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UNIVERSITY OF
MEDICINE AND PHARMACY
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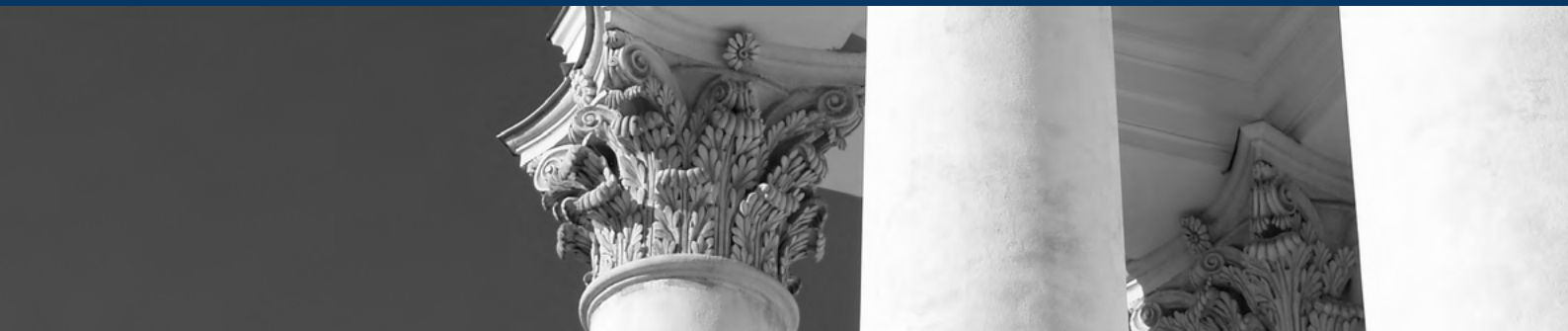
ROMANIA

"IULIU HATIEGANU" UNIVERSITY
OF MEDICINE AND PHARMACY

DOCTORAL SCHOOL NEUROSCIENCE PROGRAM

2020-2021 | SECTION 1

15 FEBRUARY, 2021
VIRTUAL MEETING



PhD NEUROSCIENCE PROGRAM COORDINATOR

Dafin F. Mureşanu

President of the European Federation of NeuroRehabilitation Societies (EFNR)

Chairman of EAN Communication and Liaison Committee

Co-Chair EAN Scientific Panel Neurotraumatology

Past President of the Romanian Society of Neurology

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

INTERNATIONAL GUEST LECTURER

Michael Chopp

Henry Ford Hospital, Department of Neurology, Detroit, MI, USA

Oakland University, Department of Physics, Rochester, MI, USA

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COURSE PROGRAM

COURSE PROGRAM

FEBRUARY 15TH, 2021

VIRTUAL MEETING

12:00 – 12:10	Welcome Address
12:10 – 12:55	Dafin F. Mureșanu/ Romania Challenges and opportunities in stroke recovery
12:55 – 13:40	Michael Chopp/ USA Physiological and molecular mechanisms mediating tissue damage after stroke
13:40 – 14:25	Michael Chopp/ USA Repair and restorative mechanisms after stroke
14:25 - 14:40	Session Break / Q&A
14:40 - 15:25	Michael Chopp/ USA Exosomes-biological nanoparticle therapy for stroke and neural injury
15:25 - 16:10	Michael Chopp/ USA Neurotrophic factors effective restorative and neurovascular protective therapy for stroke and traumatic brain injury
16:10 - 16:15	Concluding remarks

INTERNATIONAL GUEST LECTURER

MICHAEL CHOPP
USA

Michael Chopp, PhD, is Distinguished Professor of Physics at Oakland University. He has a joint appointment with Henry Ford Hospital where he is Vice Chairman for Research of the Department of Neurology, Scientific Director of the Henry Ford Neuroscience Institute, and is the Zoltan J. Kovacs Chair in Neuroscience Research.

He received his MS and doctorate degrees in Mathematical and Solid State Physics from New York University. After nearly 10 years of working as a Physicist and as a Professor of Physics, Dr. Chopp made a career change and turned his interest to translational research in neuroscience Dr. Chopp's research has primarily focused on: 1) cellular and molecular biology of ischemic cell injury, 2) the pathophysiology of stroke, traumatic brain injury, peripheral neuropathy, multiple sclerosis, and glioma, 3) combination thrombolytic and neuro and vascular protective therapies for stroke, 4) mechanisms of neuroprotection, 5) cell-based and pharmacological neurorestorative therapies for stroke, traumatic brain restorative therapies for stroke, traumatic brain injury and neurodegenerative disease, 6) molecular and cellular mechanisms underlying neurogenesis and angiogenesis and the induction of brain plasticity leading to functional and behavioral recovery after neural injury,7) treatment of glioma and breast cancer, 8) exosomes/microRNA for treatment of neurological injury and disease, and 9) magnetic resonance imaging. Dr. Chopp has 687 peer reviewed publications (h-index 111), ~ 50 book chapters and has given 459 plenary lectures and invited presentations. He has chaired National Institutes of Health (NIH) study sections and has often served as a consultant to government agencies, the U.S. National Institutes of Health, and the pharmaceutical industry.

Awards include:

2001 Top Ten Research Advances of 2001, "Treatment of Stroke with Bone Marrow Stromal Cells", American Heart Association
2005 Distinguished Scientist Award, Henry Ford Medical Group, Board of Governors
2012 Lecture of Excellence and World Stroke Organization (WSO) Award, Remodeling and rewiring the intact CNS as a treatment for Stroke, 8th World Stroke Congress, Brasilia, Brazil, October
2014 Abraham White Distinguished Science Award. "For discovery of the role of thymosin beta 4 in the treatment of brain injuries and neurodegenerative diseases; 4th International Symposium on Thymosins in Health and Disease, Washington, DC, October
2015 Thomas Willis Lecture Award, International Stroke Conference, Nashville, TN, February
2015 Doctor Honoris Cause, Universitas Medicinae Et Pharmaceuticae Artium Napocensis "Iuliu Haieganu", 5th European Teaching Course of NeuroRehabilitation, Cluj-Napoca, Romania
2016 Lecture of Excellence and Barbro B. Johansson Award, 10th World Stroke Conference, Hyderabad, India, October

DAFIN F. MUREȘANU
ROMANIA

Professor of Neurology, Senior Neurologist, Chairman of the Neurosciences Department, Faculty of Medicine, "Iuliu Hatieganu" University of Medicine and Pharmacy Cluj-Napoca, President of the European Federation of Neurorehabilitation Societies (EFNR), Chairman Communication Committee of the European Academy of Neurology (EAN), Past President of the Romanian Society of Neurology, President of the Society for the Study of Neuroprotection and Neuroplasticity (SSNN), Chairman "RoNeuro" Institute for Neurological Research and Diagnostic, Corresponding Member of the Romanian Academy, Member of the Academy of Medical Sciences, Romania and secretary of its Cluj Branch. He is member of 17 scientific international societies (being Member of the American Neurological Association (ANA) - Fellow of ANA (FANA) since 2012) and 10 national ones, being part of the executive board of most of these societies. Professor Dafin F. Muresanu is also a specialist in Leadership and Management of Research and Health Care Systems (specialization in "Management and Leadership, Arthur Anderson Institute, Illinois, USA, 1998"; "MBA – Master of Business Administration - Health Care Systems Management, The Danube University - Krems, Austria, 2003"). He has performed valuable scientific research in high interest fields such as: neurobiology of central nervous system (CNS) lesion mechanisms; neurobiology of neuroprotection and neuroregeneration of CNS; the role of the Blood-brain barrier (BBB) in CNS diseases; developing comorbidities in animal models to be used in testing therapeutic paradigms; nanoparticles neurotoxicity upon CNS; the role of nanoparticles in enhancing the transportation of pharmacological therapeutic agents through the BBB; cerebral vascular diseases; neurodegenerative pathology; traumatic brain injury; neurorehabilitation of the central and peripheral nervous system; clarifying and thoroughgoing study on the classic concepts of Neurotrophicity, Neuroprotection, Neuroplasticity and Neurogenesis by bringing up the Endogenous Defense Activity (EDA) concept, as a continuous nonlinear process, that integrates the four aforementioned concepts, in a biological inseparable manner.

Professor Dafin F. Muresanu is coordinator in international educational programs of European Master (i.e. European Master in Stroke Medicine, University of Krems), organizer and co-organizer of many educational projects: European and international schools and courses (International School of Neurology, European Stroke Organisation Summer School, Danubian Neurological Society Teaching Courses, Seminars - Department of Neurosciences, European Teaching Courses on Neurorehabilitation) and scientific events: congresses, conferences, symposia (International Congresses of the Society for the Study of Neuroprotection and Neuroplasticity (SSNN), International Association of Neurorestoratology (IANR) & Global College for Neuroprotection and Neuroregeneration (GCNN) Conferences, Vascular Dementia Congresses (VaD), World Congresses on Controversies in Neurology (CONy), Danube Society Neurology Congresses, World Academy for Multidisciplinary Neurotraumatolgy (AMN) Congresses, Congresses of European Society for Clinical Neuropharmacology, European Congresses of Neurorehabilitation). His activity includes involvement in many national and international clinical studies and research projects, over 500 scientific participations as "invited speaker" in national and international scientific events, a significant portfolio of scientific articles (231 papers indexed on Web of Science-ISI, H-index: 23) as well as contributions in monographs and books published by prestigious international publishing houses. Prof. Dr. Dafin F. Muresanu has been honoured with: „Dimitrie Cantemir" Medal of the Academy of The Republic of Moldova in 2018, Ana Aslan Award 2018 - "Performance in the study of active aging and neuroscience", for the contribution to the development of Romanian medicine, National Order "Faithful Service" awarded by the President of Romania in 2017; "Iuliu Hatieganu" University of Medicine and Pharmacy Cluj-Napoca, Faculty of Medicine, the "Iuliu Hatieganu Great Award 2016" for the best educational project in the last five years; the Academy of Romanian Scientists, "Carol Davila Award for Medical Sciences / 2011", for the contribution to the Neurosurgery book "Tratat de Neurochirurgie" (vol.2), Editura Medicala, Bucuresti, 2011; the Faculty of Medicine, "Iuliu Hatieganu" University of Medicine and Pharmacy Cluj-Napoca "Octavian Fodor Award" for the best scientific activity of the year 2010 and the 2009 Romanian Academy "Gheorghe Marinescu Award" for advanced contributions in Neuroprotection and Neuroplasticity.

ABSTRACTS

CHALLENGES & OPPORTUNITIES IN STROKE RECOVERY

DAFIN F. MUREȘANU
Chairman Department of Neurosciences University of Medicine and Pharmacy 'Iuliu Hatieganu', Cluj-Napoca, Romania

Brain damage affects all three levels of structural and functional organization: cellular and molecular level, circuitries level and dynamic network level and launches an endogenous continuous brain defense response which consists in neuroprotection (the immediate response) and neurorecovery (a later response).
Endogenous neuromodulation represents at the cellular and molecular level the optimization of common biological processes that could potentially generate cell death or promote neurodegeneration. At the circuitries and dynamic network levels, it represents the tendency in reinbalancing of functional connectivity in resting-state netwoks.

In the last years, there has been a substantial effort in understanding the brain functioning and how to enhance endogenous neuromodulation and neurorehabilitation in general, by using a large spectrum of neurotechnologies such as imaging techniques (functional magnetic resonance imaging, ligant-based positron emission tomography, diffusion-tensor imaging), quantitative electroencephalogram, magnetoencephalography, eye tracking, optogenetics, transcranial magnetic stimulation, transcranial direct current simulation, deep brain simulation, computational neuroscience and brain-computer interfaces. The combination between these technologies provide valuable information about the structure-function relationship underling resting-state networks, about the dynamic cross-talk between networks and about the abnormalities in the functional connectivity in different pathologies.

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.

Over the last decades, therapeutic approaches for stroke have significantly evolved and improved as a consequence of the implementation of modern stroke units, improvement of general medical care and more structured and early administered rehabilitation schemes.

Thrombolytic therapy with rt-PA (recombinant tissue plasminogen activator) has been developed and a number of clinical trials have recently confirmed the effectiveness of thrombectomy to be better than rtPA alone.

Except thrombolytic therapy and thrombectomy there is still no widely accepted therapy for acute ischemic stroke. Current data shows that even if advanced procedures can be used, 60% of stroke patients die or remain with a certain level of deficit. As it is widely accepted that immobilization-related complications cause over 50% of stroke patients' deaths, rehabilitation plays an important role in stroke care.

It is getting clearer that multimodal drugs may play an important role in pharmacological support of neurorehabilitation after stroke.

The results of recently published large and well-controlled clinical studies show a positive effect on neurological recovery after acute ischemic stroke.

PHYSIOLOGICAL AND MOLECULAR MECHANISMS MEDIATING TISSUE DAMAGE AFTER STROKE

MICHAEL CHOPP
Henry Ford Hospital, Department of Neurology, Detroit, MI, USA
Oakland University, Department of Physics, Rochester, MI, USA

This presentation will include discussion of: 1) mechanisms underlying cerebral damage after experimental thromboembolic stroke, secondary microvascular hypoperfusion deficits post stroke-basis for no-reflow, 2) brain heart interactions ,-demonstrating secondary cardiac adverse effects of stroke , 3) comorbidity - the effects of age, gender and diabetes on stroke outcomes, and therapeutic approaches for the treatment of experimental stroke with diabetes.

REPAIR AND RESTORATIVE MECHANISMS AFTER STROKE

MICHAEL CHOPP
Henry Ford Hospital, Department of Neurology, Detroit, MI, USA
Oakland University, Department of Physics, Rochester, MI, USA

The following will be discussed: 1) Intrinsic restorative mechanisms activated after stroke, including stimulation and coupling of neurogenesis, angiogenesis, and axonal dendritic rewiring throughout the central nervous system; 2) the role of activated astrocytes in mediating restorative events; 3) molecular and microRNA pathways that contribute to remodeling of the CNS post stroke, with an emphasis on rtPA as a potential means to stimulate neurological recovery

EXOSOMES-BIOLOGICAL NANOPARTICLE THERAPY FOR STROKE AND NEURAL INJURY

MICHAEL CHOPP
Henry Ford Hospital, Department of Neurology, Detroit, MI, USA
Oakland University, Department of Physics, Rochester, MI, USA

The following will be discussed: 1) Intrinsic restorative mechanisms activated after stroke, including stimulation and coupling of neurogenesis, angiogenesis, and axonal dendritic rewiring throughout the central nervous system; 2) the role of activated astrocytes in mediating restorative events; 3) molecular and microRNA pathways that contribute to remodeling of the CNS post stroke, with an emphasis on rtPA as a potential means to stimulate neurological recovery.

NEUROTROPHIC FACTORS EFFECTIVE RESTORATIVE AND NEUROVASCULAR PROTECTIVE THERAPY FOR STROKE AND TRAUMATIC BRAIN INJURY

MICHAEL CHOPP
Henry Ford Hospital, Department of Neurology, Detroit, MI, USA
Oakland University, Department of Physics, Rochester, MI, USA

Here, I will summarize our data on prospective, double blinded, placebo controlled preclinical studies, performed under rigorous clinical trial conditions for the treatment of stroke and TBI. In addition, I will review and provide new insight into the multiple mechanisms of action of neurotrophic factors. Data will be shown that neurotrophic factors evokes expression of Angiopoietin 1 (Ang1), which promotes blood brain barrier integrity, is anti-inflammatory and mediates axonal outgrowth. neurotrophic factors also up regulates the expression of the developmental morphogen Sonic Hedgehog (Shh). Shh stimulates cellular expression of tissue plasminogen activator (tPA), which acts as both an endogenous thrombolytic agent and plays a pivotal role in promoting neurite outgrowth and neurological recovery. In addition , I provide novel insight into how neurotrophic factors stimulates specific sets of microRNAs (miRs). miRs are small non-coding RNAs which can simultaneously post-transcriptionally regulate the translation of many genes. Shh acts to up regulate cellular expression of the miR-17-92 cluster. This cluster of miRs, has potent anti-inflammatory effects as well as promotes axonal outgrowth. Thus, we demonstrate that neurotrophic factors has multifactorial neurovascular remodeling effects on tissue which drives neurological recovery.


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