord axis: moving frontiers toward effective regeneration with smart scaffolds. In CEEPC. CEEPC 2017: Proceedings of the 11th Central and Eastern European Proteomic Conference, September 27-29, 2017, Kosice, Slovakia. 1. vyd. - Kosice; Kosice: COPYVAIT, 2017. ISBN 978-80-972017-5-3, s. 27

Murgoci, A.N. – Medvecký, L. – Cubinkova, V. – Gimeno, J-P. – Petrovova, E. – Salzert, M. – Cížkova, D. Proteomic and morphological features of rat microglia derived exosomes. In CEEPC. CEEPC 2017: Proceedings of the 11th Central and Eastern European Proteomic Conference, September 27-29, 2017, Košice, Slovakia. 1. vyd. - Kosice; Kosice: COPYVAIT, 2017. ISBN 978-80-972017-5-3, s. 36.

Cížkova, D. - Smolek, T. - Cubinkova, V. - Murgoci, A. N. - Petrovova, E. - Vdoviakova, K. - Kresakova, L. - Maloveska, M. - Cízek, M. Imunologická kontrola po traumatickom poškodení miechy. In Biologická liečba v teórii a praxi. Biologická liečba v teórii a praxi, 4. ročník. 1. vyd. - Dunajská Lužná: AH05, 2017, s. 27.

Murgoci, A. N. - Medvecký, L. - Gimeno, J.-P. - Majerová, P. - Salzert, M. - Cížkova, D. Characterization of exosomes derived from cortical and spinal cord primary microglia. In Current Status of Experimental Neuroimmunology in Slovakia. Current Status of Experimental Neuroimmunology in Slovakia: Annual meeting. 1. vyd. - Dunajská Lužná: AH05, 2017, s. 13.

Cížkova, D. - Murgoci, A. N. - Devaux, S. - Petrovova, E. - Kafka, J. - Cízek, M. - Salzert, M. Immune patrol following spinal cord injury: spatio-temporal study. In Current Status of

Experimental Neuroimmunology in Slovakia. Current Status of Experimental Neuroimmunology in Slovakia: Annual meeting. 1. vyd. - Dunajská Lužná: AH05, 2017, s. 14-15.

Hromádka, T. Introduction to biostatistics, Drug Discovery Course, Samorin, March 26-28, 2017

Hromádka, T. Introduction to clinical trials, Drug Discovery Course, Samorin, March 26-28, 2017

Hromádka, T. Cortical circuits mediating cognitive dysfunction in Alzheimer disease, Current status of experimental neuroimmunology in Slovakia, Smolenice, May 24-26, 2017

Hromádka, T. Cortical circuits mediating cognitive dysfunction in Alzheimer disease, 11th International veterinary behaviour meeting, Samorin, September 14-16, 2017

Hromádka, T. Cortical circuits—the road towards understanding Alzheimer disease, Biologická liečba v teórii a praxi 4, Bratislava, September 26, 2017

Hanes, J. Highly sensitive immunological methods. The 11th Central and Eastern European Proteomic Conference, September 27-29, 2017, Kosice

Hanes, J. Highly sensitive immunological methods. Current Status of Experimental Neuroimmunology in Slovakia, May 24-26, 2017, Smolenice, SR

Hanes, J. Vysoko citlivé imunologické metódy na stanovenie biomarkerov v krvi, Biologická liečba v teórii a praxi, Bratislava, September 26, 2017

Majerová, P.- Michalíková, A.- Kováč, A. Mozgovo-cievna bariéra ako hlavný problém biologickej liečby chorôb centrálneho nervového systému (Biologická liečba v teórii a praxi, Bratislava, Slovakia, September 26, 2017, ISBN: 978-80-971357-4-4, str. 128-133)

Majerová, P.- Sinský, J.- Michalíková, A.- Kováč, A. Použitie LC-MALDI-MS v modernej proteomickej analýze (HPLC-MS seminar, Bratislava, Slovakia, November 10, 2017, ISBN: 978-80-223-4426-5, str. 42)

Majerová, P.- Garruto, R.- Kováč, A. Vascular inflammation in Guam Parkinsonism dementia (Current status of experimental neuroimmunology in Slovakia, Smolenice, Slovakia, May 24-26, 2017)

Michalíková, A. - Majerová, P. - Cente, M. - Kittel, A. - Kováč, A. - Novák, M. Changes of the neurovascular unit in transgenic rat model for tauopathies SHR-24. Current Status of Experimental Neuroimmunology in Slovakia. May 24-26, 2017, Smolenice, Slovensko

Novák, P. - Zilka, N. - Kontšeková, E. - Kováčech, B. - Zilková, M. - Ondruš, M. - Katina, S. - Novák, M. So - how far have we gotten with anti-tau therapy as of today? Current Status of Experimental Neuroimmunology in Slovakia. May 24-26, 2017, Smolenice, Slovensko

Prcina, M. – Kazmerová, Z. – Fialová, L. - Kontšeková, E. – Novák, M. Can we predict immune response in old patients? 8th International Symposium on Experimental and Clinical Neurobiology, Kosice June 18-21, 2017

Prcina, M. – Kazmerová, Z. – Fialová, L. - Kontšeková, E. – Novák, M. Peculiarities of immune response to tau protein. Current status of experimental neuroimmunology in Slovakia. Smolenice. May 24-26, 2017

Kontšeková, E. - Zilka, N. - Novák, M. Imunoterapia v Alzheimerovej chorobe. XXXIV. Zjazd slovenských a českých alergológov a klinických imunológov so spoluúčasťou ČIS a SIMS, Horný Smokovec, Vysoké Tatry, October 18-21, 2017

Kontsekova, E. - Zilka, N. - Novak, M. Neurozápal v Alzheimerovej chorobe. XXXIV. Zjazd slovenských a českých alergológov a klinických imunológov so spoluúčasťou ČIS a SIMS, Horný Smokovec, Vysoké Tatry, October 18-21, 2017

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2.3.11. List of researchers who served as members of organising and programme committees of national conferences

No	Name	Year	Conference	Committee	Place
1.	Bhide Mangesh Ramesh	2021	Young Neuroscientists and Cutting-Edge Research	programme	online
		2020	Young Neuroimmunologists: a great hope for our healthy future	programme	online
2.	Cente Martin	2020	Young Neuroimmunologists: a great hope for our healthy future	organising	online
		2019	Advances in experimental neuroimmunology 2019	programme	Smolenice
		2019	Biologická liečba v teórii a praxi V.	programme & organising	Bratislava
		2018	Advances in slovak experimental neuroimmunology 2018	programme	Smolenice
		2017	Biologická liečba v teórii a praxi IV.	programme & organising	Bratislava
		2017	Current Status of Experimental Neuroimmunology in Slovakia	programme & organising	Smolenice
		2016	Biological Therapy in Theory and Practice III	programme & organising	Bratislava
3.	Cizkova Dasa	2021	Young Neuroscientists and Cutting-Edge Research	programme & organising	online
		2020	Young Neuroimmunologists: a great hope for our healthy future	programme	online
		2018	Current Status of Experimental Neuro-Immunology in Slovakia II	programme & organising	Kosice
4.	Filipcik Peter	2021	Young Neuroscientists and Cutting-Edge Research	programme	online
		2020	Young Neuroimmunologists: a great hope for our healthy future	programme	online

No	Name	Year	Conference	Committee	Place
		2019	Advances in experimental neuroimmunology 2019	programme & organising	Smolenice
		2019	Biologická liečba v teórii a praxi V.	programme & organising	Bratislava
		2018	Advances in slovak experimental neuroimmunology 2018	programme	Smolenice
		2018	Current Status of Experimental Neuro-Immunology in Slovakia II	programme	Kosice
		2017	Biologická liečba v teórii a praxi IV.	programme & organising	Bratislava
		2017	Current Status of Experimental Neuroimmunology in Slovakia	programme & organising	Smolenice
		2016	Biological Therapy in Theory and Practice III	programme & organising	Bratislava
5.	Hromadka Tomas	2021	Young Neuroscientists and Cutting-Edge Research	programme	online
		2020	Young Neuroimmunologists: a great hope for our healthy future	programme	online
		2018	Advances in slovak experimental neuroimmunology 2018	programme	Smolenice
		2018	Current Status of Experimental Neuro-Immunology in Slovakia II	programme	Kosice
6.	Kontsekova Eva	2021	Young Neuroscientists and Cutting-Edge Research	programme	online
		2020	Young Neuroimmunologists: a great hope for our healthy future	programme	online
7.	Kovacech Branislav	2019	Advances in experimental neuroimmunology 2019	programme	Smolenice
8.	Murgoci Adriana-Natalia	2018	Current Status of Experimental Neuro-Immunology in Slovakia II	programme & organising	Kosice
9.	Novak Michal	2019	Advances in experimental neuroimmunology 2019	programme & organising	Smolenice
		2018	Advances in slovak experimental neuroimmunology 2018	programme & organising	Smolenice
		2018	Current Status of Experimental Neuro-Immunology in Slovakia II	programme & organising	Kosice
		2017	Current Status of Experimental Neuroimmunology in Slovakia	programme & organising	Smolenice
		2016	Biological Therapy in Theory and Practice III	programme & organising	Bratislava
		2016	National Program to Conquer Alzheimer's disease and other forms of dementia	programme & organising	Smolenice
10.	Novak Petr	2017	Biologická liečba v teórii a praxi IV.	organising	Bratislava
11.	Skrabana Rostislav	2019	Advances in experimental neuroimmunology 2019	programme	Smolenice
		2018	Advances in slovak experimental neuroimmunology 2018	programme	Smolenice
		2017	Biologická liečba v teórii a praxi IV.	programme & organising	Bratislava
		2016	Biological Therapy in Theory and Practice III	programme & organising	Bratislava
12.	Smolek Tomas	2018	Advances in slovak experimental neuroimmunology 2018	programme	Smolenice
13.	Zilka Norbert	2021	Young Neuroscientists and Cutting-Edge Research	programme	online
		2020	Young Neuroimmunologists: a great hope for our healthy future	programme	online
		2018	Current Status of Experimental Neuro-Immunology in Slovakia II	programme	Kosice

No	Name	Year	Conference	Committee	Place
14.	Zilkova Monika	2019	Advances in experimental neuroimmunology 2019	programme	Smolenice
		2019	Biologická liečba v teórii a praxi V.	programme & organising	Bratislava
		2018	Advances in slovak experimental neuroimmunology 2018	programme	Smolenice
		2017	Biologická liečba v teórii a praxi IV.	programme & organising	Bratislava
		2016	National program to conquer Alzheimer's disease and other forms of dementia	programme & organising	Smolenice

2.3.12. List of researchers who received a national scientific award

No	Name	Year	Award	Bestower
1.	Cizkova Dasa	2020	Women of the year 2019	Kosice city
		2020	Personality of the year 2019	Kosice city
		2020	M.R. Stefanik award	French Embassy in Slovakia and The Ministry of Education, Science, Research and Sport of the Slovak Republic
		2018	Science and technology award	The Ministry of Education, Science, Research and Sport of the Slovak Republic
2.	Fricova Dominika	2020	L'Oreal - UNESCO for women in science	L'Oreal - UNESCO
3.	Jadhav Santosh	2020	The best publication of 2019	Slovak Immunology Society
4.	Kovac Andrej	2020	Research project with an excellent level	Slovak research and development agency
5.	Novak Michal	2017	Neuroscience Hall of Fame	Slovak Society for Neuroscience
		2017	Gold Metal of Slovak Medical Association	Slovak Medical Association
		2017	Gold Metal of University of veterinary medicine and pharmacy in Kosice	University of veterinary medicine and pharmacy in Kosice

2.4. Research grants and other funding resources

(List type of project, title, grant number, duration, total funding and funding for the institute, responsible person in the institute and his/her status in the project, e.g. coordinator “C”, work package leader “W”, investigator “I”. Add information on the projects which are interdisciplinary, and also on the joint projects with several participating SAS institutes)

- International projects

2.4.1. List of major projects of Framework Programmes of the EU (which pillar), NATO, COST, etc.

Project title: Non-globular proteins - from sequence to structure, function and application in molecular physiopathology (NGP-NET)

Project number: COST - BM1405

Duration: 31.5.2015 - 25.3.2019

Principal Investigator of NIU SAS: Rostislav Skrabana

Role of NIU SAS: Participant

Funding for NIU SAS: 16.201- €

Project title: Coordination Action in support of the sustainability and globalisation of the Joint Programming Initiative on Neurodegenerative Diseases

Project number: H2020 – JPND - 681043

Duration: 01.11.2015 – 31.10.2021

Principal Investigator of NIU SAS: Michal Novak

Role of NIU SAS: Participant

Total Funding: 2.043.283,75,- €

Funding for NIU SAS: 25.000,- €

Project title: Pathway complexities of protein misfolding in neurodegenerative diseases: a novel approach to risks evaluation and model development

Project number: H2020 – JPND - FP-829-085

Duration: 01.5.2016 – 31.12.2019

Principal Investigator of NIU SAS: Michal Novak

Role of NIU SAS: Participant

Total Funding: 2.282.875,- €

Funding for NIU SAS: 490.000,- €

Project title: Alzheimer's disease data-driven insights on individual outcomes of importance

Project number: HESOCARE-329-074 (H2020/JPND) – ADDITION

Duration: 1.5.2019 - 30.09.2023

Principal Investigator of NIU SAS: Michal Novak

Role of NIU SAS: Participant

Total Funding: 1.100.000,- €

Funding for NIU SAS: 320.000,- €

Project title: Bridging the gap between science, education and enterprise in regenerative medicine

Project number: 22020272 (Visegrad Fund)

Duration: 1.10.2020 - 20.3.2022

Principal Investigator of NIU SAS: Dasa Cizkova

Role of NIU SAS: Participant

Total Funding: 29.904,- €

Funding for NIU SAS: 0,0,- €

Project title: The tryptophan kynurenine pathway - therapeutic strategy for neuroprotection in tauopathies

Project number: CRP/SVK18-01 (ICGEB)

Duration: 1.1.2019 - 31.12.2021

Principal Investigator: Andrej Kovac

Role of NIU SAS: Coordinator

Funding for NIU SAS: 41.000,- €

- **National projects, incl. international projects with only national funding**

2.4.2. List of ERA-NET projects funded from SAS budget

Project title: Spinal cord repair: releasing the neuron-intrinsic brake on axon regeneration

Project number: No. 030

Duration: 01.1. 2017 – 31.12.2019

Principal Investigator of NIU SAS: Dasa Cizkova

Role of NIU SAS: Participant

Total Funding: 1.104.643,- €

Funding for NIU SAS: 105.000,- €

Project title: Repetitive Subconcussive Head Impacts - Brain Alterations and Clinical Consequences

Project number: No. 080

Duration: 01.1. 2017 – 31.12.2019

Principal Investigator of NIU SAS: Peter Filipcik

Role of NIU SAS: Participant

Total Funding: 955.000,- €

Funding for NIU SAS: 105.000,- €

Project title: Nanosystems conjugated with antibody fragments for treating brain infections

Project number: No. 049

Duration: 01.01.2019 – 31.12.2021

Principal Investigator of NIU SAS: Mangesh Bhide

Role of NIU SAS: Participant

Total Funding: 1.088.422,- €

Funding for NIU SAS: 75.000,- €

Project title: Neurovascular damage determines disease pathophysiology in pediatric mild traumatic brain injury: source of new biomarkers

Project number: No. 102

Duration: 01.01. 2020 – 31.12.2022

Principal Investigator of NIU SAS: Peter Filipcik

Role of NIU SAS: Participant

Total Funding: 1.014.748,- €

Funding for NIU SAS: 75.000,- €

2.4.3. List of projects of the Slovak Research and Development Agency, APVV

Project title: Etiopathogenesis of neurodegenerative diseases: focus on RNA processing regulation in development and progression of sporadic tauopathies and Alzheimer's diseases

Project number: APVV-0677-12

Duration: 01.10.2013 – 30.09.2016

Principal Investigator: Peter Filipcik

Role of NIU SAS: Coordinator

Funding for NIU SAS: 199.950,- €

Project title: Development of novel peptide based system for delivery of therapeutics into the brain

Project number: APVV-14-0547

Duration: 01.07.2015 – 30.06.2018

Principal Investigator: Andrej Kovac

Role of NIU SAS: Coordinator

Funding for NIU SAS: 244.264,- €

Project title: The model of the neuroimmune crosstalk in Alzheimer's disease

Project number: APVV-14-0872

Duration: 01.07.2015 – 30.06.2018

Principal Investigator: Norbert Zilka

Role of NIU SAS: Coordinator

Funding for NIU SAS: 248.996,- €

Project title: A novel combined therapy based on alginate biomaterials and trophic factors for spinal cord injury repair

Project number: SK-FR-2015-0018

Duration: 01.01.2016 – 31.12.2017

Principal Investigator: Dasa Cizkova

Role of NIU SAS: Coordinator

Funding for NIU SAS: 5.290,- €

Project title: Study of functional bio-implants and stem cells for CNS regeneration

Project number: APVV-15-0613

Duration: 01.07.2016 – 12.06.2020

Principal Investigator: Dasa Cizkova

Role of NIU SAS: Coordinator

Total Funding: 239.982,- €

Funding for NIU SAS: 170.000,- €

Project title: Use of animal models for tauopathies for identification of molecular pathways involved in the etiology of neurofibrillary degeneration

Project number: APVV-16-0531

Duration: 01.07.2017 – 30.10.2020

Principal Investigator: Branislav Kovacech

Role of NIU SAS: Coordinator

Funding for NIU SAS: 245.914,- €

Project title: Identification of molecular mechanisms induced by traumatic brain injury in ice hockey players

Project number: APVV-17-0668

Duration: 01.08.2018 – 31.12.2021

Principal Investigator: Peter Filipcik

Role of NIU SAS: Coordinator

Total Funding: 150.000,- €

Funding for NIU SAS: 100.000,- €

Project title: 3D In vitro Modelling of Alzheimer's Disease using Astrocytes derived from Induced Pluripotent Stem Cells

Project number: APVV-17-0642

Duration: 01.08.2018 – 31.12.2021

Principal Investigator: Eva Sykova

Role of NIU SAS: Coordinator

Funding for NIU SAS: 249.063,- €

Project title: The development of novel approaches for therapy of tauopathies using transport peptides for drugs and antibodies into the brain

Project number: APVV-18-0302

Duration: 01.07.2019 – 30.06.2022

Principal Investigator: Andrej Kovac

Role of NIU SAS: Coordinator

Total Funding: 279.075,- €

Funding for NIU SAS: 270.925,- €

Project title: Molecular biomarkers for canine brain disorders – Monitoring of the brain regeneration and efficacy of treatment

Project number: APVV-18-0515

Duration: 01.07.2019 – 30.06.2022

Principal Investigator: Norbert Zilka

Role of NIU SAS: Coordinator

Funding for NIU SAS: 249.955,- €

Project title: Inhibitory cortical circuits mediating cognitive dysfunction in Alzheimer's disease

Project number: APVV-19-0585

Duration: 01.07.2020 – 30.06.2023

Principal Investigator: Tomas Hromadka

Role of NIU SAS: Coordinator

Funding for NIU SAS: 195.000,- €

Project title: Cognitive consequences of sport-related traumatic brain injuries in adolescents in the Slovak Republic

Project number: APVV-19-0568

Duration: 01.07.2020 – 30.06.2023

Principal Investigator of NIU SAS: Igor Jurisica

Role of NIU SAS: Participant

Total Funding: 230.000,- €

Funding for NIU SAS: 114.630,- €

Project title: Development of therapeutic biomolecules blocking SARS-COV-2 infection

Project number: PP-COVID-20-0044

Duration: 16.09.2020 – 31.12.2021

Principal Investigator: Eva Kontsekova

Role of NIU SAS: Coordinator

Total Funding: 399.909,- €

Funding for NIU SAS: 244.893,- €

Project title: Molecular pathways induced by traumatic brain injury: novel biomarkers and prediction of new therapeutic targets for neurodegeneration

Project number: APVV-20-0615

Duration: 01.07.2021 – 30.06.2024

Principal Investigator: Peter Filipcik

Role of NIU SAS: Coordinator

Total Funding: 230.000,- €
Funding for NIU SAS: 140.000,- €

Project title: The double-edged sword of the plasminogen system: From homeostasis maintenance to COVID-19

Project number: APVV-20-0513

Duration: 01.08.2021 – 30.06.2025

Principal Investigator of NIU SAS: Rostislav Skrabana

Role of NIU SAS: Participant

Total Funding: 160.000,- €

Funding for NIU SAS: 24.720,- €

Project title: Examining the role of dopamine and adult neurogenesis in learned behavior of songbirds using optogenetic manipulation

Project number: APVV-20-0344

Duration: 01.07.2021 – 30.06.2025

Principal Investigator of NIU SAS: Tomas Hromadka

Role of NIU SAS: Participant

Total Funding: 210.000,- €

Funding for NIU SAS: 62.108,- €

Project title: Longitudinal Assessment of Neurodegeneration and the Correlates of Relevant Endpoints in AD

Project number: APVV-20-0447

Duration: 01.07.2021 – 30.06.2024

Principal Investigator: Petr Novak

Role of NIU SAS: Coordinator

Funding for NIU SAS: 249.552,- €

Project title: Spread of alpha-Synuclein-associated pathology across gastrointestinal organs in a mouse model and patients with Parkinson's disease

Project number: APVV-20-0331

Duration: 01.07.2021 – 30.06.2024

Principal Investigator: Alzbeta Kralova Trancikova

Role of NIU SAS: Coordinator

Funding for NIU SAS: 200.000,- €

Project title: Neuro-glia cell-based model for inter-neuronal spread of tau pathology

Project number: APVV-20-0585

Duration: 01.07.2021 – 30.06.2025

Principal Investigator: Monika Zilkova

Role of NIU SAS: Coordinator

Funding for NIU SAS::244.016,- €

2.4.4. List of projects of the Scientific Grant Agency of the Slovak Academy of Sciences and the Ministry of Education, VEGA (for funding specify only total sum obtained from all VEGA grants in particular year)

VEGA	2016	2017	2018	2019	2020	2021
Number	11	10	14	15	14	14
Funding in the year (EUR)	71.002	68.668	99.745	96.012	85.140	88.023

2.4.5. List of projects supported by EU Structural Funds

-

2.4.6. List of other projects funded from national resources

Project title: Development of new neuro-imaging approaches for preclinical diagnosis of tauopathies using transport peptides for tau specific nanobodies

Project number: 2018/24-SAV-2

Duration: 1.12.2018 - 31.12.2020

Principal Investigator: Andrej Kovac

Role of NIU SAS: Coordinator

Funding for NIU SAS: 221.930,- €

Project title: Development of the method for stratification of patients after traumatic brain injury and identification of novel therapeutic targets for personalized medicine aimed to prevention of neurodegeneration

Project number: 2018/14568:1-26C0

Duration: 01.12.2018 - 31.12.2019

Principal Investigator of NIU SAS: Peter Filipcik

Role of NIU SAS: Participant

Total Funding: 499.770,- €

Funding for NIU SAS: 100.922,- €

Project title: The role of senescence in neurodegeneration: from the molecular connection to the application and novel treatment strategies

Project number: 1085/01/02 (SASPRO)

Duration: 1.10.2021 - 30.9.2024

Principal Investigator: Dominika Fricova

Role of NIU SAS: Host organization

Funding: 204.912,- €

2.4.7. List of projects funded from private funds

Project title: Mutual collaboration agreement in neurodegenerative disease research (Grant agreement)

Duration: 03.05.2012 – 31.12.2025

Role of NIU SAS: Recipient

Funding for NIU SAS: 250.000,- € / year

2.4.8. List of projects funded from other competitive funds

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2.5. PhD studies and educational activities

The Institute of Neuroimmunology participates in a scientific collaboration and **Joint Ph.D. (Cotutelle) Study Program** with **Laboratoire PRISM – INSERM U1192, University Lille 1 in France**. The first PhD student, Mgr. Adriana Murgoci, studied under this arrangement during 2016-2018. She defended her Ph.D. thesis: “*Modulation of the microglia immune response in the context of the cross-talk between glioma and neuronal progenitor cells through extracellular vesicles*” on September 26, 2018, at UVLF Kosice/NIU SAV Bratislava, in front of an international board: Co-tutors – Prof. Michel Salzet, Ph.D. (France)/ Prof. Dasa Cizkova, DrSc. (NIU SAV, Slovakia), committee members: Prof. MVDr. Jan Motlík, DrSc (Czech Republic), Assoc. Prof. Stefania Mondell, Ph.D. (Italy), Prof. MVDr. Juraj Koppel, DrSc (Slovakia), Prof. Isabelle Fournier, Ph.D., Prof. Serge Nataf, Ph.D. (both France), Assoc. Prof. MVDr. Mangesh Bhide, Ph.D. (Slovakia).

The Joint Ph.D. program continues with another Ph.D. student (2022-2024) Lydia Ziane Chaouche, with Ph.D. thesis: “*Development and reprogramming of CAR macrophages for anti-tumor immunotherapy strategy*”. Her co-tutors are Assoc. Prof. Marie Duhamel, PhD (France)/ Prof. Dasa Cizkova, DrSc. (NIU SAV, Slovakia)

2.5.1. List of accredited programmes of doctoral studies, period of validity, source of funding

[A] Immunology 4.2.15

Period of validity: without time restriction

Source of funding: University of Veterinary Medicine and Pharmacy in Kosice

[B] Molecular biology 4.2.3.

Period of validity: without time restriction

Source of funding: Comenius University Bratislava

[C] Neuroscience 4.2.16

Period of validity: without time restriction

Source of funding: University of Veterinary Medicine and Pharmacy in Kosice

2.5.2. Summary table on doctoral studies (number of internal/external PhD students at the end of the year; number of foreign PhD students, number of students who successfully completed their theses during the year, number of PhD students who quit the programme during the year)

PhD study	2016			2017			2018			2019			2020			2021		
Number of potential PhD supervisors	16			17			17			17			23			25		
PhD students	number, end of year	defended thesis	students quitted	number, end of year	defended thesis	students quitted	number, end of year	defended thesis	students quitted	number, end of year	defended thesis	students quitted	number, end of year	defended thesis	students quitted	number, end of year	defended thesis	students quitted
Internal total	10	4	2	14	1	0	11	4	3	12	1	0	10	0	2	12	2	0
from which foreign citizens	2	0	0	2	0	0	2	1	0	2	1	0	1	0	0	1	0	0
External	2	0	0	1	1	0	0	0	0	0	0	1	1	0	0	1	0	0
Other supervised by the research employees of the institute	0	0	0	2		0	6		0	1		0	16			8		0

2.5.3. PhD carrier path – Information on the next career steps of the PhD graduates who received their degree from the institute

Year of graduation	Name	PhD carrier path
2016		
	Veronika Cubinkova	Postdoc; research scientist at the NIU SAS
	Lenka Levarska	Comenius University in Bratislava, Science Park, specialist in accounting and finance
	Tomas Smolek	Postdoc; currently research scientist at the NIU SAS;
	Ivana Zimova	Postdoc; research scientist at the NIU SAS
2017		
	Tomas Augustin	Amgen, Medical Science, Slovakia
	Alena Michalicova	Postdoc at the NIU SAS
2018		
	Veronika Brezovakova	Postdoc at the NIU SAS until April 2022
	Nina Kosikova	Roche Diagnostics, International Rotkreuz Switzerland, Clinical development and Medical Affairs, Clinical Trials
	Adriana-Natalia Murgoci	Postdoc at the NIU SAS; currently research scientist at the Institute of Environmental Medicine, Toxicology Unit, Karolinska Institutet, Stockholm, Sweden.
	Bernadeta Valachova	Postdoc at the NIU SAS; research scientist at the NIU SAS

Year of graduation	Name	PhD carrier path
2019		
	Thomas Vogels	Sylics (Synaptologics B.V.), Bilthoven, The Netherlands, Clinical trials
2020		
	Greta Vargova	Postdoc at University of California, Riverside
2021		
	Dominika Olesova	Postdoc at the NIU SAS
	Jakub Sinsky	Postdoc at the NIU SAS

2.5.4. Summary table on educational activities

Teaching	2016	2017	2018	2019	2020	2021
Lectures (hours/year)*	52	268	22	177	85	127
Practicum courses (hours/year)*	78	0	139	143	188	161
Supervised diploma and bachelor thesis (in total)	3	8	13	15	22	20
Members in PhD committees (in total)	6	4	5	1	5	5
Members in DrSc. committees (in total)	0	1	3	1	1	1
Members in university/faculty councils (in total)	2	2	2	3	4	5
Members in habilitation/inauguration committees (in total)	1	0	1	1	4	3

2.5.5. List of published university textbooks

PILIPCINEC, E. - NOVÁK, Petr - KOVÁČ, Andrej - PISTL, J. - TKACIKOVA, L. - KOSCOVA, J. - NEMCOVA, R. - SEGURADO-BENITO, I. - FEDOROVA, M. *Vybrané kapitoly zo špeciálnej bakteriológie pre farmaceutov. : Gram-negatívne baktérie..* Recenzenti: Erik Dorko, Eva Čonková. Košice : Univerzita veterinárskeho lekárstva a farmácie v Košiciach, 2018. 336 s. ISBN 978-80-8077-572-8

PILIPCINEC, E. - PISTL, J. - ŽILKA, Norbert - DORKO, E. - KOSCOVA, J. - TKACIKOVA, L. - NEMCOVA, R. - SEGURADO-BENITO, I. *Špeciálna bakteriológia. : Gram-negatívne baktérie..* Recenzenti: Monika Pipová, Andrea Lauková. Košice : Univerzita veterinárskeho lekárstva a farmácie v Košiciach, 2018. 384 s. ISBN 978-80-8077-571-1

PILIPCINEC, E. - PISTL, J. - ŽILKA, Norbert - DORKO, E. - KOSCOVA, J. - TKACIKOVA, L. - NEMCOVA, R. - SEGURADO-BENITO, I. *Špeciálna bakteriológia. : Gram-pozitívne baktérie..* Recenzenti: Monika Pipová, Andrea Lauková. Košice : Univerzita veterinárskeho lekárstva a farmácie v Košiciach, 2019. 328 s. ISBN 978-80-8077-632-9

PILIPCINEC, E. - NOVÁK, Petr - KOVÁČ, Andrej - PISTL, J. - TKACIKOVA, L. - KOSCOVA, J. - NEMCOVA, R. - SEGURADO-BENITO, I. - FEDOROVA, M. *Vybrané kapitoly zo špeciálnej*

bakteriológie pre farmaceutov. : Gram-pozitívne baktérie.. Recenzenti: Erik Dorko, Eva Čonková. Košice : Univerzita veterinárskeho lekárstva a farmácie v Košiciach, 2019. 312 s. ISBN 978-80-8077-633-6

2.5.6. Number of published academic course books

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2.5.7. List of joint research laboratories/facilities with universities

LABORATORY OF BIOMEDICAL MICROBIOLOGY AND IMMUNOLOGY (LBMI)

The laboratory was established in 1996 as a joint initiative with the University of Veterinary Medicine and Pharmacy in Kosice. The laboratory (led by Assoc. Prof. M. R. Bhide) investigates the transition of neuroinvasive pathogens through the BBB, with special emphasis on *Borrelia* and *Neisseria* species. The laboratory prominently contributed to the understanding of the mechanisms of how the pathogens pass through the BBB and how they evade the host immune system.

2.5.8. Supplementary information and/or comments on doctoral studies and educational activities – focused on what changes have occurred since the last evaluation in 2016

No	Name	Year	Award	Bestower
1.	Csicsatkova Nikoleta	2021	1st place for presentation	Young Neuroscientists and Cutting-Edge Research - conference organizers
		2020	2nd place for presentation	2020 virtual conference of young neurobiologists and phd students - conference organizers
2.	Horvath Marian	2020	3rd place for presentation	2020 virtual conference of young neurobiologists and phd students - conference organizers
3.	Kulkarni Amod	2020	2nd place for presentation	2020 virtual conference of young neurobiologists and phd students - conference organizers
4.	Macova Kristina	2021	1st place for presentation	Young Neuroscientists and Cutting-Edge Research - conference organizers
		2020	2nd place for presentation	2021 virtual conference of young neurobiologists and phd students - conference organizers
5.	Matyasova Katarina	2021	2nd place for presentation	Young Neuroscientists and Cutting-Edge Research - conference organizers
		2020	2nd place for presentation	2022 virtual conference of young neurobiologists and phd students - conference organizers
6.	Meskova Klaudia	2021	Scholarship of Dr Sedlarova-Rabanova	Fund of Dr Sedlarova Rabanova
		2021	3rd place for presentation	Young Neuroscientists and Cutting-Edge Research - conference organizers

2.6. Societal impact

2.6.1. The most important case studies of the research with direct societal impact, max. 4 for institute with up to 50 average FTE researchers per year, 8 for institutes with 50 – 100 average FTE researchers per year and so on. Structure: Summary of the impact; Underpinning research; References to the research; Details of the impact; Sources to corroborate the impact. One page per one case study

Summary of the impact

The blood-brain barrier represents the bottleneck in brain drug development and is the most important factor limiting the future growth of neurotherapeutics. Essentially 100% of large-molecule pharmaceuticals, including peptides, recombinant proteins, monoclonal antibodies, RNA interference (RNAi)-based drugs, and gene therapies, and >98% of small-molecule drugs do not cross the blood-brain barrier. We have generated a novel peptide-based brain delivery system resulting in intellectual property and scientific papers.

Underpinning research

The blood-brain barrier (BBB) is a selective barrier formed by the endothelial cells that line cerebral microvessels. The endothelial cells of the BBB are distributed along the length of the vessel and completely encircle the lumen. The periendothelial accessory structures of the BBB include pericytes, astrocytes, and a basal membrane. Endothelial cells, astrocytes, pericytes, and neurons are organized together to form the “neurovascular unit,” which is essential for the function, support, and formation of BBB [1]. The blood-brain barrier represents the major obstacle in drug development of neurotherapeutics. Essentially 100% of “larger size” neuropharmaceuticals, including peptides, recombinant proteins, monoclonal antibodies, RNA interference (RNAi)-based drugs, and gene therapies, generally do not cross the BBB. However, these compounds represent the most promising CNS drug candidates now.

In 2016 our research team, led by Dr. Kovac, began to develop a new peptide-based system for the delivery of drugs across the BBB. In the first step of the project, they focused on the preparation of the construct needed to create a 12-mer peptide phage library. In order to identify phage-bearing peptides that specifically bind to the surface of primary brain endothelial cells using the phage display method, they used a 12-mer peptide library that consisted of random peptide sequences of 12 consecutive amino acids.

During 2017-2018, they identified two peptides that bound specifically to primary endothelial cells and could traverse the BBB. The permeability of peptides was assessed using a primary rat in vitro BBB model. The results showed that both peptides are effectively internalized by primary endothelial cells, and there was no internalization or binding to non-endothelial cells [2, 3]. The permeability

obtained was in the same order of magnitude as other known BBB shuttles, such as MiniAp4, PhPro4, and NMePhe4.

Recently, they focused on the development of transport peptide-antibody conjugates (BBB shuttles) that will represent a new potential therapeutic approach for neurodegenerative diseases such as tauopathies.

References to the research

1. Michalicova A, Banks WA, Legath J, Kovac A. Tauopathies - Focus on Changes at the Neurovascular Unit. *Curr Alzheimer Res.* 2017;14(7):790-801
2. Majerova P, Hanes J, Olesova D, Sinsky J, Pilipcinec E, Kovac A. Novel Blood-Brain Barrier Shuttle Peptides Discovered through the Phage Display Method. *Molecules.* 2020 Feb 17;25(4):874.
3. Novel peptide based system for delivery of drugs into the brain. PP 24-2019 (Slovak patent)

Details of the impact

The world market for CNS drugs reached \$169.11 billion in 2021, growing at a rate of 5.7%/year. The major challenge in the CNS drug market is the delivery of modern innovative medicines into the brain. Developing therapies for neurodegenerative diseases is of the highest EU priority due to the enormous cost of medical care and the human suffering involved. Many of these diseases are proteinopathies caused by misfolded, aggregating proteins. Antibodies that recognize and remove misfolded proteins are ideally suited as proteinopathy therapeutics. The CNS has been considered off-limits to antibody therapeutics due to the BBB. However, recent advances in preclinical and clinical drug development suggest that antibodies can cross the BBB in limited quantities and act centrally to mediate their effects. Thus, technologies designed to improve antibody uptake in the brain are receiving increased attention and are likely going to represent the future of antibody therapy for neurodegeneration. Our discovery of a novel peptide-based CNS delivery system has provided the pharmaceutical industry with an innovative approach for the enhancement of delivery of protein-based biopharmaceuticals across the BBB.

2.6.2. List of the most important studies and/or other activities commissioned for the decision-making authorities, the government and NGOs, international and foreign institutes (title, name of institution, contract value, purpose (max 20 words))

Title:	National program – coordinated actions against Alzheimer's disease
Name of Institution:	Ministry of Health of the Slovak Republic
Contract value:	7.7 mil EUR (still in negotiation)
Purpose:	National programme seeks to prevent future cases of Alzheimer's disease and related dementias, and to support patients and caregivers by focusing on services, care, education, destigmatization, human rights, prevention, research, and diagnostics of Alzheimer's disease in Slovakia.

2.6.3. List of contracts and research projects with industrial and other commercial partners, incl. revenues (study title, name of institution, contract value, country of partner, purpose (max 20 words))

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2.6.4.1 List of intangible fixed assets (internally registered IP (confidential know-how), patent applications, patents granted, trademarks registered) denoting background IPR

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2.6.4.2. List of licences sold abroad and in Slovakia, incl. revenues (background IPR identification, name of institution, contract value, country of partner, purpose (max 20 words))

-

2.6.5. Summary of relevant activities, max. 300 words (describe the pipeline of valorization in terms of Number of disclosure, Number of registered IP internally, number of CCR/LIC contracts and their respective summary values, the support you are receiving in specific points internally at the institute, at SAS, externally – also the limitations and drawbacks.

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2.7. Popularisation of Science (outreach activities)

2.7.1. List of the most important popularisation activities, max. 20 items

Dr. Fricova is a founder of non-profit organization „Žijem vedu“ (www.zijemvedu.sk), which is interconnecting slovak scientists working in Slovakia and all over the world. The activities of non-profit organization include several working groups at the Ministry of Education and Government Office focused on new national strategies in order to improve slovak scientific environment.

Another contribution with national importance co-founded by Dr. Fricova is the online platform „Veda pomáha“ (Science helps) (vedapomaha.solved.fi/) interconnecting slovak specialist with the aim to provide scientific guidance for government and public during the COVID-19 pandemic. All mentioned activities are greatly supported by the institute.

Interview with prof. Michal Novak and assoc.prof. Norbert Zilka about the Lifetime Achievement Award by Alzheimer's Association awarded to prof. Novak
Place: TV/Markiza
Date: 2021

TV report about the Institute of Neuroimmunology, its cooperation with Memory Centre, and a vaccine for Alzheimer's disease
Place: TV Markiza/Reflex
Date: 2021

TV discussion about the situation in Slovak science with Dominika Fricova
Place: TV/RTVS
Date: 2021

An article about developing a vaccine for Alzheimer's disease in Slovakia - Norbert Zilka
Place: Press/Hospodarske noviny
Date: 2021

Petr Novak at the press conference for Alzheimer's disease prevention campaign by SOCIA
Place: Bratislava
Date: 2021

Interview with the director of the institute Norbert Zilka about the safety of COVID-19 vaccination
Place: TV/TA3
Date: 2021

TV discussion with the director of the institute Norbert Zilka about COVID-19 vaccination
Place: TV/Pod lampou
Date: 2021

Discussion forum with neuroscientist Tomas Hromadka
Place: RTVS/Radio Slovensko
Date: 2021

TV discussion about differences in science in Slovakia and abroad with Dominika Fricova
Place: TV/Pod lampou
Date: 2020

Director Norbert Zilka as a guest of morning broadcast at the Slovak Radio
Place: RTVS /Radio Slovensko
Date: 2020

Discussion with director Norbert Zilka about neurodegenerative diseases
Place: RTVS/Radio Slovensko
Date: 2020

A bulletin for a play about Alzheimer's disease contents information pages about the founder of the Institute prof. Novak, his work, and the Institute itself
Place: Astorka Theatre
Date: 2020

Video series with Norbert Zilka filmed by the Slovak Ministry of Health as a supporting tool for raising public awareness about COVID-19
Place: Facebook page of Ministry of Health
Date: 2020

Norbert Zilka - a regular author of articles about neurodegenerative diseases in a popular science magazine
Place: Quark magazine
Date: 2018 - 2021 (several articles per year)

Prof. Michal Novak as a speaker at TEDx Bratislava about Alzheimer's disease
Place: Slovak national theatre Bratislava
Date: 2016

Discussion forum with neuroscientist Norbert Zilka about Alzheimer's disease
Place: Place: RTVS/Radio Slovensko
Date: 2017

Presentation about Alzheimer's disease – prof. Michal Novak at the event European Researcher's Night
 Place: Bratislava
 Date: 2016

WHO prize awarded to prof. Michal Novak, the founder of the Institute of Neuroimmunology
 Place: www.health.gov.sk
 Date: 2016

2.7.2. Table of outreach activities according to institute annual reports

Outreach activities	2016	2017	2018	2019	2020	2021	total
Articles in press media/internet popularising results of science, in particular those achieved by the Organization	4	22	22	24	30	49	151
Appearances in telecommunication media popularising results of science, in particular those achieved by the Organization	0	1	5	0	6	16	28
Public popularisation lectures	3	5	6	8	4	14	40

2.8. Background and management. Infrastructure and human resources, incl. support and incentives for young researchers

2.8.1. Summary table of personnel

2.8.1.1. Professional qualification structure (as of 31 December 2021)

	Degree/rank				Research position		
	DrSc./DSc	CSc./PhD.	professor	docent/ assoc. prof.	I.	II.a.	II.b.
Male	4	17	3	4	3	14	3
Female	3	16	2	1	3	5	11

I. – director of research with a degree of doctor of science/DrSc.

II.a – Senior researcher

II.b – PhD holder/Postdoc

2.8.1.2. Age and gender structure of researchers (as of 31 December 2021)

Age structure of researchers	< 31		31-35		36-40		41-45		46-50		51-55		56-60		61-65		> 65	
	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B
Male	0,0	0,0	1,0	1,0	4,0	4,0	3,0	2,5	4,0	3,8	2,0	1,5	3,0	2,6	0,0	0,0	3,0	3,0
Female	0,0	0,0	3,0	3,0	2,0	1,0	2,0	2,0	3,0	2,7	0,0	0,0	1,0	0,9	1,0	1,0	1,0	1,0

A – number

B – FTE

2.8.2. Postdoctoral fellowships (list of positions with holder name, starting date, duration. Add brief information about each fellow's career path before and after receiving PhD degree, etc.)

2.8.2.1. MoRePro and SASPRO fellowships

MUDr. RNDr. Dominika Fricova, PhD., 1.10.2021 - 30.09.2024 group leader
Evolution of mitochondrial genomes at Faculty of Natural Sciences Comenius University /Parkinson's disease at Mayo clinic and NIU SAS

2.8.2.2. Stefan Schwarz fellowships

Mgr. Adriana-Natalia Murgoci, PhD., 1.6.2019 - 30.9.2019 researcher
(fellowship was terminated after she left the institute)
Neuroscience at NIU SAS/Neuroscience at NIU SAS and Toxicology at Karolinska Institutet

2.8.2.3. Postdoctoral positions from other resources (specify)

All postdoctoral positions at NIU SAS are paid from international and national grants and AXON grants

Brandoburova Petra, Mgr., PhD. 1.10.2017- 28.2.2018 researcher
Neuropsychology/ Neuropsychology at Memory center

Brezovakova Veronika, MVDr., PhD. 5.9.2018 - 31.3.2022 researcher
Molecular and cellular neuroscience/ Molecular and cellular neuroscience at NIU SAS

Hladka Julia, Mgr., PhD. 1.10.2017 - 28.2.2018 researcher
Speech therapy/ Speech therapy at Memory center

Kulkarni Amod, Mgr., PhD. 1.5.2019 - 30.6.2022 researcher
Microbiology and neuroscience at UVLF/ Microbiology and neuroscience at NIU SAS

Majerova Petra, Mgr., PhD. 1.10.2016 - open researcher
Immunology/proteomics and metabolomics at NIU SAS

Mate Veronika, MVDr., PhD. 1.10.2016 - open researcher
Transgenic animal models/ Transgenic animal models at NIU SAS

Olesova Dominika, PharmDr. PhD. 1.9.2021 - 31.8.2022 researcher
Proteomics/ Proteomics at NIU SAS

Palova Denisa, Mgr., PhD. 1.11.2019 - 31.10.2025 researcher
Biology of physical activity at Biomedical research center SAS/cellular neuroscience at NIU SAS

Polcik Michalicova Alena, PharmDr., PhD.	1.9.2017 - open	researcher
<i>Blood-brain barrier/ Blood-brain barrier at NIU SAS</i>		
Prcina Michal, Mgr., PhD.	1.10.2016 - 31.3.2019	researcher
<i>Prion diseases/Immunology-flow cytometry NIU SAS</i>		
Smolek Tomas, MVDr. Mgr., PhD.	1.10.2016 - open	group leader
<i>Transgenic animal models/ Transgenic animal models at NIU SAS</i>		
Sinsky Jakub, Mgr. PhD.	1.9.2021 - 31.8.2022	researcher
<i>Proteomics/ Proteomics at NIU SAS</i>		
Uhrinova Ivana, MVDr., PhD.	1.10.2016 - 30.9.2022	researcher
<i>Transgenic animal models/ Transgenic animal models at NIU SAS</i>		
Weisova Petronela, Mgr., PhD.	1.10.2016 - 15.7.2019	researcher
<i>Researcher at SVFA SR/cellular neuroscience at MFPL Vienna and NIU SAS</i>		

2.8.3. Important research infrastructure introduced during the evaluation period with the information about the sources of funding (max. 2 pages)

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2.9. Supplementary information and/or comments on all items 2.1 – 2.8 (max. 2 pages in total for the whole section)

Human resources

Since 2005, NIU SAS has been receiving funds from the SAS budget to cover salaries of 31 employees (FTE—Full Time Equivalent). Since 2017, however, the average number of employees at NIU SAS has been 48. The difference between the allocated FTE and the actual number of employees has been covered from additional resources, mostly from international grants, grants with biotech companies and only partially from national grants. However, Slovak grant agencies either do not allow for salaries and wages to be included in the budget (VEGA), or the planned expenditures on salaries and wages are significantly reduced by expert panels (APVV). In addition, structural funds which represent another source of income, have not been available for Bratislava region for several years (see below).

During the past 17 years, our FTE has not been increased by a single employee, despite the fact that we have applied for an increase multiple times. NIU SAS has always been one of the most highly rated institutes within SAS, but the rating has never been taken into account.

Research infrastructure

Capital expenditures have not been eligible for APVV (Slovak Research and Development Agency, a national grant agency) grant calls for more than a decade. The sole exception was the “covid call” (PP-COVID 2020), in which capital expenditures (up to 65% of eligible project expenditures) were allowed to be used for scientific equipment and infrastructure.

In the EU Structural Funds during 2016-2021 there were no opportunities to participate in calls in which we could obtain funds for the renewal and completion of scientific infrastructure. In general, the Bratislava region is excluded from calls for infrastructure support. The calls for Bratislava region are limited overall, regardless of capital expenditures.

Moreover, no investment funds were allowed in funding calls which targeted less developed regions outside the Bratislava region. For implementation of such projects outside the eligible region, it was possible to use up to 15 % of the project budget (so-called 15% flexibility rule) outside the eligible region with positive effects and benefits for the eligible region.

Most institutions in the Bratislava region could not apply for funds for the development of scientific infrastructure. Only selected institutions participating in the Operational Programme Research and Innovation (call codes: OPVaV-2012/4.2/08-RO and OPVaV-2013/4.2/09-RO) and receiving funds from already supported projects for university science parks and research centers development were eligible to apply for such funds.

3. Implementation of the recommendations from the previous evaluation period

I. The institute needs redefining its complex structure as compared to few researchers, many of whom work only part-time

The number of researchers with a university degree increased from **12.388 FTE** per year (2012-2015) to **26.03 FTE** per year during 2016-2021, despite the fact that the Institute salary budget has remained the same for the last 17 years. This increase in FTE is accompanied by an increase in the number of PhD supervisors and PhD students (see the following point below).

The Institute’s organizational structure has been inspired by top international research organizations, namely MRC LMB in Cambridge (UK). The structure is based on a combination of medium and small research groups composed of research scientists, PhD students, and technicians, which allows for a highly specialized, focused, and flexible research.

The medium-sized groups (Proteomics & Metabolomics, Integrated Neuromics, Immunology and Neuroimmunology, Computational Neurobiology, Laboratory of Biomedical Microbiology and Immunology, Molecular and Cellular Neurobiology) have broader research interests and also include personnel working in the Institute’s animal facility. The smaller groups (Structural Proteomics,

Systems Neuroscience, Parkinson's disease research laboratory, Center of Regenerative Medicine) are either newly established (Regenerative medicine), and/or led by a young researcher (D. Fricova in the Parkinson's lab), or have narrower research interests (crystallography, neural circuits, stem cells in neuro-regeneration).

II. The Institute needs attracting and promoting younger researchers and should be more active in leading the PhD students to the degrees.

The number of PhD students has increased from **14** in the years 2014 and 2015 to **12+16** (at NIU SAS + at other institutions) in 2020 and **14+8 in 2021**. Several students were funded by external sources to support increasing interest in the PhD programme at the Institute. The number of PhD supervisors has also increased.

To attract young researchers, students and young postdocs are encouraged to improve and broaden their skills by taking part at a traineeship at recognized partner laboratories or in courses:

PhD students:

- *Jakub Sinsky*, (Sept 2018-April 2019) traineeship at the Faculty of Science, University of South Bohemia in České Budějovice (Czech Republic).
- *Dominika Olesova*, (Sept 2019-Dec 2019) traineeship in the group of Assoc. Prof. David Friedecky at the Faculty of Medicine, Palacky University in Olomouc (Czech Republic)
- *Sandra Mihaljevic*, (Sept 2018-Jan 2019) traineeship at the Theodor Kocher Institute, Medical Faculty of the University of Bern (Switzerland)
- *Klaudia Meskova*, (Jan-Feb 2019) University of Ljubljana, Prof. Jurij Lah, Faculty of Chemistry and Chemical Technology, (Slovenia)
- *Klaudia Meskova*, (June 10-16, 2018), FEBS practical crystallization course, Advanced methods in macromolecular crystallization VIII, Nove Hradky (Czech Republic)
- *Nikoleta Csicsatkova*, *Katarina Matyasova*, and *Sara Porubska* attended the IRIS 2020 Summer school (Sep 2020), organized by Academy Research Organization (NGO) (Slovakia)
- *Greta Vargova* (Oct 2016-Sep 2017) traineeship in *Dinu Albeanu* group at the Cold Spring Harbor Laboratory, New York, USA.

Postdocs:

- *Ondrej Cehlar*, (Dec 2018-Mar 2019) in the group of Dr. Jozef Hritz, Protein structure and dynamics group, CEITEC, Masaryk university, Brno (Czech republic)

PhD students actively participate at national and international conferences allowing them to present and discuss their work with other scientific groups and opinion leaders:

PhD students – scientific presentations	2016	2017	2018	2019	2020	2021
Posters at national conferences		2	1		3	
Lectures at national conferences		2	14	7	4	7
Posters at international conferences		3	3	5		3
Lectures at international conferences	1		1			2

In August 2018 a PhD student gave lecture at the Axon Repair Meeting in Prague:

MURGOČI, Adriana-Natalia. “Evaluation expression of GFP in DRGs cultured in vitro.” Axon Repair Meeting, Prague, Czech Republic, August 30 – 31, 2018.

In 2019, NIU SAS organized an international conference, MESIA 2019, 4th Meeting of Middle-European Societies for Immunology and Allergology, at which one of our PhD students delivered a lecture:

MIHALJEVIĆ, Sandra. Changes of the choroid plexus barrier in tauopathies. 4th Meeting of Middle-European Societies for Immunology and Allergology, MESIA 2019, Samorin, Slovakia, November 28-30, 2019.

In 2020, NIU SAS organized in a cooperation with the Slovak Society for Neuroscience and the Slovak Immunological Society an online conference “*Young Neuroimmunologists: A great hope for our healthy future*”. The conference was specifically aimed at PhD students and young postdocs-neuroscientists to present their research and discuss their results and future plans with more than 80 participants.

In 2021, NIU SAS organized in a cooperation with the Slovak Society for Neuroscience and the Slovak Immunological Society the second edition of the online conference “*Young neuroscientists and cutting-edge research*” for PhD students and young postdocs-neuroscientists where they presented their research, discussed their results, and future plans. The conference was attended by more than 80 participants.

- Dominika Olesova delivered a lecture at the international 3rd Mini-symposium on The Blood-Brain Barrier from Basic to Clinical Research, Shimane (Japan), in March 2021:
Lipid accumulation in brain tissue and CSF correlates with neurofibrillary pathology in a transgenic rat model for tauopathy. In Mini symposium on the blood brain barrier. 3rd Mini symposium on the blood brain barrier. Online, March 26 - 27, 2021, Izumo, Shimane Japan
- In June 2021, Katarina Martonova Heskova gave a lecture “*Flexible platform for production of proteins of a quality and quantity suitable for structural studies*” at The First student conference on structural biology, organized by Czech society for structural biology and Biotechnology institute, Czech Academy of Sciences.
- Thomas Vogels delivered talks at AAIC Neuroscience Next 2020 Meeting:

AAV Vector to Study the Consequences of Astrocytic Tau Pathology, AAIC Neuroscience Next 2020,

- and also at AD/PD conference in March 2021:

AAV vectors to study the functional consequences of neuronal and astrocytic tau pathology using in vivo 2-photon imaging. AD/PD 2021 The 15th International Conference on Alzheimer's & Parkinson's Diseases. 9-14 March 2021

III. There is a need for more international research grants, which bring in longer-term financial stability for working groups (ERC, other H2020 full grants)

The Institute systematically builds collaborating ties with groups and laboratories (see below under "Collaboration") in Europe and the USA. The collaborations resulted in several publications and international projects listed below. These projects facilitate formation of consortia that will bring in larger projects and strengthen sustained funding.

Running funded projects:

Horizont 2020, ADDITION (1.5.2019 / 30.4.2022): M. Novak (Co-Investigator, Coordinator: Karolinska Institutet, Sweden), "*Alzheimer's disease data-driven insights on individual outcomes of importance*". **Funding: 320'000 €**

Horizont 2020, No. 681043 (1.11.2015 / 30.4.2021): M. Novak (Co-Investigator, Coordinator: INSERM, France), "*Coordination Action in support of the sustainability and globalisation of the Joint Programming Initiative on Neurodegenerative Diseases*" **Funding: 25'000 €**

H2020 – JPND - FP-829-085 (01.5.2016 – 31.12.2019): M. Novak (Co-Investigator), "*Pathway complexities of protein misfolding in neurodegenerative diseases: a novel approach to risks evaluation and model development*" **Funding: 490'000 €**

ERANET, Neu-Vasc (1.1.2020 / 31.12.2022): P. Filipcik (Co-Investigator, Coordinator: IBS, Spain), "*Neurovascular damage determines disease pathophysiology in pediatric mild traumatic brain injury: source of new biomarkers*" **Funding: 75'000 €**

ERANET, EURONANOMED 2018-049 (1.1.2019 / 31.12.2021): Mangesh R. Bhide (Co-Investigator, Coordinator: IBS, Spain), "*Nanosystems conjugated with antibody fragments for treating brain infections*" **Funding: 75000 €**

ERA-NET No. 030 (01.1. 2017 – 31.12.2019): Dasa Cizkova (Co-investigator) "*Spinal cord repair: releasing the neuron-intrinsic brake on axon regeneration*" **Funding: 105'000 €**

ERA-NET No. 080 (01.1. 2017 – 31.12.2019): Peter Filipcik (Co-investigator) "*Repetitive Subconcussive Head Impacts - Brain Alterations and Clinical Consequences*" **Funding: 105'000 €**

ICGEB: CRP/SVK18-01 (2019-2021): Andrej Kováč, "*The tryptophan kynurenine pathway - therapeutic strategy for neuroprotection in tauopathies*", **Funding: 41'000 €**

In addition to international projects already running at the Institute, in 2021 our researchers submitted projects in the following schemes: ERANET (1 project, approved), THE MICHAEL J. FOX FOUNDATION (1x, not approved), ICGEB (2x, not approved), and 2 projects in Horizon Europe 2021-2027/ JPND (1 approved), H2020 - HORIZON-WIDERA-2022-ACCESS-04 (Excellence Hubs) – NIU as a member of a consortium, in the approval process. From June 2022, NIU SAS will join a H2020-MSCA-RISE-2019 grant 873127 InterTAU, which will be running till June 2025.

Collaborations:

- **Prof. RNDr. Peter Mikuš, PhD**, Department of pharmaceutical analysis and nuclear pharmacy, Comenius University, Bratislava, (Slovakia)

Piestansky, Juraj [UKOFAAs] (35%) - Olesova, Dominika (10%) - Galba, Jaroslav [UKOFAAs] (5%) - Marakova, Katarina [UKOFAA] (5%) - Parrak, Vojtech (5%) - Secnik, Peter (5%) - Secnik, Peter, ml. (5%) - Kovacech, Branislav (5%) - Kovac, Andrej (5%) - Zelinkova, Zuzana (5%) - Mikus, Peter [KAUT] [UKOFAA] (15%): Profiling of amino acids in urine samples of patients suffering from inflammatory bowel disease by capillary electrophoresis-mass spectrometry. *Molecules*. – 24/18 (2019), p. [1-16], art. no. 3345. - ISSN (online) 1420-3049

Piestansky, Juraj [UKOFAAs] (45%) - Galba, Jaroslav (20%) - Kovacech, Branislav (5%) - Parrak, Vojtech (5%) - Kovac, Andrej (5%) - Mikus, Peter [KAUT] [UKOFAA] (20%): Capillary electrophoresis and ultra-high-performance liquid chromatography methods in clinical monitoring of creatinine in human urine: A comparative study. *Biomedical Chromatography [elektronický dokument]*. - 34/10 (2020), p. [1-13], art. no. e4907 [print]. - ISSN (print) 0269-3879

Piestansky, Juraj [UKOFAAs] (40%) - Matuskova, Michaela [UKOFAA] (10%) - Cizmarova, Ivana [UKOFAA] (10%) - Majerova, Petra (10%) - Kovac, Andrej (10%) - Mikus, Peter [KAUT] [UKOFAA] (20%): Ultrasensitive determination of serotonin in human urine by two dimensional capillary isotachopheresis-capillary zone electrophoresis hyphenated with tandem mass spectrometry. *Journal of Chromatography A*. - Roč. 1648 (2021), p. [1-10], art. no. 462190. - ISSN (print) 0021-9673

- **Assoc. Prof. David Friedecky**, PhD, Faculty of Medicine, Palacky University Olomouc, (Czech Republic)

OLESOVA, Dominika - MAJEROVA, Petra - HAJEK, Roman - PIESTANSKY, Juraj - BRUMAROVA, Radana - MICHALICOVA, Alena - JURKANIN, Bernadeta - FRIEDECKY, Davigid - KOVAC, Andrej**.
GM3 Ganglioside Linked to Neurofibrillary Pathology in a Transgenic Rat Model for Tauopathy. In *International Journal of Molecular Sciences*, 2021, vol. 22, art. no. 12581. (2021 - Current Contents). ISSN 1422-0067.

KARLIKOVA, Radana - MICOVA, Kateřina - NAJDEKR, Lukas - GARDLO, Alzbeta - ADAM, Tomas - MAJEROVA, Petra - FRIEDECKY, David - KOVAC, Andrej. Metabolic status of CSF distinguishes rats with tauopathy from controls. In Alzheimer's Research & Therapy, 2017, vol. 9, art. no. 78. (2017 - Current Contents). ISSN 1758-9193.

- **Prof. Karel Lemr**, Faculty of Science, Palacky University Olomouc, (Czech Republic)
- **Prof. William Banks**, Division of Gerontology & Geriatric Medicine, Faculty of Medicine, University of Washington, Seattle, (USA)

BANKS, William A.** - KOVAC, Andrej - MOROFUI, Yoichi. Neurovascular unit crosstalk: Pericytes and astrocytes modify cytokine secretion patterns of brain endothelial cells. In Journal of Cerebral Blood Flow and Metabolism, 2018, vol. 38, p. 1104-1118. (2018 - Current Contents). ISSN 0271-678X.

POLCIK MICHALICOVA, Alena - BANKS, William A. - LEGATH, Jaroslav - KOVAC, Andrej. Tauopathies – Focus on Changes at the Neurovascular Unit. In Current Alzheimer Research, 2017, vol. 14, no. 7, p. 790-801. ISSN 1567-2050.

BANKS, William A. - KOVAC, Andrej - MAJEROVA, Petra - BULLOCK, K.M. - SHI, M. - ZHANG, J. Tau Proteins Cross the Blood-Brain Barrier. In Journal of Alzheimer's Disease, 2017, vol. 55, no. 1, p. 411-419.

SHI, M. - KOVAC, Andrej - KORFF, A. - COOK, T.J. - GINGHINA, C. - BULLOCK, K.M. - YANG, L. - STEWART, T. - ZHENG, D. - ARO, P. - ATIK, A. - KERR, K.F. - ZABETIAN, C.P. - PESKIND, E.R. - HU, S.C. - QUINN, J.F. - GALASKO, D.R. - MONTINE, T.J. - BANKS, William A. - ZHANG, J. CNS tau efflux via exosomes is likely increased in Parkinson's disease but not in Alzheimer's disease. In Alzheimer's & Dementia, 2016, vol. 12, p. 1125-1131. (2016 - Current Contents). ISSN 1552-5260.

- **Dr. Agnes Kittel**, Laboratory of Molecular Neurobiology, Institute of Biophysics, Biological Research Centre of the Hungarian Academy of Sciences, Szeged, (Hungary)

Majerova, Petra - Polcik Michalicova, Alena - Cente, Martin - Hanes, Jozef - Vegh, Jozef - Kittel, A. - Kosikova, Nina - Cigankova, V. - Mihaljevic, Sandra - Jadhav, Santosh - Kovac, Andrej**. Trafficking Of Immune Cells Across The Bloodbrain Barrier Is Modulated By neurofibrillary pathology in tauopathies. In PLoS ONE, 2019, vol. 14, iss. 5, art. no. e0217216, 27 pp. ISSN 1932-6203.

- **Dr. Maria Deli**, Department of Pharmacology, Institute of Experimental Medicine, Hungarian Academy of Sciences, (Hungary)

DELI, Maria - KOVAC, Andrej. Brain barriers as targets in pathologies and therapy. In Current Pharmaceutical Design, 2020, vol. 26, no. 13, p. 1403 - 1404. (2020 - Current Contents). ISSN 1381-6128.

- **Assoc. Prof. Yoichi Morofuji**, Department of Neurosurgery, University of Nagasaki, (Japan)

FUJIMOTO, Takashi - MOROFUJI, Yoichi** - KOVAC, Andrej - ERICKSON, Michelle A. - DELI, Mária A. - NIWA, Masami - BANKS, William A. Pitavastatin Ameliorates Lipopolysaccharide-Induced Blood-Brain Barrier Dysfunction. In Biomedicines, 2021, vol. 9, no. 837. (2021 - Current Contents). ISSN 2227-9059.

FUJIMOTO, Takashi - MOROFUJI, Yoichi** - NAKAGAWA, Shinsuke - KOVAC, Andrej - HORIE, Nobutaka - IZUMO, Tsuyoshi - NIWA, Masami - MATSUO, Takayuki - BANKS, William A. Comparison of the rate of dedifferentiation with increasing passages among cell sources for an in vitro model of the blood-brain barrier. In Journal of Neural Transmission, 2020, vol. 127, p. 1117-1124. (2020 - Current Contents). ISSN 0300-9564.

- **Prof. Daniela Ostatnikova**, Comenius University in Bratislava, Faculty of Medicine (Slovakia)

OLESOVA, Dominika - GALBA, Jaroslav - PIESTANSKY, Juraj - CELUSAKOVA, Hana - REPISKA, Gabriela - BABINSKA, Katarina - OSTATNIKOVA, Daniela - KATINA, Stanislav - KOVAC, Andrej**. A novel UHPLC-MS method targeting urinary metabolomic markers for autism spectrum disorder. In Metabolites, 2020, vol. 10, art. no. 443. ISSN 2218-1989.

Tomova A, Kemenyova P, Filcikova D, Szapuova Z, Kovac A, Babinska K, Ostatnikova D. Plasma levels of glial cell marker S100B in children with autism. Physiol Res. 2019 Dec 20;68(Suppl 3):S315-S323. doi: 10.33549/physiolres.934350. PMID: 31928049.

- **Prof. Abba Zubair, MD. PhD**, Mayo Clinic Comprehensive Cancer Center, Jacksonville, Florida, (USA)

Fricova, D., Korchak, J. A., & Zubair, A. C. (2020). Challenges and translational considerations of mesenchymal stem/stromal cell therapy for Parkinson's disease. NPJ Regenerative medicine, 5(1), 20. <https://doi.org/10.1038/s41536-020-00106-y>

- **Prof. Jozef Nosek, PhD**, Department of Biochemistry, Faculty of Natural Sciences, Comenius University in Bratislava, (Slovakia)

Brejová, B., Boršová, K., Hodorová, V., Čabanová, V., Gafurov, A., Fricova, D., Nebohacova, M., Vinar, T., Klempa, B., & Nosek, J. (2021). Nanopore sequencing of SARS-CoV-2: Comparison of short and long PCR-tiling amplicon protocols. PloS one, 16(10), e0259277. <https://doi.org/10.1371/journal.pone.0259277>

- **Alzbeta Trancikova Kralova, PhD**, Biomedical Center Martin, Martin, (Slovakia)

Fricova D, Harsanyiova J, Kralova Trancikova A. Alpha-Synuclein in the Gastrointestinal Tract as a Potential Biomarker for Early Detection of Parkinson's Disease. International Journal of Molecular Sciences. 2020; 21(22):8666. <https://doi.org/10.3390/ijms21228666>

- **Assoc. Prof. Matej Skorvanek, PhD**, Faculty of Medicine, Pavol Jozef Safarik University in Kosice, Kosice (Slovakia)
- **Dr. Klempa**, Biomedical Research Center, Institute of Virology, Slovak Academy of Sciences; Bratislava, Slovakia
- **Assoc. Prof. B. Brejova**, Department of Computer Science, Faculty of Mathematics, Physics and Informatics, Comenius University in Bratislava, Slovakia
- **Prof. D. Ruzek**, Institute of Parasitology, Biology Centre of the Czech Academy of Sciences, Ceske Budejovice, Czech Republic, Veterinary Research Institute, Hudcova 70, CZ-62100 Brno, Czech Republic
- **Dr. R. Sedlacek**, Czech Centre of Phenogenomics, Institute of Molecular Genetics, ASCR v.v.i, Vestec, Czech Republic

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- **Prof. Jérôme Badaut**, CNRS UMR5536, CRMSB, University of Bordeaux, Bordeaux, France.
- **Prof. Roald Bahr**, Oslo Sports Trauma Research Center, Department of Sports Medicine, Norwegian School of Sport Sciences, Oslo, Norway

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- **Prof. Inga K Koerte**, cBRAIN, Department of Child and Adolescent Psychiatry, Psychosomatics, and Psychotherapy, Ludwig-Maximilians-Universität, Munich, Germany, Department of Psychiatry, Psychiatry Neuroimaging Laboratory, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA.

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- **Prof. Lukas Zidek, Dr. Jozef Hritz**, Protein Structure and Dynamics Group, CEITEC, MUNI, Brno, Czech Republic
- **Dr. Kristaps Jaudzems**, Latvian Institute of Organic Synthesis, Department of Physical Organic Chemistry, Riga, Latvia

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IV. The formal number of publications is of international level, although the role of Institute and its other partners in actually making these papers is not clear. Publication in journals with higher IF should be a goal.

The majority of scientific papers (impacted foreign & domestic journals registered in CCC, WoS or Scopus), **86% of all papers**, published by Institute's employees do not have any affiliation or other mention of AXON Neuroscience SE biotech company. These works cover a broad range of topics:

- a) Host-pathogen interaction during the infection of bacterial pathogens (*Borrelia sp.*, *E. coli*, *N. meningitidis*, *M. tuberculosis*, *S. pneumoniae*, etc)
- b) Bioinformatic analyses of omics experiments conducted using the databases and software instruments in collaboration between NIU and Department of Medical Biophysics & Department of Computer Science, University of Toronto (Canada).
- c) Use of stem cells in the regenerative medicine of neuronal injury, especially spinal cord, often conducted in a close collaboration with the University of Veterinary Medicine and Pharmacology (Kosice, Slovakia) and Inserm, Laboratoire Protéomique, Réponse Inflammatoire et Spectrométrie de Masse-PRISM, Université de Lille (France).

- d) Development of analytical methods for quantitation of metabolites and bioactive substances in human samples by capillary electrophoresis-coupled to MS and HPLC-MS, often developed in collaboration with Faculty of Pharmacy, Comenius University (Slovakia).
- e) Biology of the blood-brain barrier and blood-CSF barrier, and their dysfunction in neurodegenerative diseases, in collaboration, besides others, with the Division of Gerontology and Geriatric Medicine, Department of Medicine, University of Washington School of Medicine (USA).
- f) Pathobiology of traumatic brain injury, biomarkers and mechanisms that lead to neurodegenerative changes later in life; In collaboration with CNRS UMR5536, CRMSB, University of Bordeaux, Bordeaux (France), Department of Sports Medicine, Norwegian School of Sport Sciences, Oslo (Norway), and Department of Child and Adolescent Psychiatry, Psychosomatics, and Psychotherapy, Ludwig-Maximilians-Universität, Munich (Germany).
- g) Pathobiology of Parkinson's disease in collaboration with Department of Neuroscience, Mayo clinic Jacksonville, Florida (USA).
- h) Development of nanoparticles for the delivery of therapeutics for CNS, in collaboration with the Department of Analytical Chemistry, Faculty of Natural Sciences, Comenius University (Slovakia).
- i) Canine dementia – molecular pathology, clinical picture and diagnostic biomarkers in collaboration with the University of Veterinary Medicine and Pharmacy, Kosice (Slovakia), and also with experts in the field outside of Slovakia: Gary Landsberg, North Toronto Veterinary Behaviour, Specialty Clinic, Thornhill, Ontario (Canada); Joseph A. Araujo, InterVivo Solutions, Toronto, Ontario (Canada); Sagi Denenberg, Langford Vets, School of Veterinary Sciences, University of Bristol, Bristol (United Kingdom)

The remaining **14%** are publications contain both NIU and AXON affiliations. These papers resulted from a mutually profitable collaboration and are solely limited to cases within the scope of AXON expertise and interest:

- a) The published work used highly sensitive bioanalytical instrumentation currently only available at AXON (Quanterix Simoa ELISA). The papers monitored CNS biomarkers in CSF and blood using the Quanterix kits.
- b) The papers presented analytical methods developed in collaboration with AXON using AXON's instrumentation (UHPLC, MS).
- c) The work was performed on AXON's proprietary and unique transgenic animal models (mice and rats) expressing human truncated tau proteins in the CNS neurons. The results describe the molecular underpinnings of the pathological cascades leading to neuronal dysfunction due to the truncated tau transgene, and might provide clues for possible future therapies (CSF and blood biomarkers, activated pathological pathways, etc).

- d) The papers resulted from a collaboration between AXON and other European institutions resulting from the clinical trials conducted by AXON.

V. Clear contractual form of collaboration between the Institute and company AXON, which fixes (inter alia) the IPR issues, would be beneficial to both parties.

We understand the debate about what kinds of collaborations should be acceptable and what kinds should not. In Slovakia, public resources are usually not directed to research programmes developing products that can be commercialised. For years, there haven't been any national programmes covering either the transition from basic research to clinical development, the so-called "valley of death" where the attrition of therapeutic inventions is extremely high, or support for IPR. The long-term strategic collaboration between the Institute and Axon Neuroscience SE biotech company is based on a Grant agreement (officially available on Institute's website). The collaboration is not based on the traditional model, where academic-industrial partnerships are part of an integrated development strategy for biotech or pharmaceutical companies. New AXON therapeutics (vaccine, antibodies) and diagnostics (based on biomarkers) were not invented at the Institute (i.e. using public resources), so NIU SAS cannot share the company's IPR. All expenses for the patent portfolio (from submission of the international PCT application to the issue of national patents at selected relevant countries) are covered exclusively by AXON.

The collaboration between the Institute and AXON is based on fee-for-service agreements (projects) and allows for exchanging ideas, sharing equipment, and publishing research papers.

During the last decade, AXON has almost exclusively focused on clinical development of a first-in-man tau vaccine. Researchers from the Institute participated in the preclinical development of the vaccine and published data in scientific journals along with AXON researchers. All instruments and equipment owned by AXON were fully available for use by the Institute employees, **even for projects not associated with AXON**. This remains a great benefit for the Institute, since in Slovakia there are no grants to cover the sourcing of new scientific and research infrastructure, and thus we do not have the opportunity to obtain state-of-the-art technology, which is a prerequisite to stay competitive with leading European scientific institutions and to become leading members of international consortia.

Finally, AXON has financed an extensive reconstruction of our animal facility and Institute premises, which were completely destroyed by fire in 2010. The company provides its unique transgenic animal models for Institute's internal research and for collaborations with European academic institutions. The company also offers a biobank facility and biological samples (where allowed by the Ethics committees and cGCP procedures) for non-profit research purposes.

Additional comments:

- **The number of teaching hours for lectures and practical courses is very low.**

The number of teaching hours at universities has increased dramatically during the evaluated period, from 17 hrs/yr in 2015 to **127 hrs/yr in 2021** (more than 100 hrs/yr throughout the whole period, see section 2.5.4.), thanks to closer collaborations with universities, especially University of Veterinary Medicine and Pharmacy in Kosice (Slovakia) and Comenius University in Bratislava (Slovakia).

- **There is a strong gender imbalance at the level of research positions.**

NIU SAS employs 58% women in general, and 49% of all scientists. Three laboratories are headed by women: Prof. Kontseková (Laboratory of Immunology and Neuroimmunology), Prof. Cizkova (Center of Regenerative Medicine) and Dr. Fricova (Parkinson's disease research laboratory).

Prof. Kontseková is also the deputy director of the Institute. Both Prof. Cizkova and Prof. Kontseková are members of the Institute's Board of Directors, which comprises four members plus the director of the Institute.

NIU SAS supports activities of several scientific societies, most notably the Slovak Society for Neuroscience and the Slovak Immunological Society. Prof. MVDr. Dasa Cizkova, DrSc. is the chairwoman of the former and Prof. RNDr. Eva Kontseková, DrSc. of the latter.

Furthermore, NIU SAS actively supports women in their professional development. In 2021, two female employees received a higher qualification degree IIa allowing them to supervise PhD students (Dr. Fricova and Dr. Brezovakova). Assoc. Prof. Cizkova was promoted to a full Professor. Finally, there are 11 female PhD students out of total 13 PhD students at NIU SAS.

- **No patents or other IPR instruments described by the Institute**

NIU SAS has applied for a patent "New peptide-based system for transporting the drugs into the brain" (Patent application: PP 24-2019).

4. Research strategy and future development of the institute for the next five years (Recommended 3 pages, max. 5 pages)

Research strategy of the institute in the national and international contexts, objectives, and methods (including the information on when the strategy was adopted)

The Institute's long-term goal is to facilitate broad interdisciplinary research for the understanding of mechanisms of neuronal degeneration, injury- and pathogen-induced deterioration and for the discovery of innovative treatments, and to support patients and their families by informing the public about the molecular basis of disease, pharmacological, and non-pharmacological therapy.

Scientific collaboration enhances research output quality. We will continue to support collaborative efforts among our research teams, as well as with other research groups in Slovakia and abroad, especially by actively supporting preparation of joint grant proposals.

We recognize that Institute's employees are its most important asset. We plan to further expand our PhD student and postdoctoral base, attracting and actively seeking excellent and talented students and postdoctoral fellows from Slovakia and other countries, by institutional investments and using external funding.

Our research strategy is to further develop and sustain research excellence in areas which are already established at the Institute and supplement those with emerging important related topics. The complementary structure of research groups at the Institute allows us to approach all research topics at different levels of description, from the molecular underpinnings, through cellular modifications, changes in brain activity, to the impact on the whole organism, including changes in biomarkers, cognitive deficits, and behavioural alterations. Our strategy is built around three main themes: basic research of pathogenic mechanisms of neurodegenerative disorders and neuronal injuries, basic research of therapeutic and regenerative approaches to brain disorders, and translational approach to disorders of the nervous and immune systems.

Research strategy and future development of the institute in the national context

One of the crucial aims for the next 5 years is to create a network of scientific and clinical institutions in the Slovak republic in order to harmonise modern diagnostic concept of dementia based on the clinical presentation and biomarker profile. The Institute has already become the main coordinator of this network and is responsible for the evaluation of molecular biomarkers in the blood and cerebrospinal fluid. The aim is to create a Slovak cohort of patients with dementia (1000 tested patients by 2025), which would allow us to participate in clinical trials on novel disease modifying drugs and to take part in international projects.

Several recently approved projects will guide research in our main focus areas.

In 2022 NIU SAS, in collaboration with the Ministry of Health of the Slovak republic, will finalise the "National Programme to fight Alzheimer's disease" and will propose the concept of the social, medical, and economic plan which may have a direct impact on Slovak society in the upcoming 10 years. An integral part of the National programme is the implementation of a novel diagnostic concept based on molecular biomarkers in clinical practice. This may improve diagnostic accuracy; patients would be diagnosed properly and treated effectively, which would lead to a lower rate of hospitalization. Utilising biomarkers to arrive at the correct diagnosis reduces costs by as much as 58%.

Research strategy and future development of the institute in the international context

The research on NIU SAS will continue to focus on various molecular and cellular underpinnings of the debilitating human and animal disorders of the central nervous system with unmet medical needs: Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, traumatic brain injury, spinal cord injury, infectious diseases affecting human brain and canine brain diseases.

1) In **Alzheimer's disease** research we will address the following topics:

- Longitudinal Assessment of Neurodegeneration and the Correlates of Relevant Endpoints in AD (Petr Novak, Norbert Zilka, 2021-2024)

The implementation and validation of the Slovak version of the Addenbrooke's Cognitive Examination version III is executed in cooperation with the Brain and Mind Centre, The University of Sydney (Australia). The clinical use of social cognition measures for the assessment of neurocognitive disorders (the SIGNATURE Initiative) is being worked out in cooperation with University of Trento CiMeC, Rovereto (Italy).

- Neuro-glia cell-based models for the inter-neuronal spread of tau pathology (Eva Kontsekova, Monika Zilkova, Branislav Kovacech, 2021-2025)

Spread of abnormal forms of the neuronal protein tau through the brain is currently seen as the main culprit responsible for neuronal dysfunction and death of CNS neurons. Glial cells appear to play a dual role in this process. Their timely activation seems to reduce the spread of tau pathology, while chronic activation leads to excessive release of inflammatory molecules that worsen the disease outcome. In our project we aim to establish a co-culture of human primary astrocytes and microglia (from Alzheimer's disease and control post-mortem human brains) with human iPSC-derived neurons and identify glial factors (and metabolic clues) that influence the spread of pathological tau proteins from neuron to neuron.

- Non-pharmacological interventions for Alzheimer's disease patients (Petr Novak, Norbert Zilka, Andrej Kovac, 2023-2026)
- Movement of pathological proteins across the brain barriers (Andrej Kovac, Petra Majerova, Jozef Hanes, 2022-2025)

Alzheimer's disease is identified worldwide as one of the public health priorities due to the increase in prevalence with age. There is an urgent need for earlier and better diagnostics and disease-modifying treatments. The project will be focused on the one of the most important parts of brain research, on brain barriers and its role in neurodegenerative diseases. In our project we will analyse movement of tau protein in extracellular space and across the brain barriers.

- Development of novel therapeutic approaches for Alzheimer's disease (Andrej Kovac, Petra Majerova, Jozef Hanes, 2022-2025)

Brain diseases are among the less understood and poorly treatable conditions. Despite the rapid growth in recent years in the drug development, there is still a low success rate of effective therapies focused on disease of the central nervous system. The blood-brain barrier (BBB) presents a challenge to the delivery of drugs into the brain. Several strategies try to overcome BBB and promote efficient and specific crossing through BBB of therapeutically relevant drugs. The aim of the project is to develop novel antibodies for brain transport that allow delivery of

drugs or biologicals into the brain. We expect to identify novel brain delivery receptor mediated system based on discovered antibodies specifically binding to brain endothelial cells receptors.

- Neuronal circuits mediating cognitive dysfunction in neurodegenerative disorders (Tomas Hromadka, 2021-2025)

How the specific molecular and morphological changes associated with tauopathies affect information processing in neuronal circuits and translate into distinct and cognitive deficits is unclear. Yet, resolving the changes in neuronal activity is crucial for understanding the impact of neurodegeneration on brain function. Using a combination of experimental approaches in vivo we study the changes in activity and function of well-defined cortical cell-types during neurodegeneration in rodent models of tauopathies created using AAV vectors. We aim to uncover the principles of functional organization of neuronal circuits in healthy and diseased brains. Such organization would relate directly the detailed structure of cortical circuits to perception and behaviour in brain disorders.

2) ***Parkinson's disease***

- Spread of alpha-synuclein-associated pathology across gastrointestinal organs in a mouse model and patients with Parkinson's disease (Dominika Fricova, Alzbeta Trancikova, 2021-2024)

3) ***Traumatic brain injury***

- Molecular pathways induced by traumatic brain injury: novel biomarkers and prediction of new therapeutic targets for neurodegeneration. The research will be supported by APVV, VEGA, ERANET grants, several other grant applications were submitted in 2022, either in collaboration with Comenius University in Bratislava, Trnava University or Oslo Sport Trauma Research Centre (Peter Filipcik, Martin Cente, 2022 – 2025).

We have also created a network focusing on brain alterations and clinical consequences of repetitive head impacts in adolescents that includes Ludwig-Maximilians-University in Munich, Katholieke Universiteit Leuven, Tel Aviv University, Oslo Sports Trauma Research Center and University Medical Center Utrecht.

NIU SAS is a member of consortium together with University of Bordeaux, Institute of Functional Genomics in Montpellier, Ludwig-Maximilians-University in Munich and University of Calgary investigating the neurovascular damage and novel biomarkers for mild traumatic brain injury.

4) ***Amyotrophic lateral sclerosis***

- We became a partner of the JPND international project “A premotor disease signature for ALS” (Norbert Zilka, Andrej Kovac, Petra Majerova, 2022-2025), which aims to develop a clinico-molecular fingerprint of premotor gene mutation carriers that will shed light on the molecular pathogenesis of ALS and allow for a timelier diagnosis. The fingerprint will improve

diagnostic accuracy, but also yield information about molecular and pathophysiological causes driving ALS. NIU SAS is the national coordinator for the Slovak republic.

5) Drug delivery systems to target pathogens

- Drug delivery systems are being designed to cross the human BBB and target neuroinvasive pathogens like *Borrelia*, *Neisseria* and West Nile virus. In vitro BBB models either in the form of 2D transwells or 3D spheroids are being generated to test the molecular cross talk between meningo-encephalitis - causing pathogens and human cells. These in vitro models will be used to evaluate the ability of drug delivery systems to cross BBB (Mangesh Bhide, Amod Kulkarni, 2022 – 2025).

6) Cell signalling related to COVID-19 virus

- Mechanisms of immune memory, duration of protection and correlates of protection are poorly understood for SARS-CoV-2 virus. Therefore, the aim of the study is a comprehensive quantitative and qualitative longitudinal analysis of adaptive immunity in adult subjects and in children after infection with SARS-CoV-2 or after vaccination. Our challenge is to identify the critical components of adaptive immunity, both humoral and cellular, which are needed to control and to prevent the viral infection. The project will be a collaboration with National Institute of Children's Diseases, Bratislava, Slovakia (Eva Kontseková, 2022 - 2024).
- We also aim to perform transcriptome analysis of human alveolar epithelial cells and/or human hepatocarcinoma cells exposed to spike protein of SARS-CoV-2 to disentangle cell signalling events of host cells during SARS-CoV-2 internalization. Simultaneously, the single stranded oligonucleotides (aptamers) binding to spike protein of SARS-CoV-2 will be developed as potential therapeutic molecules (Mangesh Bhide, Amod Kulkarni, 2022 – 2025).

7) Structural biology of non-globular proteins involved in neurodegenerative processes

- Basic research of fundamental principles governing the fate of the entirely or partially non-globular proteins causing neurodegenerative disorders (tau protein, amyloid beta peptide, alpha synuclein, prion protein, huntingtin etc.) has been largely reinforced by the recent developments in structural biology methods, namely cryoEM and NMR. We are collaborating with NMR and cryoEM groups in CEITEC, Brno and LIOS, Riga on structural investigation of tau protein pathological forms. Team of Rostislav Skrabana in consortium with NMR group at the Institute of Chemistry SAS received funding for project investigating the role of small structural motifs in disordered, non-globular proteins. (Rostislav Skrabana, Ondrej Cehlar, Milos Hricovini, 2022-2025)