THE SOCIETY FOR THE STUDY OF NEUROPROTECTION AND NEUROPLASTICITY

Academia de Științe Medicale din România

UMF IULIU HAȚIEGANU UNIVERSITY OF MEDICINE AND PHARMACY CLUJ-NAPOCA

TEL AVIV UNIVERSITY

UPPSALA UNIVERSITET

SNR societatea de neurologie din romania

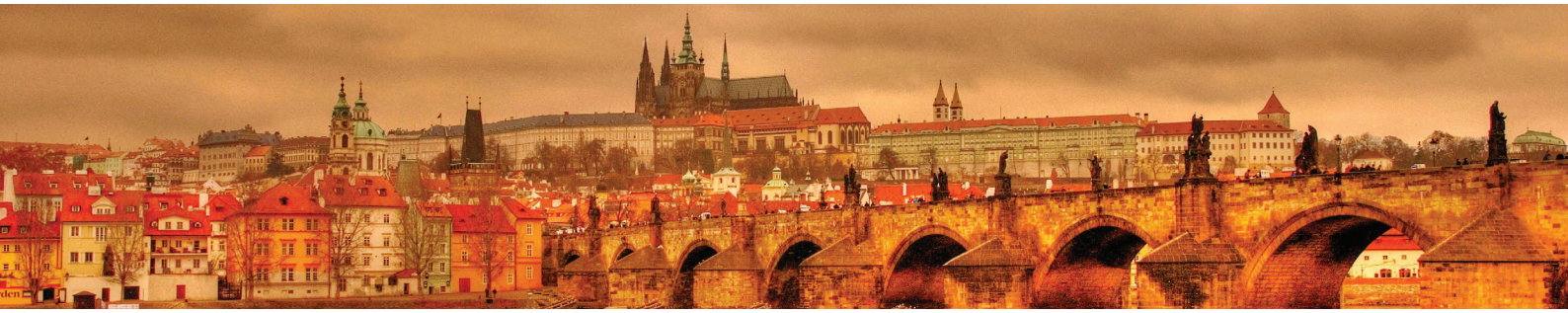
DONAU UNIVERSITÄT KREMS

# 9th CONGRESS OF THE SOCIETY FOR THE STUDY OF NEUROPROTECTION AND NEUROPLASTICITY

## Final Program and Abstract Book

**31 OCTOBER - 3 NOVEMBER 2013**

**Hilton Prague Old Town Hotel | Prague | Czech Republic**



# CONGRESS CHAIRMEN

## Dafin F. Mureşanu

President of the Romanian Society of Neurology

Professor of Neurology, Chairman Department of Clinical Neurosciences, University of Medicine and Pharmacy "Iuliu Haţieganu", Cluj-Napoca, Romania

President of the Society for the Study of Neuroprotection and Neuroplasticity (SSNN)

## Natan M. Bornstein

Professor of Neurology at the Tel-Aviv University Sackler Faculty of Medicine, Israel

Vice President of the World Stroke Organization (WSO)

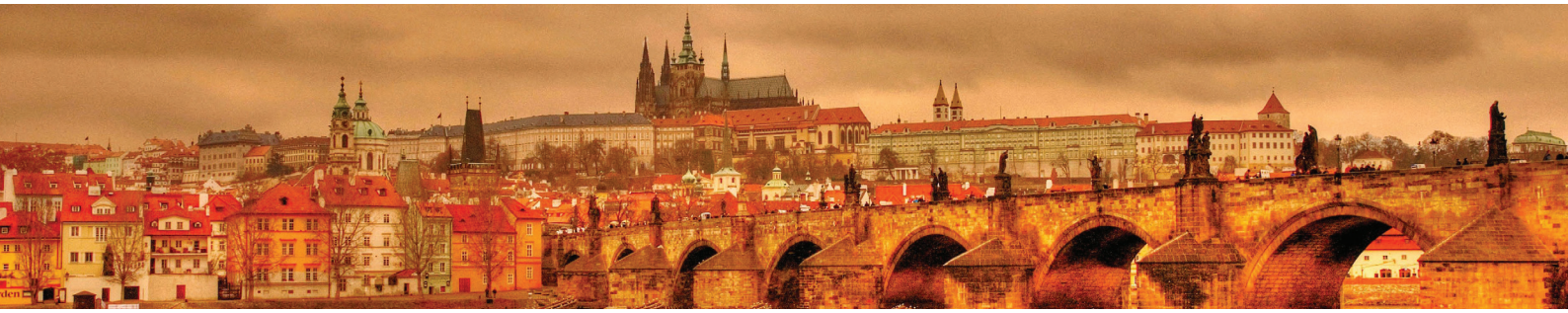
Head of Stroke Unit at the Tel-Aviv Medical Center

Chairman of the Israeli Neurological Association

# FACULTY

/in alphabetical order

Angelo Antonini /Italy
Jaroslaw Aronowski /USA
Leontino Battistin /Italy
Natan Bornstein /Israel
Eva Feldman /USA
Marc Fisher /USA
Natalia Gulyaeva /Russia
Pavel Kalvach /Czech Republic
Amos Korczyn /Israel
Dafin F. Mureşanu /Romania
Michaela Pinter /Austria
Bogdan O. Popescu /Romania
Giorgio Sandrini /Italy
Hari Shanker Sharma /Sweden
Stephen Skaper /Italy
Johannes Vester /Germany
Gregory del Zoppo /USA



# ORGANIZERS

The Society for the Study of Neuroprotection and Neuroplasticity
www.ssnn.ro

Romanian Academy of Medical Sciences
www.adsm.ro

"Iuliu Haţieganu" University of Medicine and Pharmacy Cluj-Napoca, Romania
www.umfcluj.ro

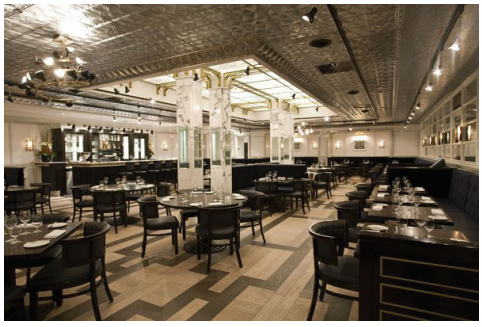
Tel Aviv University
www.tau.ac.il

Uppsala University
www.uu.se

Romanian Society of Neurology
www.neurology.ro

Danube-University Krems
http://www.donau-uni.ac.at/

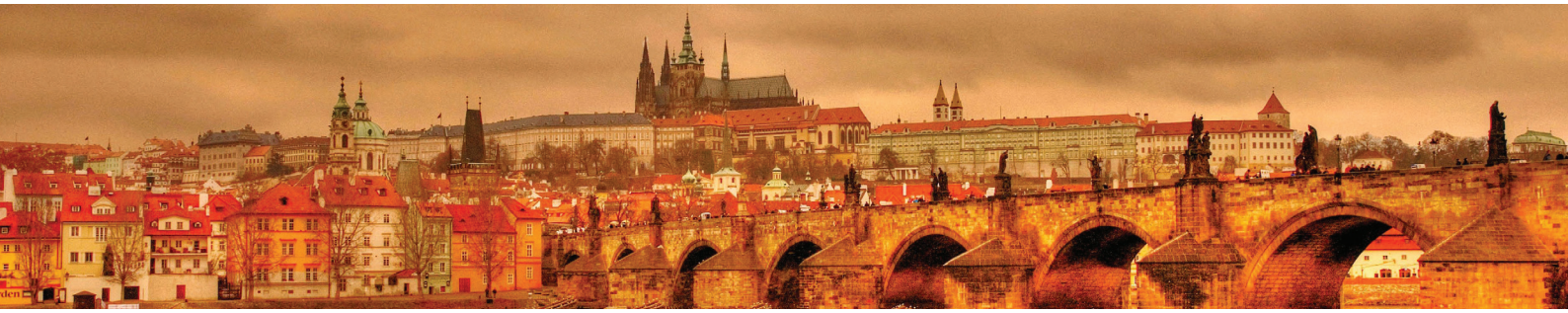
## CONGRESS VENUE



Hilton
PRAGUE OLD TOWN

# HILTON PRAGUE OLD TOWN HOTEL

Hilton Prague Old Town
V Celnici 7, 11121 Prague 1, Czech Republic
Tel: +42 2 218 22100 Fax: +42 2 218 22100
http://www.hiltonpragueoldtown.com/



## Scientific Secretariate

The Society for the Study of
Neuroprotection and Neuroplasticity
Cluj-Napoca, Romania
33A Teleorman Street
Office phone: +40264431924
E-mail:contact@ssnn.ro

## Congress Registration Desk

All congress materials and documentation will be available at the SSNN booth. The congress staff will be pleased to help you with all enquiries regarding registration, congress materials and program.
Please do not hesitate to contact the staff members if there is something they can do to make your stay more enjoyable.

## Registration Fees

The registration fee is 450 Euro.

## Payment Options

Beneficiary Address:

PERFECT TRAVEL

Cluj-Napoca, Str. Teleorman nr. 33/A
Romania
Bank account: RO20DAFB1017001184666EU03
Bank name: BANK LEUMI ROMANIA - CLUJ BRANCH
BIC: DAFBRO22XXX
Bank Adress: Cluj-Napoca, P-ta Unirii nr. 15, Romania

## Contact

If you need further information regarding payment details, please contact:
Doria Constantinescu
doria@perfecttravel.ro
Phone: +40757 096 111

## Participants Registration Fee Includes:

Admission to all scientific sessions during the congress
Conference materials (delegate bag, final program and abstract book etc.)
Admission to Lunches, Dinners and Coffee Breaks

## On-Site Registration

On-site registration will be processed on a first-come, first-served basis.
Priority will be given to pre-registered delegates.
Depending on the number of on-site registered delegates, availability of congress bags may be limited.

## Name Badges

Participants are kindly requested to wear their name badge at all times during the congress.
The badge constiutes admission to the scientific sessions, coffee breaks and lunches.

## Congress Language

The congress language is English.
Simultaneous translation will not be provided.

## Changes In Program

The organizers cannot assume liability for any changes in the congress program due to external or unforeseen circumstances.

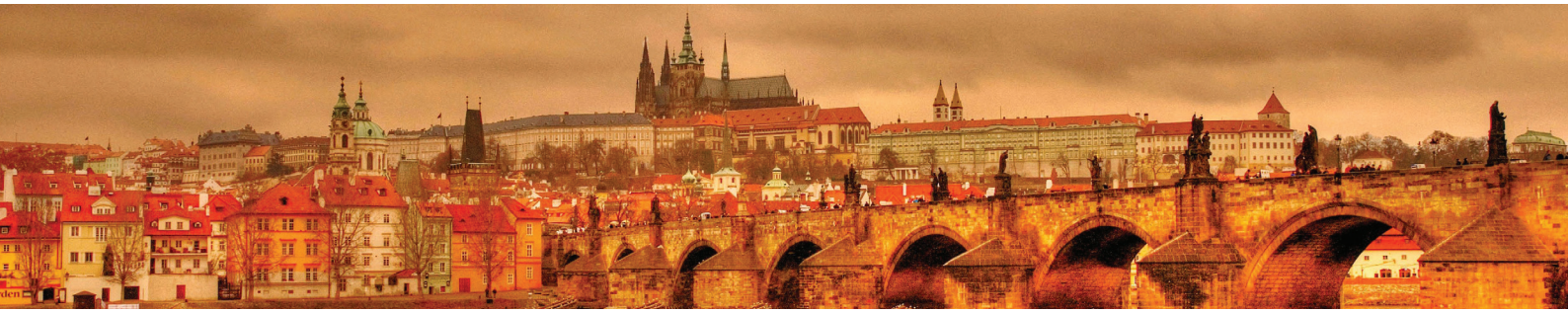
## Contact

If you need further information regarding technical details, please contact:
Ovidiu Selejan/e-mail/ovidius@ssnn.ro
For updates and details please visit our website/www.ssnn.ro

# SCIENTIFIC PROGRAM

# OCTOBER 31ST, 2013

| | |
|---|---|
| 18:50 – 19:00 | Welcome Address<br>Dafin F. Mureșanu (Romania), Natan Bornstein (Israel) |
| Session 1<br>Chairperson: | Natalia Gulyaeva (Russia), Hari Shanker Sharma (Sweden) |
| 19:00 – 19:20 | Hari Shanker Sharma (Sweden)<br>Neuroprotective Effects of neurotrophic factors in Traumatic Brain Injuries. An Experimental Study Using Dose Escalation Study in the Rat |
| 19:20 – 19:40 | Bogdan O. Popescu (Romania)<br>Traumatic Brain Injury:<br>Therapeutic Windows Versus a Therapeutic Continuum |
| 19:40 – 20:00 | Natalia Gulyaeva (Russia)<br>Neuroinflammation in Neuronal Plasticity and Pathology:<br>Focus on Hippocampus |
| 20:00 – 20:20 | Stephen Skaper (Italy)<br>Astrocyte-Microglia Cooperation in the Expression of a Pro-Inflammatory Phenotype |
| 20:20 – 20:35 | Discussions |
| 20:45 | Welcome reception<br>Zinc restaurant & Zinc Bar, Ground Floor |



## NOVEMBER 1ST, 2013

| | |
|---|---|
| Presidential Session Chairperson: | Natan Bornstein (Israel), Dafin F. Mureşanu (Romania) |
| 09:00 – 09:30 | Dafin F. Mureşanu (Romania)<br>CNS Protection and Recovery - The Promise and the Challenges |
| 09:30 – 10:00 | Natan Bornstein (Israel)<br>Stress and Post - Stroke Cognitive Impairment |
| 10:00 – 10:30 | Eva Feldam (USA)<br>Intraspinal Stem Cell Transplantation in ALS |
| 10:30 – 11:00 | Gregory del Zoppo (USA)<br>The Neurovascular Unit and its Susceptibility to Ischemia |
| 11:00 – 11:30 | Coffee Break |
| Session 3 Chairperson: | Eva Feldam (USA), Gregory del Zoppo (USA) |
| 11:30 – 11:50 | Amos Korczyn (Israel)<br>Idiopathic Parkinson's Disease - a Disease or a Syndrome? |
| 11:50 – 12:10 | Angelo Antonini, Leontino Battistin (Italy)<br>The Role of Apomorphine in the Treatment of Parkinson's Disease? |
| 12:10 – 12:30 | Leontino Battistin (Italy)<br>Historical Aspects of Parkinson's Disease and Famous Parkinsonians |
| 12:30 – 12:45 | Discussions |
| 13:00 – 14:00 | Lunch |

| | |
|---|---|
| Session 4<br>Chairperson: | Amos Korczyn (Israel), Giorgio Sandrini (Italy) |
| 14:00 – 14:20 | Marc Fisher (USA)<br>Is there a Future for Neuroprotection? |
| 14:20 – 14:40 | Jaroslaw Aronowski (USA)<br>PPARγ and Nrf2 in Neuroprotection After Intracerebral Hemorrhage and Ischemia |
| 14:40 – 15:00 | Pavel Kalvach (Czech Republic)<br>Natural Aging of Cerebral Parenchyma. Tissue Changes in Imaging. |
| 15:00 – 15:15 | Discussions |
| 15:15 – 15:45 | Coffee Break |
| Session 5<br>Chairperson: | Marc Fisher (USA), Pavel Kalvach (Czech Republic) |
| 15:45 – 16:05 | Giorgio Sandrini (Italy)<br>Stroke Rehabilitation: When to Start and How Long |
| 16:05 – 16:25 | Michaela Pinter (Austria)<br>Role of rTMS in Stroke Rehabilitation |
| 16:25 – 16:45 | Johannes Vester (Germany)<br>A New Start in Traumatic Brain Injury Clinical Research |
| 16:45 – 17:00 | Discussions |
| 20:30 | Traditional Czech Dinner<br>Vikarka Restaurant |

# ABSTRACTS

# THE ROLE OF APOMORPHINE IN THE TREATMENT OF PARKINSON'S DISEASE

ANGELO ANTONIONI

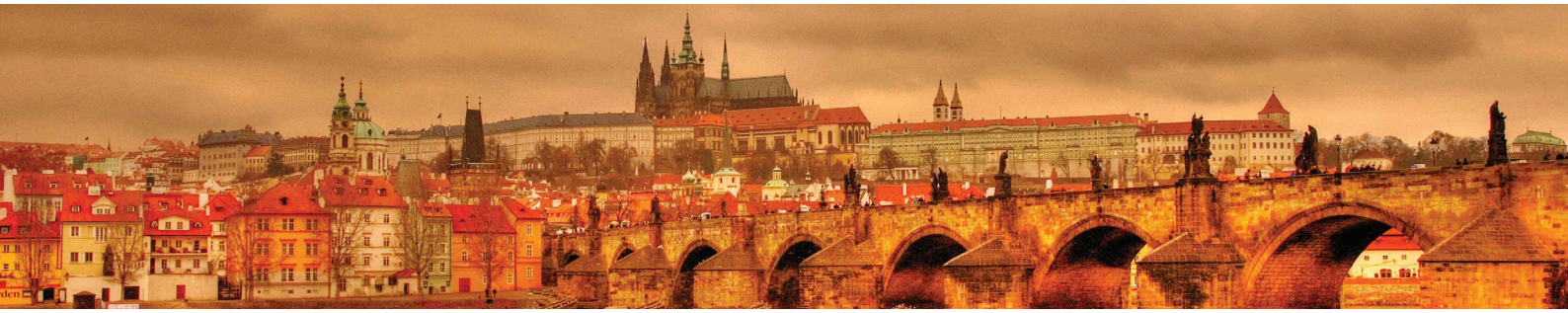
IRCCS San Camillo Hospital, Venice – 1st Neurology Clinic, University Hospital of Padua, Italy

Apomorphine is the oldest dopaminergic medication and was initially known for its emetic properties. It was initially used for Parkinson's disease over 60 years ago but later ignored for many years following levodopa introduction. It is also the most potent dopamine agonist and its administration can provide symptom relief comparable to levodopa. Apomorphine exerts its antiparkinsonian effect by direct stimulation of striatal postsynaptic dopamine D1 and D2 receptors. The drug has a rapid absorption after subcutaneous injection (Cmax 20 min), and a short half-life (almost 43 min), and this is consistent with its rapid onset of action, with effects apparent within 5–15 minutes of subcutaneous administration. Clinical studies and evidence-based reviews generally support a role for apomorphine infusion as an effective option for patients with PD and severe fluctuations, poorly controlled by conventional oral drug treatment with an improvement in OFF-time between 50% and 80% as well as dyskinesia. While the benefit on off time is consistent across all studies, dyskinesia improvement generally occurs after a few weeks or months of continuous dopaminergic stimulation as a result of wider therapeutic window. Moreover it can be best achieved with apomorphine monotherapy that may require high infusion doses.
Intermittent subcutaneous apomorphine (penjet) may instead be suitable for the long-term acute treatment of OFF episodes in patients with advanced PD. Apomorphine injections can be a particularly helpful in the management of patients who undergo surgical procedures and cannot take medication by mouth or to treat additional severe non-motor symptoms occurring during OFF periods.

References:

Antonini A, Tolosa E Apomorphine and levodopa infusion therapies for advanced Parkinson's disease: selection criteria and patient management. Expert Rev Neurother. 2009 Jun;9(6):859-67

Antonini A, Isaias IU, Rodolfi G A 5-year prospective assessment of advanced Parkinson disease patients treated with subcutaneous apomorphine infusion or deep brain stimulation J Neurol. 2011 Apr;258(4):579-85



## PPARγ AND NRF2 IN NEUROPROTECTION AFTER INTRACEREBRAL HEMORRHAGE AND ISCHEMIA

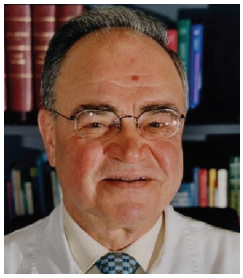
JAROSLAW ARONOWSKI

University of Texas Health Science Center, Department of Neurology, Houston, Texas, USA

Recently transcription factors PPARγ and Nrf2 emerged as new promising targets for the treatment of cerebrovascular diseases including ischemic and hemorrhagic stroke. It is now recognized that besides their established role in metabolic processes in adipose tissue and acute phase response, PPARγ and Nrf2 (respectively) appears to be abundant in the brain where they play a key role in cell signaling in neurons and glia. PPARγ and Nrf2 also act as auspicious pleiotropic regulators of lipid and glucose metabolism, mitochondrial function, inflammation, oxidative stress, differentiation, phagocytosis, cell cycle and cell death. Such amalgam of multimodal biological effect of PPARγ offers a unique suitability for PPARγ and Nrf2 activating agents to help combat manifold pathogenic pathways underlying brain damage caused by stroke.

To study the mechanisms of how PPARγ and Nrf2 may help brain after stroke, we employed pharmacologic agents that alter these transcription factors, as well as neuron- and microglia-specific PPARγ knockout mice. Animal models of ischemic (modeled by the middle cerebral artery occlusion) and hemorrhagic (modeled by intracerebral injection of autologous blood) stroke, as well as tissue culture systems simulating stroke events were employed.

Our in vitro studies indicate that PPARγ and Nrf2 acts as endogenous cytoprotective modulator for most brain cells and protect them from various types of injury. Stroke itself induces expression of PPARγ and Nrf2 while activation of PPARγ or Nrf2 with pharmacological agents protects brain from damage caused by both ischemic and hemorrhagic stroke. In agreement with the notion of these pharmacological studies, mice lacking PPARγ in neurons as compared to control developed more brain damage after ischemic stroke, corroborating an important role of PPARγ in protecting neurons. This increased vulnerability of neurons was associated with impaired expression of PPARγ- and Nrf2- targeted anti-oxidative enzymes and selected mitochondrial protein and coincided with increased oxidative stress in neurons. Increased ischemic injury was also evident in mice lacking PPARγ in microglia. This neuroprotective effect however is likely due to a secondary damage since mice deficient in PPARγ showed increased dysfunction, as compared to wild type mice, only after more than 24h following the stroke. Finally, after hemorrhagic stroke, PPARγ in microglia appeared to help in the cleanup of hematoma from the hemorrhagic brain by improving the efficiency of microglia/macrophage-mediated phagocytosis of erythrocytes and other cellular debris. This PPARγ effect is likely mediated via increased expression of scavenger receptor, CD36 (PPARγ target gene), improved anti-oxidative capacity and reduced pro-inflammatory response.



# HISTORICAL ASPECTS OF PARKINSON'S DISEASE AND FAMOUS PARKINSONIANS

LEONTINO BATTISTIN

Department of Neurosciences, University-Hospital, Padova, Italy

Research Hospital for Neurorehabilitation, IRCCS San Camillo, Venice, Italy

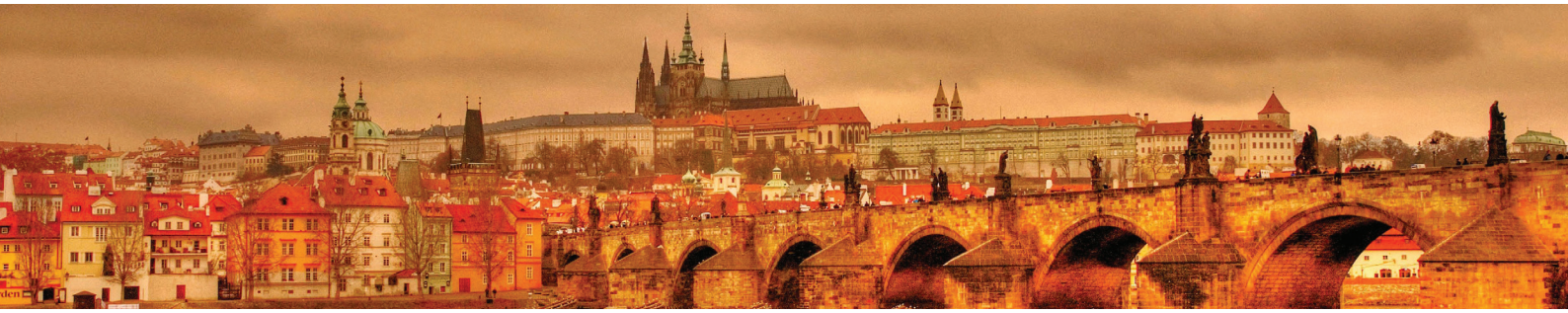
The book "An essay on Shaking Palsy" was published in 1817 by James Parkinson. He was a general physician but with interests also in geology and paleontology. He also was quite active in social and political activities somewhat related to the French Revolution.

Even though his description of the disease was quite precise, his name was linked to the disease only 40 years later by the great Jean Martin Charcot. Nevertheless he received very little attention by the english medical scientific community and in 1912 the american scientist J.G. Rowntree wrote of him "english born, english grown, forgotten by the english and by the entire world, this was the fate of James Parkinson". If this is the official history of this disease, there are facts indicating that such disease was also known in the very ancient history. As a matter of fact, in the indian medicine, that is Ayurveda, there are descriptions of parkinsonian symptoms, named Kampavata, that seems dated 5000 years before Christ; also, it is quoted a tropical legume "Muruna Pruriens" that was found to be a natural source of L-dopa. There are citations of parkinsonian symptoms also in the Bible, both the Old and New Testament, particularly in the Ecclesiaste and Luca Gospel.

There are also descriptions of this disease in the papers of Galeno, but also of Paul of Aegina and of persian medicine. We should also quote the papers of Leonardo da Vinci, and the artistic works of Shakespeare.

During the history, many famous persons suffered of this disease, in all the fields, like science, politics, theatre, sport. So, we'll do a description of some of these personalities, like Francisco Franco, Adolf Hitler, Muhammed Ali, Mao Tse Tung, The Pope John Paul II, Deborah Kerr, Katherine Hepburn, Yasser Arafat, Giovanni Natta, Abdus Salam, Salvador Dalì and others.

Finally, we'll underline that some of these famous people were, or are even now, very much engaged in the social aspects of Parkinson's disease, including the ones related to basic and clinical research in this field and the funds raising for such a research.



# INTRASPINAL STEM CELL TRANSPLANTATION IN ALS

The FDA-approved trial, "A Phase 1, Open-label, First-in-human, Feasibility and Safety Study of Human Spinal Cord-derived Neural Stem Cell Transplantation for the Treatment of Amyotrophic Lateral Sclerosis, Protocol Number: NS2008-1," has been completed in 15 patients with amyotrophic lateral sclerosis (ALS). Our overall objective was to assess the safety and feasibility of stem cell transplantation into lumbar and/or cervical spinal cord regions in ALS. Patient cohorts consisting of 3 ALS patients each followed a "risk escalation" paradigm progressing from non-ambulatory to ambulatory patients receiving unilateral (n=5) or bilateral (n=10 total) lumbar or cervical injections. The final cohort of 3 patients, Group E, received cervical injections and had previously received bilateral lumbar injections. All injections delivered 100,000 cells in a 10 ←l volume, for a dosing range between 500,000 to 1.5 million cells over the 18 surgeries. The procedure was well-tolerated by all patients with minimal perioperative or postoperative complications. Although this was a safety trial, clinical progression was monitored and will be reported. Advanced analyses on Group E outcome data revealed preliminary insight into potential windows of stem cell biological activity and identified assessment measures that closely correlate with disease progression. Overall, results demonstrate that lumbar, cervical and dual-targeted intraspinal transplantation of stem cells in ALS patients is feasible and well-tolerated, supporting future trial phases examining therapeutic dosing and efficacy. Phase 2 of the trial commenced September 2013 and initial results of 3 cervical transplantation surgeries will be reported. This study was funded by Neuralstem, Inc.

EVA FELDMAN[1]

Jonathan D. Glass[2]
Nicholas M. Boulis[3]
ALS Trial
Study Team*

1. Department of Neurology, University of Michigan, Ann Arbor, MI USA

2. Department of Neurology, Emory University School of Medicine, Atlanta, GA USA

3. Department of Neurosurgery, Emory University School of Medicine, Atlanta, GA USA

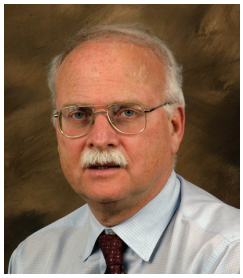
4. Neuralstem, Inc., Rockville, MD USA

5. Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA USA

6. A. Alfred Taubman Medical Research Institute, University of Michigan, Ann Arbor, MI USA

* The ALS Trial Study Team:

Jayna Bordeau[2]
Jayna Duell[1]
Thais Federici[3]
Stephen Goutman[1]
Thomas G. Hazel[4]
Junguk Hur[1]
Karl Johe[4]
Meraida Polak[2]
Seward B. Rutkove[5]
Stacey A. Sakowski[6]

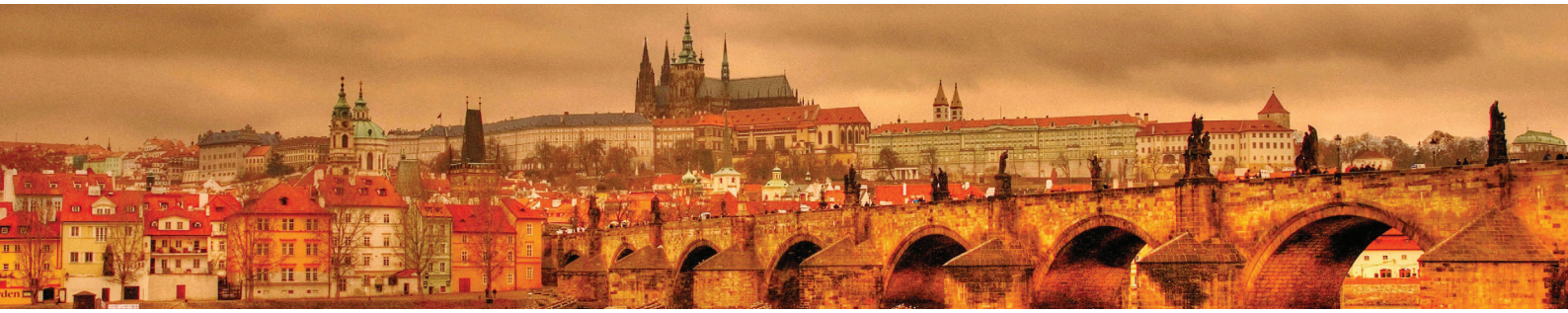


## IS THERE A FUTURE FOR NEUROPROTECTION?

MARC FISHER

Department of Neurology, University of Massachusetts Medical School. USA

All prior drug development programs of neuroprotective agents were unsuccessful for a variety of reasons related to both preclinical assessment and the design/ implementation of clinical trials. The neuroprotection hypothesis of improving functional outcome related to salvaging ischemic brain tissue is strongly supported by robust preclinical data for many agents. In the future, monotherapy neuroprotection trials will be difficult but could be performed in under utilized centers with drugs that have very promising and complete preclinical results. Additional approaches for the testing and use of neuroprotective agents should be considered. Novel approaches would include; extending penumbral survival for the later use of reperfusion therapy, reducing reperfusion injury after successful reperfusion and using drugs with both neuroprotective and recovery enhancing effects as exemplified by granulocyte colony stimulating factor and citicoline. To maximize outcome after stroke, the combined use or reperfusion and neuroprotection is likely to be needed so we need to begin to perform carefully designed trials with this combination.



## NEUROINFLAMMATION IN NEURONAL PLASTICITY AND PATHOLOGY: FOCUS ON HIPPOCAMPUS

NATALIA GULYAEVA

Institute of Higher Nervous Activity and Neurophysiology, Russian Academy of Sciences, Moscow, Russia

Neuroinflammation is regarded as one of common pathways in CNS pathologies, including both neurodegenerative diseases and neuropsychiatric illnesses. Adaptive/beneficial at the first stages, neuroinflammation further becomes deadaptive/detrimental, and recruitment of inflammatory cells is known to drive the secondary damage cascades. Microglia are nervous system-specific cells participating in brain development, maintenance of the neural environment, response to injury, and repair. Microglia facilitate the coordinated responses between the immune system and the brain, assist in synaptic remodeling and plasticity, and is central to mediating the effects of neuroinflammation. Activated microglia release a number of cytokines and chemokines, which in turn activate many signal transduction pathways. An increase in the inflammatory profile of the CNS and altered microglial function has behavioral and cognitive consequences. Hippocampal neurons demonstrate selective vulnerability to different extreme factors, a phenomenon not explained yet. Recently we have shown that an increased susceptibility to inflammatory processes may underlie the vulnerability of hippocampal neurons. Since proliferation process and neuronal differentiation are susceptible to proinflammatory environment, existence of major neurogenic niche in the dentate gyrus also contributes to selective vulnerability of hippocampus.

# NATURAL AGING OF CEREBRAL PARENCHYMA. TISSUE CHANGES IN IMAGING

PAVEL KALVACH[1]

Jiří Keller[2]
Tomáš Peisker[1]

1. Dept. of Neurology, Charles University, 3rd Medical Faculty, Prague, Czech Republic

2. Dept. of Radiology, Hospital Na Homolce, Prague, Czech Republic

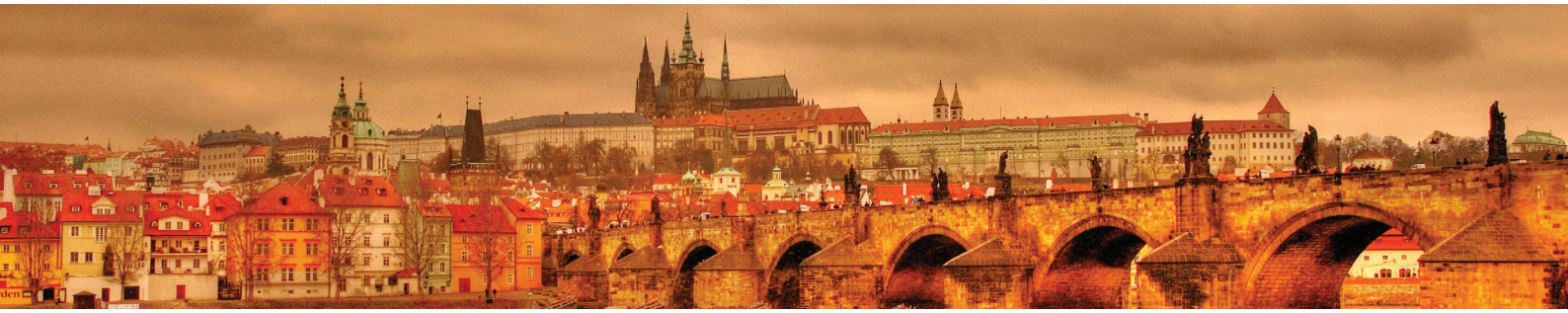
Similarly as all organs of the human body, deteriorating changes affect also our brain already since early adulthood. Research and literature tend to distinguish particular diseases as causes for these gradual deficits. Although such categories are clearly adequate for the presenile dysfunction, they are much less meaningful in advanced age.

In our presentation we review changes in the human brain, detected by neuroradiological investigations along with histological degenerative and ischaemic phenomena reported in literature. Findings, classically considered as typical for Alzheimer's dementia, others, classically reported as typical for vascular dementia as well as those, revealed in other specific dementias bear nevertheless many common features and converge into a complex picture in the advanced senescence. The failing cerebral perfusion is one of its most prominent culprits.

We have carried out measurements of vasoregulatory capacity in 40 elderly "healthy subjects" using ultrasonographic Doppler evaluation of systolic and diastolic velocities in middle cerebral artery. The findings were compared with the intensity of leukoaraiosis in these persons expressed in the Fazekas scale. The capacity for vasodilatation after breath-holding and vasoconstriction after hyperventilation showed only a weak correlation with the intensity of white matter lesions. The most closely associated factor with the extent of leukoaraiosis appeared to be the index of peripheral resistance. Our search in literature resulted into a new knowledge, that the blood supply to the whole hemisphere is not the crucial phenomenon, but rather its disproportional distribution to the white and gray matter respectively.

Besides we also collected pilot measurements of cerebral mean diffusivity and fractional anisotropy in persons with leukoaraiosis, along with recording their cerebral perfusion in the gray and white matter by arterial spin labeling.

Our findings, demonstrating the increase of mean diffusivity (MD) and decrease of fractional anisotropy (FA) in leukoaraiosis, corresponding with districts of reduced cerebral blood flow will be interpreted as a consequence of the failing vasoregulation specifically in the white matter. The neuroradiological features will be presented in correlation with histological deterioration of this tissue.



# IDIOPATHIC PARKINSON'S DISEASE - A DISEASE OR A SYNDROME?


AMOS KORCZYN

Department of Neurology, Tel-Aviv University Medical School, Ramat Aviv, Israel



Many different nosological entities can lead to parkinsonism. Sometimes, the etiology and mechanisms are known and understood (vascular, neuroleptic, Mendelian genetic, post-intectious etc). Among the neurodegenerative diseases causing parkinsonism, a large number are termed idiopathic Parkinson's disease (IPD). Lately, polymorphisms in severel genes have been established as being related to IPD. These cases are thought to be caused by a heterogeneous combinations of contributions of several genes and environmental factors.

The Mendelian genes causing Parkinson's disease (PD) can be divided to these related to mitochondrial dysfunction and oxidative stress, proteasome dysfunction and protein mishandling, lysosomal dysfunction, etc. Several other lines of evidence – biochemical, pharmacological etc. support the separation of mechanisms.

It is suggested that IPD is actually a clinical syndrome, caused by a heterogeneous combination of different genetic and environmental factors. Thus, primary disease prevention is impractical. Downstream changes, like apoptosis, are also unlikely targets for intervention. However, using metabolomics, therapy against the process responsible for the neurodegeneration is feasible, leading to disease course modification.

# CNS PROTECTION AND RECOVERY - THE PROMISE AND THE CHALLENGES

DAFIN F. MUREŞANU

Chairman Department of Clinical Neurosciences

University of Medicine and Pharmacy "Iuliu Hatieganu", Cluj-Napoca, Romania

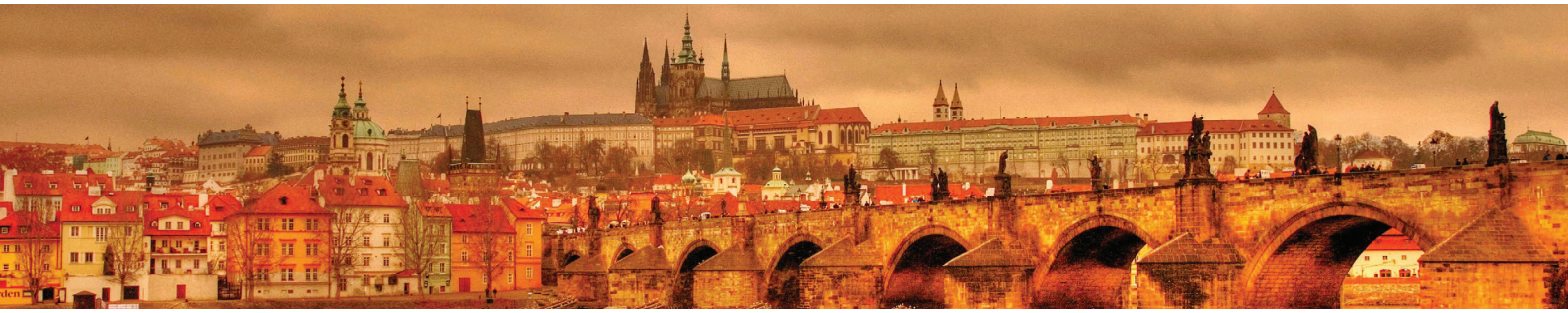
Neurological disorders, especially stroke, traumatic brain and spinal cord injuries, as well as degenerative diseases, represent a leading cause of long term disability all over the world. Many advances have been done in the treatment of these pathologies, mostly confined to acute phase, especially in stroke (e.g. thrombolysis, mechanical recanalization, augmentation of cranial perfusion, etc). The need to identify therapeutic methods, able to limit brain and spinal cord damage or enhance recovery of motor function through neuroprotective and neurorestorative mechanisms when administered at later time points, is desirable. Neurorecovery is the positive outcome that produces clinically relevant results with immediate functional and late structural effects. Neurorecovery depends on the adaptive plasticity of the undamaged nervous tissue, and of the non-affected elements of functional network. Initial size and location of injury are the main factors that determine the extent of recovery in brain and spinal cord lesions.

Neurorecovery can be enhanced by pharmacological intervention, physical activity, electromagnetic stimulation, psychological support, environmental stimulation or any demonstrated combinations of these factors capable of improving the patient's condition after brain and spinal cord injuries. From the pharmacological perspective, it is clear that the focusing on molecules that are capable of mimic the function of endogenous molecules with multimodal and pleiotropic neuroprotective effects is the best approach in neurorecovery, especially when they are associated with intensive physical training.

Biological agents (e.g., neurotrophic factors and related molecules) with modulating and multimodal effects are better pharmacological agents for brain and spinal cord protection and recovery, because they usually have also pleiotropic neuroprotective effect. That is why they are capable of pharmacologically bridging acute neuroprotective processes with the long-term recovery processes.

There are many animal and human studies trying to elucidate the cellular and molecular mechanisms of plasticity of the nervous system. A better understanding of the mechanisms underlying the neuroplasticity will reflect in a more efficient and comprehensive treatment.

This presentation will focus on the validity of different methods able to stimulate neurorecovery after brain lesions.



## ROLE OF rTMS IN STROKE REHABILITATION


MICHAELA PINTER

Professor of Neurorehabilitation –Research at the Danube University Krems, Austria

Deputy Head of the Department for Clinical Neuroscience and Preventive Medicine

Scientific Consultant of the Neurological Rehabilitätation Centre Allentsteig, Austria


In recent years, efforts have focused on investigating the neurophysiological changes that occur in the brain after stroke, and in developing novel strategies such as additional brain stimulation to enhance sensorimotor and cognitive recovery.

In the 1990s, repetitive transcranial magnetic stimulation (rTMS) was introduced as a therapeutic tool for improving the efficacy of rehabilitation for recovery after stroke. It is evident that disturbances of inter-hemispheric processes after stroke result in a pathological hyperactivity of the intact hemisphere.

The rationale of using rTMS as a complementary therapy is mainly to decrease the cortical excitability in regions that are presumed to hinder optimal recovery by low frequency rTMS delivered to the unaffected hemisphere, while high frequency rTMS delivered to the affected hemisphere facilitate cortical excitability. However, the exact mechanisms of how rTMS works are still under investigation.

There is a growing body of research in stroke patients investigating the effect of rTMS in facilitating recovery by modifying cortical and subcortical networks. Clinical trials applying rTMS already yielded promising results in improving recovery of sensorimotor and cognitive functions.

All together, in combination with conventional therapeutic approaches rTMS has a potential to become a complementary strategy to enhance stroke recovery by modulating the excitability of targeted brain areas.

In future studies, emphasis should be placed on selecting patient populations to determine whether treatment response depends on age, lesion acuteness, or stroke severity. Furthermore, it is important to identify parameters optimizing the beneficial effects of rTMS on stroke recovery, and to monitor their long-term effects.


Keywords: repetitive transcranial magnetic stimulation, stroke rehabilitation.

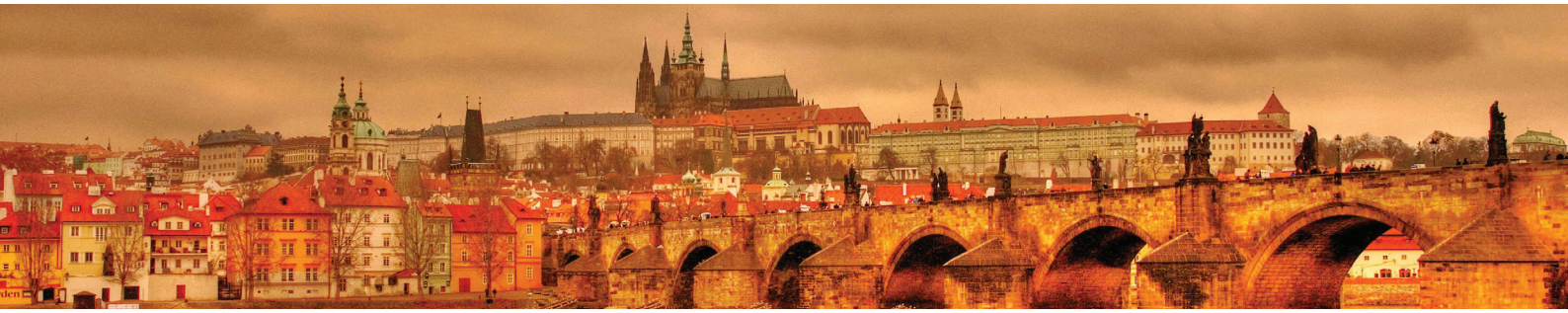
# TRAUMATIC BRAIN INJURY: THERAPEUTIC WINDOWS VERSUS A THERAPEUTIC CONTINUUM

One of the leading causes of death and disability in young adults remains the traumatic brain injury (TBI). Unfortunately, past and recent clinical trials in TBI did not identify an efficacious therapeutic intervention in the acute phase, able to rescue significant brain tissue and prevent death or permanent invalidity. Neuroprotection is still considered an important strategy for TBI, targeting deleterious biochemical reactions which induce secondary tissue damage. In this paper I will discuss therapeutic targets in TBI and I will focus on neurotrophic factors, brain-self multimodal molecules involved in regulation of apoptosis, cell signaling, synapse maintenance and neuroplasticity. I will also summarize the concept of therapeutic time windows and introduce the concept of a therapeutic continuum.

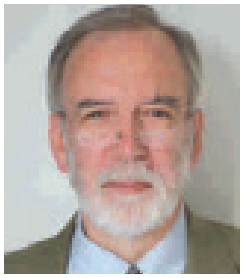
BOGDAN O. POPESCU

Department of Neurology, Colentina Clinical Hospital – CDPC, School of Medicine, 'Carol Davila' University of Medicine and Pharmacy, Bucharest, Romania

Department of Molecular Medicine, 'Victor Babes' National Institute of Pathology, Bucharest, Romania



# STROKE REHABILITATION: WHEN TO START AND HOW LONG




GIORGIO SANDRINI

Department of Neurological Rehabilitation
IRCCS "C. Mondino" Foundation, Institute of Neurology
University of Pavia, Pavia, Italy


In spite of the large number of patients suffering from stroke and the great number of studies documenting the efficacy of rehabilitation in those patients, when to start rehabilitation after acute stroke is often argument of debate In several cases, initiating rehabilitation in acute phase post-stroke appears to be influenced by patients clinical characteristics (degree of lesion, critical conditions, etc.) and living circumstances.
Patients treated in stroke unit present a better outcome when compared with the other patients.

Early verticalization seems to be able to improve gait recovery.
Preliminary evidence about the efficacy of robotics used in early phase in post-stroke patients are reported in literature.
On the other hand, the duration of treatment is equally a controversial argument.
In particular, in the last years numerous studies investigated the efficacy of rehabilitation in so-called "chronic stroke"

Very recently brain imaging studies on patients with chronic stroke have shown evidence for reorganization of areas showing functional plasticity after a stroke, showing that structural plasticity is possible even after 6 months.
Several rehabilitation approaches were proposed in chronic stroke, including telerehabilitation.

Due to the high cost of a long lasting treatment new approaches were proposed, including adapted physical activity.
New technologies could be useful for improving recovery, including cognitive function, in chronic stroke .

# NEUROPROTECTIVE EFFECTS OF NEUROTROPHIC FACTORS IN TRAUMATIC BRAIN INJURIES. AN EXPERIMENTAL STUDY USING DOSE ESCALATION STUDY IN THE RAT

HARI SHANKER SHARMA[1]

Dafin F. Muresanu[2]
Ranjana Patnaik[3]
Herbert Mössler[4]
Aruna Sharma

1. Laboratory of Cerebrovascular Research, Department of Surgical Sciences, Anesthesiology & Intensive Care Medicine, Uppsala University Hospital, Uppsala, Sweden.

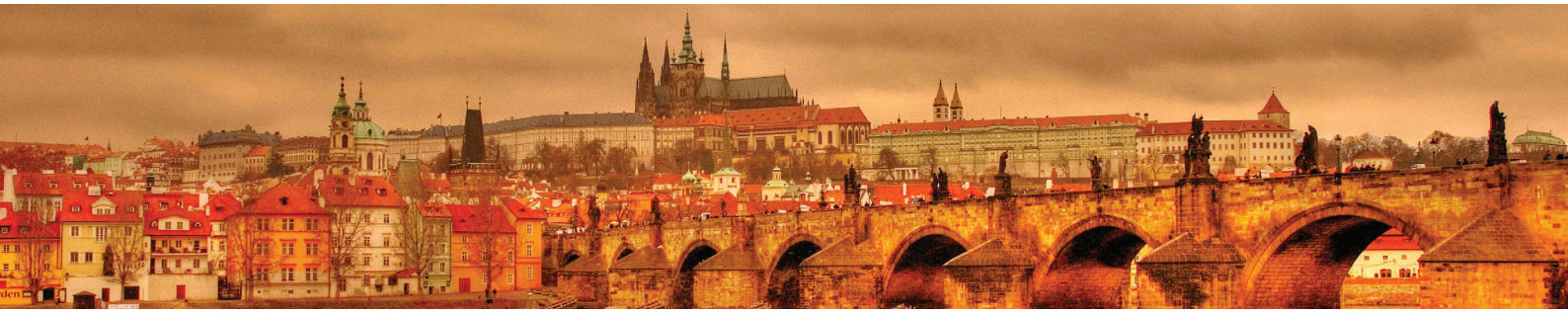
2. Dept of Neurosciences, University Hospital, University of Medicine & Pharmacy, Cluj-Napoca, Romania

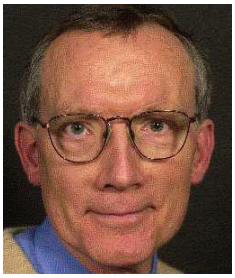
3. Dept.Of Biomaterials, School of Biomedical Engineering, Indian Institute of Technology, Banaras Hindu University, Varanasi, India.

The possibility that neurotrophic factors could induce neuroprotection in traumatic brain injuries in a dose related matter was examined in this investigation in rat models. Traumatic brain injuries (TBI) was produced in anesthetized rats by opening of the right and left parietal bone (4 mm2) and making a longitudinal lesion of the cerebrla cortex (about 3 mm deep and 5 mm long). In another model of concussive brain injury, a blunt force of 0.224 N was delivered on the right parietal bone on the intact skull by dropping a weight of 114.6 g from the 20 cm height through a guided tube. These animals were allowed to survive 5 h after injury. In a separate group of rats Cerebrolsyin was given in a dose escalated fashion (see below). In these traded or untreated animals, blood-brain barrier function, brain edema, neuronal injuries as well as behavioral dysfunction using standard sensory motor dysfunction was examined using well-established protocol in our laboratory.

The biochemical and physiological data suggest that neurotrophic factors up to certain extent (2.5, 5 and 10 ml/kg equivalent doses) induced a dose dependent neuroprotection and attenuated behavioral dysfunction following brain injuries. However, further escalation of the dose ca. 10 ml/kg to 15 ml/kg (equivalent doses) no greater effects were seen on these pathophysiological or behavioral parameters examined in our model. This suggests that neurotrophic factors in a dose of 10 ml/kg appears to be maximum effective in attenuating traumatic brain injuries induced brain pathology. Interestingly, when these escalated doses are given after 30 min to 4 h after brain injury the beneficial effect was still observed on pathology and sensory motor function up to 12 h after trauma. Moreover when repeated doses were administered starting from 4 h to 12 h after injury, the beneficial effects are present until 24 h after trauma.

These observations are probably the first to show that neurotrophic factors have has a dose-response effects and repeated administration after injury could still be beneficial for long time as the drug is able to thwart brain pathology and behavioral dysfunction after trauma 12 h after the last dose given





# ASTROCYTE-MICROGLIA COOPERATION IN THE EXPRESSION OF A PRO-INFLAMMATORY PHENOTYPE


STEPHEN SKAPER

Massimo Barbierato
Laura Facci
Carla Argentini
Carla Marinelli
Pietro Giusti

Dipartimento di Scienze del Farmaco, Università degli Studi di Padova, 35131 Padova, Italy



Inflammation is fundamentally a protective cellular response aimed at removing injurious stimuli and initiating the healing process. However, when prolonged, inflammation overrides the bounds of physiological control and eventually becomes destructive. Inflammation increasingly surfaces as a key element in the pathobiology of chronic pain, neurodegenerative diseases, stroke, spinal cord injury, and perhaps even neuropsychiatric disorders. Glial cells not only serve supportive and nutritive roles for neurons, but also respond to protracted stress and insults by up-regulating inflammatory processes. The complexity of studying glial activation in vivo has led to the widespread adoption of in vitro approaches, for example the use of the bacterial toxin lipopolysaccharide (LPS, a ligand for toll-like receptor 4 (TLR4)) as an experimental model of glial activation. Astrocyte cultures frequently contain minor numbers of microglia, which can complicate interpretation of responses. In the present study, enriched (<5% microglia) astrocytes cultured from neonatal rat cortex, spinal cord and cerebellum were treated with the lysosomotropic agent L-leucyl-L-leucine methyl ester to eliminate residual microglia, as confirmed by loss of microglia-specific marker genes. L-Leucyl-L-leucine methyl ester treatment led to a loss of LPS responsiveness, in terms of nitric oxide and cytokine gene up-regulation and mediator (pro-inflammatory cytokines, nitric oxide) output into the culture medium. Surprisingly, when astrocyte/microglia co-cultures were then reconstituted by adding defined numbers of purified microglia to microglia-depleted astrocytes, the LPS-induced up-regulation of pro-inflammatory gene and mediator output far exceeded that observed from cultures containing the same numbers of microglia only. Similar behaviors were found when examining interleukin-1ß release caused by activation of the purinergic P2X7 receptor. Moreover, comparable results were obtained with engagement of TLR2 and TLR3, pointing to the generality of this phenomenon. Given that astrocytes greatly outnumber microglia in the central nervous system, these data suggest that a similar interaction between microglia and astrocytes in vivo may be an important element in the evolution of an inflammatory pathology.

## A NEW START IN TRAUMATIC BRAIN INJURY CLINICAL RESEARCH

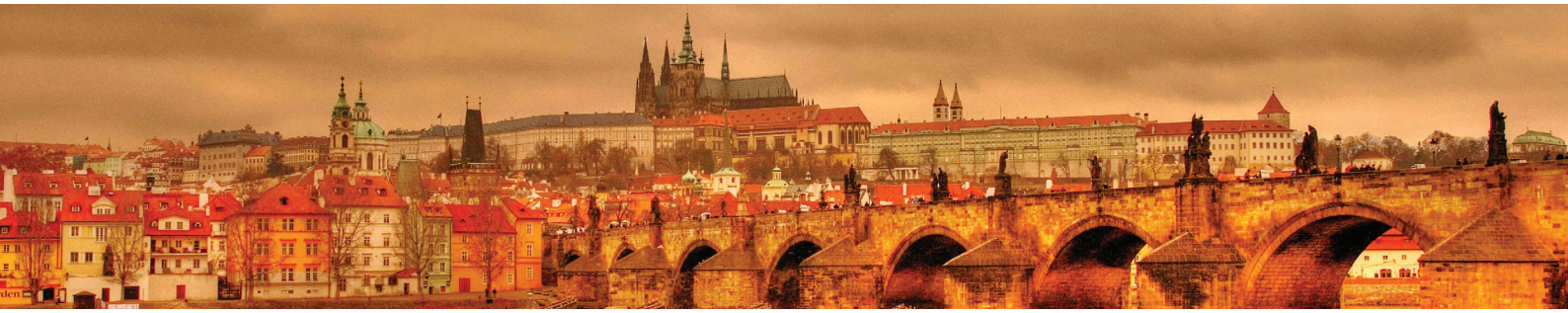
JOHANNES VESTER

IDV Data Analysis and Study Planning, Krailling, Germany

Preparing for the future starts with learning from the past. Over the past thirty years, not a single TBI trial with a traditional design has succeeded to demonstrate statistical significance on neuroprotective agents. Almost all the inconclusive studies used a single outcome measure approach, which is certainly not capable of identifying all the important deficits affecting TBI patients:

IMPACT recommendations state: “outcome after TBI is by definition multidimensional including neurophysical disabilities and disturbances of mental functioning” (2010).

We will discuss the various requirements for a multidimensional approach and present the basic biometric design of the CAPTAIN trial. It will be the first TBI study with an assumption-free “true” multidimensional approach based on full outcome scales. We will also discuss other lessons from the past as undersized studies, loss of power by inefficient scales, the problem of dichotomization, loss by heterogeneity of study population and the problem of low center quality, again with recommendations for the future and their implementation within the framework of the CAPTAIN trial.



# THE NEUROVASCULAR UNIT AND ITS SUSCEPTIBILITY TO ISCHEMIA


GREGORY DEL ZOPPO

Departments of Medicine and Neurology
University of Washington
Seattle, Washington


Cerebral microvessels and their recipient neurons, as well as other components of the "neurovascular unit," suffer a sequence of consistent and complex changes following focal cerebral ischemia. The neurovascular unit (NVU) is both a structural and conceptual framework that involves the functional interactions among the cells and their environment during normal conditions and following injury. Cerebral capillaries consist of the endothelium, the extracellular matrix (ECM) of the basal lamina, and the astrocyte end-feet. A specific feature of the CNS microvasculature, not found in other beds, is the permeability barrier ("blood-brain" barrier). While there is substantial evidence that neuronal stimulation can alter flow through the dependent cerebral microvessel bed, evidence that the microvascular endothelium-matrix-astrocyte complex communicates with the neuron is growing.

Observations made during early focal cerebral ischemia, suggest that a tight capillary-neuron relationship exists: i) Responses to focal cerebral ischemia. Events within the microvasculature and adjacent neurons, following the onset of focal ischemia, occur simultaneously, rather than sequentially, despite the relative resistance of the endothelium to ischemic injury. ii) Microvessel-neuron distance relationships. In the primate striatum, the microvessel-neuron ([m-n]) distance relationship distribution is highly ordered and consistent. Within 2 hours following middle cerebral artery occlusion (MCA:O), neurons most distant from their nearest microvessel are significantly more likely to display evidence of injury within the ischemic core. This response appears neuron-selective (e.g. $GAD^-$ neurons) within 2 hours of MCA:O. This consistent and highly-ordered response to focal ischemia implies a close functional relationship between individual microvessels and their nearest neighboring neuron. iii) Matrix proteolysis. Within hours following MCA:O, there is significant loss of laminin-1, fibronectin (cellular), collagen IV, and perlecan (HSPG) from the microvessel ECM. iv) Matrix receptor responses. Simultaneously, there is loss of both 1 integrin (endothelium) and dystroglycan (astrocyte end-feet) immunoreactivity, which coincides with increased microvessel permeability in the ischemic core. v) Matrix protease responses. There is significant up-regulation of pro-MMP-2, together with its direct (MT- and MT3 MMP) and indirect (u-PA/u-PAR) activation apparatus. pro-MMP-2 expression is linearly associated with neuron injury and with the volume of cell injury. u-PA/u-PAR, cathepsin L, and heparanase appear simultaneously within microvessels from neighboring neurons, suggesting that the appearance on these two structures is coordinated. This may represent local release by these structures, and/or by intervening cells (e.g., microglia). Both ultrastructural and adhesion receptor responses to hypoxia/ischemia by microvessel endothelial cells and astrocytes indicate that responses in these two cell populations are somehow coordinated. These matrix-receptor responses to focal cerebral ischemia impact the integrity of the inter-endothelial cell portion of the permeability barrier, as well as the microvessel matrix. Both the temporal and spatial aspects of these responses suggest that capillary-neuron processes are related or coordinated.

The evolution of injury in the ischemic core is complex. These events occur at the outset of this evolution. Clearly, reperfusion of the stricken territory-at-risk limits the extent of the injury.

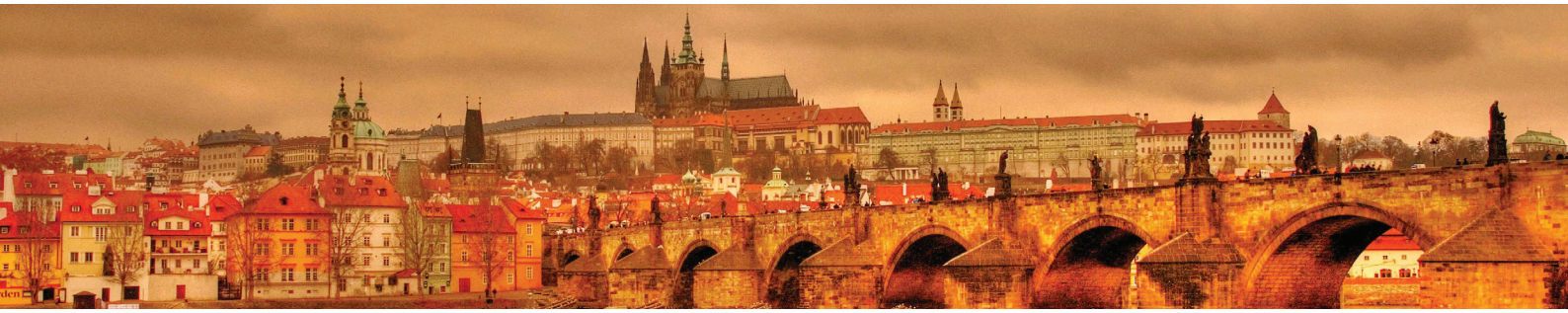
More problematic are the events that occur in the microvasculature and neurons required for recovery. The cellular relationships within the NVU are permanently disturbed by 24 hours after MCA:O. Evidence demonstrates that the regions of reversible injury are scattered throughout the injury core. There is also evidence that the early events set in motion the release of substances that may: i) stimulate angiogenesis, and/or ii) provide for limited neuron repopulation. While coordinated angiogenesis and neuron population occur during development there is still limited evidence that the cellular responses to injury are coordinated. Hurdles to recovery include i) matrix disruption, ii) products of matrix proteolysis, and iii) processes of innate and peripheral inflammatory responses that may not "reset" the CNS tissue in the injured regions.

Unanswered questions include how stroke acutely injures both nonvascular and vascular tissues within the brain, how the cell components of the NVU communicate, the roles of matrix environment in the function of the cells of the NVU, and how to improve the outcomes of potential treatments during ischemic stroke in view of this information. They also support the observation that clinical trials focused on neuron preservation, without reperfusion, may have limited utility without consideration of the remainder of the NVU. These issues will be explored during the presentation.

# CURRICULUM VITAE

# ANGELO ANTONINI
/ITALY

Angelo Antonini joined the Parkinson Institute in Milan, Italy in November 1997. He is now medical coordinator for Information Technology and Clinical Research at the Department of Neuroscience of the Hospital 'Istituti Clinici di Perfezionamento' in Milan, Italy. He is also aggregate Professor of Neurology at the University of Milan-Bicocca. He earned his medical degree from the Università degli Studi di Roma 'La Sapienza', Rome. In November1990 he completed his neurology training with honors and then undertook a visiting fellowship at the PET Department Paul Scherrer Institute, Villigen, Switzerland before starting his PhD in neuroradiology under the supervision of Professor Klaus Leenders. In 1995 he received the first award from the National Parkinson Foundation for 'young researchers in Parkinson's disease'. In 1996 he was awarded the Junior Faculty Award 1996/97 from United Parkinson Foundation and Parkinson's Disease Foundation for his research in the field of Parkinson's disease. His research interests include neuroimaging as well as cognitive and behavioral aspects of Parkinson's disease. His research also focuses on the use of continuous subcutaneous infusion of apomorphine and subthalamic nucleus deep brain stimulus (STN-DBS) in the treatment of serious motor fluctuations and dyskinesia of patients suffering from advanced Parkinson's disease. During his academic career he has published over 150 peer-reviewed manuscripts, over 200 abstracts and several book chapters. He serves as reviewer for the main neurology journals and is on the editorial board of Movement Disorders.



# JAROSLAW ARONOWSKI
/USA

PRESENT TITLE:

Professor and Roy M. and Phyllis Gough Huffington Chair in Neurology and Vice-Chairman for Research
Director of Stroke Research

UNDERGRADUATE EDUCATION/
GRADUATE EDUCATION:

1974 – 1982
Medical School, Warsaw, Poland
1982 –1985
Polish Academy of Sciences, Department of Pharmacology
1992
Polish Academy of Sciences, PhD

POSTGRADUATE TRAINING:

1982 - 1985
Instructor, Medical School (Warsaw, Poland),
Department of Pharmacodynamics
The Institute of Physiology
1985 - 1985
Research Assistant
Texas Research Institute of Mental Sciences at Houston
1985 - 1994
Research Associate
University of Texas Medical School at Houston
Departments of Neurology & Neurobiology and Anatomy

ACADEMIC APPOINTMENTS:

1994 – 2002
Assistant Professor, Department of Neurology
University of Texas Medical School at Houston
2003 - 2008
Associate Professor, Department of Neurology
Director of Stroke Research
University of Texas Medical School at Houston
2008 - present
Professor (tenured), Department of Neurology
Director of Stroke Research
University of Texas Medical School at Houston

1999 - present
Faculty Member –Professor, Graduate School of Biomedical Sciences, University of Texas at Houston
2012 – Vice Chairman of Neurology, for Research

PROFESSIONAL ORGANIZATIONS:

NATIONAL:

American Society for Neurochemistry
American Association for the Advancement of Science
New York Academy of Science
American Heart Association (Stroke Council)

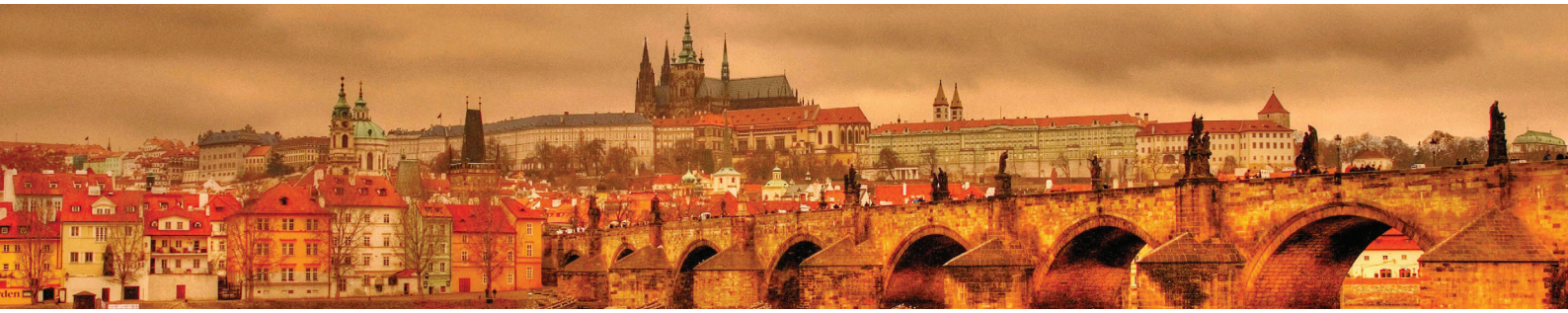
INTERNATIONAL:

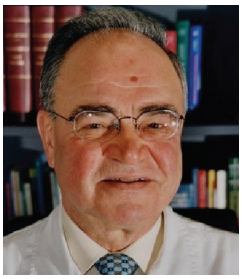
The International Society for Cerebral Blood Flow & Metabolism (Presently – on Board of Directors)

Society for Neuroscience

HONORS AND AWARDS:

First award in the National Competition for the best Master Thesis – Poznan, Poland (1983)





# LEONTINO BATTISTIN
/ITALY

Graduated in Medicine at the University of Padova Medical School in 1963; Specialist in Neurology in 1967. During the years 1967-1970 he was Research Fellow at the Institute for Neurochemistry, Columbia University, New York, USA.

Full Professor of Neurology from 1980 and then Director of the Department of Neurosciences of the Medical School of the University of Padova from 1989 to 2009. He is the Scientific Director of the Research Hospital for Neurorehabilitation, IRCCS San Camillo, Venice, from 2005.

He has been member of the Executive Council of the Italian Society of Neurology and the President of the Italian Society for Parkinson's Disease; he is member of the Executive Committee on Extrapiramidal Disorders and of the one on Dementia of the World Federation of Neurology and Chairman of the Research Group for Organization and Delivery of Neurological Services; he has been Vice-President for Europe of the World Federation of Neurology during the years 2001-2005, and he is the President of the European Society for Clinical Neuropharmacology during the years 2000-2008; he is a member of numerous International Scientific Societies, and Fellow of the American Academy of Neurology. He is also a member of the Editorial Board of international journals of neuroscience and clinical neurology.

He has organized various International Symposia on specific themes of neuroscience; he was also the President of the 11th World Congress on Parkinson's Disease that was held for the first time in Italy in 1994.

He has published more than 250 papers in various international and national journals and edited ten volumes on specific arguments of neurology; his main scientific interests have always been cerebral metabolism and function expecially in degenerative diseases of the nervous system, like Parkinson's and Alzheimer's disease, as well as in cerebrovascular diseases and in neurorehabilitation.

# NATAN BORNSTEIN
/ISRAEL

EDUCATION

| | |
|---|---|
| 1970-73 | University of Sienna, Medicine, Sienna, Italy |
| 1973-79 | Technion Medical School, Hifa, Medicine, MD, 1979 |

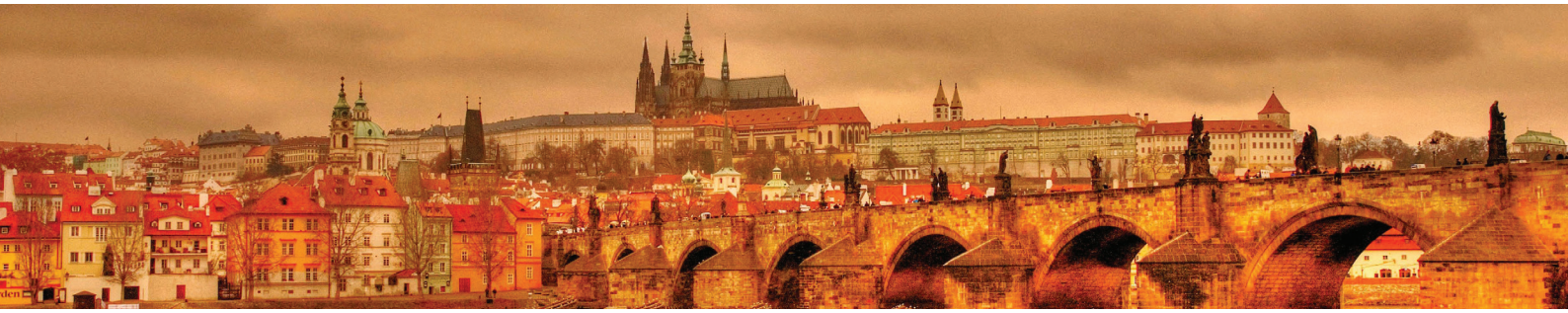
Date of receiving specialixation certificate: 11 September, 1984
Title of Doctoral dissertation: Dextran 40 in acute ischemic stroke
Name of Supervisor: Dr. Jacob Vardi

FURTHER EDUCATION

| | |
|---|---|
| 1978-83 | Tel-Aviv University, Sackler Faculty of Medicine, neurology (residence), Israeli Board certified in Neurology, 1983 |
| 1979-83 | Tel-Aviv University, Sackler Faculty of Medicine, Post graduate studies in Neurology |
| 1984-87 | Sunnybrook Medical Center, University of Toronto, M.R.C stroke, Fellowship |

ACADEMIC AND PROFESSIONAL EXPERIENCE

| | |
|---|---|
| 1982-1995 | Tel-Aviv University, Neurology, instructor |
| 1991-present | European stroke Conference (ESC), Executive committee |
| 1995-1999 | Tel-Aviv University, Neurology, Senior lecturer |
| 1995 | Eliprodil CVD 715 clinical trial, Steering Committee |
| 1995-1997 | International Stroke Study (IST), Steering Committee |
| 1995-1999 | American Academy of Neurology, Member of the International Affairs Committee |
| 1996 | Asymptomatic Carotid Stenosis and Risk of Stroke(ACSRS), Advisory Committee |
| 1996-present | The Mediterranean Stroke Society (MSS), President |
| 1996-2002 | EFNS, Management Committee |
| 1997-2009 | Israeli Neurological Association, Secretary |
| 1999-present | Tel-Aviv University, Neurology, Associated Professor |
| 2001- present | European Society Neurosonology and Cerebral Hemodynamics (ESNCH) Executive committee |
| 2005-present | Neurosonolgy Research Group, Executive committee |
| 2006-present | European Master in Stroke Medicine, Member of faculty |
| 2006-2008 | NEST II clinical Trial, Steering Committee |
| 2006-present | SENTIS clinical Trial, Steering Committee |
| 2006-present | CASTA Trial, Steering Committee |
| 2006-present | Brainsgate clinical Trial, Steering Committee |
| 2008- present | World Stroke Association (WSO), Vice president |
| 2009-present | Israeli Neurological Association, Chairman |
| 2009-present | European Stroke Organization (ESO), Member on the board of directors |
| 2010- | NEST III clinical Trial, Steering Committee |



PROFESSIONAL ACHIEVEMENTS- EDITORIAL BOARD

| | |
|---|---|
| 1991-present | Neurological Research Journal, Guest Editor |
| 1991-present | STROKE, Member of the editorial board |
| 1998-present | European Journal of Neurology, Member of the editorial board |
| 1999-present | Journal of Cerebrovascular disease, Member of the editorial board |
| 2000-present | Journal of Annals of Medical Science, Consulting Editor |
| 2001-present | Journal of Neurological Science (Turkish), Member of the editorial board |
| 2001-present | Acta Clinica Croatica, Member of the editorial Counsil |
| 2003-present | Italian Heart Journal, International Scientific Board |
| 2003-present | Journal of Neurological Sciences, Guest Editor |
| 2004-present | Turkish Journal of Neurology, International Advisory Board |
| 2005-present | Archives of Medical Sciences (AMS) , Member of the Editorial Board |
| 2006-present | Journal of Cardiovascular Medicine, International Scientific Board |
| 2006-present | International Journal of Stroke, Editorial Board |
| 2006-present | Acta Neurologica Scandinavica, Editorial Board |
| 2009-present | American Journal of Neuroprotection& Neurogeneration (AJNN) Member of the Editorial Board |
| 2010 | Neurosonology, International Editorial Board |
| 2010 | Frontiers in Stroke, Review Editor |

PROFESSIONAL ACHIEVEMENTS- REVIEWER

| | |
|---|---|
| 1998-present | Lancet, Ad Hoc reviewer |
| 1998-present | Diabetes and its complications, Ad Hoc reviewer |
| 1999-present | Journal of Neuroimaging, Reviewer |
| 1999-present | Journal of Neurology, Ad Hoc reviewer |
| 2000-present | Neurology, Ad Hoc reviewer |
| 2003-present | Israeli Medical Association Journal (IMAJ), Reviewer |
| 2003-present | Acta Neurologica Scandinavica, Ad Hoc reviewer |
| 2006-present | Journal of Neurology, Neurosurgery & Psychiatry, Reviewer |
| 2010- | European Neurology, Ad Hoc reviewer |

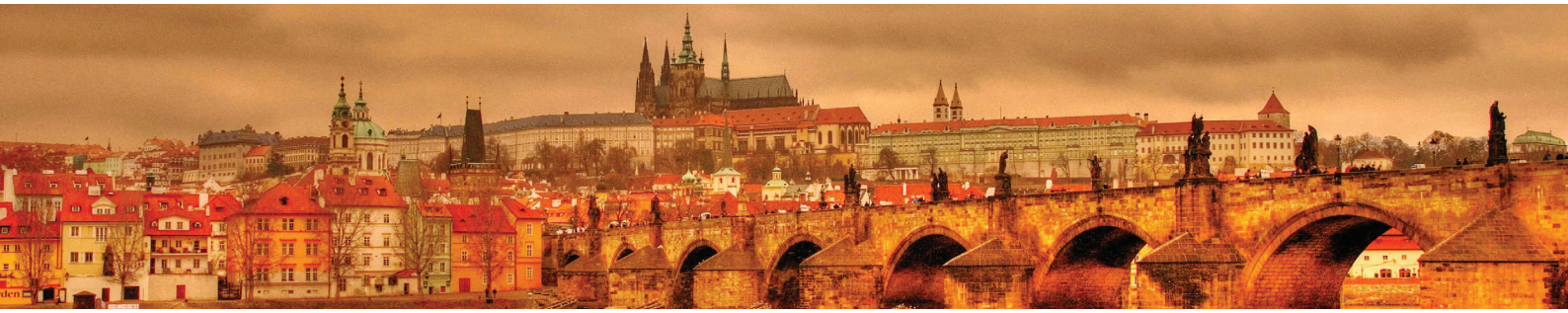
MEMBERSHIP IN PROFESSIONAL SOCIETIES

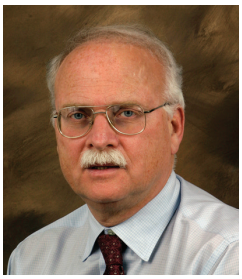
| | |
|---|---|
| 1977-present | Israeli Medical Association |
| 1983-present | The Israeli Neurological Association |
| 1985-present | Stroke Council of the American Heart Association (Fellow) |
| 1986-present | American Academy of Neurology |
| 1986-present | Neurosonology Research Group of the World Federation of Neurology |
| 1987-present | Stroke Research Group of the World Federation of Neurology |
| 1990-2008 | International Stroke Society |
| 1995-2008 | European Stroke Council |
| 1995-present | Mediterranean Stroke Society (MSS) |
| 1998-present | European Neurosonology Society |
| 2005-present | World Stroke Organization (WSO) |
| 2008-present | Fellow of the European Stroke organization (FESO) |

# EVA FELDMAN
/USA

Dr. Eva Feldman is the University of Michigan Russell N. DeJong Professor of Neurology, Director of the A. Alfred Taubman Medical Research Institute, Director of the Program for Neurology Research & Discovery, and President of the American Neurological Association. Using a multifaceted approach consisting of active research programs in basic, translational and clinical research, she is devoted to understanding the pathogenic mechanisms that trigger neurodegeneration in the central and peripheral nervous systems and to identifying novel therapies.

As one of America's most influential neurologists and scientists, Dr. Feldman has over 280 original articles and her research has significantly advanced neurology and healthcare, particularly for amyotrophic lateral sclerosis (ALS) and diabetic neuropathy (DN). She is a thought leader on cellular therapies, and is leading the first and only FDA-approved clinical trial examining direct intraspinal stem cell transplantation in ALS patients, a trial that has exhibited no serious adverse events through Phase I completion. She is also pursuing innovative approaches to model ALS and study disease mechanisms and treatments using induced pluripotent stem cell technology, an approach that will enable a novel strategy to study the most common forms of ALS. Her research in diabetic neuropathy has also defined new causes and identified novel therapies. She was the first to identify and investigate the role of lipids in diabetic complications, and her idea that impaired glucose tolerance can present as neuropathy has changed standards of clinical practice to now mandate glucose tolerance tests for all patients presenting with neuropathy. Developed by Dr. Feldman, the Michigan Neuropathy Screening Instrument is now used clinically to evaluate neuropathy and in countless clinical trials across the nation. Dr. Feldman also serves as director of the A. Alfred Taubman Medical Research Institute, which supports cutting-edge, "high-risk, high reward" research, and she is President of the American Neurological Association, only the 3rd woman in 137 years to hold this prestigious post. Overall, her research and innovative translational advances have led to new disease therapies, changed clinical guidelines, and identified her as an opinion leader in neurology and healthcare, and she has also made a tremendous impact on the medical and scientific communities through her leadership. She is recognized as one of the preeminent neurologists of our time.





# MARC FISHER

/USA

Dr. Fisher has a long track record in performing MRI-based experiments in rat stroke models to evaluate the presence and evolution of the ischemic penumbra. Using diffusion/perfusion MRI his experimental group has evaluated the effects of therapies on the progression of the diffusion/perfusion mismatch. Recently, they have shown that high-flow 100% oxygen therapy initiated early after embolic stroke in rats markedly inhibits the expansion of the ischemic core on diffusion imaging and extended the time window for successful reperfusion. Dr. Fisher has extensive experience in organizing and implementing clinical acute stroke therapy trials with a particular interest in imaging-based trials. He has performed these trials with co-investigators at multiple sites around the world. He has a long history of patient care in both the outpatient and inpatient setting with an emphasis on patients with cerebrovascular disorders. He has published extensively with over 250 peer-reviewed articles and has edited or co-edited 13 books. He currently serves as editor-in-chief of Stroke.

# NATALIA GULYAEVA

/RUSSIA

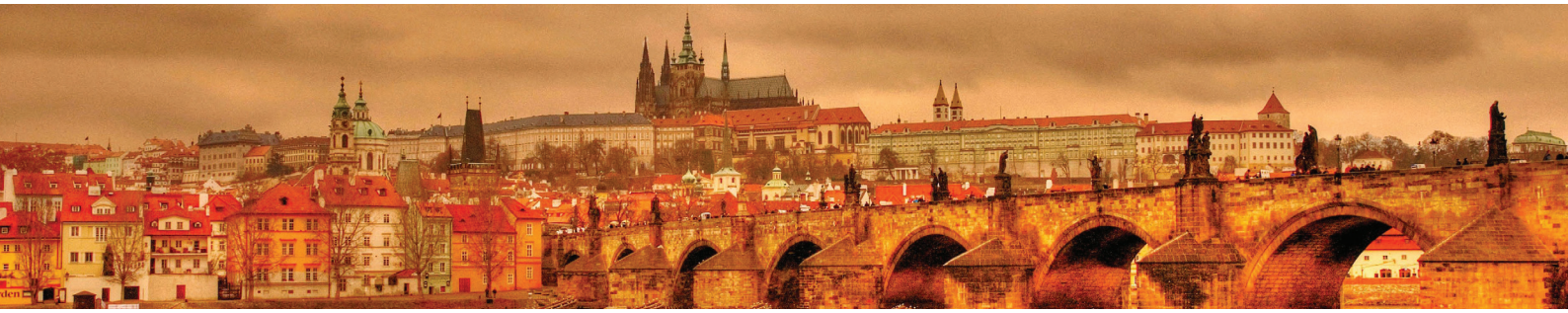
Natalia Gulyaeva is Deputy Director of the Institute of Higher Nervous Activity and Neurophysiology, Russian Academy of Sciences, Moscow, and the Chair of the Department of Functional Biochemistry of the Nervous System. Dr. Gulyaeva's research focuses on molecular mechanisms underlying neuronal cell death and neuronal plasticity in models of cerebral pathologies.

Natalia Gulyaeva graduated from Moscow State University, where she received MS and PhD degrees in Biochemistry. She received the DSc degree in Pathophysiology in the Institute of Higher Nervous Activity and Neurophysiology, Russian Academy of Sciences, Moscow.

Prof. Gulyaeva is the Deputy Director of the Institute of Higher Nervous Activity and Neurophysiology RAS, and the Chair of the Department of Functional Biochemistry of the Nervous System.

Dr. Gulyaeva's research field covers neurochemistry, pathophysiology, neurophysiology and is related to cerebral pathologies (epilepsy, stroke, ALS, depression) including animal models and human studies. Her research interests are focused on molecular mechanisms of neurodegeneration and neuronal plasticity (nitric oxide and free radical-mediated processes; proteases; neuroinflammation; neurogenesis; neurotrophic factors). Translational research is among her prior interests.

Prof. Gulyaeva is the Editor-in-Chief of "Neurochemical Journal", Associate Editor of "Journal of Higher Nervous Activity", Handling Editor of "Journal of Neurochemistry", member of Editorial Boards of "Neurochemical Research" and "Metabolic Brain Disease"; the Scientific Secretary of Russian Society for Neurochemistry.



# PAVEL KALVACH

## /CZECH REPUBLIC

Board certified neurologist since 1975. He studied Charles University, Medical faculty in Prague. PhD on „Cerebral perfusion“ in 1984. In 1988 appointed chairman of Dept. of Neurology, Cz Institute for Postgraduate Medicine, with responsibility for neurological board certifications in Czechoslovakia. 1991-1994 he attended a collaborative research on „Cerebrovascular disease“, 4 x 3 months at Yale, USA. In 1996 -2006 worked as chairman of Dept. of Neurology, 3rd Medical faculty, Charles University in Prague. In the European Federation of Neurological Societies (EFNS) appointed General secretary in 1999 (4 years) and later Vicepresident in 2003 (4 years). Main author of „Cerebral ischemia and haemorrhage“, 3 editions in Czech, awarded by 2 national prices in Czechoslovakia.

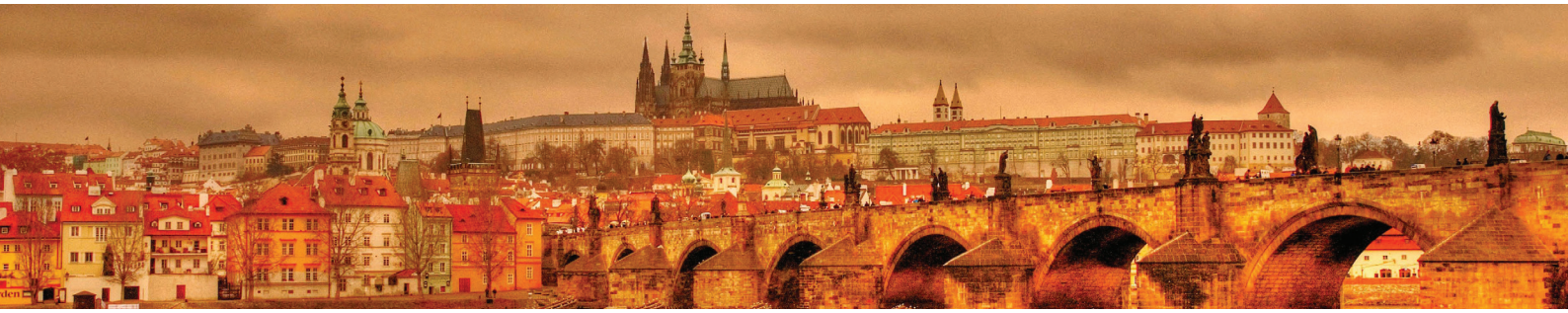
# AMOS KORCZYN
/ISRAEL

Professor Korczyn graduated from the Hebrew University – Hadassah Medical School in Jerusalem in 1966 (MD), where he also received an MSc degree in pharmacology (cum laude) in 1966. He trained in neurology at Beilinson Hospital and at the National Hospital for Nervous Diseases, Queen Square, London. He was the Chairman of the Department of Neurology at the Tel-Aviv Medical Center since 1981 until 2002, and the incumbent of the Sieratzki Chair of Neurology at Tel-Aviv University, 1995-2010. Professor Korczyn has a particular interest in neurodegenerative diseases. He has authored or co-authored over 600 articles in peer-reviewed journals, as well as chapters in books, etc. He edited several books and Special Issues in Journals, and is co-Editor of the Journal of the Israeli Neurological Association (JINA) since 2009. He is or has been an Editorial Board member of 20 international journals, and organized several neurological conferences, mainly in the field of dementia, Parkinson's disease and other degenerative brain disorders, as well as CONy – the International Congress on Controversies in Neurology. Professor Korczyn also served on advisory boards in several drug discovery programs.

Professor Korczyn is the Chairman of the Scientific Administrative Board of the Israeli Alzheimer's disease association (EMDA), and member of the SAB of Alzheimer Disease International, and has been the chairman of the WFN Research Committee for Neuropharmacology.

Professor Korczyn is an honorary member of the neurological societies of Israel, Serbia, Poland and Russia.

Professor Korczyn's H-index is 39.



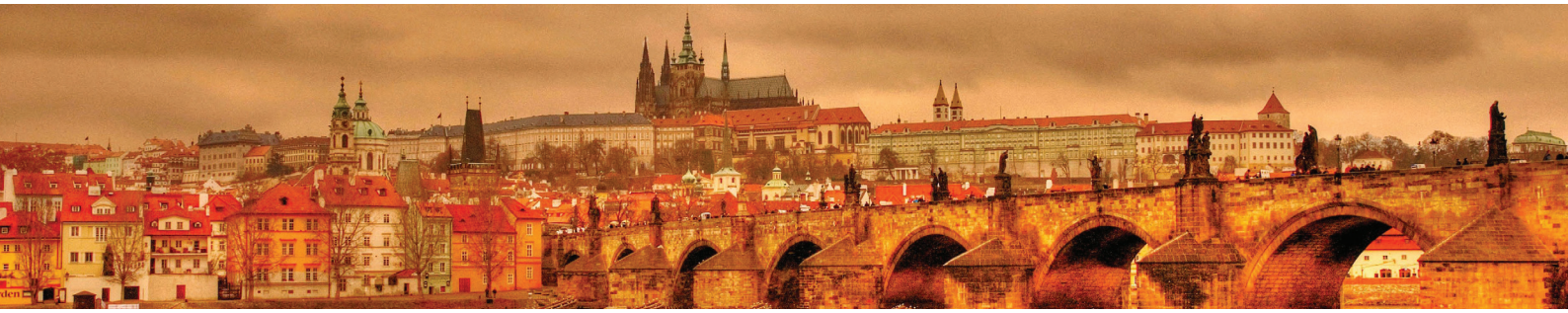
# DAFIN F. MUREŞANU
/ROMANIA

Muresanu Fior Dafin, MD, PhD, MBA, FANA, is the President of the Romanian Society of Neurology, Professor of Neurology, Chairman of the Neurosciences Department, University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca, member of the Academy of Medical Sciences, Romania. He also acts as the President of the Society for the Study of Neuroprotection and Neuroplasticity. In these roles, he is involved as member of the faculty in international educational programs of European Master (i.e. European Master in Stroke Medicine, University of Krems), organizer and co-organizer of European and international schools and courses (International School of Neurology, European Stroke Organisation Summer School, Danubian Neurological Society Teaching Courses). His activity includes involvement in many clinical studies and research projects, memberships in the executive board of many national and international societies, participations as invited speaker in national and international congresses, a significant portfolio of scientific articles (77 papers indexed on Web of Knowledge-ISI) as well as contributions in monographs and books published by prestigious international publishing houses. In the last 7 years, he was also invited as speaker in over 200 scientific events both national and abroad. Prof. Dr. Muresanu has been honoured with the Faculty of Medicine, University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca "Octavian Fodor Award" for the best scientific activity of the year 2010 and the 2009 Romanian Academy of Medical Sciences "Gheorghe Marinescu Award" for advanced contributions in Neuroprotection and Neuroplasticity.

# MICHAELA PINTER
/AUSTRIA

PROFESSIONAL CAREER

| | |
|---|---|
| 1977-1983 | Medical School University Vienna |
| 1984-1991 | Internship Neurological Hosiptial Rosenhügel, Vienna, Austria |
| 1991 | Neurologist |
| 1991-1999 | Assistant Medical Director Neurological Hospital Rosenhügel and Maria Theresien Schlössel, Vienna, Austria |
| 1993-1997 | Post-doc fellowships at the Division of Restorative Neurology and Neurobiology, Baylor College, Houston, USA (Univ. Prof. DDr. Milan R. Dimitrijevic) |
| 1999-2008 | Medical Director of the Neurological Rehabilitation Centre Rosenhügel, Vienna, Austria |
| 2001 | Venia Docendi for Neurology at the Medical University, Vienna, Austria |
| 2001 | Master of advanced study for hospital management MAS |
| since 2009 | Scientific Consultant of the Neurological Rehabilitätation Centre Allentsteig, Austria |
| since 2009 | Full Professor of Neurorehabilitation –Research at the Danube University Krems, Austria<br>Deputy Head of the Department for Clinical Neuroscience and Preventive Medicine |



# BOGDAN O. POPESCU
/ROMANIA

Bogdan O. Popescu - born March 8th, 1971 in Bucharest, Romania.
Address: Department of Neurology, School of Medicine, 'Carol Davila' University of Medicine and Pharmacy, Colentina Clinical Hospital, 19-21 Sos. Stefan cel Mare, sector 2, 020125, Bucharest, Romania.
Academic Education and Appointments

| | |
|---|---|
| 1996 | MD, 'Carol Davila' University School of Medicine, Bucharest, Romania |
| 1997 - 2002 | Resident in Neurology, University Hospital Bucharest |
| 2000 - 2009 | Assistant Professor, 'Carol Davila' University School of Medicine |
| 2001 | PhD, 'Carol Davila' University School of Medicine - suma cum laudae |
| 2002 - 2008 | Neurologist, University Hospital Bucharest |
| 2004 | PhD, Karolinska Institute, Stockholm, Sweden |
| 2005 - | Head of Laboratory of Molecular Medicine, 'Victor Babeş' National Institute of Pathology, Bucharest, Romania |
| 2008- | Senior Neurologist |
| 2009 - 2012 | Lecturer, 'Carol Davila' University School of Medicine |
| 2009 - | Senior Researcher, 'Victor Babeş' National Institute of Pathology, Bucharest, Romania |
| 2012 - | Associate Professor, 'Carol Davila' University School of Medicine and Head of Neurology Unit II, Colentina Clinical Hospital |

AWARDS

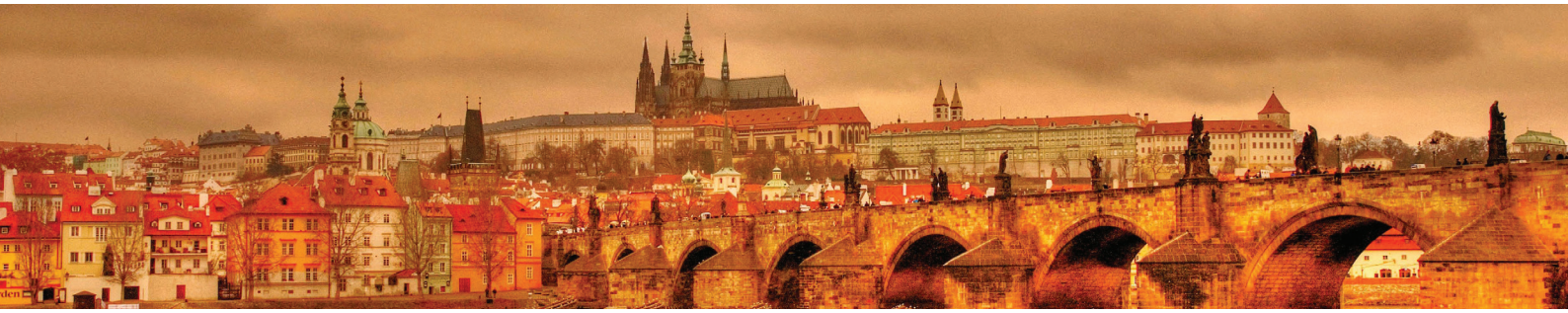
| | |
|---|---|
| 1999 | Beaufour-Ipsen prize for the best research study in neurology |
| 2000 | Young histochemist award - International Society of Histochemistry and Cytochemistry |
| 2004 | Diploma of scientific merit – 'Victor Babeş' National Institute of Pathology |
| 2007 | Romanian Academy award for medical research |
| 2010 | 'Science and Art National Foundation Award of Excellence for research in the field of Neuroscience and Neuropathology |

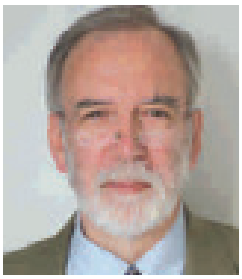
OTHER CURRENT ACTIVITIES

Guest editor for Alzheimer's review series at Journal of Cellular and Molecular Medicine
Executive editor of Romanian Journal of Neurology
President elect of the Romanian Society of Neurology (2017-2021) and former Secretary General (2001-2013)
Research director of the Society for the Study of Neuroprotection and Neuroplasticity
Director, Victor Babeş' National Institute of Pathology, Bucharest, Romania

SELECTED PUBLICATIONS

1. Popescu BO, Gherghiceanu M, Kostin S, Ceafalan L, Popescu LM. Telocytes in meninges and choroid plexus. Neurosci Lett. 2012, 516:265-9.
2. Hort J, O'Brien JT, Gainotti G, Pirttila T, Popescu BO, Rektorova I, Sorbi S, Scheltens P; EFNS Scientist Panel on Dementia. EFNS guidelines for the diagnosis and management of Alzheimer's disease. Eur J Neurol. 2010, 17:1236-48.
3. Popescu BO, Toescu EC, Popescu LM, Bajenaru O, Muresanu DF, Schultzberg M, Bogdanovic N. Blood-brain barrier alterations in ageing and dementia. J Neurol Sci, 283:99-106, 2009.
4. Cowburn RF, Popescu BO, Ankarcrona M, Dehvari N, Cedazo-Minguez A. Presenilin-mediated signal transduction. Physiol Behav. 2007;92:93-7.
5. Hansson CA, Popescu BO, Laudon H, Cedazo-Minguez A, Popescu LM, Winblad B, Ankarcrona M. Caspase cleaved presenilin-1 is part of active gamma-secretase complexes. J Neurochem. 2006;97:356-64.
6. Popescu BO, Ankarcrona M. Mechanisms of cell death in Alzheimer's disease: role of presenilins. J Alzheimers Dis. 2004;6:123-8.
7. Popescu BO, Cedazo-Minguez A, Benedikz E, Nishimura T, Winblad B, Ankarcrona M, Cowburn RF. Gamma-secretase activity of presenilin 1 regulates acetylcholine muscarinic receptor-mediated signal transduction. J Biol Chem. 2004;279:6455-64.
8. Cedazo-Mínguez A, Popescu BO, Blanco-Millán JM, Akterin S, Pei JJ, Winblad B, Cowburn RF. Apolipoprotein E and beta-amyloid (1-42) regulation of glycogen synthase kinase-3beta. J Neurochem. 2003;87:1152-64.
9. Popescu BO, Oprica M, Sajin M, Stanciu CL, Bajenaru O, Predescu A, Vidulescu C, Popescu LM. Dantrolene protects neurons against kainic acid induced apoptosis in vitro and in vivo. J Cell Mol Med. 2002;6:555-69.
10. Popescu BO, Cedazo-Minguez A, Popescu LM, Winblad B, Cowburn RF, Ankarcrona M. Caspase cleavage of exon 9 deleted presenilin-1 is an early event in apoptosis induced by calcium ionophore A 23187 in SH-SY5Y neuroblastoma cells. J Neurosci Res. 2001;66:122-34.





# GIORGIO SANDRINI
/ITALY

Giorgio Sandrini is Full Professor of Neurology and Chairman of the Department of Neurology and Neurorehabilitation at the Institute of Neurology, "C. Mondino" Foundation, University of Pavia, Pavia, Italy.

He is Director of Postgraduate School in Neurophysiopathology and Chairman of the Section of Clinical and Rehabilitative Neurology, University Department of Brain and Behavioral Sciences.

He is President of the Scientific Committee of the Research Consortium on Adaptive Disorders and Headache. He is President of the European Federation of the Neuro-Rehabilitation Societies and Past-President of the Italian Society of Neuroehabilitation.

He is Chairman of the International Headache Society Italian Linguistic Special Interest Group and Chairman of the European Federation of Neurological Societies Task Force on Neurophysiological Tests and Neuroimaging Procedures in Non-acute Headache.

His main FIELDS OF INTEREST are:

Neurorehabilitation, pathogenetic mechanisms, classification and treatment of Headache and Neuropathic Pain; neurophysiology of pain and autonomic system; movement disorders,.

SCIENTIFIC ACTIVITY: he has published more than 200 indexed papers. He has edited or co-edited several scientific books and Congress Proceedings.

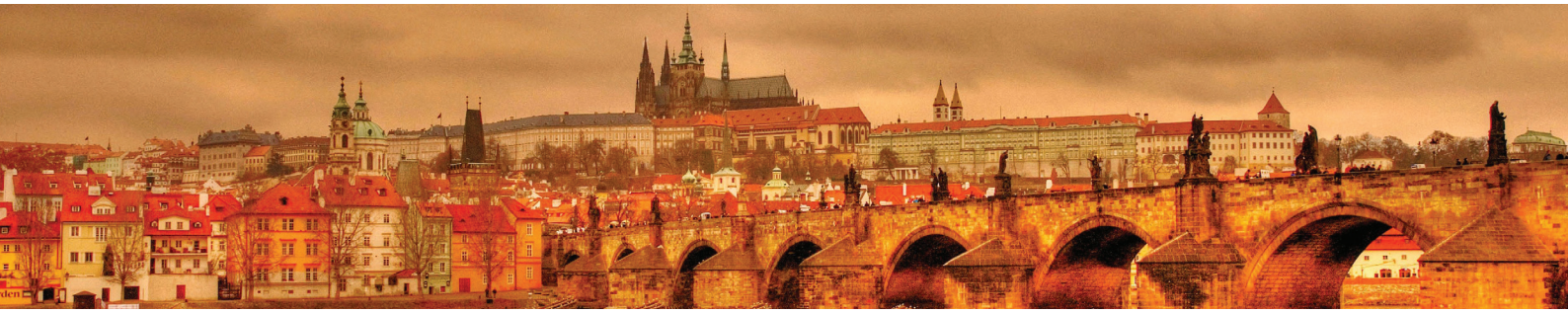
He organised numerous National and International Congresses.

He participated as investigator / principal investigator or coordinator, to numerous clinical trials carried out according to the GCP on treatment of headache , neuropathic pain or stroke.

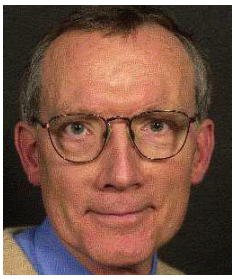
# HARI SHANKER SHARMA
/SWEDEN

Hari Shanker Sharma, Director of Research (CNS Injury & Repair), University Hospital, Uppsala University is Professor of Neurobiology (MRC), Docent in Neuroanatomy (UU) and is currently affiliated with Department of Surgical Sciences, Division of Anesthesiology and Intensive Care Medicine, Uppsala University, Sweden. Hari Sharma was born on January 15, 1955 in an Industrialist town Dalmianagar (Bihar), India. He did his Bachelor of Science with Honors from the prestigious L. S. College Muzaffarpur in 1973 and secured 1st position in his batch. He obtained his Master Degree from Bihar University with special expertise in Cell Biology in 1976 and awarded Gold Medal of Bihar University for securing 1st potion in the 1st Class. Hari Sharma joined the group of Professor Prasanta Kumar Dey, a neurophysiologist by training in the Department of Physiology, Institute of Medical; Sciences, Banaras Hindu University, Varanasi in 1977 to obtain Doctor of Philosophy Degree (D.Phil.) in Neurosciences and was awarded Ph.D. in 1982 on "Blood-Brain Barrier in Stress." Hari Sharma after carrying out a series of Government of India funded Research Projects on the BBB and brain dysfunction (1982–1987), joined the lab of Neuropathology at Uppsala University with Professor Yngve Olsson in 1988 to investigate passage of tracer transport across the BBB caused by stress or traumatic insults to the Brain and Spinal cord at light and electron microscopy. Dr. Sharma awarded the prestigious Alexander von Humboldt Foundation Fellowship of German Government (1989–1991) to work on hyperthermia induced BBB dysfunction at the ultrastructural level in the laboratory of Professor Jorge Cervós-Navarro (a living "Legend in Neuropathology in Europe"). Dr. Sharma joined again Uppsala University and established a network of collaboration on "Experimental CNS Injury Research Group" as a lead investigator with eminent collaborators in various parts of Europe, USA, and Australia (1991–). On his work on hyperthermia Dr. Sharma received the prestigious Neuroanatomy award "Rönnows Research prize" of Uppsala University for "best neuroanatomical research of the year 1996" followed by the Award of the Degree of Doctor of Medical Sciences of Uppsala University in Neuroanatomy in 1999 and selected for the Best Thesis Award of the Medical faculty, "The Hwassers Prize" of 1999. On his meticulous works on the Blood Brain barrier and Brain edema (2000–2003) Dr. Sharma earned the prestigious title of "Docent in Neuroanatomy" of Medical Faculty, Uppsala University in April 2004. Currently his main research interest is Neuroprotection and Neuroregeneration, in relation to the Blood-brain barrier in stress, trauma, and drugs of abuse in health and disease.

Dr. Sharma on his research on brain pathology and neuroprotection in different models received the prestigious awards from The Laerdal Foundation of Acute Medicine, Stavanger, Norway, in 2005 followed by Distinguished International Scientists Collaboration Award by National Institute on Drug Abuse (NIDA), Baltimore, MD (2006–2008). His recent work on 5-HT3 receptor mediated neuroprotection in morphine withdrawal induced neurotoxicity won the coveted prize of Best Investigator Award 2008 and Best Scientific Presentation by European Federation of the International Association for Study of Pain (ISAP), and Awarded during their VI Annual Meeting in Lisbon, September 9–12, 2008. His recent research is aimed to find out the role of nanoparticles in Neurodegeneration and Neuroprotection using various treatment strategies that is supported by European Aerospace Research and Development (EOARD), London, UK and US Air Force Research Laboratory, Wright Patterson Air Force Base, Dayton, Oh, USA. On his works on Blood–brain barrier in hypertension and diabetes together with Romanian colleagues, University of Medicine and Pharmacy "Iuliu Hatieganu," Cluj-Napoca, Romania awarded Dr. Sharma with Honorary Doctorate of Medical Sciences in 2009. Dr. Sharma's work over 30 years on the blood-brain barrier and brain edema won him the US Neurosurgeon Dr. Anthony Marmarou Award (2011) by the International Brain Edema Society at their 15th Congress in Tokyo, Japan, November 20–24, 2011. His works on Nanoneuroscience and development of nanomedicine to treat the CNS injuries has won accolades at various



Government and International Scotties or Organization across the World. Accordingly Dr Sharma was decorated with the most prestigious "Hind Rattan Award 2012" on the eve of Republic Day of India 25th January 2012 and Mahatma Gandhi Pravasi Gold Medal on October 12, 2012 in House of Lords, London, UK. Hari Sharma was also invited to organize and chair Nanosymposium in Society for Neuroscience meetings in Chicago (2009), San Diego (2010), Washington DC (2011) and New Orleans (2012). Hari Sharma has published over 380 research papers, 75 reviews, 12 monographs, and 70 international book chapters and edited 15 book volumes. He served as Guest Editor of Curr. Pharm. Desig. (2005, 2007, 2010–); J. Neural. Transmiss. (2006, 2011–) and is founding Editor-in-Chief of Int. J. Neuroprotec. Neuroregen. (2004–), UK. Dr. Sharma is on board of various International Journals including CNS and Neurological Disorders-Drug Targets, USA, Journal of Neurodegeneration and Regeneration, USA (2009–) and is associate editor of Journal of Nanoscience and Nanotechnology (Nanoneuroscience 2006–), USA, Review Editor—Frontiers in Neuroengineering (2007–), Frontiers in Neurorestoratology, and Associate Editor of Frontiers in Aging Neuroscience (2008–), Frontiers of Fractal Physiology (2010–), Switzerland, Journal of Neurorestoratology, Dove Medical press, London, UK (2012–), Webmed Central, Neurology Faculty, Advisory Board Member (2010–), World Journal of Pharmacology (2011–), Journal of Physical Medicine and Rehabilitation, USA (2012–). Dr. Sharma served as volume editor of several progress in Brain research series (Volumes 104, 115, 162 and 180), International review of Neurobiology (Volume 82 and 102) and other Springer Volumes on Spinal cord injury (1988) and Handbook of Neurochemistry (2009) apart from stand alone books (Elsevier, Springer and Academic Press since 1994). Dr. Hari Sharma is invited to join several National Academies of repute including New York Academy fo Science, USA (since 1994–); International Academy of Stress, New York (2003–), Swedish Academy of Pharmaceutical Sciences (2010–). Dr. Sharma has served as an expert evaluator and advisor to various Boards, Councils and Institutions for their Research Grants including Wellcome Trust, London, UK (2011–); Catalan Agency for Health Information and Quality, TV3 (2010–), European Commission Projects (2002–), European Nanomed Council (2009–), Ministry of Health Science Foundation; Medical research Council and University Commission of Grants in various countries in Europe, USA, UK, Canada, Hong Kong, Singapore and in Australia. Some of the notable organizations include: Australia and New Zealand Health Council (2000–); University Commission of Grants, Hong Kong (2002–), Singapore Medical Council, Singapore (2003–); UK Charity Organization "Research on Ageing: Help the Aged" (2003–); Euro Nanomed (2010–). Dr. Sharma is designated as ambassador of the City of Uppsala 2007, by Uppsala County administration and Uppsala Tourism for promoting Uppsala, Sweden as International Research Collaboration/Meetings and Conference Destination. Dr. Hari Sharma is married to Aruna Sharma (nee Bajpai) since 23rd April 1979 and has two sons. His political affiliations belong to Swedish Social Democrat Party (Socialdemokraterna, Sverige) where he is associated with the development of Education and Research matters in Sweden actively. Contact information: Hari S. Sharma, voice and fax: +46-18-243899, cell phone: +46 70 641 9843; e-mail: Sharma@surgsci.uu.se



# STEPHEN SKAPER
/ITALY

STUDIES: B.S. (chemistry) Illinois Institute of Technology (1969); Ph.D. (biochemistry) University of South Dakota (1973); Laurea in chemistry, University of Padova (1990)

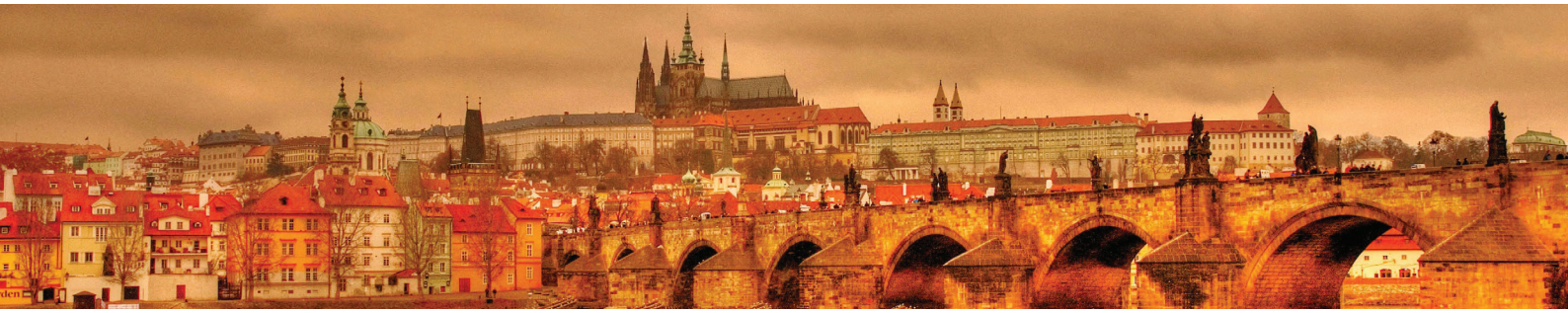
CAREER: NIH Postdoctoral Fellow, Department of Medicine, University of California, San Diego (1973-1976); Fellow in Human Genetics, Department of Pediatrics, Case Western Reserve University, Cleveland, Ohio (1977); Postgraduate Research Biologist, Department of Biology, University of California, San Diego (1978); Assistant Research Biologist, Department of Biology, University of California, San Diego (1979-1982); Associate Research Biologist, Department of Biology, University of California, San Diego (1983-1987); Head, Laboratory of Neuropharmacology, Neuroscience Research Laboratories, Fidia S.p.A. - Abano Terme, Italy (1987-1993); Principal Scientist and Head, Laboratory of Cell Biology, Researchlife S.c.p.A. (a Lifegroup Company), Biomedical Research Center, St. Thomas Hospital, Castelfranco Veneto (TV), Italy (1993-1996); Visiting Professor, Department of Pharmacology, University of Padova, Padova, Italy (1997); Assistant Director, Molecular Neurobiology Research, SmithKline Beecham Pharmaceuticals, New Frontiers Science Park, Harlow, United Kingdom (1998-2001); Senior Team Leader, Migraine and Stroke Research, Neurology & GI Centre of Excellence for Drug Discovery, GlaxoSmithKline R & D Limited, Harlow, United Kingdom (2002-2003); Senior Team Leader, Neuro Cell Sciences/ Neurodegeneration Research, Neurology & GI Centre of Excellence for Drug Discovery, GlaxoSmithKline R & D Limited, Harlow, United Kingdom (2004-2007); Senior Team Leader, Target Validation Dept (Cognition and Pain), Centre of Excellence for Drug Discovery, GlaxoSmithKline R&D Limited, Harlow, United Kingdom (2008); Adjunct Professor, Department of Pharmacology and Anesthesiology, University of Padova, Faculty of Medicine, Padova, Italy (2009-present).

PROFESSIONAL MEMBERSHIPS: Sigma CI (The Scientific Research Society); Phi Lambda Upsilon (honorary chemistry society); Alpha Chi Sigma (professional society in chemistry/chemical engineering); Society for Neuroscience; International Society for Cerebral Blood Flow and Metabolism

JOURNALS EDITED: Editor-in-Chief, CNS & Neurological Disorders – Drug Targets; Editor-in-Chief, Clinical CNS Drugs; Associate Editor, American Journal of Neuroprotection and Neuroregeneration; Editorial Board Member, Nature Scientific Reports (Neuroscience); Councilor, International Association of Neurorestoratology
REVIEW PANELS: The Wellcome Trust (UK), Biotechnology and Biological Sciences Research Council (BBSRC) (UK), Austrian Science Fund (ad hoc review panel to evaluate interdisciplinary doctoral programmes in neuroscience)

RESEARCH INTERESTS: Molecular biology and cellular mechanisms of cell death in CNS aging and neurodegenerative disorders and neuroinflammation.Track record of drug discovery project leadership in kinases, ion channels, G-protein-coupled receptors, DNA repair enzymes, growth factors, identification and optimization of tools for target validation studies, utilising RNAi, conditional and viral knockdown\outs\ins, transcriptomics, proteomics and in vitro cell-based disease or mechanism relevant assays in rodent systems.

PUBLICATIONS: OVER 240 publications in the neurosciences, including book chapters and symposia proceedings.



PATENTS: Pharmaceutical compositions containing monosialoganglioside GM1 or derivative thereof suitable for the treatment of Parkinson's disease (Patent No.: US 6,620,792 B1), use of CRF receptor agonists for the treatment or prophylaxis of diseases, for example neurodegenerative diseases (US 2003/0186867 A1), treatment of conditions with a need of GSK-3 inhibition (PCT WO 02/062387 A1), use of CRF receptor agonists for the treatment or prophylaxis of diseases, for example neurodegenerative diseases (PCT WO 01/72326 A1), use of monosialoganglioside GM1 or N-dichloro-acetyl-lyso-GM1 for preventing or reversing neuronal degeneration induced by long term treatment with L-DOPA in the therapy of Parkinson's disease (EP 0 770 389 A1)

REVIEWER FOR JOURNALS: Journal of Neuroscience, PNAS, Nature Reviews, The FASEB Journal, Journal of Neurochemistry, Journal of Neuroinflammation, Neurobiology of Disease, Neurobiology of Aging, Glia, Apoptosis, Molecular & Cellular Neuroscience, Journal of Pharmacology and Experimental Therapeutics, Neuroscience, British Journal of Pharmacology, Neuropharmacology, European Journal of Pharmacology, Journal of Neurological Sciences

# JOHANNES VESTER
/GERMANY

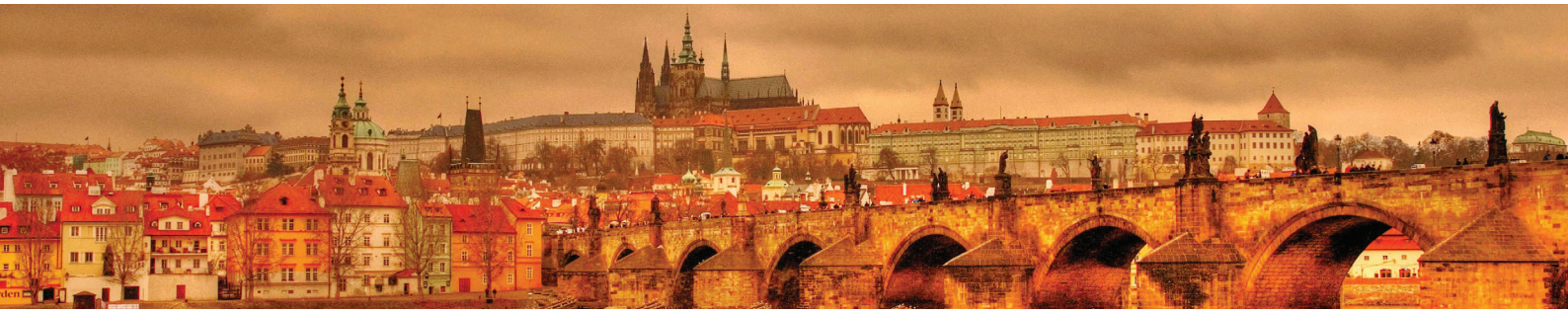
Born, 1952, he specialized in Veterinary Medicine between 1971 and 1974 at the University in Munich, then changed to the University in Cologne in 1974 and specialized in Human Medicine from 1974 to 1980. In 1976 to 1979, he additionally studied biometric methods for pharmacology and clinical research at the Institute for Data Analysis and Study Planning in Munich.

While studying human medicine, he completed research work on pattern recognition in the visual brain and developed a pharmacodynamic Neuron Simulation Model at the Institute for Medical Documentation and Statistics of the University at Cologne.

From 1985 to 1995, he was member of the Ultrahigh Dexamethasone Head Injury Study Group and leading biometrician of the German GUDHIS Study.

Since 1982 he holds advanced training courses on biometry for professionals in clinical research and university establishments. His work also involves human engineering of biometric software and GCP-compliant tutorials for biometric appraisal of clinical studies.

Since 1995 he cooperates closely with the Institute for Data Analysis and Study Planning as Senior Consultant for Biometry & Clinical Research. He planned and evaluated about 150 randomized clinical studies worldwide and is member of various international advisory boards including participation as biometric expert in regulatory authority panels and in FDA, EMEA, and BfArM hearings.



# GREGORY DEL ZOPPO
/USA

EDUCATION:

| | |
|---|---|
| 1966-1970 | B.S., Honors, Chemistry, University of Washington<br>Seattle, Washington |
| 1970-1973 | M.S., Biology (Molecular Biology, Neurophysiology)<br>California Institute of Technology, Pasadena, California |
| 1973-1977 | M.D.<br>University of Washington School of Medicine, Seattle, Washington |

PROFESSIONAL TRAINING AND POSITIONS HELD:

| | |
|---|---|
| 1977 | Externship<br>The National Hospital, Institute of Neurology, Queen Square<br>London WC1N 3BG, U.K. |
| 1977 - 1978 | Internship, Internal Medicine (Categorical)<br>St. Louis University Affiliated Hospitals, St. Louis, Missouri |
| 1978 - 1980 | Residency, Internal Medicine (Categorical)<br>University of Oregon Health Sciences Center, Portland, Oregon |
| 1979 | Senior House Officer and Registrar (Locum), Neurology<br>The National Hospital, Institute of Neurology<br>Queen Square, London WC1N 3BG, U.K. |
| 1980 - 1982 | Fellowship, Clinical Hematology/Medical Oncology<br>University of Oregon Health Sciences Center (Oregon Health Sciences University),<br>Portland, Oregon |
| 1982 - 1986 | Senior Research Associate<br>Department of Basic and Clinical Research, Scripps Clinic and Research Foundation<br>La Jolla, California |
| 1983 -2007 | Member<br>Division of Hematology/Medical Oncology, Scripps Clinic, La Jolla, California |
| 1986 - 1992 | Assistant Member<br>Department of Basic and Clinical Research/Molecular and Experimental Medicine<br>The Scripps Research Institute, La Jolla, California |
| 1986 - 1987 | Gastprofessur of the Deutsche Forschungsgemeinschaft (DFG) - Nr. Aa 2/75-1<br>Abteilung Neurologie, Klinikum RWTH, Aachen, Federal Republic of Germany, |
| 1989 - 1991 | Director, Coagulation Laboratory<br>Department of Clinical Pathology, Scripps Clinic and Research Foundation,<br>La Jolla, California |
| 1992 - 1997 | Associate Member |
| 1997 -2007 | Associate Professor, Department of Molecular and Experimental Medicine<br>The Scripps Research Institute, La Jolla, California |

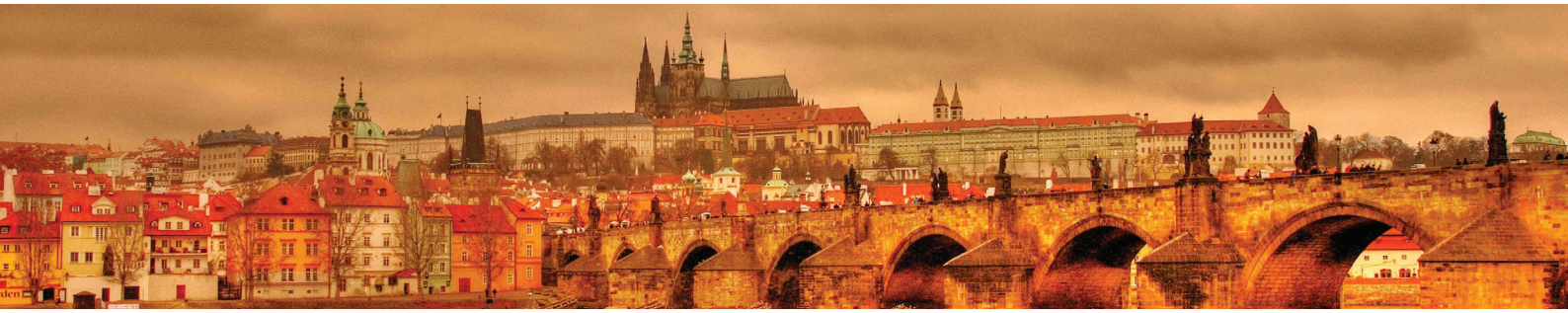
| | |
|---|---|
| 2007-Present | Professor, Department of Medicine<br>Division of Hematology, University of Washington, Seattle, Washington |
| 2007-Present | Adjunct Professor, Department of Neurology<br>University of Washington, Seattle, Washington |
| | Hospital Positions Held (in addition to the above): |
| 1982-2007 | Green Hospital of Scripps Clinic<br>La Jolla, California |
| 2007-Present | University of Washington, Haborview Medical Center<br>Seattle Cancer Care Alliance, Seattle, Washington |

HONORS AND AWARDS:

| | |
|---|---|
| 1969 | Phi Beta Kappa, Phi Eta Sigma, Phi Lambda Upsilon |
| 1970 | Baccalaureate Honors - Magna cum laude |
| 1977 | Merck Manual Award |
| 1986 | Gastprofessur, der Deutsche Forschungs◂gemeinschaft (DFG) - Nr. Aa 2/75-1<br>Abteilung Neurologie (Vorstand: K. Poeck), Klinikum, RWTH, Aachen,<br>Federal Republic of Germany |
| 1996 | Ad hoc Member, Neurology "A" Study Section, NIH, NINDS |
| 1997 - 2004 | Member, Neurology "A"/BDCN-1 Study Section, NIH, NINDS |
| 2001 | Ad hoc Member, AACR - 6 Study Section, NIH, NHLBI |
| 2001 -present | Member, Progress Review Group (PRG) for Stroke, NIH, NINDS |
| 2004 | NINDS Javits Neuroscience Investigator Award |
| 2005 | William M. Feinberg, M.D. Memorial Lecture in Stroke, University of Arizona |
| 2005 | Visiting Professor, Department of Neurology, University of California -<br>Irvine, 30-31 August, 2005 |
| 2005 - 2006 | Member, ZRG1, BINP - L (01) Study Section, NIH, NINDS |
| 2007 | Member, Review Session on Neuroscience, for the Excellence Initiative by the German Federal and State Governments to Promote Science and Research at German Universities, of the Deutsche Forschungsgemeinschaft (DFG), Bonn, 4-6 July, 2007 |
| 2008 | Member, Review Session of the Canadian Stroke Network, Washington,<br>D.C., 25 January, 2008 |
| 2008 - 2010 | Chair, Acute Neural Injury and Epilepsy (ANIE) Study Section, NIH |
| 2012 | Member, Review Panel for the LS 19 Life Sciences, Centres for Excellence in the Neurosciences Initiative, of the Deutsche Forschungsgemeinschaft (DFG),<br>Berlin, 9-11 January, 2012 |
| 2012 | The Thomas Willis Award, American Heart Association/American Stroke Association,<br>1 February, 2012 |
| 2012 | Election to Honorary Membership of the Japanese Society of Neurology (JSN),<br>22 May, 2012 |

BOARD CERTIFICATIONS:

| | |
|---|---|
| | American Board of Internal Medicine (ABIM) |
| 1981 | Internal Medicine |
| 1982 | Hematology<br>Medical Oncology (Board-eligible) |



PROFESSIONAL ORGANIZATIONS:

Fellow (FAHA), Council on Stroke; American Heart Association/American Stroke Association
Fellow (FAHA), Council on Arteriosclerosis, Thrombosis, and Vascular Biology,
American Heart Association

Member, Society for Neuroscience
Member, International Society of Thrombosis and Haemostasis
Member, International Society of Cerebral Blood Flow and Metabolism
Member, American Neurological Association

Member, International Stroke Society (now part of World Stroke Organization)
Member, American Society of Hematology
Member, American College of Physicians
Member, Association of American Physicians
Member, American Association for the Advancement of Science
Member, Molecular Medicine Society
Member, New York Academy of Sciences

TEACHING RESPONSIBILITIES:

Courses:

| | |
|---|---|
| 1986-2007 | Fellowship lectures on hemostasis/thrombosis (2-4 per year) |
| 2007-Present | Annual lectures in HuBIo552 course on hemostasis/thrombosis<br>Co-leader of small group sessions under HuBio552 |


THE SOCIETY FOR THE STUDY OF NEUROPROTECTION AND NEUROPLASTICITY

www.ssnn.ro