



# Accreditation 2012 – 2015

## Institute of Neurobiology SAS



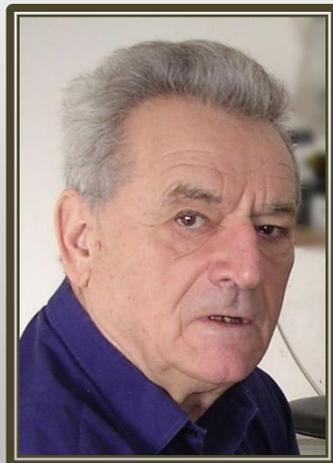
Jan Galik, PhD.

## Introduction to the Institute

The Institute of Neurobiology SAS has its roots in the Institute of Experimental Biology SAS, which was originated in 1964. In 1969, after part of the Institute separated as the Institute of Animal Physiology SAS, **prof. Jozef Marsala, the father of Slovak neurosciences**, became director of the Institute.

Due to substantial changes in the research direction towards neurobiology, namely ischemic injury of nervous tissue, the Institute was renamed to **the Institute of Neurobiology SAS in 1977**.

The main research focus of new institute was cerebral ischemia and it had two main methodological branches – histology and biochemistry



**Today, the Institute of Neurobiology SAS is vital, ambitious institution with focused research plan, good regional cooperation, and it is established in international neuroscience network.**

The two original methodological branches

- histology
- biochemistry

ramified into complex methodological coverage:

- Immunohistochemistry
- Morphology
- Molecular biology
- Proteomics
- Behavioral methods
- Electrophysiology
- In vitro methods
- Cell and tissue culturing



Allowing thus multidisciplinary approach.

During accreditation period the staff of INb SAS was around 40 persons (including PhD students and technical workers). Our institutional budget was about 320 000 €, which covered almost 100% of our salaries, and less than 50 % of expenses for water, energies, building and infrastructure maintenance. All other expenses - full coverage of research projects, and the rest of indirect costs came from competitive sources.

	2012	2013	2014	2015
Institutional budget (income)	323 000 (258 300)	318 000 (258 800)	298 700 (253 900)	314 600 (261 600)
Competitive sources	109 686	129 382	129 235	148 109
SF EU projects	1 031 069	1 201 898	213 692	345 597

During the assessment period INb SAS was successful in obtaining 6 projects supported by EU SF (3 as coordinator, 3 as partner), of which 3.8 million EUR was assigned to our Institute. Within these projects INb SAS obtained financial coverage for 7 postdoctoral and 6 technical assistant positions.

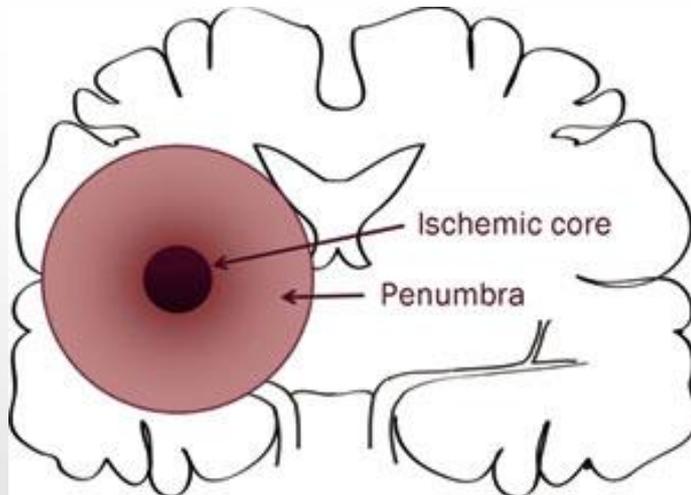
In the past four years 2012 – 2015 our research, which is based on the **study of mechanisms of nervous tissue injury**, was organized into several partially **overlapping** directions:

- ❑ Ischemic tolerance, pre- and post-conditioning of injured CNS tissue
- ❑ Spinal trauma – models and therapy
- ❑ In vitro, cellular and non-cellular therapy, using biomaterial matrices
- ❑ Regeneration of peripheral nerve
- ❑ Postnatal neurogenesis and neural progenitor production

The research is multidisciplinary, and each of these research directions has potential of translational research.

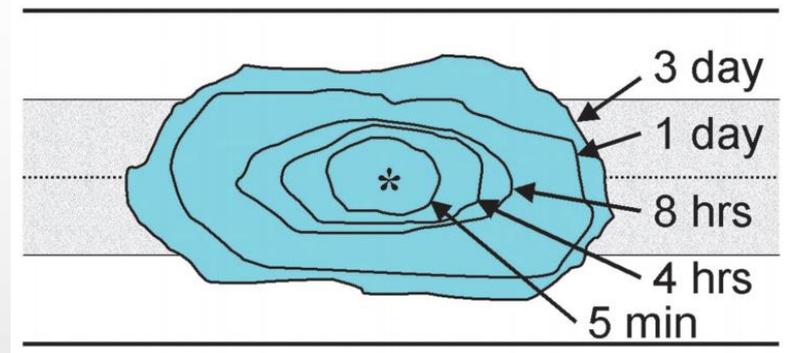


Our research is focused to reduce nervous tissue injury...



~~Ischemic core~~

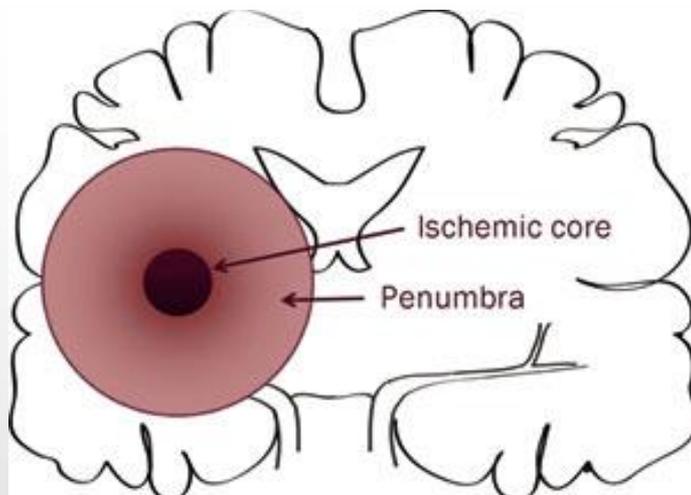
Ischemia affected tissue  
Penumbra



~~Primary injury~~

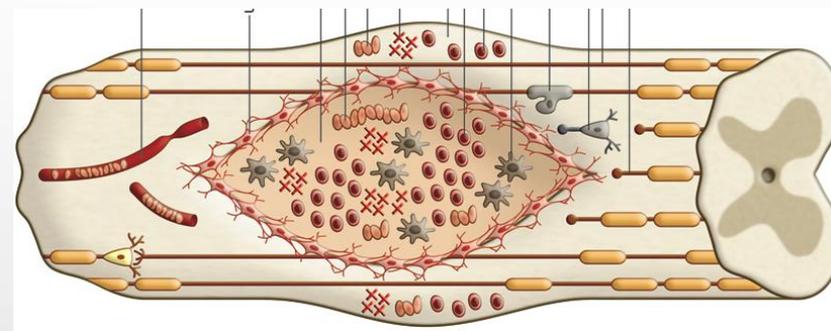
Secondary injury

**Our research is focused to reduce nervous tissue injury...**



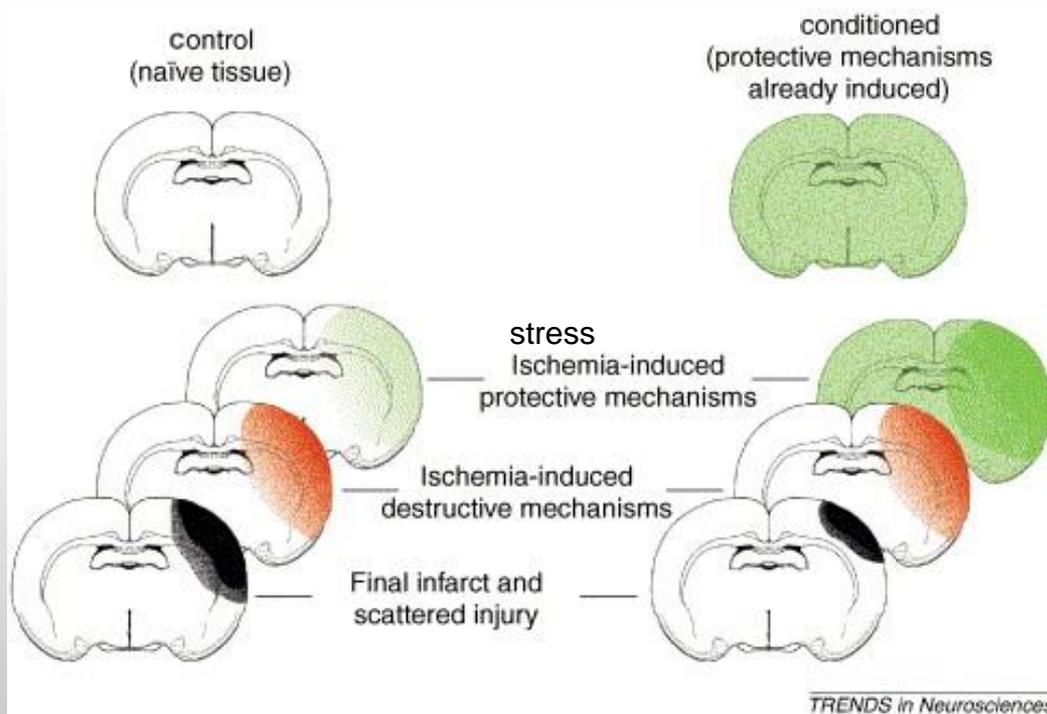
Stimulation endogenous mechanisms  
minimizing excitotoxic and toxic free  
oxygen radicals formation

Conditioning – stimulation of endogenous  
mechanisms of protection



Reduction of excitotoxicity and free radicals production  
Modulation of inflammation and edema  
Blocking adverse glial activity (glial scar)  
Stimulation of myelination and beneficial glial activity

## Conditioning

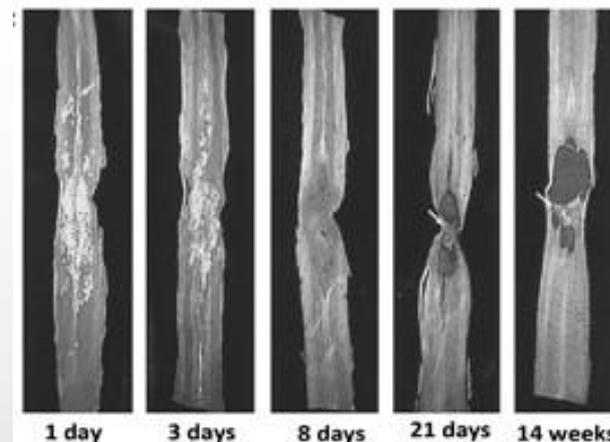
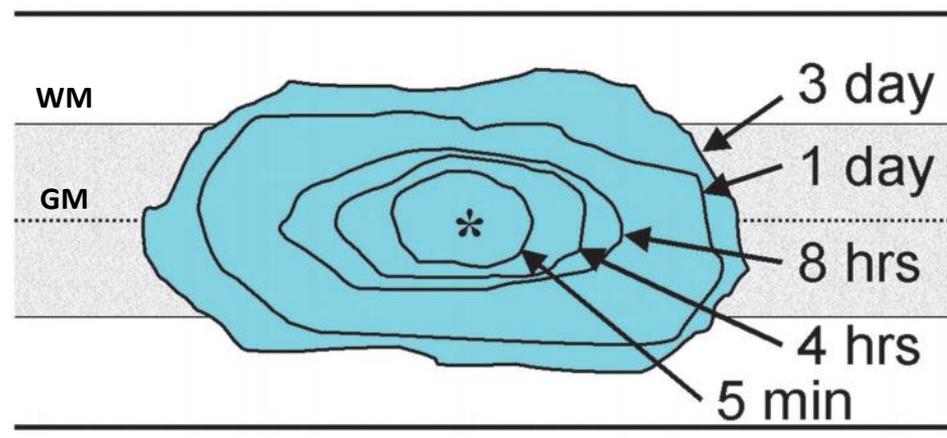


From: Dirnagl U., Simon R.P., Hallenbeck J.M., Ischemic tolerance and endogenous neuroprotection

### Important results

- Neuroprotective signals generated by conditioning are **transmitted to the brain via circulating blood**
- CNS tissue can be protected by **remote conditioning**, e.g. stress to skeletal muscle
- **These findings are important from the clinical point of view. They imply an effective way of therapy for the injured CNS**

## Spinal cord trauma

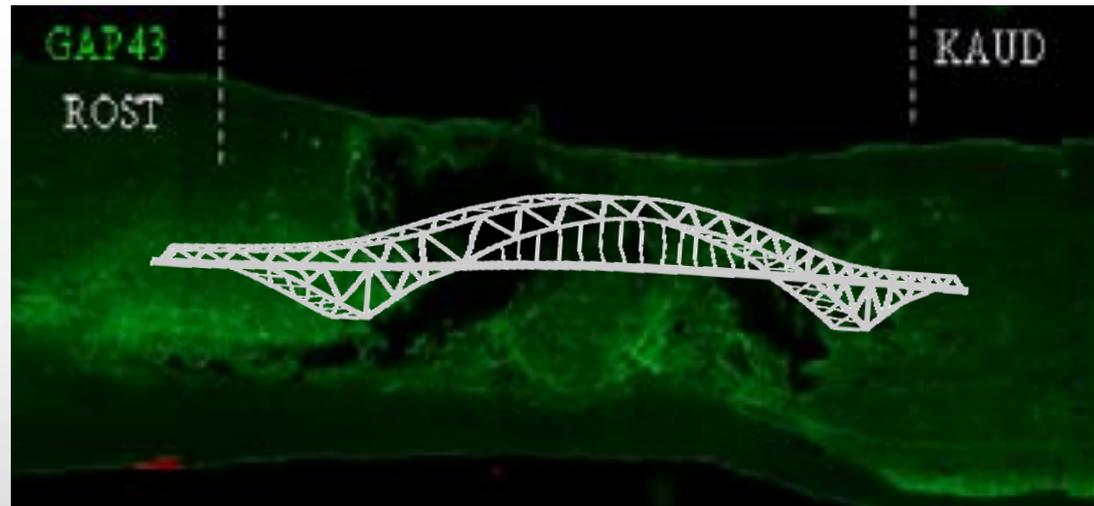


### Important results

Locally applied hypothermia have beneficial effect to edema reduction, and to reduction of secondary injury

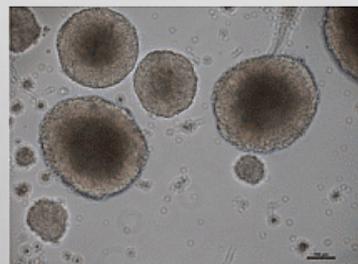
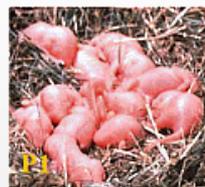
These findings together with methodological description were summarized in a document that was sent as recommendation to the Slovak Ministry of Health

## ... and to recover functionality of injured tissue



- Stimulation of neuroregeneration (trophic factors)
- Stimulation and directing axonal regrowth
- Blocking of axonal growth inhibitory factors
- Biomaterials with cells and/or trophic factors delivery

# Cell and tissue culture



neurospheres formation

tissue dissociation,  
enzymes

single cell suspension



proliferation (bFGF, EGF)/10 DIV

differentiation 14 DIV

(-GFs, +FCS), adhesive substrate

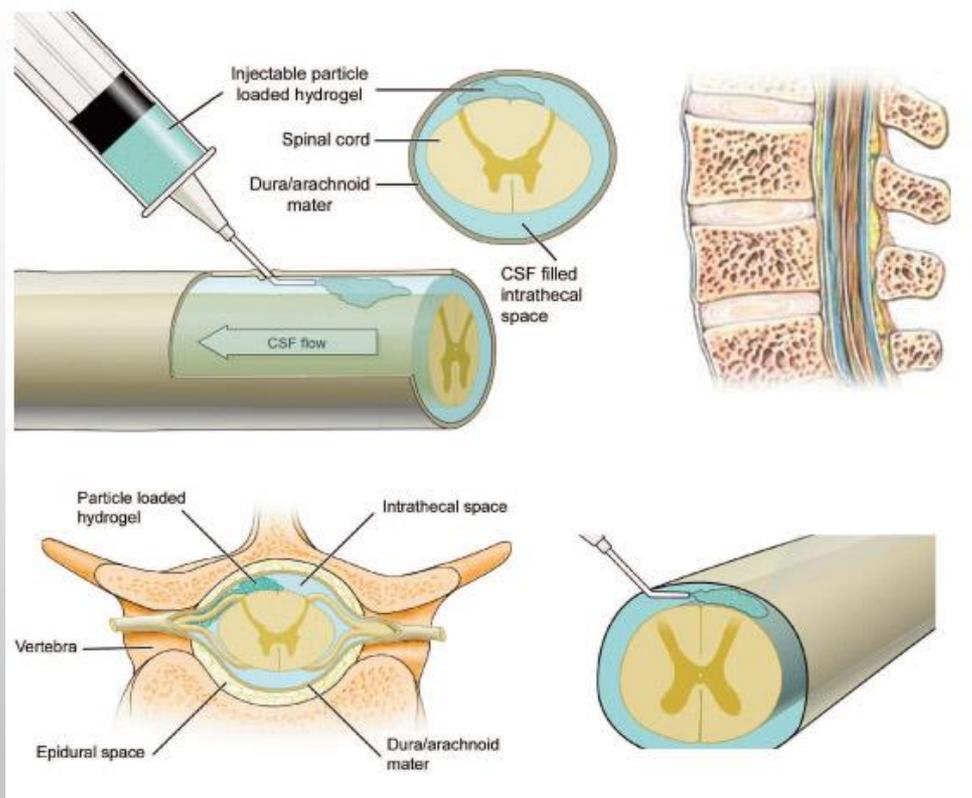
ICCH methods

neurons-MAP2

astrocytes-GFAP

oligodendrocytes-RIP

## Cells and / or biomaterial matrices injection



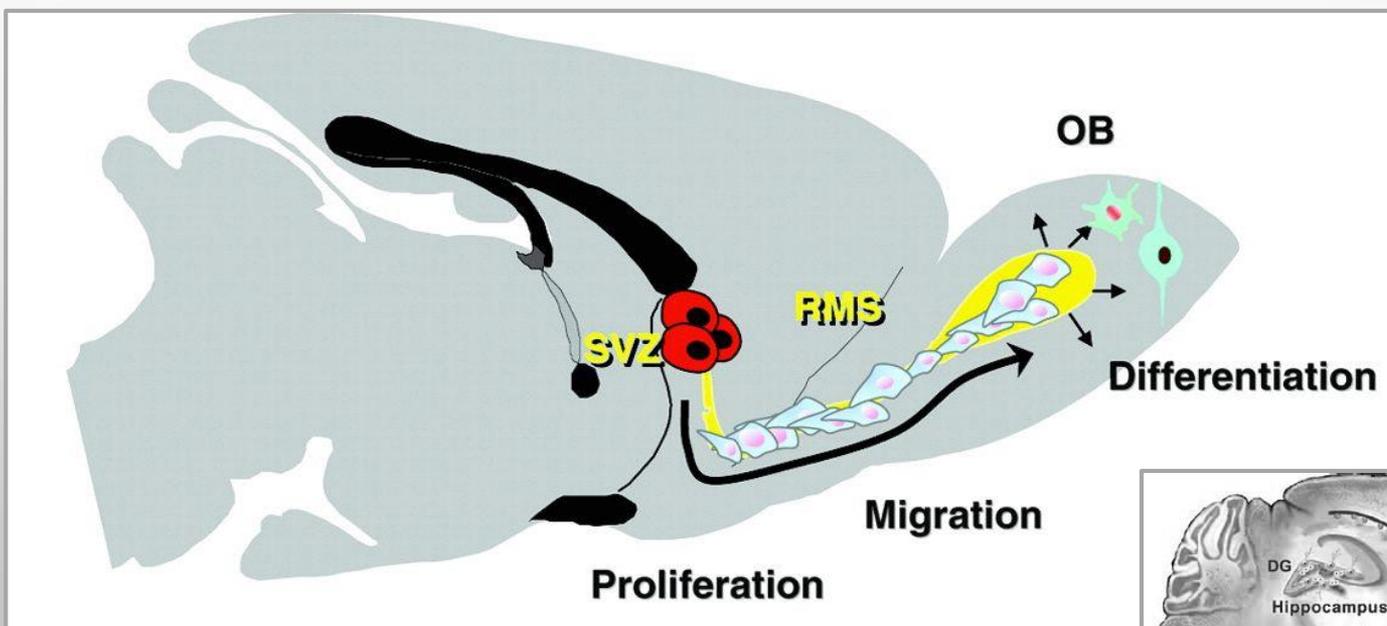
## Important results

- Biomaterial based on alginate, enriched with trophic factors was transplanted in SCI rats.
- Continuous supply of bioactive molecules protected spinal cord tissue – increased number of surviving neurons, outgrowing corticospinal fibers and blood vessels
- These findings correlated with functional behavioral tests
- **These results suggest the possible therapeutic application of active alginate implants with various active molecules for the treatment of spinal cord injury.**

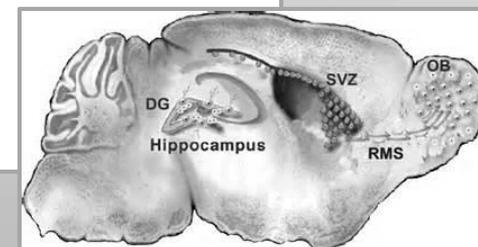
## Adult neurogenesis

Understanding of mechanisms of adult neurogenesis can lead to new therapeutic strategies in the treatment of brain recovery after injury, or in neurodegenerative diseases.

The main source of stem and immature cells is in the brain subventricular zone (SVZ).

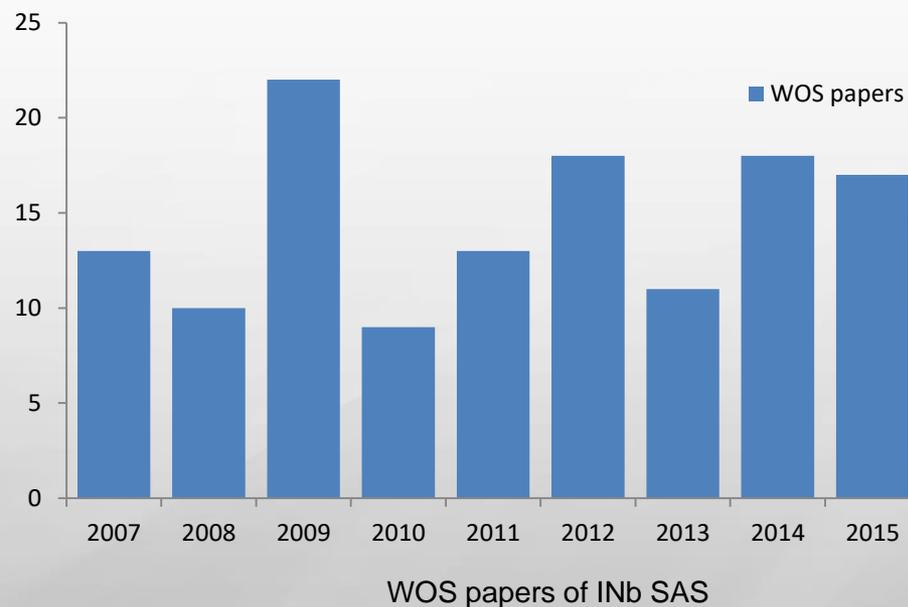


From: Abrous D.N., Koehl M., Le Moal M., Adult Neurogenesis: From Precursors to Network and Physiology., *Physiol.Reviews*, 2005



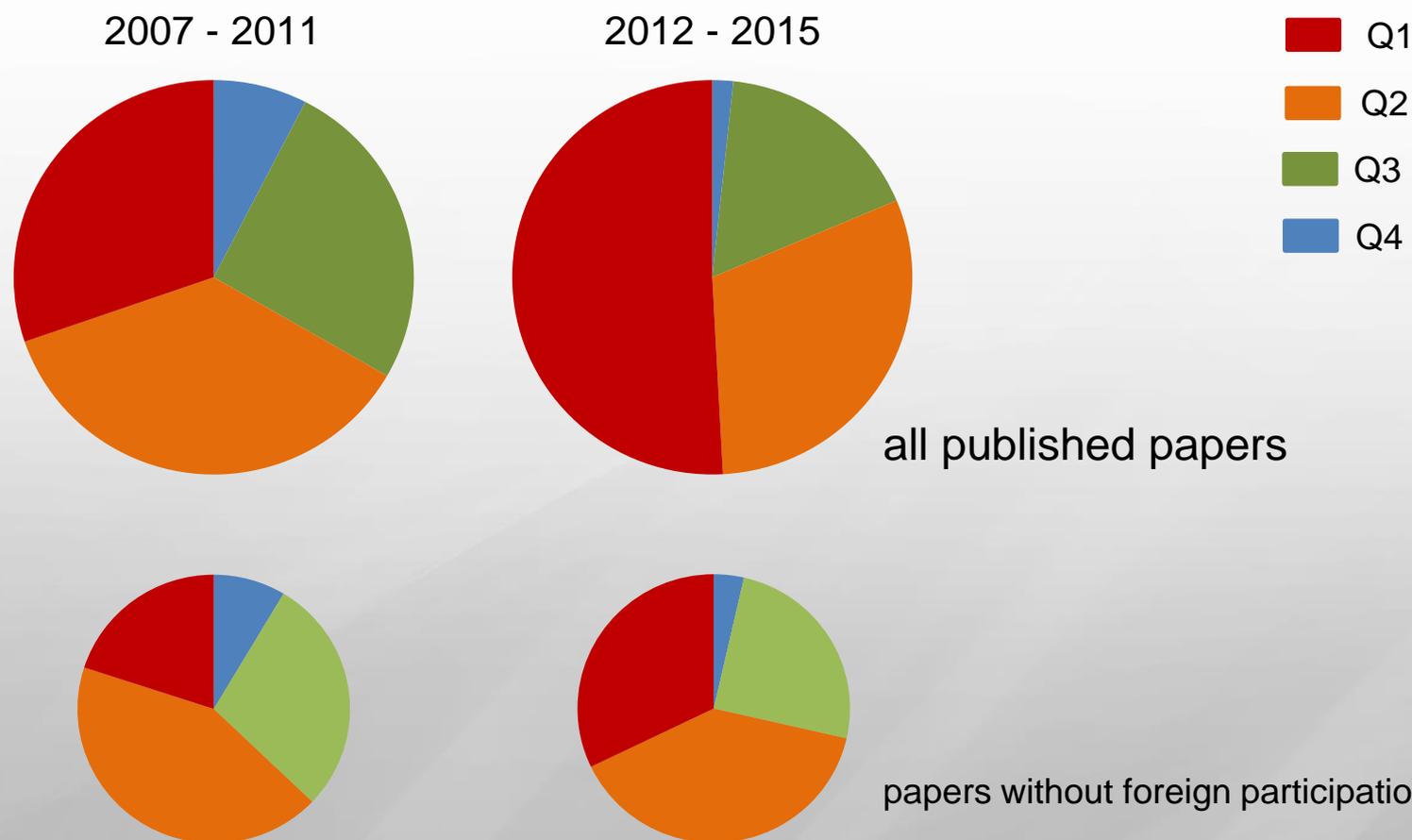
## Research outputs

Annual number of publications during last years is relatively stable, with slight increase in this accreditation period.

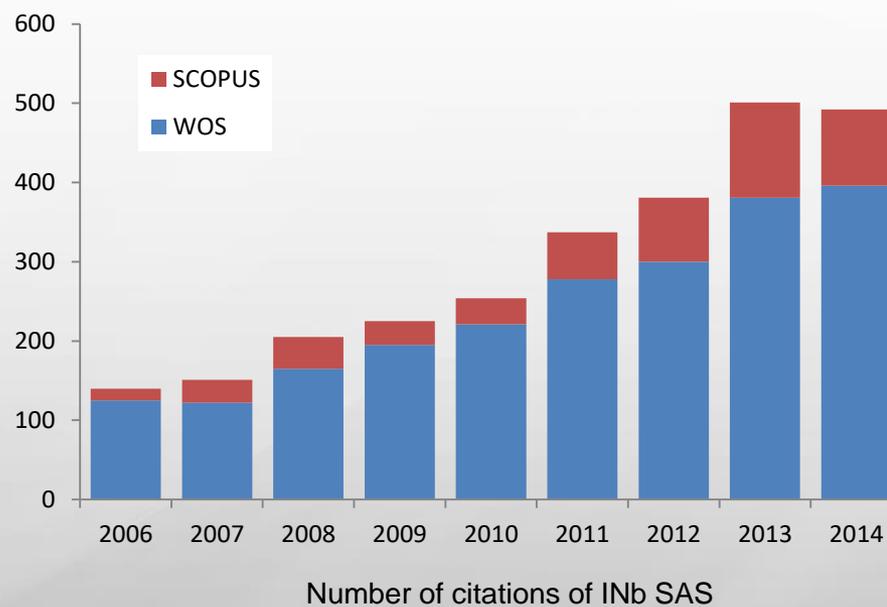


### Comparison in quality of papers since the last accreditation period

Proportions of papers published in journals belonging to different quartiles in Neurosciences



### Increasing quality is reflected in increasing rate of citations



## National collaboration

### Collaboration with universities

- University of P.J. Safarik, Kosice – Medical and Natural Sciences faculties
- University of veterinary medicine and pharmacy, Kosice
- Technical university in Kosice
- Comenius University – Jessenius Medical Faculty
  - Common workplaces
  - Common projects (VEGA, APVV)
  - Pre- and post-gradual education
  - Participation in commissions for bachelor, diploma and dissertation works

### Collaboration with clinical institutions

- Neurosurgery clinic of University Hospital, Kosice
- Tissue bank of the University Hospital of L. Pasteur
  - Participation in big common projects – Neureg, Trauma, Medipark
  - Common research projects (VEGA, APVV)

### International collaboration

- ❑ **Czech Republic:** Institute of Animal Physiology and Genetics AS CzR, Libechov  
Institute of Experimental Medicine AS CzR, Prague
- ❑ **France:** Université de Lille, Lille
- ❑ **Hungary:** University in Szeged, Szeged
- ❑ **Poland:** Medical research center PAS of M. Mossakowski, Warsaw
- ❑ **Portugal:** University of Coimbra, Coimbra
- ❑ **Spain:** Hospital of Ramon y Cajal, Madrid  
University of Alcalá; University del País Vasco, Leioa
- ❑ **Ukraine:** Bogomoletz Institute of Physiology UAS, Kiev
- ❑ **USA:** University of California San Diego, San Diego  
Miller Medical School, Miami  
National Institute of Mental Health, Bethesda  
Neuralstem company, Rockville

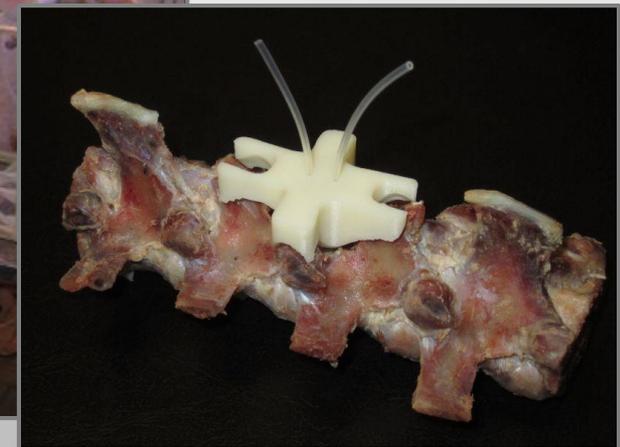
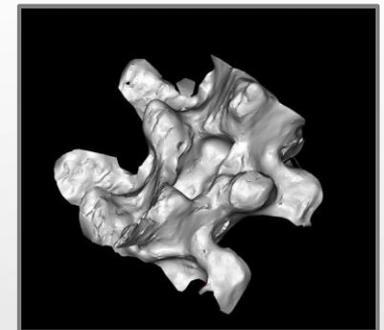
### Research of socially relevant diseases

- ❑ **Stroke and trauma** are listed among the costly brain diseases. In Europe, stroke is the third most frequent cause of death and a leading cause of disability.
- ❑ **Spinal cord injury (SCI)** leads most frequently to permanent paralysis and a range of serious dysfunctions. The number of spinal cord-injured patients in Europe has been estimated at over 500 000.
- ❑ **Adult neurogenesis**, our findings lead to collaboration with psychiatrists to introduce testing of olfaction for diagnosis of some psychiatric diseases and early diagnosis of neurodegenerative disorders.



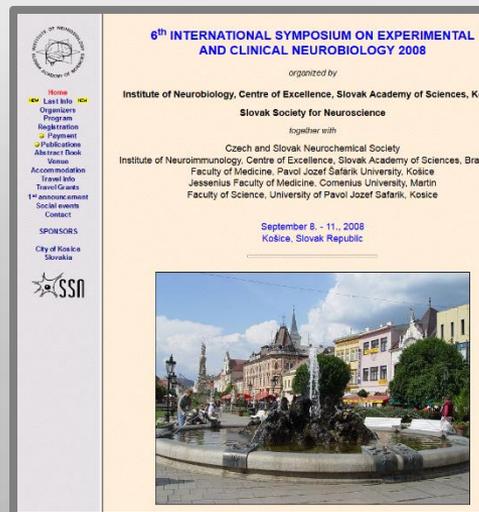
## Social impact

INb SAS participated in **translational projects aimed towards preclinical testing** (funded with EU Structural Funds), which studied the principle of CNS protection by means of conditioning, and the treatment of traumatic spinal cord injury (SCI).



## Organization and support of neuroscience in Slovakia

- ❑ INb SAS initiated and founded the **Slovak Society for Neuroscience (SSN)**, which brought membership to FENS and IBRO to Slovak neuroscientists.
- ❑ INb SAS founded **Association for Support of Neuroscience Research** with the aim to collect extra budget financial resources, and to promote neuroscience in public
- ❑ INb SAS in collaboration with Medical faculty UPJS created the **first post-graduate study program Neuroscience** in Slovakia
- ❑ INb SAS organizes regular **international symposia**, which cover all aspects of neuroscience research



## Science Popularization

Since a fundamental part of science financing comes from public sources, we have accountability towards public. **Science Cafes** organized by INb SAS became part of cultural life in Kosice, also **Days of open Institute** and **Night of researchers** are regular part of educational process of biology teachers in regional secondary schools.



### 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 from CNS injuries

**The vision is the common participation of researchers from INb SAS with clinical experts on clinical tests of effective therapeutic method for treatment of injured CNS tissue, which were based on findings of the Institute of Neurobiology SAS.**

### Research strategy

Research will be oriented on **neuroregeneration**, which is aimed at promoting the regrowth and repair of nervous system tissues. Our strategy is to **keep research focused**, 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



### Objectives

- Identification of neuroprotective factors circulating in the blood of conditioned animals...
- Regulation of inflammatory response during development of secondary SCI...
- Endogeneous (endurance training) and exogeneous (gene therapy) stimulation of neurotrophins...
- Innovative cell-based approaches targeting regeneration of neural tissue...
- Postnatal development in the neurogenic area...
- Relationships between alterations in adult neurogenesis and neurodegenerative diseases...

### Management

Networking – to utilize potential of collaboration on regional level within regional academic and clinical institutions, especially in MEDIPARK project.

Internationally to send young researchers abroad, recruit foreign scientists, organize international symposia, and utilize schemes of EU calls.

Partnerships – with a biomedical oriented institution or consortium, which is big enough to cover all necessary bureaucracy, to provide all administrative services, and which has much bigger financial and personal buffering capacity. It would increase our chance to be successful in obtaining EU grants.

Personnel policy – generational exchange, staff internationalization

### Aim: Increase of productivity of INb SAS in competitive environment

Strengths	Weaknesses
<ol style="list-style-type: none"> <li>1. Long-time tradition in basic research, experienced research teams</li> <li>2. Good instruments infrastructure</li> <li>3. Good regional and international collaboration</li> <li>4. Flexibility in research</li> <li>5. Increasing tendency in citation response</li> </ol>	<ol style="list-style-type: none"> <li>1. Small size of institution, not enough researchers and team leaders</li> <li>2. Publication activity does not match the potential of the Institute</li> <li>3. Absence of supportive infrastructure</li> <li>4. Low effectiveness in obtaining EU projects</li> <li>5. Slow qualification growth</li> </ol>
Opportunities	Threats
<ol style="list-style-type: none"> <li>1. Extra budget financial sources</li> <li>2. PhD students from foreign countries</li> <li>3. Participation in Medipark project</li> <li>4. Location in the region</li> </ol>	<ol style="list-style-type: none"> <li>1. Failures and maintenance of expensive instruments from SF EU.</li> <li>2. Public procurement delays and threats</li> <li>3. Governmental economical priorities (budget, support of grant agencies)</li> <li>4. Legislature – research limiting, economical</li> <li>5. Frequent and too high administrative burden</li> </ol>

**The Institute of INb SAS has great potential for further development in the future. Because our research program is:**

**Worldwide relevant, and socially important** - CNS diseases belong to the major health problems in Europe, and their rate is likely to increase. In developed countries neuroscience is one of the most prestigious and fastest-growing areas in biomedical sciences. We are making every effort to bring neurosciences in Slovakia up to their proper level of importance.

**Complementary to the mosaic of Slovak neuroscience and biomedical research** – there is a potential for collaboration in any biomedical oriented consortium.

**Focused** – well defined, multidisciplinary with a long-lasting tradition – for almost 40 years the basic pillars of INb SAS research program have been CNS injuries.

**Whole institutional** – the whole Institute is focused on the main research plan, each laboratory's study is directed towards the common aim.

**Has a regional aspect** – 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. 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.



Thank you

**Thank you for your attention**