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

Period: January 1, 2012 - December 31, 2015

1. Basic information on the institute:

1.1. Legal name and address:

Institute of Neurobiology Slovak Academy of Sciences, Šoltésovej 4-6, 040 01 Košice

1.2. URL of the institute web site:

http://www.neurobiology.sk

1.3. Executive body of the institute and its composition

Directoriat	Name	Age	Years in the position
Director	RNDr. Nadežda Lukáčová, DrSc RNDr. Ján Gálik, CSc	59 56	1.3.2011 - 30.6.2015 since 1.7. 2015
Deputy director	RNDr. Ján Gálik, CSc RNDr. Nadežda Lukáčová, DrSc	56 59	1.3.2011 - 30.6.2015 since 1.7. 2015
Scientific secretary	RNDr. Jaroslav Pavel, PhD RNDr. Lucia Slovinská, PhD	43 41	1.3.2011 - 30.6.2015 since 1.7. 2015

1.4. Head of the Scientific Board

MVDr. Ivo Vanický, CSc

1.5. Basic information on the research personnel

1.5.1. Number of employees with university degrees (PhD students included) engaged in research projects, their full time equivalent work capacity (FTE) in 2012, 2013, 2014, 2015, and average number of employees in the assessment period

	2012		2013		2014		2015		total		
	number	FTE	number	FTE	number	FTE	number	FTE	number	averaged number per year	averaged FTE
Number of employees with university degrees	26,0	22,100	27,0	24,540	27,0	23,280	25,0	20,270	**105,0**	**26,3**	**22,548**
Number of PhD students	8,0	7,000	8,0	7,000	9,0	8,000	12,0	11,000	**37,0**	**9,3**	**8,250**
Total number	34,0	29,100	35,0	31,540	36,0	31,280	37,0	31,270	**142,0**	**35,5**	**30,798**

1.5.2. Institute units/departments and their FTE employees with university degrees engaged in research and development

Research staff	2012		2013		2014		2015		average	
	No.	FTE	No.	FTE	No.	FTE	No.	FTE	No.	FTE
Institute in whole	26,0	22,100	27,0	24,540	27,0	23,280	25,0	20,270	**26,3**	**22,548**
1. Department of neurodegeneration, plasticity and repair (since 1. 9. 2014)					17,0	13,530	12,0	11,270	**14,5**	**12,400**
2. Department of regenerative medicine and cell therapy (since 1. 9. 2014)					10,0	9,750	9,0	9,000	**9,5**	**9,375**

1.6. Basic information on the funding of the institute

Institutional salary budget and others salary budget

Salary budget	2012	2013	2014	2015	average
Institutional Salary budget *[thousands of EUR]*	257,956	258,675	253,501	268,247	**259,595**
Other Salary budget *[thousands of EUR]*	70,793	83,448	74,920	40,195	**67,339**

1.7. Mission Statement of the Institute as presented in the Foundation Charter

The Institute of Neurobiology of the Slovak Academy of Sciences (INB SAS) was created through the transformation of the former Institute of Experimental Biology of the Slovak Academy of Sciences (founded 1964) and it was officially registered on January 1st, 1977. According to the Foundation Charter issued by the Presidium of the Slovak Academy of Sciences, the Institute of Neurobiology is a scientific organization with the budgetary form of financial management. The main mission of the Institute is to conduct basic research into the central nervous system (CNS) under physiological and pathological conditions. Research activities are focused on understanding relationships between blood circulation and the nervous system, especially during circulatory and metabolic disorders. Efforts are being made to elucidate the pathological mechanisms of the stroke, a major disorder of the CNS, as well as spinal cord injury. The scientific program of the Institute is closely associated with clinical research promoting integrative studies based on a multidisciplinary approach. As a respected research institution, the Institute provides consultancy services and expertise related to its main activities. The scientists at the Institute are involved in both undergraduate and postgraduate training of students in neurobiology in accordance with current legislation. The important mission of the Institute is to publish scientific results in periodical and nonperiodical printed media, particularly in the field of cell biology and pathology, neurobiology, neurophysiology, neurochemistry, neuropathology, developmental toxicology and teratology, molecular pharmacology, immunopharmacology, molecular embryology, stem cells and nervous tissue regeneration.

1.8. Summary of R&D activity pursued by the institute during the assessment period in both national and international contexts, (recommended 5 pages, max. 10 pages)

Priority results achieved in brain and spinal cord research at the Institute since 2012

The Institute of Neurobiology (INb) SAS is the leading academic institution in the field of CNS injury in the Slovak Republic, with the focus shifting into regeneration, neuroplasticity and various protective effects. A large portion of our research output is the result of international cooperation within the EU research area (Czech Republic, Spain, France, Poland, Portugal), or other countries worldwide (Israel, USA).

As stated in the mission of the Institute (see WEB) "The main field of our research consists of socially relevant diseases of the nervous system caused by insufficient blood supply (ischemia) and by direct insult (trauma), and their treatment using principles of regenerative medicine". In the past four years 2012-2015 these two general objectives were studied in four, partially overlapping research directions:

- Spinal trauma therapy – cellular approach using biomaterial matrices
- Postnatal neurogenesis and neural progenitor production
- Spinal trauma therapy - pharmacological and physical approach
- Ischemic tolerance, pre- and post-conditioning of injured CNS tissue

Research was carried out in six laboratories, organized within two departments. The most important topics of the Institute are described below.

<u>Spinal trauma therapy - cellular and biomaterial approach</u>

In cooperation with partners from *Laboratoire Protéomique, Réponse Inflammatoire et Spectrométrie de Masse, University of Lille, France,* we introduced innovative methods of molecular imaging technology: matrix-assisted laser desorption / ionization (MALDI) and imaging mass spectrometry. Together we analyzed bioactive substances produced by resting and activated microglia under *in vitro* conditions and identified a number of products of mesenchymal stem cells that significantly inhibited the activated microglia (1). More than 300 proteins and peptides were identified in rat spinal cord injured tissue, which are involved in regeneration as well as degeneration and apoptotic processes. In the segments above the lesion (rostral) and in the central lesion especially chemokines and cytokines were identified, or factors affecting neurogenesis. In the segments below the lesion (caudal), we observed the presence of particular factors related to necrosis. Conditioned media obtained from various segments of the damaged spinal cord were added to the nutrient media for the in vitro cultivated cell culture (microglial line / BV2, dorsal ganglia). It was found that the conditioned media of the different segments were able to differently activate microglia, and to stimulate the growth of nerve fibers in dorsal root ganglia. The acquired data can be associated with different polarization of activated microglia and macrophages (M1 / M2) along the rostro-caudal axis after acute injury (2). In collaboration with another group from the *Center of Regenerative Medicine and Stem Cell Research, Ben-Gurion University of the Negev, Beer Sheva, Israel* we have developed and designed biomaterial based on alginate, with the ability to bind and release epidermal growth factor (EGF), and fibroblast growth factor - 2 (bFGF). The biomaterial was settled under *in vitro* conditions with neural progenitor cells obtained from experimental animals. The concentration of growth factors released within the first week *in vitro* was optimal for cell division and formation of neurospheres. During the following 14 days, the concentrations of growth factors decreased, which stimulated the migration of cells from neurospheres and their terminal differentiation into neurons, astrocytes and oligodendrocytes. The results confirm that this 3D alginate-based biomaterial with continuous growth-factor release represents an optimal environment for the long-term survival and differentiation of neural progenitors *in vitro (3).* This biomaterial was also used for transplantation studies in rats with compression injury of the spinal cord. A continuous supply of these bioactive molecules at the injury site considerably protected the spinal cord tissue, which contained a higher number of surviving neurons (ChAT motoneurons) above and below the lesion. In the central lesion containing biomaterial we observed outgrowing corticospinal fibers and blood vessels. Immunohistochemical detection correlated with behavioral tests, which confirmed the functional improvement of the spinal-cord injured rats treated with alginate and bioactive molecules in comparison with untreated rats.

These results suggest the possible therapeutic application of active alginate implants with various active molecules for the treatment of spinal cord injury *(4).*

Postnatal neurogenesis

Another possible way of treating and repairing injured tissue is to study the endogenous capacity of the nervous system. Our study focused on understanding one of the most exciting fields of neuroscience: adult neurogenesis. The study of this topic could lead to the development of new therapeutic strategies directed toward improving neuronal replacement after injury or neurodegeneration, as well as to consideration of this phenomenon in terms of prevention. We investigated the main neurogenic area of the brain, which is represented by the subventricular zone (SVZ), rostral migratory stream (RMS) and olfactory bulb (OB). We published original data for the existence of functional connections: synapses of nitric oxide-producing neurons in the rat RMS and thereby extended knowledge about the possible regulation of neurogenesis *via* established neuronal circuitry (6).

The mechanisms involved in regulation of postnatal neurogenesis by exogenous factors still remain unclear. Exposure of adult rats to artificial or naturalistic odor induced selective expression of Fos protein in the SVZ/RMS/OB system. The obtained morphological/behavioral data provide new evidence that some cells in the neurogenic area have complete prerequisites necessary for Fos signal transduction (7). It was previously found that blood vessels in the RMS and the OB serve as a migratory scaffold for newborn neurons in adult mice. We presented the first detailed description of the arrangement of blood vessels, neuroblasts and astrocytes in the rat RMS. The organization of blood vessels, astrocytes and neuroblasts in the RMS of adult rats suggests that the scaffold for migrating neuroblasts is established by contribution of blood vessels and astrocytes alike (8).

Spinal trauma therapy - pharmacological and physical approach

One of the possible therapeutic solutions for suppressing and totally reducing undesirable secondary processes after SCI is the application of hypothermia: the reduction of physiological body temperature, which has minimal effect on the metabolism and body functions. The conclusions of our study confirm that hypothermia had only a partial neuroprotective effect on the preservation of neurons in the dorsal and ventral horn of the spinal cord, which correlated with significant improvement in motor and vegetative functions after some intervals of survival time. On the other hand, hypothermia resulted in development of the sensitive abnormality called allodynia *(5).*

The effect of locally-applied hypothermia was also used in translational experiments on minipigs. We have developed a highly-reproducible model of traumatic spinal cord injury at lumbar level using a computer-controlled compression device. This model is useful for experimental purposes in preclinical studies. It was used in Slovakia for the first time. Ice-cold saline (4°C) was carried through a special spinal perfusion chamber, created with 3D printing technology, using a peristaltic pump (the flow 2ml/min). This cold perfusion created local hypothermia of the lesion site (L3) lasting for 5 hours, while the body temperature remained stable during the whole perfusion period. The temperature of solutions in the perfusion chamber was maintained at 19°C. The results of this study provide evidence of considerable loss of neurofilament immunoreactivity (NF-IR) and tissue degradation seen at the lesion site and 3 cm caudally, as well as cranially 9 weeks after SCI (8N, 15N and 18N force). It shows that local hypothermia has beneficial effects on the number of neurofilaments, and on gray and white matter preservation, and, although without statistical significance, also on functional improvement.

Original results were obtained in experiments focused on the study of molecular mechanisms in the spinal cord following experimentally-induced trauma (compression and transection at various segmental levels) and ligation of peripheral nerves. We examined the mechanisms leading to progressive development of spinal hyper-reflexia. We clearly demonstrated that neuronal nitric oxide synthase (nNOS) plays a key role in excitability of α-motoneurons. A single dose of nitric oxide synthase blocker NNLA (60mg/kg) applied on the 10th day after spinal cord injury, or Baclofen (GABA-B agonist) therapy, reduced nNOS expression in α-motoneurons and suppressed symptoms of spasticity. We experimentally demonstrated that a single dose of AMPA antagonist NGX424 (1 mg, i.t. or 3,6,12 mg.kg-1, s.c.), nitric oxide synthase blocker

NNLA (60 mg/kg, i.m.) or α2-adrenergic agonist Tizanidine (1 mg/kg, i.t.) can effectively modulate chronic spasticity in patients who are tolerant to Baclofen treatment (9,10,11). In collaboration with the *Center for Neurosciences and Cell Biology, Coimbra, Portugal*, we revealed that glutamate-dependent nitric oxide (NO) temporal dynamics *in vivo,* measured using NO-selective microelectrodes in specific brain regions did not fully overlap with the pattern of nNOS expression, suggesting that, complementary to the distribution of nNOS, the local regulation of NO synthesis/decay pathways critically determines the effective NO concentration sensed by a target within the diffusional spread of this free radical (12). Original results were also achieved in cooperation with our partners from the *Department of Cellular Signaling, Mossakowski Medical Research Center, Polish Academy of Sciences,* suggesting that endurance training, which enhances the expressions of BDNF and its receptor TrkB, lastingly upregulates the key elements of the NO/sGC/cGMP pathway in brain regions vital for the execution and coordination of locomotor movements. We found that favorable extrapyramidal motor effects of endurance training are related to changes in specific motor control-related subcortical brain regions (13). Previous experiments suggested that Angiotensin II (Ang II) released into the blood circulation could modulate the excitability of sensory circuits at the level of the spinal cord and associated afferent fibers originating from dorsal root ganglion neurons. Systemic continual administration of subpressor doses of Ang II on the 7th day of survival after chronic ligation of rat sciatic nerve caused tactile, heat and cold hyperalgesia, which means increased sensitivity to neuropathic pain. This effect was mediated by AT1 receptors, since blocking these receptors by selective antagonist Losartan prevented increased sensitivity. Our experiments suggest that Ang II through AT1 receptor activation is an important regulatory factor in neuropathic pain sensitivity and plays an important role in the injury of large-sized primary afferent neurons and activation of satellite glial cells elicited by chronic constriction injury of the sciatic nerve (14).

Ischemic tolerance

Promising results, with great translational potential, were obtained studying the phenomenon of ischemic tolerance, especially the mechanism and cell pathways resulting in a tolerant phenotype of neuronal cells affected by ischemia. In the last five years we have concentrated on the role of antioxidant defense and excitotoxicity in building ischemic tolerance. Beside the model of global ischemia, our investigation was extended to a model of focal cerebral ischemia and toxic brain injury and novel strategies for tolerance induction (also called conditioning), including remote tolerance and cross-tolerance. All these methods clearly demonstrated the potential of glutamate for monitoring the progress of ischemia and the efficacy of therapy. Ischemia/toxic brain injury leads to marked elevation of blood and tissue glutamate (15, 16). On the other hand, conditioning renews protein synthesis in affected cells and activates mechanisms resulting in rapid elimination of glutamate from brain tissue and/or in the circulatory system, which could otherwise impede brain-to-blood glutamate efflux mechanisms (17). Activation of this glutamate elimination machinery significantly improves survival of damaged neurons and memory performance (18). The crucial point for successful activation of ischemic tolerance is the timing of conditioning. We have found that in the model of focal ischemia-reperfusion, post-therapeutic intervention should be applied within three hours of reperfusion at most for the best neuroprotection (rapid conditioning) (19). In this time the antioxidant capacity and protein synthesis activity of cells surrounding the infarct are still preserved (17, 18). As described previously, the best therapeutic potential in permanent focal ischemia is within the first hour after the attack. We showed that preserved integrity of the mitochondrial membrane and the incompletely developed process of apoptosis may contribute to a better therapeutic outcome. With prolonged ischemia the blood-brain barrier is gradually disrupted and the apoptotic pathway of cell death is activated, resulting in infarct expansion from the core to surrounded tissue (19). In contrast to this, in global ischemia rapid therapy, delayed conditioning, or a combination of rapid and delayed conditioning should be applied to prevent neuronal death (20). Very important information resulting from the recent period is the fact that signals responsible for activation of neuroprotective mechanisms generated by conditioning (pre- or post-) are transmitted to the brain via circulating blood, and may even be transferred from animal to animal (21). This finding, that neuroprotection can be transmitted to injured nervous tissue even hours after injury attack, is very important information from the clinical point of view. It implies an effective way of therapy for the injured CNS. This information, together

with our previous results, was the basis for a patent application and has become the focus of our scientific direction for the coming period.

Project activity

During the assessment period, funding became a major challenge for the Institute, in the context of decreasing governmental funding, and rising administrative costs. INb SAS was successful in obtaining 6 projects supported by EU SF (3 as coordinator, 3 as partner) with a total amount of 5 million EUR, of which 3.8 million EUR was assigned to our Institute. Thanks to the project entitled “Center of Excellence for Neuroregeneration Research” (NEUREG), our Institute substantially improved its instrument infrastructure, which widened our scope of innovative experimental approaches. During the last 4 years we implemented or improved techniques such as MALDI mass spectrometry, in vitro techniques, cell and tissue cultures, molecular biology, in vitro and in vivo electrophysiology, and advanced behavioral testing. Intensive effort was devoted to improving the personnel situation in the Institute: within the EU SF projects INb SAS obtained funds for full financial coverage for 7 postdoctoral and 6 technical assistant positions.

1. Cizkova D., Devaux S., Le Marrec-Croq F., Franck J, Slovinska L., Blasko J., Rosocha J., Spakova T., Lefebvre Ch., Fournier I., Salzet M.: Modulation properties of factors released by bone marrow stromal cells on activated microglia: an in vitro study, Sci Rep., 4:7514. doi: 10.1038/srep07514, 2014, IF = 5.578
2. Cizkova D., Le Marrec-Croq F., Franck J., Grulova I., Devaux S., Lefebvre Ch., Fournier I., Salzet M.: Alterations of the protein composition along the rostro-caudal axis after spinal cord injury: Proteomic, in vitro and in vivo analyzes. Frontiers in Cellular Neuroscience, 8, art. no. 105, 2014, IF = 4.175
3. Cizkova D., Slovinska L., Grulova I., Salzet M., Cikos S., Kryukov O., Cohen S.: The influence of sustained dual-factor presentation on the expansion and differentiation of neural progenitors in affinity-binding alginate scaffolds, J Tissue Eng Regen Med., 2013, IF = 2.826
4. Grulová I., Slovinska L., Blasko J., Devaux S., Wisztorski M., Salzet M, Fournier I., Kyukov O., Cohen S, Cizkova D.: Delivery of Alginate Scaffold Releasing Two Trophic factors for spinal cord injury repair, Sci Rep. 5:1-19, 2015, IF = 5.578
5. Grulova I., Slovinska L., Nagyova M., Cizek M., Cizkova D.: The effect of hypothermia on sensory-motor function and tissue sparing following spinal cord injury. The Spine Journal, 13:1881-1891, 2013, IF = 3.355
6. Blasko, J., Fabianova, K., Martoncikova, M., Sopkova, D., Racekova, E.: Immunohistochemical Evidence for the Presence of Synaptic Connections of Nitrergic Neurons in the Rat Rostral Migratory Stream. Cell. Mol. Neurobiol., 33:753–757, 2013, IF=2.293
7. Fabianová, K., Martončíková, M., Fabian, D., Blaško, J., Račeková, E.: Diverse effect of different odor stimuli on behavior and Fos protein production in the olfactory system neurogenic region of adult rats. Behav. Brain Res., 265:38-48, 2014, IF=3.391
8. Martončíková, M., Fabianová, K., Schreiberová, A., Blaško, J., Almašiová V., Račeková, E.: Astrocytic and vascular scaffolding for neuroblasts migration in the rostral migratory stream. Curr. Neurovasc. Res., 11:321-329, 2014, IF=2.735
9. Kisucká A., Hricová Ľ., Pavel J., Strosznajder JB., Chalimoniuk M., Langfort J., Gálik J., Maršala M., Radoňak J., Lukáčová N.: Baclofen or nNOS inhibitor affect molecular and behavioral alterations evoked by traumatic spinal cord injury in rat spinal cord. Spine J. 15(6):1366-78, 2015, IF: 2.800
10. Kakinohana O., Scadeng M., Corleto JA., Sevc J., Lukacova N., Marsala M.: Development of AMPA receptor and GABA B receptor-sensitive spinal hyper-reflexia after spinal air embolism in rat: a systematic neurological, electrophysiological and qualitative histopathological study. Exp Neurol., 237(1):26-35, 2012, IF=2.843
11. Corleto JA., Bravo-Hernández M., Kamizato K., Kakinohana O., Santucci C., Navarro MR., Platoshyn O., Cizkova D., Lukacova N., Taylor J., Marsala M.: Thoracic 9 Spinal Transection-Induced Model of Muscle Spasticity in the Rat: A Systematic Electrophysiological and Histopathological Characterization. PLoS One., 10(12):e0144642, 2015, IF=3.234
12. Lourenço CF., Ferreira NR., Santos RM., Lukacova N., Barbosa RM., Laranjinha J.: The pattern of glutamate-induced nitric oxide dynamics in vivo and its correlation with nNOS expression in rat hippocampus, cerebral cortex and striatum. Brain Res., 1554:1-11, 2014, IF=2.828
13. Chalimoniuk M., Chrapusta SJ., Lukačova N., Langfort J. Endurance training upregulates the nitric oxide/soluble guanylyl cyclase/cyclic guanosine 3',5'-monophosphate pathway in the striatum, midbrain and cerebellum of male rats. Brain Res., 1618:29-40, 2015, IF=2.843
14. Pavel J., Oroszova Z., Hricova L., Lukacova N.: Effect of subpressor dose of angiotensin II on pain-related behavior in relation with neuronal injury and activation of satellite glial cells in the rat dorsal root ganglia. Cell Mol Neurobiol, 33(5):681-688, 2013, IF=2.293

15. Bonova P., Burda J., Danielisova V., Nemethova M., Gottlieb M.: Delayed post-conditioning reduces post-ischemic glutamate level and improves protein synthesis in brain. Neurochem Int., 62:854-860, 2013, IF=2.659
16. Bonova P., Burda J., Danielisova V., Nemethova M., Gottlieb M.: Development of a pattern in biochemical parameters in the core and penumbra during infarct evolution after transient MCAO in rats. Neurochem Int., 62:8-14, 2013, IF=2.659.
17. Bonova P., Danielisova V., Nemethova M., Matiasova M., Bona M., Gottlieb M.: Scheme of Ischaemia-triggered Agents during Brain Infarct Evolution in a Rat Model of Permanent Focal Ischaemia. Journal of molecular neuroscience : J Mol Neurosci, 57(1):73-82, 2015, IF: 2.343
18. Bonova P., Gottlieb M.: Blood as the carrier of ischemic tolerance in rat brain. J Neurosci Res. 93(8):1250-1257, 2015, IF=2.594
19. Danielisova V., Burda J., Nemethova M., Gottlieb M., Burda R.: An Effective Combination of Two Different Methods of Postconditioning. Neurochemical Research 37:2085-2091, 2012, IF=2.240.
20. Danielisova V., Gottlieb M., Bonova P., Nemethova M., Burda J.: Bradykinin postconditioning ameliorates focal cerebral ischemia in the rat. Neurochem Int., 72:22-29, 2014, IF=2.650
21. Lalkovicova M., Bonova P., Burda J., Danielisova V.: Effect of Bradykinin Postconditioning on Ischemic and Toxic Brain Damage. Neurochem Res., 40:1728-1738, 2015, IF=2.593

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 (ratios in percentage)

The Institute of Neurobiology of the Slovak Academy of Sciences is an academic institution and its mission is to conduct basic research into the CNS under physiological and pathological conditions. However, we have put increasing efforts into translational research. For the assessment period the ratio would be:

90% basic research / 10% applied research. The results of our research are **100% international**, as we do not study problems specific only to this region.

2.1.2 List of selected publications documenting the most important results of basic research. The total number of publications listed for the assessment period should not exceed the average number of employees with university degrees engaged in research projects. The principal research outputs (max. 5, including Digital Object Identifier - DOI) should be underlined

GRUĽOVÁ, Ivana - SLOVINSKÁ, Lucia - BLAŠKO, Juraj - DEVAUX, S. - WISZTORSKI, M - SALZET, M - FOURNIER, I - KYUKOV, O - COHEN, S - ČÍŽKOVÁ, Dáša. Delivery of alginate scaffold releasing two trophic factors for spinal cord injury repair. In *Scientific Reports*, 2015, vol., 5, p.1-19. (5.578 - IF2014). (2015 - Current Contents, Scopus, WOS). ISSN 2045-2322, **doi: 10.1038/srep13702**.

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SAGANOVÁ, Kamila - GÁLIK, Ján - BLAŠKO, Juraj - KORIMOVÁ, Andrea - RAČEKOVÁ, Eniko - VANICKÝ, Ivo. Immunosuppressant FK506: Focusing on neuroprotective effects following brain and spinal cord injury. In *Life Sciences*, 2012, vol. 91, iss., p. 77-82. (2.527 - IF2011). (2012 - Current Contents). ISSN 0024-3205**, doi:10.1016/j.lfs.2012.06.022**.

DANIELISOVÁ, Viera - BURDA, Jozef - NÉMETHOVÁ, Miroslava - GOTTLIEB, Miroslav - BURDA, R. An effective combination of two different methods of postconditioning. In *Neurochemical Research*, 2012, vol. 37, p. 2085-2091. (2.240 - IF2011). (2012 - Current Contents). ISSN 0364-3190.

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BLAŠKO, Juraj - FABIANOVÁ, Kamila - MARTONČÍKOVÁ, Marcela - SOPKOVÁ, D. - RAČEKOVÁ, Eniko. Immunohistochemical Evidence for the Presence of Synaptic Connections of Nitrergic Neurons in the Rat Rostral Migratory Stream. In *Cellular and Molecular Neurobiology*, 2013, vol. 33, p. 753-757. (2.293 - IF2012). (2013 - Current Contents). ISSN 0272-4340.

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GRUĽOVÁ, Ivana - SLOVINSKÁ, Lucia - NAGYOVÁ, Miriam - ČÍŽEK, Milan - ČÍŽKOVÁ, Dáša. The effect of hypothermia on sensory-motor function and tissue sparing after spinal cord injury. In *The Spine Journal*, 2013, vol. 13, p. 1881-1891. (3.355 - IF2012). (2013 - Current Contents). ISSN 1529-9430.

PAVEL, Jaroslav - OROSZOVÁ, Zuzana - HRICOVÁ, Ľudmila - LUKÁČOVÁ, Nadežda. Effect of Subpressor Dose of Angiotensin II on Pain-Related Behavior in Relation with Neuronal Injury and Activation of Satellite Glial Cells in the Rat Dorsal Ganglia. In *Cellular and Molecular Neurobiology*, 2013, vol. 33, no. 5, p. 681-688. (2.293 - IF2012). (2013 - Current Contents). ISSN 0272-4340.

DANIELISOVÁ, Viera - GOTTLIEB, Miroslav - BONOVÁ, Petra - NÉMETHOVÁ, Miroslava - BURDA, Jozef. Bradykinin postconditioning ameliorates focal cerebral ischemia in the rat. In *Neurochemistry International*, 2014, vol. 72, p. 22-29. (2.650 - IF2013). (2014 - Current Contents). ISSN 0197-0186.

FABIANOVÁ, Kamila - MARTONČÍKOVÁ, Marcela - FABIAN, Dušan - BLAŠKO, Juraj - RAČEKOVÁ, Eniko. Diverse effect of different odor stimuli on behavior and Fos protein production in the olfactory system neurogenic region of adult rats. In *Behavioural Brain Research*, 2014, vol. 265, p. 38-48. (3.391 - IF2013). (2014 - Current Contents). ISSN 0166-4328.

KISUCKÁ, Alexandra - HRICOVÁ, Ľudmila - PAVEL, Jaroslav - STROSZNAJDER, J.B. - CHALIMONIUK, M. - LANGFORT, J - GALIK, J. - MARSALA, Martin - RADOŇAK, J - LUKÁČOVÁ, Nadežda. Baclofen or nNOS inhibitor affect molecular and behavioral alterations evoked by traumatic spinal cord injury in rat spinal cord. In *The Spine Journal*, 2014, http://dx.doi.org/10.1016/j.spinee. 2014.08.013. (2.800 - IF2013). (2014 - Current Contents). ISSN 1529-9430.

BONOVÁ, Petra - DANIELISOVÁ, Viera - NÉMETHOVÁ, Miroslava - MATIAŠOVÁ, Milina - BONA, Martin - GOTTLIEB, Miroslav. Scheme of Ischaemia-triggered Agents during Brain Infarct Evolution in a Rat Model of Permanent Focal Ischaemia. In *Journal of Molecular Neuroscience*, 2015, vol.57, no.1, p.73-82. (2.343 - IF2014). (2015 - Current Contents). ISSN 0895-8696.

BONOVÁ, Petra - GOTTLIEB, Miroslav. Blood as the carrier of ischemic tolerance in rat brain. In *Journal of Neuroscience Research*, 2015, vol.93. no.8., p.1250-1257. (2.594 - IF2014). (2015 - Current Contents). ISSN 0360-4012.

ČÍŽKOVÁ, Dáša - SLOVINSKÁ, Lucia - GRUĽOVÁ, Ivana - SALZET, M. - ČIKOŠ, Štefan - KRYUKOV, O. - COHEN, S. The influence of sustained dual-factor presentation on the expansion and differentiation of neural progenitors in affinity-binding alginate scaffolds. In *Journal of Tissue Engineering and Regenerative Medicine*, 2015, vol. 9, p. 918-929. (5.199 - IF2014). ISSN 1932-6254.

LALKOVIČOVÁ, Mária - BONOVÁ, Petra - BURDA, Jozef - DANIELISOVÁ, Viera. Effect of Bradykinin Postconditioning on Ischemic and Toxic Brain Damage. In *Neurochemical Research*, 2015, vol. 40, no.8, p.1728-1738. (2.593 - IF2014). (2015 - Current Contents). ISSN 0364-3190. ITMS 26220220043, VEGA 2/0045/15.

ČÍŽKOVÁ, Dáša - DEVAUX, S. - LE MARREC-CROQ, F. - FRANCK, J. - SLOVINSKÁ, Lucia - BLAŠKO, Juraj - ROSOCHA, Ján - ŠPAKOVÁ, Tímea - LEFEBVRE, Ch. - FOURNIER, I. - SALZET, M. Modulation properties of factors released by bone marrow stromal cells on activated microglia: an in vitro study. In *Scientific Reports*, 2014, vol. 4, p. 7514, DOI: 10.1038/srep07514. (5.078 - IF2013). ISSN 2045-2322.

CARLETO, JA - BRAVO-HERNÁNDEZ, M - KAMIZATO, K - KAKINOHANA, O - SANTUCCI, C - NAVARRO, MR - PLATOSHYN, O - ČÍŽKOVÁ, Dáša - LUKÁČOVÁ, Nadežda - TAYLOR, J - MARŠALA, Martin. Thoracic 9 Spinal Transection-Induced Model of Muscle Spasticity in the Rat: A Systematic Electrophysiological and Histopathological Characterization. In *PLoS ONE*, 2015, vol. 10., no. 12, p.e0144642. (3.234 - IF2014). ISSN 1932-6203.

2.1.3 List of monographs/books published abroad

Chapters in scientific monographs published abroad

Hricová Ľ., Pavel J., Lukáčová N., NO-c-GMP signalling in bulbospinal respiratory pathway after cervical spinal cord injury. In *Spinal cord injures: Causes, risk factors and management*. - Nova Publishers, 2012, p. 219-235. ISBN 978-1-62081-950-0.

Račeková E., Zápotocký M., Vodička J., Poruchy čichu a chute, Kapitola 1: Anatomie, embryologie a fyziologie čichového systému, (Disorders of smell and taste, Chapter I: Anatomy, embryology and physiology of the olfactory system) - Kobzinové 3119, Havlíčkuv Brod, 580 01: TOBIÁŠ, 2012, s. 16-39. ISBN 978-80-7311-125-0.

Čížková D., Žilka N., Kážmérová Z., Slovinská L., Vanický ., Gruľová I., Cigánková V., Čížek M., Novák M., Mesenchymal stromal cells and neural stem cells potential for neural repair in spinal cord injury and human neurodegenerative disorders. In Neural stem cells and therapy, February, 2012. - Janeza Trdine 9, Rijeka, Croatia: InTech, p. 359-382, 17. Chapter, ISBN 978-953-307-958-5.

Jergová S., Neuropathic Pain Following Nerve Injury: Chapter 11, p. 179-202, In Basic Principles of Peripheral Nerve Disorders., table of contents (15 chapters). - InTech, 2012, 278 p. ISBN 978-953-51-0407-0.

Lukáčová N., Pavel J., Gálik J., Spinal cord injury - the rabbit model: 7th chapter, p. 149-158. In *Animals Models of Spinal Cord Repair*. Table of contents (14 chapters).Series title: Neuromethods, V. 76. - Uppsala: Humana Press, Springer Science + Business Media, LLC, 2013, p. 336. ISBN 978-1-62703-197-4.

2.1.4. List of monographs/books published in Slovakia

Chapters in scientific monographs published in Slovakia

Rosocha J., Spakova T., Rudinský B., Šoltýs J., Čížková D., Vaško G., Klímová E., Mezenchymálne kmeňové bunky - charakteristika a klinická perspektíva ("Mesenchymal stem cells - characteristics and clinical prospects"). In *Spinálna chirurgia II*. (*Spinal surgery II.*) - Bratislava: SAP, 2012, chap. 17, pp. 174-187. ISBN 978-80-89607-02-0.

2.1.5. List of other scientific outputs specifically important for the institute, max. 10 items

- Letter to the Ministry of Health (30.4.2015) with the recommendation, which resulted from our minipigs experiments, that in the case of unstable backbone fractures leading to traumatic spinal injury with indication of stabilizing surgery the surgeon should apply cooling of the medulla spinalis with ice cold saline.

- Prof. Martin Marsala participates in clinical trials led by Joseph Ciacci, MD, investigator and neurosurgeon at UC San Diego Health System, to investigate the safety of neural stem cell transplantation in patients with chronic spinal cord injuries (2014). The Phase I clinical trial includes eight patients in a five-year study. This clinical trial at UC San Diego Health System is funded by Neuralstem, Inc. and was launched and supported by the UC San Diego Sanford Stem Cell Clinical Center.

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

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

The years of research into ischemic nervous tissue conditioning culminated in a patent application. Patent application number 50020-2015, entitled “Method of activation of protein nature substances which are able to prevent or to limit the consequences of acute ischemic and reperfusion damage of the organism and its parts”, was submitted in April 2015, and recently it has come under national review procedure.

2.1.8. Table of research outputs (as in annual reports).

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	2012			2013			2014			2015			total			
	number	No. / FTE	No. / salary budget	number	No. / FTE	No. / salary budget	number	No. / FTE	No. / salary budget	number	No. / FTE	No. / salary budget	number	averaged number per year	av. No. / FTE	av. No. / salary budget
Scientific monographs and monographic studies in journals and proceedings published abroad *(AAA, ABA)*	0,0	0,000	0,000	0,0	0,000	0,000	0,0	0,000	0,000	0,0	0,000	0,000	**0,0**	**0,0**	**0,000**	**0,000**
Scientific monographs and monographic studies in journals and proceedings published in Slovakia *(AAB, ABB)*	0,0	0,000	0,000	0,0	0,000	0,000	0,0	0,000	0,000	0,0	0,000	0,000	**0,0**	**0,0**	**0,000**	**0,000**
Chapters in scientific monographs published abroad *(ABC)*	4,0	0,137	0,016	1,0	0,032	0,004	0,0	0,000	0,000	0,0	0,000	0,000	**5,0**	**1,3**	**0,041**	**0,005**
Chapters in scientific monographs published in Slovakia *(ABD)*	1,0	0,034	0,004	0,0	0,000	0,000	0,0	0,000	0,000	0,0	0,000	0,000	**1,0**	**0,3**	**0,008**	**0,001**
Scientific papers published in journals registered in Current Contents Connect *(ADCA, ADCB, ADDA, ADDB)*	15,0	0,515	0,058	10,0	0,317	0,039	15,0	0,480	0,059	12,0	0,384	0,045	**52,0**	**13,0**	**0,422**	**0,050**
Scientific papers published in journals registered in Web of Science Core Collection and SCOPUS *(ADMA, ADMB, ADNA, ADNB)*	3,0	0,103	0,012	1,0	0,032	0,004	3,0	0,096	0,012	5,0	0,160	0,019	**12,0**	**3,0**	**0,097**	**0,012**
Scientific papers published in other foreign journals (not listed above) *(ADEA, ADEB)*	0,0	0,000	0,000	15,0	0,476	0,058	0,0	0,000	0,000	17,0	0,544	0,063	**32,0**	**8,0**	**0,260**	**0,031**
Scientific papers published in other domestic journals (not listed above) *(ADFA, ADFB)*	1,0	0,034	0,004	0,0	0,000	0,000	1,0	0,032	0,004	0,0	0,000	0,000	**2,0**	**0,5**	**0,016**	**0,002**
Scientific papers published in foreign peer-reviewed proceedings *(AEC, AECA)*	1,0	0,034	0,004	0,0	0,000	0,000	0,0	0,000	0,000	0,0	0,000	0,000	**1,0**	**0,3**	**0,008**	**0,001**
Scientific papers published in domestic peer-reviewed proceedings *(AED, AEDA)*	8,0	0,275	0,031	11,0	0,349	0,043	16,0	0,512	0,063	9,0	0,288	0,034	**44,0**	**11,0**	**0,357**	**0,042**
Published papers (full text) from foreign and international scientific conferences *(AFA, AFC, AFBA, AFDA)*	0,0	0,000	0,000	0,0	0,000	0,000	0,0	0,000	0,000	0,0	0,000	0,000	**0,0**	**0,0**	**0,000**	**0,000**
Published papers (full text) from domestic scientific conferences *(AFB, AFD, AFBB, AFDB)*	10,0	0,344	0,039	0,0	0,000	0,000	0,0	0,000	0,000	0,0	0,000	0,000	**10,0**	**2,5**	**0,081**	**0,010**

- **Supplementary information and/or comments on the scientific outputs of the institute.**

INb SAS publication activity focuses on higher quality journals, even at the expense of a longer-review process. This trend is recognized in publications with our intenrational partners, but more importantly, also papers which were produced in our conditions. Although this effort is reflected in a smaller number of publications, their citation response is very good, which we consider more important.

Our selection of papers does not necessarily contain papers with the best IF. Some of the highest-quality papers have been published in collaboration with foreign laboratories, however we prioritize papers prepared in our conditions.

2.2. Responses to the research outputs (citations, etc.)

2.2.1. Table with citations per annum.

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) have to be listed separately.

Citations, reviews	2011		2012		2013		2014		total		
	number	No. / FTE	number	No. / FTE	number	No. / FTE	number	No. / FTE	number	averaged number per year	av. No. / FTE
Citations in Web of Science Core Collection (1.1, 2.1)	278,0	9,553	300,0	9,512	381,0	12,180	396,0	12,664	**1355,0**	**338,8**	**10,999**
Citations in SCOPUS (1.2, 2.2) if not listed above	59,0	2,027	81,0	2,568	120,0	3,836	96,0	3,070	**356,0**	**89,0**	**2,890**
Citations in other citation indexes and databases (not listed above) (3.2,4.2,9,10)	0,0	0,000	4,0	0,127	0,0	0,000	0,0	0,000	**4,0**	**1,0**	**0,032**
Other citations (not listed above) (3, 4, 3.1, 4.1)	1,0	0,034	2,0	0,063	0,0	0,000	0,0	0,000	**3,0**	**0,8**	**0,024**
Reviews (5,6)	0,0	0,000	0,0	0,000	0,0	0,000	0,0	0,000	**0,0**	**0,0**	**0,000**

2.2.2. List of 10 most-cited publications, with number of citations, in the assessment period (2011 – 2014).

ISRAEL, M.A. - YUAN, S.H. - BARDY, C. - REYNA, S.M. - MU, Y. - HERRERA, C. - HEFFERAN, Michael P. - VAN GORP, S. - NAZOR, K.L. - BOSCOLO, F.S. - CARSON, C.T. - LAURENT, L.C. - MARŠALA, Martin - GAGE, F.H. - REMES, A.M. - KOO, E.H. - GOLDSTEIN, L.S.B. Probing sporadic and familial Alzheimer´s disease using induced pluripotent stem cells. In *Nature*, 2012, vol. 482, no. 7384, p. 216-226. (36.280 - IF2011). ISSN 0028-0836, (213 cit.)

BOULENGUEZ, Pascale - LIABEUF, Sylvie - BOS, Rémi - JEAN-XAVIER, Céline - BROCARD, Cécile - STIL, Aurélie - DARBON, Pascal - CATTAERT, Daniel - DELPIRE, Eric - MARŠALA, Martin - VINAY, Laurent. Down-regulation of the potassium-chloride contransporter KCC2 contributes to spasticity after spinal cord injury. In *Nature medicine*, 2010, vol. 16, no. 3, p. 302-307. (27.136 - IF2009). ISSN 1078-8956, (112 cit.)

ARBELOA, Joana - PÉREZ-SAMARTÍN, Alberto - GOTTLIEB, Miroslav - MATUTE, Carlos. P2X7 receptor blockade prevents ATP excitotoxicity in neurons and reduces brain damage after ischemia. In *Neurobiology of Disease*, 2012, vol. 45, p. 954-961. (5.403 - IF2011). ISSN 0969-9961, (88 cit.)

ČÍŽKOVÁ, Dáša - ROSOCHA, J - VANICKÝ, Ivo - JERGOVÁ, Stanislava - ČÍŽEK, M. Transplants of human mesenchymal stem cells improve functional recovery after spinal cord injury in the rat. In *Cellular and Molecular Neurobiology*, 2006, vol. 26, no. 7-8, p.1167-1180. (2.022 - IF2005). ISSN 0272-4340, (54 cit.)

LUO, ZD - ČÍŽKOVÁ, Dáša. The role of nitric oxide in nociception. In *Current review of pain*, 2000, vol. 4, no. 6, p. 459-466. ISSN 1069-5850, (45 cit).

GOTTLIEB, Miroslav - LEAL-CAMPANARIO, R. - CAMPOS-ESPARZA, MR - SANCHEZ-GOMEZ, MV - ALBERDI, E - ARRANZ, A - DELGADO-GARCIA, JM - GRUART, A - MATUTE, C. Neuroprotection by two polyphenols following excitotoxicity and experimental ischemia. In *Neurobiology of Disease*, 2006, vol. 23, no. 2, p. 374-386. (4.128 - IF2005). ISSN 0969-9961, (42 cit).

ČÍŽKOVÁ, Dáša - MARŠALA, Jozef - LUKÁČOVÁ, Nadežda - MARŠALA, Martin - JERGOVÁ, Stanislava - ORENDÁČOVÁ, Judita - YAKSH, T. Localization of N-type Ca+ channels in the rat spinal cord following chronic constrictive nerve injury. In *Experimental Brain Research*, 2002, vol. 147, no. 4, p. 456-463. (2.306 - IF2001). ISSN 0014-4819. (34 cit.)

VANICKÝ, Ivo - URDZÍKOVÁ, Lucia - SAGANOVÁ, Kamila - ČÍŽKOVÁ, Dáša - GÁLIK, Ján. A simple and reproducible model of spinal cord injury induced by epidural baloon inflation in the rat. In *Journal of Neurotrauma*, 2001, vol. 18, no. 12, p. 1399-1407. (2.877 - IF2000). ISSN 0897-7151, (34 cit).

BURDA, Jozef - DANIELISOVÁ, Viera - NÉMETHOVÁ, Miroslava - GOTTLIEB, Miroslav - MATIAŠOVÁ, Milina - DOMORÁKOVÁ, I - MECHÍROVÁ, E - FERIKOVÁ, M - SALINAS, M - BURDA, R. Delayed postconditionig initiates additive mecanism necessary for survival of selectively vulnerable neurons after transient ischemia in rat brain. In *Cellular and Molecular Neurobiology*, 2006, vol.26, no.7-8, p. 1141-1151. (2.022 - IF2005). ISSN 0272-4340, (26 cit.)

ČÍŽKOVÁ, Dáša - GRUĽOVÁ, Ivana - SLOVINSKÁ, Lucia - VANICKÝ, Ivo - JERGOVÁ, Stanislava - ROSOCHA, J. - RADOŇAK, J. Repetitive intrathecal cetheter delivery of bone Marrow mesenchymal stromal cells improves functional recovery in a rat model of contusive spinal cord injury. In *Journal of Neurotrauma*, 2011, vol. 28, p. 1951-1961. (3.426 - IF2010). ISSN 0897-7151, (21cit).

2.2.3. List of most-cited authors from the Institute (at most 10 % of the research employees with university degree engaged in research projects) and their number of citations in the assessment period (2011– 2014).

Prof. MUDr. Martin, Maršala – 719 citations
RNDr. Miroslav Gottlieb, CSc – 399 citations
MVDr. Dáša Čížková, DrSc – 387 citations
MVDr. Ivo Vanický, CSc – 293 citations

- **Supplementary information and/or comments on responses to the scientific output of the institute.**

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

- **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.

The Institute of Neurobiology SAS strengthened its position in the international portfolio of neuroscience institutions during the evaluation period from 2012 to 2015. The main effort was devoted to preserving existing cooperation, and to building new networks with excellent scientists and institutions. The staff of the Institute has been involved in several international programs and scientific projects, as well as activities based on cooperation with excellent European universities and PhD programs.

- Dr. Cizkova participated in the COST project BM-1002 (NANONET, 2010 - 2014), the International Consortium of 11 excellent institutions under the coordination of the Netherlands Institute of Neuroscience, Royal Netherlands Academy of Arts and Sciences, Amsterdam. This COST action integrated the exciting new knowledge on intermediate filaments with novel developments in cell biology, molecular biology, medicine, (bio) chemistry, engineering, mathematics and physics. The framework of the project was directed to the 8RP proposal. The NANONET project promoted collaborative research which enabled us to study the suppression of astrocytic response following application of the bacterial enzyme ChABC (Chondroitinase ABC). The results of these experiments showed significant reduction of glial scar formation (enzymatic degradation chondroitinsulfate proteoglycan, NG2) in the primary lesion site after spinal cord injury, allowing better outgrowth and regeneration of GAP-43 positive nerve fibers. CHABC treatment in combination with cell-based transplantation represents a promising therapeutic strategy for SCI.
- International cooperation between Dr. Cizkova from the Institute of Neurobiology SAS and Prof. Michael Salzet from the University of Lille, France in 2012 started the international project APVV SK-FR 0019-11 (2012-2013) entitled “Neuroproteomics of injured spinal cord using MALDI mass spectrometry imaging after leech substances injection: towards a novel therapeutic”, which was coordinated by our Institute. The main idea of the project was to initiate the innovative molecular imaging technology MALDI (Matrix-assisted laser desorption/ionization) and MSI (mass spectrometry imaging) for determination of bioactive substances *in vivo* and *in vitro* to study neuroregeneration as well as neurodegeneration and apoptosis. The particular interest was to determine the bioactive compounds produced by: i) resting microglia ii) activated microglia or iii) factors released after spinal cord injury in rats. In collaboration with the French group, we introduced proteomic analysis of MSC products which significantly inhibit activated microglia. We managed to analyze the proteome in spinal tissue after acute spinal cord injury in rats, where we recorded the presence of specific proteins in the segments above the lesion, at the site of the lesion and below the lesion. We identified over 300 proteins and peptides which are involved in regeneration, but also in degeneration and apoptotic processes.

1. Fournier, I., Franck, J., Croq, F., Cizkova D., Lefebvre C.,Vizioli J., Sautiere PE, Salzet M.: MALDI imaging mass spectrometry: a novel technology for studying neurosciences., GLIA 61, (1), pp.S195-S195
2. Cizkova D, Le Marrec-Croq F, Franck J, Slovinska L, Grulova I, Devaux S, Lefebvre C, Fournier I, Salzet M. Alterations of protein composition along the rostro-caudal axis after spinal cord injury: proteomic, in vitro and in vivo analyses. Front Cell Neurosci. 2014, 8:105. doi: 10.3389/fncel.2014.00105. e Collection 2014
3. Cizkova D., Devaux S., Le Marrec-Croq F., Franck J., Slovinska L., Blasko J., Rosocha J., Spakova T., Lefebvre Ch., Fournier I., Salzet M., Modulation properties of bone marrow stromal cells released factors on activated microglia: in vitro study, Scientific Reports ,4: 7514, 2014

- Traditional collaborations with foreign universities continued in this assessment period as well. In 2014 INb SAS prolonged its formal international cooperation agreement with Universidad del País Vasco, Facultad de Medicina y Odontologia, Leioa, Spain, initiated in 2010. The cooperation is focused on interinstitutional collaboration in studying the molecular basis of excitotoxic brain neurodegeneration and regeneration processes. Based on this cooperation, Inb SAS researcher Dr. Gottlieb became a member of the European Committee for PhD study at the Dep. de Neurosciencia, Universidad del País Vasco, Spain in 2012, 2013, 2015. In 2015 he was awarded a Marie Curie Fellowship as part of the EU-funded project “Supporting international mobility and training in Bizkaia (B-MOB)” coordinated by our Spanish partner and focusing on the study of the neuroprotective potential of P2X7 and CALHM1 channels in ischemia.
- INb SAS became the “place of study” for three foreign PhD students from Cyprus and France in the PhD program 4.2.16 Neuroscience coordinated by the University of Veterinary Medicine and Institute of Neurobiology.
- Dr. Cizkova (INb SAS) together with Prof. Michel Salzet, director of the Proteomic Laboratory at the University of Lille 1, France and the University of Veterinary Medicine and Pharmacy in Kosice launched the Co-Tutorial PhD Program in 4.2.16 Neuroscience. Two students were accepted for co-tutorial study, Stephanie Devaux and Adriana Murgoci, who both finished their master’s degree in France.
- Important recognition of the Institute's scientific work in the field of regenerative medicine in the European context can be seen in the involvement of one of our researchers in the European projects REMEDIC European Science Foundation (membership in Steering Committee - Dr. Vanický) and Trans-European Stem Cell Therapy Consortium (Dr. Čížková). Our experts participated in evaluation of the international projects SAS-CONICET (2015) and OTKA (2012).
- The Institute of Neurobiology SAS (Dr. Lukáčová) was coordinator of bilateral cooperation with Mossakowski Medical Research Centre, Warsaw, Poland, focusing on interaction of NO synthase and calcium binding proteins in the brain stem after spinal cord injury.
- Researchers of INb SAS worked during the assessment period on the editorial boards of two international journals: General Physiology and Biophysics (Dr. Lukáčová) and Cellular and Molecular Neurobiology (Dr. Pavel).

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

“7th International Symposium on Experimental and Clinical Neurobiology”, Košice, 23 – 27 June 2013. The symposium was organised by our Institute and it focused on novel findings in the field of neurodegenerative diseases, trauma and ischemia-reperfusion injury of the CNS, molecular mechanisms underlying neurotoxicity and neuroprotection and neuroregenerative medicine. The symposium was attended by 120 participants originating from 11 countries in Europe and from the USA, including several prestigious scientists as well as neurosurgeons and neurotherapists. This symposium was also sponsored by FENS and IBRO, whose contributions were used to support young scientists.

The Institute of Neurobiology also participated in the international symposium “Behind the curtain of canine and feline dementia: from neuroscience research to treatment” held in Košice, Slovakia on 6 October 2015. This symposium focused on cognitive deficit in dogs and cats and behavioral problems connected with the aging of pets, including therapeutic interventions. The symposium was attended by 100 participants, and featured plenary lectures presented by world-recognized experts in canine behavior coming from Canada and Europe.

2.3.3. List of edited proceedings from international scientific conferences.

Programme and Abstract book of the 7th International Symposium on Experimental and Clinical Neurobiology, Košice, June 23-27, 2013, EURODOSPRINT, s.r.o., Slovakia, ISBN 978-80-263-0388-6

2.3.4. List of journals edited/published by the institute:

2.3.4.1. WOS (IF of journals in each year of the assessment period)

2.3.4.2. SCOPUS

2.3.4.3. other databases

2.3.4.4. not included in databases

- **National position of the institute**

2.3.5. List of selected projects of national importance

Project title: Centre of Excellence for neuroregeneration research
Project number: ITMS: 26220120063
Duration: 1.11.2010 / 1.8.2013
Responsible person: C/MVDr. Ivo Vanický, CSc.
Project Coordinator: Institute of Neurobiology, Slovak Academy of Sciences
The Project Partners: Associated Tissue Bank of the P. J. Šafarik University, Faculty of Medicine, University Hospital of. Louis Pasteur in Kosice; The Institute of Animal Physiology, Slovak Academy of Sciences
Total funding: 3 815 637 Eur
Funding for the Organization: ŠF EU: 1 439 987 Eur

Project title: Formation and development of a diagnostic procedure in the treatment of trauma - injured spinal cord
Project number: NFP 26220220127
Duration: 1.11.2010 / 30.4.2015
Responsible person: C/RNDr. Nadežda Lukáčová, DrSc.
Project Coordinator: Institute of Neurobiology, Slovak Academy of Sciences
The Project Partner: The University of Veterinary Medicine and Pharmacy in Košice
Total funding: 939 783 Eur
Funding for the Organization: 453 174 Eur

Project title: New possibilities to rescue neurons in the delayed neuronal death by non specific stressors
Project number: ITMS: 26220220043
Duration: 1.1.2010 / 30.6.2012
Responsible person: C/MVDr. Jozef Burda, DrSc.
Total funding: 491 090 Eur
Funding for the Organization in assessed period: 166 130 Eur

Project title: University Medical Science and Technology Park in Košice, Slovakia
Project number: 26220220185
Duration: 10.7.2013 / 30.6.2016
Responsible person: I/ RNDr. Nadežda Lukáčová, DrSc.

Project Coordinator: P. J. Šafarik University
The Project Partners: University of Veterinary Medicine and Pharmacy; Institute of Neurobiology, Slovak Academy of Sciences; Technical University in Kosice
Funding for the Organization: 356 925 Eur

Project title: Modified biomaterials and cell therapy for promoting regeneration of injured spinal cord.
Project number: APVV 0472-11
Duration: 1.7.2012 / 30.12.2015
Responsible person: C/MVDr. Dáša Čížková, DrSc.

Project title: Axonal regeneration in biosynthetic nerve guide conduits.
Project number: APVV-14-0847
Duration: 1.7.2015 / 30.6.2019
Responsible person: C/MVDr. Ivo Vanický, CSc.

Project title: Interactive methods of image acquisition and processing in microscopy using natural user interface.
Project number: APVV-0526-11
Duration: 1.7.2012 / 31.12.2015
Responsible person: I/ RNDr. Ján Gálik, CSc

Project title: Neuroproteomics of injured spinal cord using MALDI mass spectrometry imaging after leech substances injection: Towards a novel therapeutic.
Project number: SK-FR-0019-11
Duration: 1.1.2012 / 31.12.2013
Responsible person: C/ MVDr. Dáša Čížková, DrSc

2.3.6. Projects of the Slovak Research and Development Agency (APVV)

Project title: Modified biomaterials and cell therapy for promoting regeneration of injured spinal cord.
Project number: APVV 0472-11
Duration: 1.7.2012 / 30.12.2015
Responsible person: C/MVDr. Dáša Čížková, DrSc.

Project title: Axonal regeneration in biosynthetic nerve guide conduits.
Project number: APVV-14-0847
Duration: 1.7.2015 / 30.6.2019
Responsible person: C/MVDr. Ivo Vanický, CSc.

Project title: Science in Slovakia - if we do not know something, we do not feel need for it.
Project number: LPP-0178-09
Duration: 3.9.2009 / 31.8.2012
Responsible person: C/RNDr. Ján Gálik, CSc.

Project title: Mother and embryo: the influence of maternal obesity and stress on preimplantation embryo development.
Project number: APVV-0815-11
Duration: 1.7.2012 / 31.12.2015
Responsible person: I/RNDr. Enikö Račeková, CSc.

Project title: Neuroproteomics of injured spinal cord using MALDI mass spectrometry imaging after leech substances injection: Towards a novel therapeutic.
Project number: SK-FR-0019-11
Duration: 1.1.2012 / 31.12.2013
Responsible person: C/ MVDr. Dáša Čížková, DrSc

Project title: Interactive methods of image acquisition and processing in microscopy using natural user interface.
Project number: APVV-0526-11
Duration: 1.7.2012 / 31.12.2015
Responsible person: I/ RNDr. Ján Gálik, CSc

2.3.7. Projects of the Scientific Grant Agency of the Slovak Academy of Sciences and the Ministry of Education (VEGA)

Project title: Modulation somato-sensory neural pathways by Angiotensin II. Effect of Angiotensin II receptor blockade on nociceptive signaling
Project number: 2/0203/10
Duration: 1.1.2010 / 31.12.2012
Responsible person: RNDr. Jaroslav Pavel, PhD.
Funding for the Organization: 31 324 Eur

Project title: NO/ANP-mediated cGMP synthesis in neuron-glial interaction after spinal cord injury and Baclofen treatment
Project number: 2/0168/11
Duration: 1.1.2011 / 31.12.2013
Responsible person: RNDr. Nadežda Lukáčová, DrSc.
Funding for the Organization: 29 479 Eur

Project title: Study of mechanisms and regulation of ischemic tolerance
Project number: 2/0066/12
Duration: 1.1.2012 / 31.12.2014
Responsible person: MVDr. Viera Danielisová, CSc.
Funding for the Organization: 29 911 Eur

Project title: Functional consequences of altered neurogenesis in the rat olfactory system
Project number: 2/0114/12
Duration: 1.1.2012 / 31.12.2014
Responsible person: RNDr. Enikö Račeková, CSc.
Funding for the Organization: 23 802 Eur

Project title: A suppression of secondary injury of trauma-injured spinal cord using local hypothermia combined with local perfusion of neuroprotective substances
Project number: 2/0191/13
Duration: 1.1.2013 / 31.12.2015
Responsible person: RNDr. Jaroslav Pavel, PhD.
Funding for the Organization: 30 068 Eur

Project title: Cell based therapy for repair of damaged CNS tissue: in vitro model
Project number: 2/0169/13
Duration: 1.1.2013 / 31.12.2015
Responsible person: RNDr. Lucia Slovinská, PhD.
Funding for the Organization: 19 156 Eur

Project title: Transplantation of tissue constructs for the regeneration of damaged nerve fibers
Project number: 2/0183/13
Duration: 1.1.2013 / 31.12.2015
Responsible person: MVDr. Ivo Vanický, CSc.
Funding for the Organization: 19 854 Eur

Project title: Endogenous stimulation and exogenous application of neurotrophic factors to reduce secondary damage in model of spinal cord compression
Project number: 2/0173/14
Duration: 1.1.2014 / 31.12.2016
Responsible person: RNDr. Nadežda Lukáčová, DrSc.
Funding for the Organization: 30 908 eur

Project title: Blood as a medium providing the tolerance in a brain after global and focal ischemic attack
Project number: 2/0012/15
Duration: 1.1.2015 / 31.12.2017
Responsible person: RNDr. Petra Bonová, PhD.
Funding for the Organization: 18 653 Eur

Project title: Analysis of post-traumatic inflammatory and regenerative processes along the rostro-caudal axis of the spinal cord after administration of mesenchymal stem cells: an immunohistochemical and proteomic study
Project number: 2/0125/15
Duration: 1.1.2015 / 31.12.2017
Responsible person: MVDr. Dáša Čížková, DrSc.
Funding for the Organization: 20 522 Eur

2.3.8. Projects of SAS Centres of Excellence

Project title: Center of Excellence for Brain Research
Duration: 4.8.2011 / 3.8.2015
Responsible person: I/MVDr. Dáša Čížková, DrSc.
Funding for the Organization: 11 600 Eur

Project title: Centre of Excellence for Research on the regulatory role of nitric oxide in diseases of civilization
Duration: 4.8.2011 / 3.8.2015
Responsible person: I/RNDr. Nadežda Lukáčová, DrSc.
Funding for the Organization: 8 000 Eur

2.3.9. National projects supported by EU Structural Funds

Project title: New possibilities to rescue neurons in the delayed neuronal death by non specific stressors
Project number: ITMS: 26220220043
Duration: 1.1.2010 / 30.6.2012
Responsible person: C/MVDr. Jozef Burda, DrSc.
Total funding: 491 090 Eur
Funding for the Organization in assessed period: 166 130 Eur

Project title: Centre of Excellence for neuroregeneration research
Project number: ITMS: 26220120063
Duration: 1.11.2010 / 1.8.2013
Responsible person: C/MVDr. Ivo Vanický, CSc.
Project Coordinator: Institute of Neurobiology, Slovak Academy of Sciences
The Project Partners: Associated Tissue Bank of the P. J. Šafarik University, Faculty of Medicine, University Hospital of. Louis Pasteur in Kosice; The Institute of Animal Physiology, Slovak Academy of Sciences
Total funding: 3 815 637 Eur
Funding for the Organization: ŠF EU: 1 439 987 Eur

Project title: The development of the center of excellence for research of the physiology of the digestive tract - CEFT II. Phase
Project number: ITMS: 26220120043
Duration: 1.1.2010 / 1.1.2013
Responsible person: I/ MVDr. Ivo Vanický, CSc.
Project Coordinator: The Institute of Animal Physiology, Slovak Academy of Sciences
The Project Partners: Institute of Neurobiology, Slovak Academy of Sciences; Institute of Parasitology**,** Slovak Academy of Sciences
Funding for the Organization: 191 000Eur

Project title: Formation and development of a diagnostic procedure in the treatment of trauma - injured spinal cord
Project number: NFP 26220220127
Duration: 1.11.2010 / 30.4.2015
Responsible person: C/RNDr. Nadežda Lukáčová, DrSc.
Project Coordinator: Institute of Neurobiology, Slovak Academy of Sciences
The Project Partner: The University of Veterinary Medicine and Pharmacy in Košice
Total funding: 939 783 Eur
Funding for the Organization: 453 174 Eur

Project title: Competence Centre for biomodulators and nutritional supplements
Project number: ITMS: 2620220152
Duration: 1.7.2011 / 30.6.2014
Responsible person: I/MVDr. Dáša Čížková, DrSc.
Project Coordinator: The Institute of Animal Physiology, Slovak Academy of Sciences
The Project Partners: Institute of Neurobiology, Slovak Academy of Sciences; Institute of Parasitology**,** Slovak Academy of Sciences; P.J.Šafárik University; University of Veterinary Medicine; Milk Research Institute Inc.; company Imuna Pharm Inc..
Funding for the Organization: 185 040 Eur

Project title: University Medical Science and Technology Park in Košice, Slovakia
Project number: 26220220185
Duration: 10.7.2013 / 30.6.2016
Responsible person: I/ RNDr. Nadežda Lukáčová, DrSc.
Project Coordinator: P. J. Šafarik University
The Project Partners: University of Veterinary Medicine and Pharmacy; Institute of Neurobiology, Slovak Academy of Sciences; Technical University in Kosice
Funding for the Organization: 356 925 Eur

2.3.10. List of journals (published only in the Slovak language) edited/published by the institute:

2.3.10.1. WOS (IF of journals in each year of the assessment period)

2.3.10.2. SCOPUS

2.3.10.3. Other databases

2.3.10.4. Not included in databases

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

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

2013

- ČÍŽKOVÁ, D., Slovinská, L, Gruľová, I., Nagyová, M., Kafka, J., Kuricová, M., Ledecký, V., Čížek, M.: Alginate biomaterial releasing GFs promote repair of injured spinal cord: in vitro/in vivo study. FENS Featured Regional Meeting, September 11-14, 2013; Prague, Czech Republic

- LUKÁČOVÁ, N., Kisucká, A., Kucharíková, A., Hricová, Ľ., Chalimoniuk, M., Strosznajder, J.B.: Baclofen or NNLA suppress nNOS-IR in α-motoneurons after spinal cord transection. Neurochemical Conference, October 24-25, 2013; Warszaw, Poland

2014

- ČÍŽKOVÁ, D., Stem Cells and Smart Biomaterials: The Platform for Nerve Tisssue Repair and Augmentation. BIT's 7th Annual World Congress of Regenerative Medicine & Stem Cells, November 13-16, 2014; Haikou, China
- ČÍŽKOVÁ, D., In-vitro and in-vivo models for spinal cord injury repair: The platform for proteomic profiles**.** 10 eme Journeé Protéomique Université de Lille, Proteomique & Inovations, November 28, 2014, Lille, France

2015

- LUKÁČOVÁ N., Therapeutic relevance of local hypothermia after spinal cord compression: A characterization of neurofilaments in white matter pathology. Neurochemical Conference 2015: Neuropsychoimmunological mechanisms in the pathology of neurodegenerative diseases. From biomarkers to therapeutics. October 22-23, 2015, Warsaw, Poland
- RAČEKOVÁ E., Postnatal neurogenesis: immature tissue in the mature brain.16th national conference of biological psychiatry with international participation, June 3-6, 2015, Luhačovice, Czech Republic
- MARTONČÍKOVÁ M., Reorganization of blood vessels that represent scaffold for migration of neuroblasts in rostral migratory stream during early postnatal period. 16th national conference of biological psychiatry with international participation, June 3-6, 2015, Luhačovice, Czech Republic
- BURDA J., Ischemic tolerance in the injection. XXIV European Stroke Conference, May 13 – 15, 2015, Vienna, Austria

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

"7th International Symposium on Experimental and Clinical Neurobiology", Košice, Slovak Republic, June 23-27, 2013

Programme committee

- *Scientific Advisory Board:* prof. MUDr. Martin Maršala., prof. MUDr. Igor Šulla, DrSc
- *Chairman*: prof. MUDr. Martin Maršala
- *Members:* MVDr. Jozef Burda, DrSc; RNDr. Nadežda Lukáčová, DrSc; MVDr. Dáša Čížková, DrSc; MVDr. Ivo Vanický, CSc; Prof. MUDr. Igor Šulla, DrSc

Organizing commitee

- *Chairman*: RNDr. Jaroslav Pavel, PhD
- *Members:* RNDr. Juraj Blaško, PhD; RNDr. Petra Bonová, PhD; MVDr. Viera Danielisová, CSc; RNDr. Kamila Fabianová, PhD; RNDr. Ľudmila Hricová, PhD; RNDr.Ján Gálik, CSc; RNDr. Štefámia Gedrová; RNDr. Miroslav Gottlieb, CSc; RNDr. Ivana Gruľová, PhD; RNDr. Andrea Kucharíková, PhD; RNDr. Marcela Martončíková, PhD; RNDr. Miriam Nagyová, PhD; MVDr. Miroslava Némethová, PhD; RNDr. Zuzana Oroszová; RNDr. Eniko Račeková, CSc; RNDr. Kamila Saganová, CSc; RNDr. Andrea Schreiberová, PhD; RNDr. Lucia Slovinská, PhD; RNDr. Monika Závodská

„Behind the curtain of canine and feline dementia: from neuroscience research to treatment", Košice, Slovak Republic, October 6, 2015

- MVDr. Dáša Čížková, DrSc. – Scientific Committee
  – Organizing Committee

- **Position of individual researchers in a national context**

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

2012

- Burda J., Nová nádej pri liečbe akútneho zlyhania krvného zásobovania mozgu. ("New hope in the treatment of acute failure of blood supply to the brain"). Professor Club of the University of P.J. Safarik in Košice, November 13, 2012, Košice, Slovakia
- Gruľová I., Slovinská L., Nagyová M., Čížková D., A delivery of neuronal progenitors after spinal cord injury, Annual Meeting of Slovak Society for Neuroscience & Centre of Excellence for Brain Research, May 24-26, 2012, Smolenice Castle, Slovakia
- Račeková E., Blaško J., Lievajová K., Almášiová V., Martončíková M., Úloha krvných ciev v postnatálnej neurogenéze („The role of blood vessels in postnatal neurogenesis"), 15. Košický morfologický deň (15th Kosice morphological day), May 31, 2012, Košice, Slovakia
- Slovinská L., Gruľová I., Čížková D., Potenciál kmeňových buniek pre liečbu hluchoty a slepoty („The potential of stem cells for deafness and blindness treating"), Lekárske, pedagogické, sociálne a duchovné aspekty hluchoslepoty (Conference of medical, pedagogical, social and spiritual apects of deafblindness), May 18-19, 2012, Herľany, Slovakia
- Račeková E., Regenerácia a plasticita nervového tkaniva. („Regeneration and plasticity of the nervous tissue"). Meeting of the Czech society of otolaryngology and head and neck surgesy., January 19, 2012, Educational center of the hospital in Hradec Králové, Czech Republic

2013

- Burda J., Danielisová V., Bonová P., Gottlieb M., Némethová M., Burda R., Vzdialený ischemický postkondicioning klope na dvere kliník. („Remote ischemic post-conditioning is knocking on the doors of the clinics„), 16. Košický morfologický deň (15th Kosice morphological day), May 30, 2013, Košice, Slovakia
- Martončíková M., Fabianová K., Blaško J., Račeková E., Influence of odor enriched environment on the brain neurogenic region., 5th Czecho-Slovak congress of otolaryngology and head and neck surgery., May 23-25, Hradec Králové, Czech Republic
- Račeková E., Blaško J., Fabianová K., Martončíková M., Testing of functional consequences of an influence of postnatal neurogenesis in the rat olfactory system, 5th Czecho-Slovak congress of otolaryngology and head and neck surgery., May 23-25, Hradec Králové, Czech Republic

2014

- Cizkova D., Slovinská L., Blaško J., Nagyová M., Devaux S., Fournier I., Salzet M., Traumatic injury spinal cord - cell therapy and alterations of protein composition., National Program for Combating Alzheimer´s Disease – Smolenice, March 20-22, 2014.

2015

- Cizkova D., Cell Based Therapies for Neurodegenerative and Aging Disorders. The immune and nervous systems – teamwork, ageing and diseases., October 20-22, 2015, Smolenice castle, Slovakia

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

„Annual Meeting of Slovak Society for Neuroscience & Centre of Excellence in Neuroscience", May 24-27, 2012, Smolenice Castle, Slovakia
Co-organized by the Institute of Neurobiology SAS

- Programme committee: RNDr. Nadežda Lukáčová, DrSc; MVDr. Dáša Čížková, DrSc.

- **Supplementary information and/or comments documenting the international and national status of the Institute**

The Institute of Neurobiology has been cooperating with several universities such as the University of Pavol Jozef Šafárik in Košice (Faculty of Natural Sciences, Faculty of Medicine), University of Veterinary Medicine and Pharmacy in Košice, the Technical University of Košice, Jessenius Faculty of Medicine, Comenius University in Martin, and also with the Institute of Neuroimmunology SAS, the Institute of Experimental Physics SAS, and the Institute of Normal and Pathological Physiology SAS. The cooperation was carried out on several levels.

Official Partnership Agreements – Ongoing:
- University of Veterinary Medicine and Pharmacy within the project "The formation and development of diagnostic procedure for the treatment of trauma-induced spinal cord injury" supported by SF EU (since 2010);
- University of Pavol Jozef Šafárik within the project "Centre of Excellence for Neuroregenerative Research" supported by SF EU, partnership with Tissue Bank of Medical Faculty, (2009-2013);Institute of Animal Physiology SAS within the project "Competence Centre for Biomodulators and Nutritional Supplements" supported by SF EU, (2011-2014);
- Centre of Excellence for Physiology Research of Digestive Tract – II. Phase supported by SF EU (2010-2013);Institute of Neuroimmunology SAS within the project "Centre of Excellence for Brain Research" supported by SAS, (2011-2014);Institute of Normal and Pathological Physiology SAS within the project "Centre of Excellence for Research on the regulatory role of nitric oxide in diseases of civilization" supported by SAS, (2011-2014);

Official Partnership Agreements – New:
- With the University of Pavol Jozef Šafárik within the MediPark project supported by SF EU (2013), together with the University of Veterinary Medicine and Pharmacy and Technical University of Kosice.
- Between Institutes of the Slovak Academy of Sciences (Institute of Animal Physiology, Institute of Parasitology, Institute of Neurobiology) and the University of Pavol Jozef Šafárik (2014).

Joint Research Projects:
- VEGA Grant No. 1/0037/12, cooperation with the University of Veterinary Medicine and Pharmacy;
- APVV Grant No. APVV-0815-11, cooperation with the Institute of Animal Physiology SAS;
- VEGA Grant No. 1/0213/12, cooperation with Jessenius Faculty of Medicine, Comenius University;
- APVV Grant No. APVV-0526-11, cooperation with the Institute of Exper. Physics SAS;

Scientific Education:
The Institute of Neurobiology participates in pre-graduate education through lectures and practicum courses, and Bachelor and Master dissertation supervision. The Institute is a training center for two disciplines of PhD study:
- Animal Physiology – cooperation with the Faculty of Natural Sciences, University of P.J.Šafárik;
- Neuroscience – cooperation with the University of Veterinary Medicine and Pharmacy.

<u>International collaboration</u>
- Czech Republic: Institute of Physiology, Academy of Sciences of the Czech Republic, Prague; Institute of Animal Physiology and Genetics, AS CR, Libechov
- Hungary: Biological Research Center, Hungarian Academy of Sciences, Szeged; Univerzity of Szeged
- Poland: M. Mossakowski Medical Research Centre PAS, Warsaw
- Spain: Departamento de Bioquimica, Hospital Ramon y Cajal, Madrid; Departamento de Bioquimica y Biologia Molecular, Universidad de Alcala, Alcala de Henares;

Department of Neuroscience, Universidad del País Vasco, Leioa; José-Maria Delgado-Garcia, Universidad Pablo de Olavide, Sevila
- Ukraine: Bogomoletz Institute of Physiology NASU, Kiev
- USA: Department of Anesthesiology, University of California, San Diego; Miller School of Medicine, University of Miami, Miami; National Institute of Mental Health, Bethesda; Neuralstem Inc., Rockville

Membership in international scientific societies
- ESN – European Society for Neurochemistry
- ISN – International Society for Neurochemistry
- IBRO – International Brain Research Organization
- FENS – Federation of European Neuroscience Societies
- ENA – European Neuroscience Association
- ECRO – European Chemoreception Oganization
- ANG – Anatomische Geselschaft
- SFN – Society for Neuroscience
- IASP – International Association for the Study of Pain
- American Society for Neural Transplantation and Repair
- Czech and Slovak Society for Neurochemistry

2.4. Tables of project structure, research grants and other funding resources

- **International projects and funding**

2.4.1. Major projects within the European Research Area and other important project – Framework Programmes of the EU, ERA-NET, European Science Foundation, NATO, COST, INTAS, etc. (here and in items below please specify: 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"),

	Project title	Typ / Project number	Duration in months	Funding for the Institute (EUR)	Role of the Institute / Responsible person
2012	Nanomechanics of intermediate filament networks	COST/BM1002	9.11.2010 / 24.5.2014	4000	I/Čížková
2013	Nanomechanics of intermediate filament networks	COST/BM1002	9.11.2010 / 24.5.2014	4000	I/Čížková
2014	Nanomechanics of intermediate filament networks	COST/BM1002	9.11.2010 / 24.5.2014	1667	I/Čížková
2015					

2.4.2. Other international projects, incl. total funding and funding for the institute

2.4.3. Other important, international projects and collaborations without direct funding (max. 10 projects)

Project title: Study of the neuroprotective potential of P2X7 and CALHM1 channels in ischemia
Project number: B-MOB (Maria Currie Mobility)
Duration: 20.3.2015 / 30.6.2016
Responsible person: RNDr. Miroslav Gottlieb, CSc
Co-ordinator: Achucarro Basque Center for Neuroscience Fundazioa
Partner: Institute of Neurobiology, Slovak Academy of Sciences

Project title: The response of nitric oxide synthase and calcium-binding proteins in brain stem after spinal cord injury
Project number: Polish-Slovak Joint Research Project - MAD
Duration: 1.1.2010 / 31.12.2012
Responsible person: C/ RNDr. Nadežda Lukáčová, DrSc - Slovak Academy of Sciences
Responsible person: C/ prof. Malgorzata Chalimoniuk, PhD - Mossakowski Medical Research Centre, Polish Academy of Sciences, Warsaw, Poland

Project title: Scientific exchange programme between Switzerland and the new member states of the EU.
Project number: SCIEX-NMS
Duration: 1.1.2013 – 31.12.2013
Responsible person: C/ RNDr. Mária Lalkovičová
Co-ordinator: Dept of Developmental and Cell Biology, University of Fribourg, Switzerland
Partner: Institute of Neurobiology, Slovak Academy of Sciences

- **National projects and their funding**

2.4.4. Projects supported by the Slovak Research and Development Agency (APVV)

Role of the Institute e.g. coordinator “C”, investigator “I”.

	Project title	Typ / Project number	Duration in months	Funding for the Institute (EUR)	Role of the Institute / Responsible person
2012	Modified biomaterials and cell therapy for promoting regeneration of injured spinal cord	APVV 0472-11	1.7.2012 / 30.12.2015	25634	C/Čížková
	Mother and embryo: the influence of maternal obesity and stress on preimplantation embryo dvelopment	APVV-0815-11	1.7.2012 / 31.12.2015	1599	I/Račeková
	Neuroproteomics of injured spinal cord using MALDI mass spectrometry imaging after leech substances injection: Towards a novel therapeutic	SK-FR-0019-11	1.1.2012 / 31.12.2013	2645	C/Čížková
	Science in Slovakia - if we do not know something, we do not feel need for it.	LPP-0178-09	3.9.2009 / 31.8.2012	11878	C/Gálik
	Interactive methods of image acquisition and processing in microscopy using natural user interface	APVV-0526-11	1.7.2012 / 31.12.2015	6156	I/Gálik
2013	Modified biomaterials and cell therapy for promoting regeneration of injured spinal cord)	APVV 0472-11	1.7.2012 / 30.12.2015	47066	C/Čížková
	Neuroproteomics of injured spinal cord using MALDI mass spectrometry imaging after leech substances injection: Towards a novel therapeutic	SK-FR-0019-11	1.1.2012 / 31.12.2013	2645	C/Čížková
	Mother and embryo: the influence of maternal obesity and stress on preimplantation embryo dvelopment	APVV-0815-11	1.7.2012 / 31.12.2015	3237	I/Račeková
	Interactive methods of image acquisition and processing in microscopy using natural user interface	APVV-0526-11	1.7.2012 / 31.12.2015	8263	I/Gálik
2014	Mother and embryo: the influence of maternal obesity and stress on preimplantation embryo dvelopment	APVV-0815-11	1.7.2012 / 31.12.2015	3326	I/Račeková
	Modified biomaterials and cell therapy for promoting regeneration of injured spinal cord	APVV 0472-11	1.7.2012 / 30.12.2015	47050	C/Čížková
	Interactive methods of image acquisition and processing in microscopy using natural user interface	APVV-0526-11	1.7.2012 / 31.12.2015	6032	I/Gálik
2015	Modified biomaterials and cell therapy for promoting regeneration of injured spinal cord)	APVV 0472-11	1.7.2012 / 30.12.2015	40250	C/Čížková
	Mother and embryo: the influence of maternal obesity and stress on preimplantation embryo dvelopment	APVV-0815-11	1.7.2012 / 31.12.2015	3478	I/Račeková
	Interactive methods of image acquisition and processing in microscopy using natural user interface	APVV-0526-11	1.7.2012 / 31.12.2015	4995	I/Gálik
	Axonal regeneration in biosynthetic nerve guide conduits.	APVV-14-0847	1.7.2015 / 30.6.2019	21900	C/Vanický

2.4.5. Projects supported by the Scientific Grant Agency of the Slovak Academy of Sciences and the Ministry of Education (VEGA) for each year, and their funding

VEGA	2012	2013	2014	2015
Number	12	14	12	11
Funding in the year (EUR)	61774	68781	72827	77486

[1]

[1] Excluding projects for the popularisation of science

- **Summary of funding from external resources**

2.4.6. List of projects supported by EU Structural Funds

Project title: New possibilities to rescue neurons in the delayed neuronal death by non specific stressors
Project number: ITMS: 26220220043
Duration: 1.1.2010 / 30.6.2012
Responsible person: C/MVDr. Jozef Burda, DrSc.
Total funding: 491 090 Eur
Funding for the Organization in assessed period: 166 130 Eur

Project title: Centre of Excellence for neuroregeneration research
Project number: ITMS: 26220120063
Duration: 1.11.2010 / 1.8.2013
Responsible person: C/MVDr. Ivo Vanický, CSc.
Project Coordinator: Institute of Neurobiology, Slovak Academy of Sciences
The Project Partners: Associated Tissue Bank of the P. J. Šafarik University, Faculty of Medicine, University Hospital of. Louis Pasteur in Kosice; The Institute of Animal Physiology, Slovak Academy of Sciences
Total funding: 3 815 637 Eur
Funding for the Organization: ŠF EU: 1 439 987 Eur

Project title: The development of the center of excellence for research of the physiology of the digestive tract - CEFT II. Phase
Project number: ITMS: 26220120043
Duration: 1.1.2010 / 1.1.2013
Responsible person: I/ MVDr. Ivo Vanický, CSc.
Project Coordinator: The Institute of Animal Physiology, Slovak Academy of Sciences
The Project Partners: Institute of Neurobiology, Slovak Academy of Sciences; Institute of Parasitology**,** Slovak Academy of Sciences
Funding for the Organization: 191 000Eur

Project title: Formation and development of a diagnostic procedure in the treatment of trauma - injured spinal cord
Project number: NFP 26220220127
Duration: 1.11.2010 / 30.4.2015
Responsible person: C/RNDr. Nadežda Lukáčová, DrSc.
Project Coordinator: Institute of Neurobiology, Slovak Academy of Sciences
The Project Partner: The University of Veterinary Medicine and Pharmacy in Košice
Total funding: 939 783 Eur
Funding for the Organization: 453 174 Eur

Project title: Competence Centre for biomodulators and nutritional supplements
Project number: ITMS: 2620220152
Duration: 1.7.2011 / 30.6.2014
Responsible person: I/MVDr. Dáša Čížková, DrSc.
Project Coordinator: The Institute of Animal Physiology, Slovak Academy of Sciences
The Project Partners: Institute of Neurobiology, Slovak Academy of Sciences; Institute of Parasitology**,** Slovak Academy of Sciences; P.J.Šafárik University; University of Veterinary Medicine; Milk Research Institute Inc.; company Imuna Pharm Inc..
Funding for the Organization: 185 040 Eur

Project title: University Medical Science and Technology Park in Košice, Slovakia
Project number: 26220220185
Duration: 10.7.2013 / 30.6.2016
Responsible person: I/ RNDr. Nadežda Lukáčová, DrSc.
Project Coordinator: P. J. Šafarik University

The Project Partners: University of Veterinary Medicine and Pharmacy; Institute of Neurobiology, Slovak Academy of Sciences; Technical University in Kosice
Funding for the Organization: 356 925 Eur

2.4.7. Summary of external resources of the EU Structural Funds (ERDF/ESF)

Role of the Institute in the project, e.g. coordinator "C", work package leader "W", investigator "I".

Year	Project title	Project number	Duration in months	Funding for the Institute (EUR)	Role of the Institute
2012	New possibilities to rescue neurons in the delayed neuronal death by non specific stressors	ITMS: 26220220043	1.1.2010 / 30.6.2012	166 130	C/Burda
	Centre of Excellence for Neuroregeneration Research	ITMS: 26220120063	1.11.2010 / 1.8.2013	547 235	C/Vanický
	The development of the centre of excellence for the research of digestive tract physiology - CEFT II. phase	ITMS: 26220120043	1.1.2010 / 1.1.2013	0	I/Vanický
	Formation and development of a diagnostic procedure in the treatment of trauma - injured spinal cord	ITMS: 26220220127	1.11.2010 / 31.10.2013	147 784	C/Lukáčová
	Competence centre for biomodulators and nutritional supplements	ITMS: 2620220152	1.7.2011 / 30.6.2014	169 920	I/Čížková
2013	Competence Centre for biomodulators and nutritional supplements	ITMS: 2620220152	1.7.2011 / 30.6.2014	13 300	I/Čížková
	MEDIPARK - University Medical Science and Technology Park in Košice	ITMS: 26220220185	10.7.2013 / 31.12.2014	7 211	I/Lukáčová
	Formation and development of a diagnostic procedure in the treatment of trauma - injured spinal cord	ITMS: 26220220127	1.11.2010 / 31.10.2013	97 635	C/Lukáčová
	Centre of Excellence for neuroregeneration research	ITMS: 26220120063	1.11.2010 / 1.8.2013	892 752	C/Vanický
	The development of the centre of excellence for the research of digestive tract physiology - CEFT II. phase	ITMS: 26220120043	1.1.2010 / 1.1.2013	191 000	I/Vanický
2014	Competence Centre for biomodulators and nutritional supplements	ITMS: 2620220152	1.7.2011 / 30.6.2014	1 820	I/Čížková
	MEDIPARK - University Medical Science and Technology Park in Košice	ITMS: 26220220185	10.7.2013 / 30.6.2015	25 305	I/Lukáčová
	Formation and development of a diagnostic procedure in the treatment of trauma - injured spinal cord	ITMS: 26220220127	1.11.2010 / 30.4.2015	186 567	C/Lukáčová
2015	MEDIPARK - University Medical Science and Technology Park in Košice	ITMS: 26220220185	10.7.2013 / 30.6.2016	324 409	I/Lukáčová
	Formation and development of a diagnostic procedure in the treatment of trauma - injured spinal cord	ITMS: 26220220127	1.11.2010 / 30.4.2015	21 188	C/Lukáčová

External resources	2012	2013	2014	2015	total	average
External resources (milions of EUR)	1,734	1,202	0,214	0,381	**3,531**	**0,883**
External resources transfered to coooperating research institute (milions of EUR)	0,703	0,000	0,000	0,000	**0,703**	**0,176**

- **Supplementary information and/or comments on research projects and funding sources**

Financial resources from EU Structural Funds, which were several folds higher than our annual institutional budget, had substantial impact on the Institute infrastructure. To obtain resources for realization of our scientific projects, we regurarily applied for the project from governmental APVV agency, as well from the SAS Scientific Grant Agency. We had ambitions to get also EU projects (FP7, H2020, SASPRO), however, non of our proposal was accepted.

2.5. PhD studies and educational activities

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

During the assessed period the Institute of Neurobiology provided postgraduate education in two accredited programs:

- 4.2.10 Animal Physiology by the Faculty of Natural Sciences at P.J.Šafárik University, guarantor RNDr. Nadežda Lukáčová, DrSc, 2007 – ongoing
- 4.2.16 Neurosciences by the University of Veterinary Medicine and Pharmacy in Košice, guarantor MVDr. Dáša Čížková, DrSc, 2012 – ongoing

  INb SAS was the first institution in Slovakia which created a postgraduate programme: entitled "Neurosciences", it was developed in collaboration with the Medical Faculty of P. J. Šafárik University in Košice (2006-2008.). After the University lost its accreditation (the guarantor of the program left), the „Neurosciences" program was accredited again in collaboration with the Veterinary University in Košice, as a result of an EU SF project.
  Within the „Neuroscience" program Dr. Cizkova (INb SAS) together with Prof. Michel Salzet, director of the Proteomic Laboratory at the University of Lille 1, France and the University of Veterinary Medicine and Pharmacy in Kosice launched the Co-tutorial PhD Program. Two students from France were accepted for this co-tutorial study course.

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

PhD study	31-12-12			31-12-13			31-12-14			31-12-15		
Number of potential PhD supervisors	16			16			15			12		
PhD students	number	defended thesis	students quitted	number	defended thesis	students quitted	number	defended thesis	students quitted	number	defended thesis	students quitted
Internal	7,0	3,0	0,0	7,0	2,0	0,0	8,0	1,0	0,0	11,0	0,0	0,0
External	1,0	0,0	0,0	1,0	0,0	0,0	1,0	0,0	0,0	1,0	0,0	0,0
Other supervised by the research employees of the institute	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0

2.5.3. Summary table on educational activities

Teaching	2012	2013	2014	2015
Lectures (hours/year)[2]	39	39	39	22
Practicum courses (hours/year)[2]	0	0	39	84
Supervised bachelor theses (in total)	3	6	2	0
Supervised diploma theses (in total)	7	8	12	9
Supervised PhD theses (in total)	9	9	9	12
Members in PhD committees (in total)	3	6	5	3
Members in DrSc. committees (in total)	0	2	2	0
Members in university/faculty councils (in total)	0	0	0	1
Members in habilitation/inauguration committees (in total)	1	2	4	2

2

2.5.4. List of published university textbooks

Gajdoš M., Šulla I., Szilasiová J., Foltánová T., Kollová A., Lukáč I., Balik V., Gajdoš J., Šulla I.jr., Základy neurochirurgie: Učebnica pre lekárov a študentov všeobecného lekárstva (The basis of neurosurgery: The textbook for medical doctors and for students of general medicine). Košice, 416 s. ISBN 978-80-8152-003-7.

Račeková E., Zápotocký M., Vodička J., Poruchy čichu a chute, Kapitola 1: Anatomie, embryologie a fyziologie čichového systému, (Disorders of smell and taste, Chapter I: Anatomy, embryology and physiology of the olfactory system) - Kobzinové 3119, Havlíčkuv Brod, 580 01: TOBIÁŠ, 2012, s. 16-39. ISBN 978-80-7311-125-0.

Šulla I., Pohľad neurochirurga na mozgové krvácania hypertonikov. (The view of neurosurgeon on cerebral bleeding in hypertonic patients.) In e-lerning portal of the Slovak medical chamber, Bratislava: Slovak medical chamber, 2012. ISSN 1338-4392. Available on the WEB: <www.i-med.sk>.

Šulla I., Ochorenia driekových medzistavcových platničiek a syndróm cauda equina. (Spinal discs diseases and cauda equine syndrome) In e-lerning portal of the Slovak medical chamber, Bratislava: Slovak medical chamber, 2012. ISSN 1338-4392. Available on the WEB: <www.i-med.sk>.

Šulla I., Dyzrafické vývinové chyby chrbtice a miechy. (Dysraphic developmental deformations of the spine and spinal cord.) In e-lerning portal of the Slovak medical chamber, Bratislava: Slovak medical chamber, 2012. ISSN 1338-4392. Available on the WEB: <www.i-med.sk>.

2.5.5. Number of published academic course books

2 Do not include time spent with bachelor, diploma or PhD students during their supervising

2.5.6. List of joint research laboratories/facilities with universities

Official Partnership Agreements:

- Joint research workplace with the University of Veterinary Medicine and Pharmacy within the project “The formation and development of diagnostic procedure for the treatment of trauma-induced spinal cord injury” supported by SF EU (since 2010)
- Joint research workplace with P. J. Šafárik University within the project ”Centre of Excellence for Neuroregenerative Research" supported by SF EU, partnership with the Tissue Bank of the Medical Faculty of P. J. Šafárik University (since 2009)
- Joint research laboratories with P. J. Šafárik University within the MediPark project supported by SF EU (2013). MediPark was designed in order to build up the university Science Park for applied research and its transfer into clinical practice as an excellent national and international centre in the field of biomedicine. It is based on collaboration between the University of P. J. Šafárik, the University of Veterinary Medicine and Pharmacy, the Technical University and the Institute of Neurobiology SAS.
- Joint research workplace of the Slovak Academy of Sciences (Institute of Animal Physiology, Institute of Parasitology, Institute of Neurobiology) and P. J. Šafárik University (2014). This joint scientific workplace was established in order to support research projects, scientific and educational activities, popularization and application of results in social practice.

- **Supplementary information and/or comments on doctoral studies and educational activities**

- Our Institute has also provided undergraduate teaching: semestral lectures “Neurophysiology” and “Experimental methods in physiology” (Dr. Gálik), practicals in “Animal Physiology” and “Etology” (Dr. Tomko), and the lecture “Neural cell physiology” (Dr. Čížková)
- RNDr. Stanislava Jergová, PhD, post-doctoral position at the National Institutes of Health, Craigh Neilsen Foundation, University of Miami Miller School of Medicine (2008-2013)
- Mgr. Mária Lalkovičová was granted a one-year study stay at the University of Freiburg in Switzerland, Dept. of Developmental and Cell Biology, within the Scientific Exchange Program between Switzerland and the New Member States of the EU (SCIEX-NMS, 2012).
- Three foreign students (France, Cyprus) applied for PhD study at our Institute. They are supervised by Dr. Čížková and Dr. Martončíková.
- In 2014, within the Erasmus program, three students from Warsaw were trained at the Institute (Dr. Lukáčová Dr. Galik, Dr. Pavel).
- Over the past period, our students have been successful in obtaining travel grants mainly for international symposiums and training courses.

  (e.g. 8th FENS Forum of Neuroscience 2012, Barcelona, Spain – 2 students; FENS-IBRO School 2012; Bertinoro, Italy – 1 student; 7th International Symposium on Experimental and Clinical Neurobiology, Kosice, Slovakia 2013 – 6 students; Images of the spinal cord: from functionally identified neurons to functional recovery, Warsaw, Poland, 2013 – 3 students).
- Our students obtained several awards in competitions for the best scientific work on the doctoral seminar in memory of Academician Boda, 2012-2015, Kosice.

2.6. Social impact

2.6.1. List of the most important results of applied research projects.

The project "New possibilities to save neurons in the process of delayed neuronal death by nonspecific stressors“ was funded with EU Structural Funds. We found that remote postconditioning, performed with 20 min of tourniquet ischemia applied to the hind limb is a simple method able to effectively stop the onset of neurodegeneration and prevent occurrence of massive muscle cell necrosis, even when used two days after the adverse

event. Surviving neurons retained a substantial capacity of their learning and memory ability. The procedure of tourniquet postconditioning can be used in clinical medicine after cardiac arrest, hypertensive shock and other transient ischemic attacks, as well as apoptosis-inducing intoxications. The therapeutic window after permanent focal ischemia is substantially shorter, so postconditioning should be used as soon as possible, and similarly to other attacks can be used repeatedly. It is important to note that tourniquet application increases blood pressure to about 30% higher values than before its application, which can be dangerous in the case of possible bleeding. The principle of nervous tissue protection by means of postconditioning is the subject of a patent application (see 2.1.7.).

The project "Formation and development of a diagnostic procedure in the treatment of traumatic spinal cord injury", funded with EU Structural Funds, consisted of a pre-clinical study for the treatment of traumatic spinal cord injury (SCI). Traumatic SCI has devastating consequences for patients, and current treatments are controversial or of limited efficacy. We investigated the neuroprotective efficacy of local hypothermia after spinal cord compression (8N, 15N and 18N impact trauma at L3 level) in minipigs, induced by a computer-controlled impactor device allowing us to gain a clinically relevant minipig model of chronic spinal cord trauma. Local hypothermic perfusion (4°C) of the lesion site was performed through a special perfusion chamber with saline or oxygenated culture DMEM/F12 medium starting half an hour after spinal cord compression and maintained for five hours, with the aim of stopping the spread of injury, and the complex cascade of events that follow the primary insult. We found that saline hypothermia leads to gray and white matter sparing, and to substantial sparing of neurofilaments in segments away (rostrally +3, +2, +1 and caudally -1, -2, -3) from the lesion site, i.e. in spinal cord sections that are likely to be affected by secondary injury. In particular, we demonstrated that saline hypothermia after 8N SCI, causing the sparing of axons in lateral funiculi at +1 and -1 (improvement by 25% and 19%), showed favorable neurological outcomes. The animals presented faster recovery of hind limb function and the ability to walk from one to three steps with consistent plantar-hoof stepping at nine weeks. Such improvements were not observed in the group subjected to more severe SCI. The application of local hypothermia in this computer-controlled minipig compression model provided data analogous to the impact of such treatments in patients (Ahmad et al., 2014; Hansebout and Hansebout, 2014). The most important results were summarized in a document that was sent to the Ministry of Health on April 30, 2015. The recommendation resulting from this study is that in the case of unstable backbone fractures leading to traumatic spinal injury with indication of stabilizing surgery, the surgeon should apply cooling of the medulla spinalis using ice-cold saline.

2.6.2. List of the most important studies commissioned for the decision-making authorities, the government and NGOs, international and foreign institutes

MVDr. Dáša Čížková, DrSc

- member of the Council of Medical Sciences of Slovak Research and Development Agency
- member of the Accreditation Commission of the Ministry for Education for the research program "Veterinary Sciences"

Prof. MUDr. Igor Šulla, DrSc

- member of the Accreditation Commission of the Ministry for Education for the research program "Medical Sciences"
- member of the editorial board of "Zdravotníctvo a sociálna práca" (Health and Social Work)
- expert's reports from the field of neurosurgery for the Slovak Health Care Supervision Authority

2.6.3. List of contracts and research projects with industrial and other commercial partners, incl. revenues

The Institute of Neurobiology (INb) SAS participated in the project financed with EU Structural Funds (EU SF) entitled: Competence Center for Biomodulators and Nutritional Supplements (PROBIOTECH, ITMS code 2620220152, duration 1 July 2011 – 30 June 2014, with total funds for INB SAS of 219 960 EUR). The strategic objective of the project was to create a competence center focusing on advanced research in collaboration with the private sector. The project involved several academic institutions and private companies: the Institute of Animal Physiology (IAP) SAS, INb SAS, Institute of Parasitology (IP) SAS, P.J.Šafárik University (UPJS), University of Veterinary Medicine (UVM), Milk Research Institute company and Imuna Pharm company. INb SAV participated together with IAP SAS and IP SAS in activity 1.1, i.e. setting up laboratories for scientific testing. The aim of the activity was to test microbial production strains using modern molecular-biological methods and to standardize existing methodologies. Based on our experience in analysing nNOS, eNOS and iNOS in the nervous system, we adapted our methodologies to identify nNOS and NADPH in intestinal tissue. We also optimized flow cytometry methods to identify apoptosis / necrosis of stromal stem cells (BMSCs). Furthermore, we modified the method of Annexin V / Propidium Iodide labeling, which allowed us to quantify the number of apoptotic and necrotic cells and the population of BMSCs that might provide optimal antimicrobial potential. With the allocated funds, INb SAS obtained Night OWL, an unique imaging system for *in vivo* detection of fluorescent proteins and visualization of cells labeled with fluorescent markers.

During the evaluated period INb SAS participated in building the University Biomedical Science and Technology Park (MEDIPARK Košice). The objective of the project was to create a top national and international center for applied research and its transfer into practice in the field of biomedicine. The project (MEDIPARK Košice, ITMS code 26220220185) was supported with EU SF (356 925 EUR). INb SAS in cooperation with three major institutions in Košice (P. J. Šafarik University, University of Veterinary Medicine and Pharmacy, and the Technical University) integrated human potential with expertise in biomedical sciences, and they built important research infrastructure. With the allocated funds INb SAS obtained several unique items of equipment (slide scanner, treadmill and instruments for behavioral testing of small laboratory animals). There are five core research programs in Medipark. Our Institute together with the Faculty of Medicine of P. J. Šafarik University created the Neurosciences research program. The aim of this program is to use innovative approaches for the prevention of severe neurological disability after spinal cord injury or stroke. Based on our experience with CNS ischemia, by studying the phenomenon of ischemic tolerance we obtained promising results with great translational potential. We also developed a clinically relevant minipig model of chronic spinal cord trauma at lumbar level and optimized conditions for application of local spinal cord hypothermia. Medipark Košice created the basis for scientific interactions between academic institutions and the business sector in biomedical research and development and subsequent transfer of the results into clinical practice.

2.6.4. List of licences sold abroad and in Slovakia, incl. Revenues

- The ownership rights of MVDr. Viera Danielisová, PhD (Institute of Neurobiology, SAS) to patent no. EP 0514789 B1, entitled "Use of 1- (5-oxo- hexyl) -3-methyl-7-n-propyl-xanthine and vascular surgery" were transferred from Sanofi-Aventis Deutschland GmbH to the company Solace Pharmaceuticals Inc., Boston, USA. Revenue for the organization: 13 333.34 USD.

2.6.5. List of most important social discourses under the leadership or with significant participation of the institute (max. 10 items)

Screening of olfactory functions in European countries. Pleasantness of odorants was evaluated in several European countries (Czech Republic, Italy, Slovak Republic, Germany). INb SAS participated in this study by testing a group of healthy subjects using its “New Test of Odour Pleasantness”. The aim of this study was to standardize olfactometry tests for clinical practice.

J. Vodicka[1], P. Bronthankova[1], G. Ottaviano[2], D.T. Nguyen[3], E. Racekova[4], M. Martoncikova[4], Y. Furukawa[5], [1]Department of Otorhinolaryngology and Head and Neck Surgery, Regional Hospital Pardubice; Faculty of Health Studies, University of Pardubice, Czech Republic [2]Department of Neurosciences, Otolaryngology section, University of Padova, Italy [3]Centre Hospitalier Universitaire de Nancy, Department of Ear, Nose, and Throat–Head and Neck Surgery, Nancy, France [4]Institute of Neurobiology, Slovak Academy of Sciences, Kosice, Slovakia; [5]Smell & Taste Clinic, Department of Otorhinolaryngology, Technische Universitaet Dresden, Germany.,
Evaluation of pleasantness of odorants in several European countries. Chemical Senses, 40: 294, 2015

2.6.6. Summary of relevant activities, max. 300 words

2.7. Popularisation of Science (outreach activities)

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

1. Organization of and active participation in "Science Cafes“, which are informal lectures and debates for the public popularizing science outside of academic spaces. Our “Science Cafes” are already accepted as a regular part of cultural life in Kosice. There were 42 presentations in the assessment period 2012 – 2015.
2. Administration of the “Popular Science” web portal for science popularization (http://www.popularnaveda.sk).
3. Regular annual organization of "Open Institute Day“, to present our work to students and the general public (2012 - 2015).
4. Regular annual active participation in daylong mass science shows visited by thousands of people: Night of Researchers, Piknik Naukowy (Poland), 2012 – 2015.
5. Active participation in the "Steel Park” interactive science center project (http://www.steelpark.sk). The Institute designed and built four interactive stands to demonstrate the electrical properties of the human body. The center was opened in 2012, and since that time it has been visited by tens of thousands of visitors.
6. Active participation in citywide cultural events such as the installation and presentation called "BioArt - Life Affairs“ in the DIG Gallery; or the"One Cell Sound" installation in the Old Synagogue during the White Night in Kosice.
7. Publishing of the "Košické neuročriepky” (Kosice’s neuro-fragments) bulletin presenting our projects and neuroscience problems for students and the public, distributed in printed and electronic forms (2012)
8. Participation in TV and radio discussions such as the TV show "Talks over midnight" in national TV TA3 (Dr. Galik: Brain – facts and secrets), the program EUROSKOP in TV TA3 (Dr. Lukáčová); multiple presentations in local radios.
9. Popularizing articles: Quark: Journal of popular science for young people "How to save the injured spinal cord” (9/2012, author: Dr. Lukáčová), Medical newspaper "Progress in the research of slerosis“, (2014, author: Dr. Lukáčová).
10. Exhibitions of attractive, large-scale micro-photographs, showing neuronal cells with simple short descriptions for the public in schools and public places.

2.7.2. Table of outreach activities according to institute annual reports

Outreach activities	2012	2013	2014	2015	total
Articles in press media/internet popularising results of science, in particular those achieved by the Institute	4	2	1	2	9
Appearances in telecommunication media popularising results of science, in particular those achieved by the Institute	3	4	5	3	15
Public popularisation lectures	8	14	11	5	38

- **Supplementary information and/or comments on popularisation activities, max. 300 words**

Popularization is an integral part of our everyday work. An important impulse for our popularization effort was support from the APVV agency grant entitled “Science in Slovakia - if we do not know something, we do not feel the need for it.” (2009–2012, Dr. Gálik). This project has finished, but many activities have survived. Our most effective form of science popularization is the organization of Science Cafes. We organize them on a monthly basis, and they have become an integral part of cultural life in Kosice. Another tool for science popularization is our web portal called “Popular Science” (http://www.popularnaveda.sk). We have also published a bulletin called “Košické neuro-čriepky” (Kosice’s neuro-fragments); however, for an institution of our size it was too time consuming, so we temporarily suspended its publication. The Institute is active in many forms of cultural activity in Kosice. We regularly participate in the annual mass science show known as the Night of Researchers in a large shopping mall; we are frequently invited to participate in installations and presentations by the cultural community in Kosice. Our “Open Institute Days” are very traditional and popular, especially for teachers and students in secondary schools. Every year our Institute welcomes 100-300 students. Our popularization activities have also brought us an invitation to the biggest popularization event in central Europe, the Piknik Naukowy, which takes place in the largest sports stadium in Warsaw, Poland, and it is attended by 100-150 000 visitors. We participated in this three times during the assessment period. Another appreciation of our popularization effort was the invitation to be part of the “Steel Park” interactive science center in Kosice (http://www.steelpark.sk). Our Institute is the only non-technical institution among all institutes and faculties in Kosice which actively participate in the project. Our activities were rewarded with two SAS Prizes for science popularization awarded by the SAS Presidium, one individual (Dr. Gálik, 2013) and one team prize (2014).

2.8. Background and management. Human resources and implementation of recommendations from previous assessment

2.8.1. Summary table of personnel

Personnel	2012	2013	2014	2015
All personnel	43,0	44,0	39,0	32,0
Research employees from Tab. Research staff	26,0	27,0	27,0	25,0
FTE from Tab. Research staff	22,100	24,540	23,280	20,270
Average age of research employees with university degree	46,8	47,5	49,2	47,6

2.8.1.1. Professional qualification structure (as of 31.12. 2015) FEMALE

FEMALE	AGE								
Number of	< 30	31 - 34	35 - 39	40 - 44	45 - 49	50 - 54	55 - 59	60 - 64	> 65
DrSc. / prof.						1	1		
II.a / Assoc. prof.		1		2	1	1		1	
Other researchers PhD./CSc.		4	2	1					
doc. / Assoc. prof.									

2.8.1.2. Professional qualification structure (as of 31.12. 2015) MALE

MALE	AGE								
Number of	< 30	31 - 34	35 - 39	40 - 44	45 - 49	50 - 54	55 - 59	60 - 64	> 65
DrSc. / prof.						1			
II.a / Assoc. prof.				1		1	1	1	
Other researchers PhD./CSc.		1							
doc. / Assoc. prof.									

2.8.2. Postdoctoral and mobility scheme

2.8.2.1. Postdoctoral positions supported by national and international resources

2.8.2.2. Postdoctoral positions supported by external funding

RNDr. Juraj Blaško, PhD
RNDr. Kamila Fabiánová, PhD
RNDr. Milina Matiašová, PhD
Support from the SF EU project: University Medical Science and Technology Park in Košice (Medipark, Košice), - ITMS 26220220185
PI: RNDr. Nadežda Lukáčová, DrSc. (7/2013-6/2015)

RNDr. Alexandra Kisucká, PhD
RNDr. Marcela Martončíková, PhD
RNDr. Andrea Stropkovská, PhD
RNDr. Kamila Fabiánová, PhD
Support from the SF EU project: Formation and development of a diagnostic procedure in the treatment of trauma - injured spinal cord, – ITMS 26220220127
PI: RNDr. Nadežda Lukáčová, DrSc. (11/2010-4/2015)

2.8.2.3. SAS stipends and SASPRO stipends

2.8.2.4. Internal funding - the Slovak Academy of Sciences Supporting Fund of Stefan Schwarz

RNDr. Juraj Blaško, PhD. – 1.1. 2015 – 31.12.2018

2.8.3. Important research infrastructure *(max. 2 pages)*

- **Proteomics** – MALDI TOF-TOF mass spectrometer (UltraleXtreme, Bruker) with the level of detection of less than 10^{-15} mol. The kit includes nano-HPLC chromatography (Dionex UltiMate 3000) which allows 2D nano-high performance liquid chromatography. The chromatography connects to a spotting device called Proteineer FC, which deposits fractions on MALDI targets, which are further directly analyzed in the spectrometer and evaluated by the ProteinScape 2.1 server system, which is

directly connected to MASCOT and PHENYX databases, and saved to their own servers.

- **Tissue sample preparation** – laser microdissection system to cut samples out of individual cell populations or subcellular structures (Leica LMD6500), vibratom, cryostats (Leica CM1510 S), automatic station for paraffin embedding (Bio Optica CD1000), cooled ultracentrifuge allowing subcellular fractionation of microgram tissue quantities (Beckman Optima TLX),
- **Molecular biology and biochemistry** – system for 1-D, 2-D electrophoresis band scanning and analysis (Biorad GelDoc), Western blot setup with sensitive camera and SW, PCR and Real time PCR (BioRad CFX96), Typhoon Trio reader - multifunctional laser scanner, for scanning and analysis of 1 or 2D gels stained with fluorescent dyes, chemiluminescent agents or marked radioactive substances, with maximum resolution of 25 μm (GE Healthcare), spectrophotometers (Specord 210 Plus).
- **Microscopy** – confocal microscope (lasers 405, 488, 532 and 635 nm, a spectral confocal detector in the minimum range of 440 to 720 nm; one detector for observation in transmitted light), slide scanner for large area sections (Leica), several fluorescent microscopes with camera and SW (Olympus, Leica, Nikon), professional software for image analysis (Image Pro)
- **Cell and tissue culture** – inverted fluorescent microscope with camera, SW and heated incubation chamber for live-cell culture monitoring (Nikon Eclipse Ti-E), programable freezing apparatus for freezeng cryovials and packs (Nicool Freezal, Air Liquide), air decontamination unit Plasmair (Air in space), CO_2 incubators, laminar flow boxes.
- **Behavioral testing** – equipped for all kinds of behavioral tests necessitated for injured brain and spinal cord evaluation: motor, sensory and pain, memory and learning, emotional tests: open field, water maze, and other mazes with monitoring (Noldus Ethovison XT), system for quantitative assessment of footfalls and gait in rats and mice (Noldus Catwalk XT), five-line treadmill for small laboratory animals (Bioseb), elevated maze, von Frey fiber test, olfactometer for evaluation of olfactory functions with four channels (Knosys), the whole set of instruments from Ugo Basile - active and passive avoidance tests for rats and mice, rotarods for rats and mice, hot/cold plate tests, tail flick test, grip strength test.
- **Electrophysiology, in vivo** – several setups (amplifiers, stimulators, data interfaces) for vital-sign monitoring (body temperature, EEG, ECG, EMG, breathing), spinal evoked potential monitoring, unit activity recordings, implantable telemetry system for monitoring biopotentials in traumatically injured animals (Emka).
- **Electrophysiology, in vitro** – patch clamp setup for cellular electrophysiology, recording of individual cells in cerebral and spinal slices and cell cultures using an upright fluorescent microscope (Molecular devices).
- **Vivarium** - automatic washing and disinfection machine for animal cages (Steelco AC 1200), laminar flow changing stations (Tecnipalst CS45 EVO)
- **Surgery rooms** – operating microscopes for small-animal surgery (Leica M320), vital-function monitor for surgery room, stereotactic apparatuses (Stoelting), vaporizers for inhalation anesthesia, laser blood flow meter: two units for non-invasive measurement of blood flow using the Doppler effect, one unit for partial oxygen pressure measurement, and a 1 mm probe for non-invasive blood flow measurement (PeriFlux System 5000), spinal compression apparatus to induce controlled traumatic spinal cord injury (custom made), station for terminal perfusion of smal experimental animals.
- **General laboratory equipment** – laboratory fume hoods, deep freeze boxes, freezers, ice makers, automatic washing machine for laboratory glass, and other laboratory equipment.
- **Other measuring equipment** – *in vivo* fluorescent imaging system (Night Owl), radioactive gamma-ray measuring device.
- **3D fabrication** – equipment for the fabrication of a plastic perfusion chamber for perfusion of injured spine. It contains a non-contact 3D laser scanner (eScan, 3D digital), modeling software (Rhinoceros), and a 3D printer (uPrint).

2.8.4. Description of how the results and suggestions of the previous assessment were taken into account

There were no specific suggestions and tasks which had to be performed by the organization. The overall evaluation statement was:
The strengths of the Institute are: very good research infrastructure, the research teams are very well interconnected in common topics.
Weaknesses: suboptimal orientation on clinical research, relatively low number of scientific publications.

To address the weaknesses, we tried to put emphasis on translational research with possible outputs to clinical practice. During the assessment period our Institute implemented (along with others) two translational projects financed by EU SF (Dr. Lukáčová, Dr. Burda). Both projects focused on preclinical studies. During the projects' implementation we utilized our collaboration with neurosurgeons and clinical veterinary doctors. They were members of the project teams, helping us with the surgeries, bringing in the clinical point of view, and also supporting better and direct transfer of the project results into clinical practice. Another project focusing on the transfer from science into clinical practice is the Medipark project. Medipark is a science and technology formation, an excellent national and international center for applied research, and for the transfer of its results into practice in the field of biomedicine. The Institute of Neurobiology SAS is one of the active partners in this project.

The second comment related to the number of publications. We are fully aware, that in spite of the fact, that the average number of published papers slightly increased from 13,8 in last accreditation period to 16 in recent period, our production is not satisfactory. The number of our papers has been relatively stable throughout the last 4 years, however, the quality expressed by their IF significantly increased. More than 50% of published papers (35 of 64) has IF above median in Neurosciences (IF2015 = 2,419). In addition, the last 4 years were years of continuing implementation of 6 large scale projects, which, in conditions of the institution of our size, is exhausting productivity to significant level.

In an effort to increase the activities that support status of the Institute within international context we also prepared and submitted five FP7 and H2020 projects. Unfortunately, none of them was accepted.

- **Supplementary information and/or comments on management, research infrastructure, and trends in personnel development**

Research in the Institute is organized in two departments, with a total of six laboratories:

- Department of Neurodegeneration, Plasticity and Repair
  - Laboratory of neurochemistry and neurophysiology
  - Laboratory of proteomics
  - Laboratory of electrophysiology and functional diagnostics
- Department of Regenerative Medicine and Cellular Therapy
  - Laboratory of cell culture and biomaterials
  - Laboratory of neuroregeneration, neurotransplantation and pharmacotherapy
  - Laboratory of neuromorphology and developmental neurobiology

The Institute of Neurobiology SAS is a vital research institute with a focused research program, experienced research teams and excellent regional cooperation with universities and clinical departments. INb SAS has been succesful in competitions for 6 EU Structural Funds, and we obtained substantial financial resources which were used to modernize our laboratory infrastructure to the standard European level. There is great potential for further development of the Institute. However, it is often limited by external factors.

Since there is no legal way yet to expand the Institute, we are actively looking for possibilities to obtain project resources (from H2020, SF EU, APVV) for some new job positions. In the evaluated period we were able to provide funds for seven postdoc and six technical assistant positions through involvement in EU SF projects.

Another way is our partnership in the University biomedical research and technological park (MEDIPARK). This project has created a platform for mutual collaboration of all important academic institutions in Kosice. There are opportunities here for mixed research teams, joint teams with clinicians, spaces and equipment for special laboratories with necessary certifications (clean rooms, GMO laboratories, etc.). INb SAS is thus an integral part of the biomedical community in Kosice.

However, these short-term solutions are not enough to solve the problem of our future existence satisfactorily. We see a long-term solution in partnerships. All SAS Institutes are going to be transformed into public research institutions in a short time. In 2015 we participated in the process of creating of the SAS Biomedical Research Center. Due to many unsolved problems regarding administration, personnel and account matters connected with our remote geographical location, we did not join the Center at that time. However, we are fully aware that to be part of a biomedically-oriented institution, which is big enough to cover all necessary bureaucracy, to provide all administrative services, and which has much bigger financial and personal buffering capacity, is essential for our future existence.

3. Research strategy and future development of the institute for the next five years (2016-2020) **(**Recommended 3 pages, max. 5 pages)

3.1. Present state of the art in both the national and the international contexts

Neuroscience is one of the fastest-growing areas in biomedical sciences. Brain diseases represent a major public health problem. They may cost as much as 45% of the annual health budget in Europe. With an aging population the prevalence of brain disorders will dramatically increase, and there is an urgent need to find means to reduce their burden and economic impact.

Research at the Institute of Neurobiology has been traditionally focused on neurodegeneration associated with transient ischemia and traumatic injury to the central nervous system. These topics are directly associated with major health problems in Europe. Stroke and trauma are listed among the 12 most costly brain diseases, and their annual costs in Europe are calculated as €22 billion and €3 billion respectively. Acute cerebrovascular diseases occur with an incidence of 200 cases per 100 000 people per year, making them the most frequent organic CNS disorders. In Europe, stroke is the third most frequent cause of death and a leading cause of disability. However, the only effective treatment to have been approved for acute stroke to date is lysis of the clot obstructing the artery that supplies the affected brain region. Future research must focus on those pathophysiological mechanisms which can be influenced by therapeutic strategies in order to prevent or mitigate the development and propagation of ischemic damage.

The number of spinal cord-injured patients in Europe has been estimated at over 500 000. About half of these patients are the victims of traffic accidents, and more than half occur in the 16-30 age group, men being more frequently affected (80%). Spinal cord injury (SCI) leads most frequently to permanent paralysis and a range of serious dysfunctions affecting the bladder, bowel, and reproductive and cardiovascular systems. In SCI, the initial impact results in a primary lesion with axonal disruption and haemorrhage leading to secondary damage mechanisms including inflammation and oxidative stress. There is enormous potential for the further development of neuroprotective strategies which reduce one or more of the key mechanisms involved in secondary tissue damage. The versatility of stem cells and progenitors has led to substantial interest in the use of such cells for transplant-mediated replacement strategies. Since severed axons often have to traverse areas of scar tissue and cystic cavitation at the lesion site, a number of tissue engineering approaches have been explored to bridge the gap, and more sophisticated biomaterials are contributing to this approach.

INb SAS is well equipped to tackle the existing range of research problems. There is a certified animal facility, surgery rooms with stereotaxy and microsurgery equipment, laboratories for histology, immunohistochemistry, biochemistry, molecular biology, proteomics, microscopy, electrophysiology, behavioral testing, and also for cell and tissue cultures.

INb SAS is well embedded in the network of national and international research and academic institutions. We have joint workplaces with P.J.Safarik University and the University of Veterinary Medicine and Pharmacy in Kosice. We are part of the big project of University Science and Technology Park (MEDIPARK) in Kosice, together with all local universities. We have formal agreements and active cooperation with several internationally-recognized research institutions, especially in France, Poland, Ukraine, Spain and Portugal. INb SAS initiated the foundation of the Slovak Neuroscience Society, which is a corporate member of FENS and IBRO. Our effort in international cooperation is to help interconnect neuroscientists and clinicians into a functional center or association for spinal cord injury research. We try to implement this idea through the regular organization of international symposia, where we invite all the relevant authorities.

3.2. Research strategy of the institute in the national and the international contexts, objectives and methods

INb SAS Fundamental Goals

- To achieve better understanding of the nervous system functioning, pathological mechanisms and plasticity after CNS disorders;
- To translate basic discoveries into treatment and recovery promotion from CNS injuries.

Research strategy

As set out in our mission statement, we focus on neuroregeneration research which is aimed at promoting the regrowth and repair of nervous system tissues. This includes the generation of new neuronal cells, cell transplantation as well as promoting axon regrowth and remyelination of damaged neurons. Taking into account the size of the Institute, our strategy is to keep our research focused. For the next four years we have defined three main fields of research:

- Ischemic brain injury – stimulation of endogenous repair mechanisms
- Traumatic spinal injury – minimizing secondary injury
- Cell-based therapy – using cultured cells or secretoma, and study of adult neurogenesis.

Stimulation of endogenous repair mechanisms in injured nervous tissue

One direction of the neuroscience research that has been developed at the Institute of Neurobiology SAS is the study of the phenomenon of ischemic tolerance. Ischemic tolerance represents a complex and relatively undescribed process. Considering the ominous stroke prevalence prediction for the next decade, our scientific interest will be focused on collecting novel information about tolerance from the basic research and to bridge it with clinical data. We have found that the information responsible for induction of tolerance to ischemic conditions in brain tissue is transmitted via circulating blood. This information could be stimulated endogenously, but could be transferred from donor to recipient as well. Our main target in the long-term future will be to elucidate the complex pathophysiological mechanisms underlying the spread of ischemic/ischemic-reperfusion damage to nervous tissue and expansion of the ischemia-triggered destruction process. Effort will be put into finding and effective timing of neuroprotective strategies in various clinical condition-simulated models. Primarily, our research strategies will apply non-invasive and clinically acceptable stimuli to induce tolerance to ischemic condition in two very frequent animal models of brain ischemia. For generalization of relevant results we are expecting novel advanced *in vitro* and *in vivo* approaches and models. Besides detailed description of the metabolic and cellular pathway leading to a tolerant phenotype that is crucial for implementation to practice, we aim to link the relevant data resulting from basic research to real clinical situations; especially for patients affected by weak to moderate stroke and recurrent stroke. The phenomenon of ischemic tolerance represents a conservative process; our results would therefore be applied to other models of acute and chronic diseases of the central and peripheral nervous system.

Objectives:

The main objectives for the next evaluation period are derived from our key findings. Our main effort for the next evaluation period is the characterization and identification of neuroprotective factors circulating in the blood of conditioned animals, detailed description of the pathway leading to their production, and testing of bioreactivity and therapeutic properties with respect to potential application of results in translational research.

Reduction of secondary injury after trauma-injured spinal cord

The outcome of spinal cord injury (SCI) depends on the extent of secondary damage produced by a series of cellular and molecular events initiated by the primary trauma. The final pathohistological lesion is far greater than identifiable in the first few hours after traumatic injury. The extent of secondary injury for many patients is a limiting factor in the subsequent recovery. Intensive research of the pathological changes occurring in the injured spinal cord in recent years has resulted in the identification of many targets for treatment. However, the final results of clinical trials are mostly negative and none of the promising therapies has been fully accepted in clinical practice. To date, there is no efficient and trustworthy clinical treatment available for SCI patients. Repair of the injured spinal cord has to include halting the spread of secondary tissue damage in order to save as many neurons as possible, including the curbing of inflammation, neutralizing inhibitory factors, reducing scar formation, promoting guided nerve fibre growth across the area of injury, and enabling the formation of nerve connections. Based on these factors, a combinatorial strategy is necessary for successful treatment and repair.

It has been suggested that an uncontrolled immune system mediates cell death and inhibits axonal growth in SCI, and requires exogenous control to achieve net benefit. Regulated inflammatory response after SCI in the direction of tissue repair can be more beneficial rather than its blocking, which is a commonly used approach in many experimental works. This supposes that effective treatment for SCI requires a combinatorial approach including regulated inflammatory response together with the promotion of axonal regrowth and guidance.

Objectives:

To focus on the regulation of inflammatory response during development of secondary injury and promotion of axonal regrowth and guidance in time- and dose-dependent manner within acute and chronic phases with the aim of improving neurological function after SCI.

To utilize the beneficial effects of endogeneous (endurance training) and exogeneous (gene therapy) stimulation of neutrophins, rehabilitation and controlled non-invasive muscle electrostimulation as supporting approaches for subsequent recovery.

Cell-based therapy

The incidence of spinal cord injury is far less widespread compared to brain diseases, but its impact on human beings and society is equally important. Despite all efforts and attempts, there is no effective treatment for spinal cord-injured patients. One of the promising challenges is transplantation strategy. Embryonic stem cells have the widest potential due to their pluripotency. Due to the ethical and legal restrictions in this country regarding the use of embryonic cells, we need to focus on stem cells or precursors from adult or fetal sources. We will study the therapeutic potential of cultured cells using several approaches. *Cellular therapy* – we will use neural stem cells (NSCs) and mesenchymal stem cells (MSCs) in cellular therapies to improve clinical outcomes after spinal cord injury (SCI). We will focus on better understanding of neuro-glial interactions and their modifications after SCI. *Acellular therapy* – we will use proteomics analysis to study the complete protein network of cells by analyzing all the proteins produced by these cells, understanding their structure and their functions in CNS injuries. *Biomaterials* – to use tissue engineering with biodegradable polymer scaffolds loaded with different growth-promoting cells (Schwann cells, neural progenitor cells, MSCs) and various growth factors to bridge the gaps, and to promote axonal regeneration and functional restoration in the spinal cord. *Regeneration of peripheral nerve fibers* – to test biosynthetic implants seeded with Schwann cells to repair peripheral nerves, with the plan to use optimized implants to enhance regeneration of nerve fibers in CNS white matter.

Objectives:

To study innovative cell-based approaches (cellular, acellular, biomaterial) targeting the repair and regeneration of neural tissue with the aim of enhancing the regenerability and plasticity of the injured spinal cord. To use neurotransplantation techniques to transplant immature or genetically-modified cells, biomaterial implants, or secretome application.

Adult neurogenesis:
To find an optimal cell replacement therapy, we have to understand the detailed mechanisms of immature neural cell ontogeny. The study of adult neurogenesis (AN) is one of the most exciting and fast-moving fields of neuroscience. Over the last two decades a large amount of data has been obtained on anatomical organization, functional regulation and the integration of newly-born neurons in the main neurogenic areas (the subventricular zone and the subgranular zone). Full understanding of AN is indispensable for its possible exploitation in brain repair. However, many facts and concepts remain still unexplained and unknown. There is also the suggestion that neurogenesis is linked with clinically-relevant problems of neurodegenerative diseases. As the causes of most cases of prevalent neurodegenerative diseases are unknown, we plan to investigate a possible link between altered neurogenesis and neurodegeneration. We have observed that individual processes of neurogenesis can be significantly affected by different exogenous factors like stress and various types of radiation, which can play an important role in neurodegenerative disease development.

Objectives:

To study postnatal development in the neurogenic area with emphasis on the arrangement and role of blood vessels in neuroblast migration and molecules regulating processes of neurogenesis.

To study relationships between specific alterations in adult neurogenesis and early symptoms of some neurodegenerative diseases, which can be a key to better understanding of the role of postnatal neurogenesis in the pathogenesis of neurodegenerative diseases.

New methodological approaches:
Innovation is essential for advancement in basic neuroscience because new technologies and methods can open up new areas of scientific inquiry. The most innovative methodological addition with precise therapeutic potential will be the possibility to work with GMO, to use gene therapies. Within the next five years we plan to use a novel spinal subpial AAV-based gene delivery technique which permits potent spinal parenchymal AAV-mediated transgene expression in experimental animals. This technique has potential for direct clinical application aimed at spinal gene upregulation or silencing in general.
Another methodological addition will be the membrane electrophysiology (patch clamp) for both, tissue slices and cell culture cells. It will bring more detailed view on functional status of the cells (neural progenitors), on responses of the cells to specific agents (ischemic tolerance study) and on molecular mechanisms of such interactions.

Personnel policy
Sustained progress requires not only the translation of scientific ideas toward clinical application, but also an increase in the number of neuroscientists and good communication between researchers doing basic and applied research. There is a gap between young and senior scientists, so the INb SAS has to systematically recruit a diverse and talented scientific workforce and PhD students to sustain the next generation of researchers. We have to ensure that research will be intellectually rewarding and a viable career.

Popularization of science
Since a fundamental part of science financing comes from public sources, we have public accountability. For this reason science popularization is an integral part of our strategy also for the coming period. Our Institute is one of the most active popularizing institutions within SAS. We will keep up well-proven methods of communication with students and the general public (science cafes, presentations, WEBs, media, exhibitions, seminars), as well as trying new ones.

Project proposals submited to 7RP or H2020	2012	2013	2014	2015
Institute as coordinator	0	0	1	0
Institute as participant	1	0	2	1

4. Other information relevant for the assessment

The Institute of Neurobiology SAS has great potential for further development in the future. These are some arguments supporting this view. Our research program is:

- **Worldwide relevant, and socially important** - CNS diseaseas belong to the major health problems in Europe, and their rate is likely to increase. The cost of brain disorders to the European economy is calculated 45% of the annual European health budget and is comparable to that of cancer, cardiovascular diseases and diabetes together. These figures justify the gradual increase in research funding, and attract the attention of current scientific research to this field of biomedicine.
  In developed countries neuroscience is one of the most prestigious and fastest-growing areas in biomedical sciences, and Institutes studying the nervous system belong among the most important research institutions. We are making every effort to bring neurosciences in Slovakia up to their proper level of importance in scientific terms, as well as in the social, economic and public health context.
- **Complementary to the mosaic of Slovak neuroscience and biomedical research** – there is no institution studying the nervous system in such completeness, with emphasis on damaging injuries. There is potential therefore for collaboration in any biomedically oriented consortium.
- **Focused - well defined, multimethod with a long-lasting tradition** – for almost 40 years since its foundation, the basic pillars of INb SAS research program have been CNS injuries, ischemic and traumatic. All methods have been implemented to see the problem in its complexity.
- **Whole institutional** – the whole Institute is focused on the main research plan. Each laboratory studies problems from different aspects but it is directed towards the common aim of CNS injury and repair.
- **Has a regional aspect** - the fact that we are far from the center gives our institution even more important value. INb SAS represents an opportunity for specialized study for the students, a research institution for the qualification growth of clinical staff, and for experimental realization of their ideas. The Institute is a rather attractive place for the students of all universities in Kosice: P. J. Safarik University (Medical and Natural Sciences faculties), the University of Veterinary Medicine and Pharmacy, and also the Technical University for interdisciplinary studies. Last but not least, there is the promotion and popularization of science and neuroscience as a whole. Without such centers the differences between regions would expand, and the regions depopulate.

The Slovak Republic does not have specific legislation regulating research and work with stem cells, embryonic cells, and other progenitor cells. These problems are judged according to other, non-specific laws and regulations, which allow various and ambiguous ways of explication. This creates an ambiguous legal situation without clear and solid definitions. INb SAS will continue to initiate discussions about legislature regulating cell-based research in Slovakia.

For more information, please, see our WEB page: http://www.neurobiology.sk/index.php/en

Košice, 5. 8. 2016

RNDr. Ján Gálik, CSc.
Director of INb SAS