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FUNDATIA JURNALULUI Journal of Medicine and Life

E A N

TASK FORCE FOR RARE NEUROLOGIC DISEASES

TEACHING COURSE

7 - 9 SEPTEMBER 2017

"IULIU HATIEGANU" UNIVERSITY OF MEDICINE AND PHARMACY

"IULIU HATIEGANU" AUDITORIUM | 23 GHEORGHE MARINESCU STREET | CLUJ -NAPOCA | ROMANIA

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Past President of the Romanian Society of Neurology

Chairman "RoNeuro" Institute for Neurological Research and Diagnostic

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Dept. Medicine, Surgery and Neurosciences, Medical School, University of Siena, Italy

Chair of the EAN Rare Neurological Diseases Task Force

FACULTY

IN ALPHABETICAL ORDER

Ovidiu Băjenaru / Romania

Jean-Marc Burgunder / Switzerland

Anna Czlonkowska / Poland

Antonio Federico / Italy

Holm Graessner / Germany

Maurizio Leone / Italy

Albert Ludolph / Germany

Maria Judit Molnár / Hungary

Dafin F. Mureșanu / Romania

Alessandra Rufa / Italy

Johann Sellner / Austria

Antonio Toscano / Italy

GENERAL INFORMATION

REGISTRATION DESK

All materials and documentation will be available at the registration desk located at SSNN booth.
The staff will be pleased to help you with all enquiries regarding registration, 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.

LOGISTIC PARTNER:

SYNAPSE
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LANGUAGE

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

CHANGES IN PROGRAM

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

NAME BADGES

Participants are kindly requested to wear their name badge at all times. The badge enables admission to the scientific sessions and dinners.

FINAL PROGRAM & ABSTRACT BOOK

The participants documents include the program and abstract book which will be handed out at the registration counter.

COFFEE BREAKS

Coffee, tea and water are served during morning coffee breaks and are free of charge to all registered participants.

MOBILE PHONES

Participants are kindly requested to keep their mobile phones turned off while attending the scientific sessions in the meeting rooms.

CURRENCY

The official currency in Romania is RON.

ELECTRICITY

Electrical power is 220 volts, 50 Hz. Two-prong plugs are standard.

TIME

The time in Romania is Eastern European Time (GMT+2).

ACADEMIC PARTNERS

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Opera Cluj-Napoca
www.operacluj.ro

SCIENTIFIC PROGRAM

THURSDAY, SEPTEMBER 7TH, 2017

09:00 – 09:30	***OPENING REMARKS***
09:30 – 10:30	Antonio Federico (Italy) A general approach to the diagnosis and care of rare neurologic diseases and the EAN Role: a Pandora box for neurology
10:30 - 11:00	Holm Graessner (Germany) ERNs: which are the changes in clinical practice for neurology
11:00 – 11:30	***COFFEE BREAK***
11:30 – 13:00	Jean-Marc Burgunder (Switzerland) Rare Neurologic diseases presenting with movement disorders a. Ataxia, spastic paraparesis b. Huntington's and parkinsonism
13:00 – 14:00	***LUNCH BREAK***
14:00 – 15:00	Antonio Federico (Italy) Late onset Neurometabolic Diseases: dementias, leucoencephalopathies, movement disorders, etc
15:00 – 16:30	Antonio Federico (Italy) Rare Neurologic disorders (late onset) presenting with leukoencephalopathy (non-metabolic)
16:30 – 17:00	***COFFEE BREAK***

THURSDAY, SEPTEMBER 7TH, 2017

17:00 – 17:30	Maurizio Leone (Italy) Guidelines for rare diseases
17:30 – 18:00	Anna Czlonkowska (Poland) Wilson's disease
17:30 – 20:00	***CASE DISCUSSION***
20:00 – 21:00	***DINNER***

FRIDAY, SEPTEMBER 8TH, 2017

09:00 – 10:00	Maria Judit Molnar (Hungary) Informatic supports and data banks for diagnosis of rare neurologic diseases
10:00 – 11:00	Antonio Toscano (Italy) Rare Neurologic disorders presenting with Myopathy
11:00 – 11:15	***COFFEE BREAK***
11:15 – 12:15	Antonio Toscano (Italy) Metabolic myopathies
12:15 - 13:15	Dafin Muresanu (Romania) Rare neurologic disorders in the context of rare causes of stroke
13:15 – 14:15	***LUNCH***
14:15 – 15:15	Antonio Toscano (Italy) Skin, muscle and nerve biopsies for diagnosis of rare diseases
15:15 – 16:15	Albert Ludolph (Germany) Rare Neurologic Diseases presenting with motor neuron disease
16:15 – 17:15	Jean-Marc Burgunder (Switzerland) Perspective on treatment of rare neurologic disorders
19:00	***SPECIAL CULTURAL AND NETWORKING EVENT***

SATURDAY, SEPTEMBER 9TH, 2017

08:00 – 08:30	Alessandra Rufa (Italy) Eye movements for diagnosis of rare neurologic diseases
08:30 -09:00	Ovidiu Bajenaru (Romania) Epilepsy in Tuberous Sclerosis Complex
09:00 -09:30	Johann Sellner (Austria) Spinal cord infarction
09:30 – 09:45	***COFFEE BREAK***
09:45 – 11:00	***ROUND TABLE*** Coordinators: Antonio Federico and all speakers

Current therapeutic opportunities for rare neurologic diseases

- Niemann Pick type C, Gaucher, Lysosomal diseases
- Mitochondrial diseases and LHON
- CTX
- Glycogenosis
- Wilson and other chelating therapies
- Muscle spinal atrophy
- Others

11:00 – 11:10 ***CONCLUSIONS & CLOSING REMARKS***

ABSTRACTS

EPILEPSY IN TUBEROUS SCLEROSIS COMPLEX

OVIDIU BĂJENARU
University of Medicine and Pharmacy "Carol Davila" Bucharest, Romania

TSC is a multisystem disorder that results from mutations in TSC1 (hamartin) or TSC2 (tuberin) genes. TSC1/TSC2 complex can influence neuronal and synaptic structures as well as neurotransmission: tumor growth suppressors, agents that regulate cell proliferation and differentiation. TSC is one of the leading genetic causes of epilepsy, often refractory to treatment. Mutations in TSC1/TSC2 complex modify the mTOR cascade, which influnces the normal development of normal cortical neurons and their excitability, leading to cortical dysplasia, focal deficits, neurocognitive impairment and epilepsy. Epilepsy in TSC is generally treated with specific antiepileptic drugs and eventualy surgery. In cases of refractory epilepsy associated with TSC, recently a new therapeutic approach based on mTOR inhibition, associated with classical therapeutic algorithm, proved its efficiency in a recent clinical trial. This could be seen as an example of disease modifying therapy and a potential antiepileptogenic approach.

ERSPECTIVE ON TREATMENT OF RARE NEUROLOGIC DISORDERS

JEAN-MARC BURGUNDER
Professor of Experimental Neurology at the Faculty of Medicine of the University in Bern, Switzerland

A most precise diagnosis as possible will best guide treatment in rare neurological disorders. In rare instances, a thorough diagnostic work up, including extensive metabolic investigations, exome or even genome sequencing, may lead to a the discovery of a very specific defect, which can be treated appropriately. Such treatment may range from a small molecule to a complex treatment to decrease gene expression or to modulate brain activity. One example of the first is the discovery of mutations in SLC19A3 in a basal ganglia disorder responsive to biotin treatment, of the second antisense oligonucleotides treatment in spinal muscular atrophy.

Clinical research on silencing abnormal gene expression with different techniques in a number of rare neurologic disorders is well in progress. This is complemented by novel preclinical research on gene modification and repair.

For the time being, more frequently, treatment will be symptomatic either solely or complementary because therapy of the cause may not fully alleviate all aspects of the phenotype. Rare neurological disorders usually have a very complex phenotype

including cognitive and psychiatric changes with movement disorders, dysphagia and dysarthria, sometimes alongside with autonomic and neuromuscular changes as well as systemic ones. For this reason, a multidisciplinary team involving specialists from the involved fields, both physicians and allied health, is mandatory. Finally, the needs and wishes of the patient and his family are important to guide management. In order to do this it is important to provide appropriate information, including limitations in therapeutic options at the present time.

RARE NEUROLOGIC DISEASES PRESENTING WITH MOVEMENT DISORDERS

JEAN-MARC BURGUNDER
Professor of Experimental Neurology at the Faculty of Medicine of the University in Bern, Switzerland

Abnormal movements are often part of the phenotype in rare neurologic disorders and are usually quite similar to those found in more frequent disorders. They may be hyperkinetic, like chorea, myoclonus, dystonia, ataxia, bradykinetic or spastic and often occur in combination. They sometimes are the major symptom and sign, like leg spasticity in hereditary spastic paraplegia, or ataxia in spinocerebellar ataxias, more often part of a complex syndrome like chorea in Huntington's disease. Clues to recognise rare neurologic disease presenting with movement disorders include a positive family history, and early onset. The presence of a complex phenotype with cognitive and psychiatric involvement, malformations, and systemic involvement also provides hints for a rare disorder. Differential diagnosis from common diseases may be quite difficult at movement disorder onset and a thorough evaluation is needed, specifically with the aim to recognise rare disorders, which may be treated in order to avoid later complications. In any case, it is very important to closely follow-up the patient in the course of the disorder, this is needed to further precise diagnosis as the syndrome develops, but also to address specific problems as they present at later stages.

Diagnostic work up is based on detailed clinical investigation, which includes neurological examination with cognitive and psychiatric assessment as well as general physical check-up. Typically, brain MRI and laboratory investigations will be performed. Molecular genetic assessment, either guided by the phenotype allowing single gene testing in well-defined phenotypes, or exome sequencing in other cases may provide the genetic diagnosis.

WILSON'S DISEASE

ANNA CZŁONKOWSKA

2nd Department of Neurology, Institute of Psychiatry and Neurology
and Department of Pharmacology, Warsaw Medical University, Poland

Wilson's disease (WD) is relatively rare, inherited as an autosomal recessive disorder, due to copper accumulation and toxicity. WD may present with a variety of hepatic (40%), neurological (40%) or behavioral (15%) signs and symptoms between age of 5 to 50 years. Hepatic diseases as hepatitis, cirrhosis, liver failure occur most often in the second decade of life. Neurological symptoms occur at older age. Dystonia, postural or rest tremor, dysarthria, drooling or gait disturbances may dominate. Most common psychiatric symptoms, at disease onset, which start and often coincide with neurological forms, are incongruous behavior, irritability, aggression but may be also severe depression or psychosis. The diagnosis in the early stage may be difficult due to diverse manifestations. The characteristic feature of the disease Kayser-Fleischer rings is present in almost all neurological, but in less than 50% hepatic cases. Family history of hepatic or extrapyramidal disorders can be very helpful. First laboratory diagnostic tests which should be done are serum ceruloplasmin, copper concentration (decreased) and urinary excretion of copper (increased). DNA analysis is now the gold standard, but due to high number of mutations in WD gen not always positive result is obtained. In doubtful cases radioactive copper incorporation to ceruloplasmin and liver biopsy can be performed. Neuroimaging techniques as MR play an important role in diagnosis and monitoring of the treatment. The spontaneous course of the disease varies enormously but untreated many patients will die in the first 5 years after onset of the initial symptoms. Chelating therapy (d-penicillamine and treientine) or zinc salts initiated early and maintain for whole life dramatically changes WD prognosis. In future gene therapy seems possible.

A GENERAL APPROACH TO THE DIAGNOSIS AND CARE OF RARE NEUROLOGIC DISEASES AND THE EAN ROLE: A PANDORA BOX FOR NEUROLOGY

ANTONIO FEDERICO
Dept Medicine, Surgery and Neurosciences, Medical School, University of Siena, Italy.
Chair Scientific Committee EAN and Chair of EAN TF Rare Neurologic Diseases

Rare Neurological diseases are a Pandora Box for Neurology.

The list of the Rare diseases encloses more then 5000 disorders, half of them have a neurological interest, with involvement of the Central and Peripheral nervous system or Muscle or all.

They are underdiagnosticated and a global effort is necessary to improve their knowledge, the possibility to have a correct diagnosis by dissemination of information and culture on them and research, leading to possible treatments (the majority of them are without treatments and in all countries has started a cooperative effort for "orphan drugs".

In USA, since 30 years ago has been stimulated the interest on these disorders, followed 10 year later by the European Community.

Several Scientific Societies have started to have a promoting role on this field.

Since Neurology , as speciality, has the major role in the diagnosis and care of this disease, and basic and applied neurosciences in the research on their pathogenesis, EAN have the main responsibility for the promotion of the knowledge of these disorders, of the informations and of the research within the neurological community in Europe.

The Scientific Committee of the EAN organized a Task Force to Rare Neurologic Diseases, that will have a strict relationship with the Subspecialities Panels. It have members from all the different Panels (the Chairmen (ex officio), another member and a delegate from the Patient Associations) and young Neurologists (from each panels).

This could be an interesting action of the EAN Board, either from the political and ethical point of vue (orphans diseases and orphan drugs) either from a practical point of vue, giving to our members facilities to be informed on this topics and stimulating interactions for the different groups in Europe involved into research .

The aims of the TF is:

- Stimulation the redaction of a list of Rare Neurological Diseases, with main symptoms and diagnostic criteria and guidelines for diagnosis

- Evaluation of the facilities for diagnosis of RND in Europe (produce a list of facilities and address), with the indication where are the main centers interested in the different disorders, where is possible to do the genetic, biochemical and other laboratory tests, etc
- Promotion of an analysis of the attitude of European Neurologist to RND and which is the state of the art of this issue in the different European countries;
- Stimulation to promotion of registries for RND, data bank and biobanks. These are main aims of the EU, with Research projects in the Biomed Program.
- Stimulation to create European Networks for RND for diagnosis and research.
- Promotion of Teaching courses in Europe.
- Information Service for Rare Neurological Diseases, within the EAN, that will be able, with the collaboration of the different experts present in the WG, to answer to questions from patients, families and doctors (on line). Information service on new data, new findings, research founds, treatments, etc. Discussion on Rare Cases, within the Section on Web page where cases will be described and experts from SSP will answer.

With this activity, the EAN recognizes the primary role of neurologists in the care of these disorders, the necessity to improve the level of the organization of the Neurological Units in Europe and of the formation of neurologists in the care of rare neurological disorders. But also we will stimulate a better integrated relationship with Patient Associations.

We will also focused our attention on the clinical approach to a Rare Neurologic Disease and some guidelines for the diagnosis.

GENETIC LEUCODYSTROPHIES AS A MODEL OF OLIGODENDROCYTE DYSFUNCTION

ANTONIO FEDERICO
Dept Medicine, Surgery and Neurosciences, Medical School, University of Siena, Italy.
Chair Scientific Committee EAN and Chair of EAN TF Rare Neurologic Diseases

Leukodystrophies are a group of orphan genetic diseases that primarily affect the white matter (WM) of the brain. Glial cells play a major role in the structural, metabolic and trophic support of axons.

Diversity of the genetically determined defects that interfere with glial cell functions explain the large heterogeneity of leucodystrophies that may be classified:

- According to neuropathology (staining: ortochromatic, metachromatic, sudanophilic; site of demyelination: sparing U fibres,etc; associated findings)
- According with clinical aspects (peripheral nerve, muscle, eye involvement, macrocephaly, tendinous xanthomas, premature aging,, skin and bone changes, endocrine involvement: adrenocortical or ovarian insufficiency, diabetes, etc)
- According to biochemical abnormalities
- According to molecular genetic abnormalities.

We will describe the main well known forms (Adrenoleucodystrophy, Metachromatic Leucodystrophy, Krabbe Disease) and some rarer conditions as Vanishing White Matter disease, Vacuolating Leucodystrophy, Alexander disease, etc, describing the clinical findings for clinical suspicion and the pathogenetic mechanisms.

LATE ONSET NEUROMETABOLIC DISEASES: DEMENTIAS, LEUCOENCEPHALOPATHIES, MOVEMENT DISORDERS, ETC.

ANTONIO FEDERICO
Dept Medicine, Surgery and Neurosciences, Medical School, University of Siena, Italy.
Chair Scientific Committee EAN and Chair of EAN TF Rare Neurologic Diseases

The biochemical pathogenesis of many hereditary diseases of the nervous system and muscle has in the recent years been very much investigated: for many diseases an enzyme defect and metabolic substances accumulating in the tissues or in biological fluids have been identified facilitating the diagnosis of a large number of genetic metabolic encephaloneuromyopathies.

Beside the well known infantile- and juvenile-onset diseases, an increasing number of cases with a slowly progressive disease and adult onset have been described, the pathogenesis of which is linked to the same congenital defect of lysosomal, mitochondrial or peroxysomal metabolism as the early onset forms, but in which the onset of the clinical manifestations is delayed in adult age.

We will report the most recent data on the metabolic basis of several disorders mainly involving neurons (characterized by dementia, epipepsy, etc), oligodendrocytes (presented with leucoencephalopathies) , basal ganglia (with

particular regards to the different forms of Parkinsonism, dystonia, and other movement disorders etc).

From a metabolic point of view, we will summarize the clinical and biochemical aspects of the disorders related to

- Storage material for a primary lysosomal dysfunction of lipid metabolism
- Plasma membrane lipid changes due to peroxisomal impairment
- Cell cholesterol trafficking disturbancies
- Energy metabolism impairment
- Chromosomal instability and Dna repair
- Cell nutrients deficiency
- Small vessel diseases
- Disorders of Heavy Metal Metabolism
- Disorders of Neurotransmitter Metabolism
- Disorders of intermediary metabolism
- Disorders of mechanism of DNA Damage and Repair

For all of them we will describe clinical signs, diagnostic work-up and possible therapeutic strategies.

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ERNs: WHICH ARE THE CHANGES IN CLINICAL PRACTICE FOR NEUROLOGY

HOLM GRAESSNER
University Hospital Tübingen, Germany

European Reference Networks (ERNs) have been created so that the best specialists from across Europe could join their efforts to tackle rare medical conditions that require highly specialised healthcare and a concentration of knowledge and resources. The objectives of the ERNs are seen best achievable at EU level. These encompass better access of patients to highly specialised and high quality and safe care, European co-operation on highly specialised healthcare, pooling knowledge, improving diagnosis and care in medical domains where expertise is rare, helping Member States with insufficient number of patients to provide highly specialised care, maximising the speed and scale of diffusion of innovations in medical science and health technologies and being focal points for medical training and research, information dissemination and evaluation.

The European Reference Network for Rare Neurological Diseases (ERN-RND)

is one of 24 ERNs which started to work in March 2017 and is a network of 32 Healthcare Providers from 13 EU member states. To achieve its objectives it will pursue two main approaches that will change clinical practice for neurology. Firstly, it will focus on knowledge management for RND. Through consolidating knowledge and expertise scattered across countries, ERN-RND will give healthcare providers access to a much larger pool of expertise. This will result in better chances of RND patients to receive an accurate diagnosis and evidence-based management. Secondly, using a dedicated IT platform and telemedicine tools ERNs will implement "virtual multidisciplinary consultation" to review diagnosis and treatment of complex rare disease patients in advisory boards of medical specialists across different disciplines. This way, the medical knowledge and expertise will travel rather than the patients.

GUIDELINES FOR RARE DISEASES

MAURIZIO LEONE

Director of the Neurology Unit at the Clinical Research Institute IRCCS "Casa Sollievo della Sofferenza" in San Giovanni Rotondo, Italy

Rare Diseases (RD) are frequently life-threatening or seriously debilitating conditions, which can cause significant morbidity and mortality, can severely affect quality of life, and can confer a social and economic burden on families and communities. Knowledge of RDs is poorer and treatments opportunities are fewer than for other diseases. These conditions are, by their nature, encountered very infrequently by clinicians; thus, clinical practice guidelines are potentially very helpful in supporting clinical decisions, health policy and resource allocation.

Most of the available evidence for therapy of RDs comes from observational studies with many limitations, or even from case reports or case series. Randomized clinical trials (RCT) are rare and difficult to perform. In this setting, small sample size is the main concern, and RCTs may not allow for the more conventional statistical analysis. Thus there is a need for improved designs for small trials. The possibility to use alternative clinical trial designs for the evaluation of interventions should be explored in this particular disease-treatment-outcome setting.

Guidelines for RD are clearly affected by the lack of evidence from RCTs. Other drawbacks and shortcomings include difficulties to identifying groups of patients (often unclear diagnostic criteria), and defining relevant outcomes (few studies on patient-reported outcomes, frequent use of surrogate outcomes, time-length of some outcomes). Applying the strategy, commonly known as "PICO" (patient, intervention, comparator, outcome), is not always possible. All these difficulties

lead to a paucity of RD guidelines of high quality.

However, notwithstanding these difficulties, the EAN considers the production of neurological guidelines in RDs a primary tool to improve clinical practice in European Neurology. The use of the GRADE system (Grading of Recommendations, Assessment, Development and Evaluation) adopted by EAN for frequent diseases may be challenging in producing guidelines for RDs.

RARE NEUROLOGIC DISEASES PRESENTING WITH MOTOR NEURON DISEASE

ALBERT LUDOLPH
Department of Neurology, University of Ulm, Germany

The term motor neuron diseases describes a syndrome which comprises clinically those syndromes which are characterized by predominant motor neuron involvement. However, it is now well-known, that so called motor neuron diseases are multisystem degenerations and other diseases such as Parkinson's disease are also affecting motor neurons.

The most relevant and frequent motor neuron disease is amyotrophic lateral sclerosis. Recently, the formal pathogenesis has been delineated by Heiko Braaks group. The disease spreads along the association fibers of the cortex and affects those subcortical nuclei which are monosynaptically connected with cortical neuronal groups. Syndromes like progressive muscular atrophy (PMA) and primary lateral sclerosis (PLS) can be easily integrated into this concept. Also the minor frontal deficits of ALS patients are part of this staging effort. The spinal muscular atrophies (SMA's), however, can be not be integrated into this effort.

Therapeutically the concept of initiation and propagation is attractive for further developments; there are genetically-based concepts (antisense oligonucleotides) which are also currently in the therapeutic focus.

INFORMATIC SUPPORTS AND DATA BANKS FOR DIAGNOSIS OF RARE NEUROLOGICAL DISORDERS

MÁRIA JUDIT MOLNÁR
Institute of Genomic Medicine and Rare Disorders, Hungary

The importance of the use of the artificial intelligence (AI) has increasing importance in these days. Computer processing power is doubling every 18 months and the amount of healthcare data is doubling every 18 months. It has special importance in the field of the rare disorders since in every month a new gene is associated with human disease. Presently we know cc. 8.000 rare human diseases and about 60-70% of them is related to the nervous system.

It would take a physician cc. 160 hours/week of reading to stay up to date on the latest literature. The John Hopkins Study in the USA revealed that cc. 40,500 patients died of misdiagnosis a year. Many of them had rare neurological disorders. The management of this huge amount of data is really challenging for the human brain. On the other side our human cognition has some distortions, such as perception of disease prevalence, recall bias, order effect, framing, anchoring, the management of the potential hypotheses is limited. All these factors support the fact that we have to use the artificial intelligence in the everyday clinical diagnostic and treatment of the rare neurological disorders.

The presentation will offer the introduction into the field of estimation tools, diagnostic tools and therapeutic decisions tools supported by AI. The workshop will clarify why databanks and registries are important even in the everyday clinical praxis, how we get an Improved diagnosis with help of evidence-based decision support, how we can use different softwares for the interpretation of next-generation diagnostics and disease-gene discovery and how artificial intelligence and machine learning can be useful for clinical diagnostic.

RARE NEUROLOGIC DISORDERS IN THE CONTEXT OF RARE CAUSES OF STROKE

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

According to the World Health Organization, 15 million people suffer stroke worldwide each year. Of these, 5 million die and another 5 million are permanently disabled. Europe averages approximately 650,000 stroke deaths each year.

Stroke is the number one cause of permanent disability globally and the second most common cause of dementia. Although stroke among young adults is generally considered a rare event, with a previous study reporting that about 5% of all strokes in the United States occurred in a young adult population aged between 18 and 44 years, there is growing evidence of an increasing trend of stroke in young adults. It has been documented that stroke incidence in young adults aged between 20 and 54 years has significantly increased between 1999 and 2005.

Many risk factors for cerebrovascular diseases have been established including no modifiable factors such as age, gender, and race, as well as acquired risk factors such as hypertension, smoking, diabetes, and obesity. These factors, however, only account for a portion of the stroke risk suggesting that other variables, including genetics, must be involved in the etiology of stroke. The exact contribution of genetics to the incidence of stroke still remains largely unknown; however, it is clear that stroke can result from both monogenic and polygenic diseases. Common monogenic causes of stroke include cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) and its autosomal recessive form, CARASIL, as well as sickle cell disease, and Fabry disease.

Among rarer monogenic and polygenic causes of stroke we have: mitochondrial encephalomyopathy, lactic acidosis, and stroke like episodes (MELAS), hereditary endotheliopathy with retinopathy, nephropathy, and stroke (HERNS), homocystinuria, moyamoya disease, and inherited connective tissue disorders, including type IV collagen α1- chain gene (COL4A1) mutation, Marfan syndrome, and vascular Ehlers–Danlos syndrome (VEDS).

Despite all recent advances in neuro-technologies applied for stroke diagnostic, up to a third of strokes are rendered cryptogenic or of undetermined etiology. This number is specifically higher in younger patients. At times, inadequate diagnostic workups, multiple causes, or an under-recognized etiology contributes to this statistic.

The current presentation will give a brief overview related to most studied rare causes of stroke: aortic arch atheroma, cervical dissection, PFO & ASA, hereditary conditions, thrombophilia, acquired hypercoagulable status and vasculitis.

EYE MOVEMENT DISORDERS IN NEUROMETABOLIC DISEASES

ALESSANDRA RUFA

Neurologist and Neurophthalmologist at the Neurometabolic Unit of the University of Siena, Italy

Neurometabolic diseases, are a heterogeneous group of genetic diseases presenting in infancy or adolescence but also in adulthood. Due to the different penetrance and phenotypic variability, adult presentation can differ from classic childhood onset phenotypes, leading to a significant diagnostic delay or diagnostic failure. Infantile forms are often characterized by severe clinical and neurological presentation with death in the first decade. Neurological symptoms in infantile forma, often include: movement disorders, hypotonia, epilepsy, visual and hearing problems and are associated with multi organ failure. Adult phenotype are characterized by slow progression of neurological disturbances including movement disturbances, cognitive decline and psychiatric symptoms . Beside visual problem due to retinal neurodegeneration or cataracts, abnormalities of eye movements, are also common and can even be the presenting symptom.

Eye movement disorders can be classified as central or peripheral disorders. Central forms are frequently seen in lysosomal storage disorders, while peripheral forms are a key feature of mitochondrial disease. Furthermore, oculogyric crisis is an important symptom in disorders affecting dopamine syntheses or transport.

In adult patients with unexplained psychiatric symptoms, cognitive decline and movement disorders, a special focus on examination of eye movements is important and can serve as a relatively simple clinical tool to detect a neurometabolic disease. Early diagnosis is important because available treatments in some neurometabolic diseases, can prevent further damage.

CURRICULUM VITAE

OVIDIU BĂJENARU
ROMANIA

Corresponding Member of the Romanian Academy
Member of the Romanian Academy of Medical Sciences of Romania
Professor of Neurology and Director of the Clinical Neuroscience Department at the University of Medicine and Pharmacy "Carol Davila" Bucharest, Chairman of the Department of Neurology – University Emergency Hospital Bucharest

- Graduate of the Faculty of Medicine – University of Medicine and Pharmacy (UMF) „Carol Davila" Bucharest (1983)
- Specialist in Neurology (1989), Senior Neurologist (1994); competence in MRI diagnostic in neurologic disorders (1991)
- PhD (1993) - UMF „Carol Davila" Bucharest
- 2006: Doctor Honoris Causa –University „Ovidius" – Constanta
- Postdoctoral specialization at the University „René Descartes" (Paris) during 1993-1994, in clinical Neurology (CHU „Saint-Anne" and „Kremlin-Bicetre") and research grants in Clinical and Experimental Neurophysiology (CHU „Cochin-Port Royale" and Faculté de Medecine Paris V)
- 2001-2013: President of the Romanian Society of Neurology
- Since 2013: Honorary President ad vitam of the Romanian Society of Neurology
- Since 2001: Coordinator and Chairman of all annual National Congresses of the Romanian Society of Neurology and many other scientific events and teaching courses organized for neurologists in Romania
- Visiting Professor in Vietnam (2013) and Kazakhstan (2015), on behalf of WFN
- Member of the Executive Committee of ENS (European Society of Neurology) between 2005-2009, of the Scientific Committee of ECTRIMS (2004-2009)
- Member of European Academy of Neurology (since 2014), American Academy of Neurology, International Parkinson's Disease and Movement Disorders Society, European Stroke Organisation, Danube Neurological Association (member of the Scientific Board and Deputy Secretary General), and others
- Since 2008: official representative of Romania for UEMS - European Board of Neurology (secretary of the Executive Committee between 2010-2015) and member of the examination board for the title of European Neurologist
- Author of more than 1000 scientific papers reported and published in scientific journals, among 147 cited in ISI Web of Science (Hirsch index 16) and Pubmed. Author

of chapters in 2 international books of neurology and author and co-author in more than 15 medical books published in Romania.

- Coordinator of the National Diagnostic and Treatment Guidelines in Neurological Disorders
- National Principal Investigator and Investigator in more than 50 international, multicentric, controlled clinical trials in: stroke, Parkinson's disease and movement disorders, multiple sclerosis, dementia, epilepsy, and others.
- Director of more national research grants
- 9 awards of excellency in medicine from different socio-professional national and international organizations, the Romanian Ministery of Health and the Romanian Orthodox Patriarchate
- Initiator and coordinator of the National Medical Programs of the Ministery of Health and National Health Insurance System for the treatment of: acute stroke, multiple sclerosis, rare neurological diseases, advanced Parkinson's disease (1999 – 2015)
- President of Consultative Commision of Neurology of the Ministery of Health and National Health Insurance System (2008 – 2015)

JEAN-MARC BURGUNDER
SWITZERLAND

Jean-Marc Burgunder has graduated in Medicine at the Faculty of Medicine in Bern, Switzerland, and trained in internal medicine, neurology and neuroscience in Switzerland and at the Institutes of Mental Health in Bethesda, USA. He is a Professor of Experimental Neurology at the faculty of medicine of the University in Bern. He has spent some years as a Professor of Medicine at the National University of Singapore. He is a visiting Professor of Neurogenetics at the Central South University in Changsha and at the Sichuan University in Chengdu (China). He also holds a position as an adjunct professor at the Sun Yat Sen University in Guangzhou in China. He is now Medical Director of the Siloah Neurocenter, Chair of the EHDN Executive Committee, Co-Chair of the Specialist Scientists Panel on Neurogenetics of the European Academy of Neurology.

He is director of the NeuroZentrum Siloah in Gümligen (Bern). The centre is devoted to the care of patients with rare neurological disorders including Huntington's disease, along with the provision of general neurology services for the area.

ANNA CZŁONKOWSKA
POLAND

Prof. Anna Członkowska MD, PhD finished Medical Academy in Warsaw. Since 1985, she is employed in the 2nd Department of Neurology in the Institute of Psychiatry and Neurology in Warsaw (till end of 2013 as the head of the department, currently is the professor in this department). She is since years also collaborating with Department of Pharmacology , Warsaw Medical University.

Her main interests are: stroke (epidemiology, treatment, rehabilitation), neuroimmunology (multiple sclerosis, local and systemic immunity in neurodegeneration) and Wilson's disease. She has passed several fellowships in neuroimmology and neuropathology (UK, Germany, USA) and participated in many academical and sponsored clinical studies.
She served as a member of the International Consortium at EUROWILSON. Since 1969, has cared for 900 patients with Wilson Disease and established a database. She cooperates with WD centers across Europe and has evaluated the clinical course of WD (with a focus on the efficacy of current therapies). She has also completed basic research for the evaluation of pathogenesis of WD.

She is the member of Polish Academy of Arts and Sciences, member correspondent of Polish Academy of Science, American Neurological Association, German Society of Neurology and she is Fellow of the Royal College of Physicians of Edinburgh.

ANTONIO FEDERICO
ITALY

Prof. Antonio Federico, born in Polla (Sa) on the 25.08.48, from 1990 is full professor of Neurology at the University of Siena , Director of the Unit Clinical Neurology and Neurometabolic Disease.

He was Director of the Department of Neurological, Neurosurgical and Behavioural Sciences, University of Siena (2002-2008).

He received the degree in Medicine and specialization in Nervous and Mental Diseases, summa cum laude, at the University of Naples in 1972 and 1975 respectively. He received the Lepetit Award for the best degree dissertation in 1972.
His biological training was in the Institute of Biochemistry as student and after in Physiology of the University of Naples, and in the Centre de Neurochimie of CNRS, in Strasbourg, directed by prof. Mandel where he worked in the years 1973-75. He also collaborated with many international research groups, in different countries where he spent in the past years some times: in Montreal (Prof. Andermann, Karpati and Shoudgbridge), in London (dr A. Harding and prof. Morgan-Hughes), in Toronto (dr.Robinson), in Bonn (prof. von Bergmann) , in Paris (dr.Baumann), in Baltimore (proff. Moser and Naidu), in Oxford (prof. Matthews), etc.
His clinical formation was made at the Medical School of the University of Naples, in the Dept, Neurology, and after in Siena, where he moved on 1980 with his mentor, prof. G.C. Guazzi. Associated professor in Neurology in 1982, since 1990 he is full professor of Neurology, Medical School, University of Siena.
In 2013, he received honoris causa degree in Medicine at University Carol Davila, Bucharest, Rumania.

In the years 1990-96 he was Secretary of the Italian Society of Neurology. In the years 2006-08 was President of the Italian Society of Neurology.

He coordinated the Study Group on Clinical Neurogenetics of the Italian Society of Neurology.

He has been referee for projects evaluation in the area of Orphan drugs and Orphan diseases for Biomed Projects from EU, for MURST, CNR and Istituto Superiore di Sanità, and other national and international funding agencies, etc.

He is member of the Second Opinion Group of the American Leucodistrophy Association.

Associated editor of Neurological Sciences in the past 3 years. From 2012, he is Editor-in Chief.

He is author of more than 500 article quoted by Pubmed. He is author of a chapter on Cerebrotendinous Xanthomatosis, Vinken and Bruyn Edts, Handbook of Clincal Neurology, vol 49, Neurodystrophies and Neurolipidoses. On the book McKusick's Mendelian Inheritance in Man,. Ed.1992, Catalog of Autosomal Dominant and Recessive Phenotypes he is cited for 3 different diseases. He was editor of the book Late Onset Neurometabolic diseases (A.Federico, K. Suzuki and N.Baumann Edts), Karger 1991, and many other books from Italian and international Publishing Companies.
Recently he published (2015) Manuale di Neurologia Pratica and Neurologia and Assistenza infermieristica, for students.

His main field of interest is related to neurometabolic, neurodegenerative and rare diseases, investigated from a genetic, metabolic, neuroimaging and clinical point of vue.

Summary of the academic involvements:
- Director of the Section Neurological Sciences, Dept Neurological , Neurosurgical and Behavioural Sciences (2000-2012)
- Director of the Research Center for the Diagnosis, Therapy and Prevention of the Neurohandicap and Rare Neurological Diseases, until the 2010
- Vice-Dine of the Medical School, University of Siena (2003-2006)
- Director of the Postgraduate School of Neurology, University of Siena, from 2006 up to 2014.
- Director of the PhD School in Cognitive and Neurological Sciences, University of Siena (from 2000 up to date)
- Coordinator of the Section of the Univ. Siena of the PhD Program Neurosciences, Univ. Florence.
- Research delegate for the Dept Medicine, Surgery and Neurosciences (2013-)
- Vice-Rector of the University of Siena, from 1st april 2016.

Medical Involvements
- Director of the OU Clinical Neurology and Neurometabolic Diseases, University Hospital of Siena Medical School.
- Director of the Regional Reference Center for Rare Diseases
- Regional Coordinator of the Network for Rare Neurological Diseases, Tuscany Region.
- Member of several Ministry of Health and Regional Committees
  National and International Commitments
- President of the Italian Society of Neurology (2009-11)
- Italian delegate to the World Federation of Neurology
- Italian Delegate to the European Union of Medical Specialists (Section Neurology)
- Italian Delegate and Chairman of the Neuromediterraneum Forum and President
- Consultive Member of the European Brain Council

- Editor – in – Chief of Neurological Sciences, Springer Verlag Editor. He is in the Editorial Board of many national and international journals.
- Member of the American Panel United Leucodystrophies.
- Member of the Scientific Committee of AISM (Associazione Italiana Sclerosi Multipla)
- Chairman of the Scientific Committee of the European Academy of Neurology
- Chairman of Neuromediterraneum Forum
- Co-Chairman of Research group of WFN Migration Neurology

Member of the Scientific Societies:
- Società Italiana di Neurologia (Past Secretary, President, Past-President and Member of the Committee)
- Society for the Inborn Errors of Metabolism
- Italian Association of Neuropathology
- SINDEM (Italian Association of Dementias)
- Italian Association for Parkinson's disease
- Italian Association of Neurogeriatrics (Member of the Scientific Committee)
- Italian Stroke Forum
- European Academy of Neurology (Member of the Board and Chairman of the Scientific Committee)
- American Academy of Neurology
- World Federation of Neurology (Co-Chair Section of Migration Neurology)
- Neuromediterraneum Forum (President)

His present positions are:
full professor of Neurology, University of Siena, Medical School
- Director of Unit Clinical Neurology and Neurometabolic Diseases, Siena Hospital.
- Past-Director of the Section Neurological Diseases of the Department of Neurological and Behavioural Sciences of the University of Siena since the 2012, at the fusion of this Department in the Dept Medicine, Surgery and Neurosciences.
- Italian Delegate to the World Federation of Neurology and to European Academy of Neurology Council.
- Past- President of the Italian Society of Neurology (President years 2009-2011)
- From 1995 he is Director of a PhD Programme on Applied Neurological Sciences at University of Siena, from 2004 of the European PhD Programme and European School of Doctorate of Applied Neurological Sciences. Since 2011 he is director of the PhD Programme on Cognitive and Neurological Sciences at University of Siena.
- He is Italian member of the Committee of European Union of Medical Specialists, in the section Neurology.
- Delegate for Research in the Dept. Medicine, Surgery and Neurosciences.
- Coordinator for the Tuscany Region of the Network on Rare Neurological Diseases.
- On 2013, he received Honoris Causa degree from the University Carol Davila, Bucharest
- Chairman of the Neuromediterraneum Forum
- Editor in Chief of Neurological Sciences, Springer-Verlag Editor.
- Co-Editor of many international journals.
- On the 2014 was nominate WHO consultant for Rare Neurological Diseases.

- From june 2014, he is Chairman of the Scientific Committee and Member of the Board of the European Academy of Neurology
- From February 2015 Co-Chairman of the Research Group Migration Neurology of the World Federation of Neurology.
- From the 1st april 2016, vice-Rector of the University of Siena.

HOLM GRAESSNER
GERMANY

Holm Graessner is Executive Director of the Rare Disease Centre, since 2010, at the University and University Hospital Tübingen, Germany.

He is Coordinator of the European Reference Network for Rare Neurological Diseases (ERN-RND).

He received his PhD "Summa cum laude" in 2004 and, then, he obtained his MBA degree in 2008.

From 2003 until now, he has been coordinating and managing more than 10 EU funded collaborative projects. The main focus of these projects are rare and neurological diseases, among them EUROSCA, MEFOPA, SENSE-PARK, MULTISYN, NEUROMICS and PROOF.
He has been co-leading one of the four working groups of the German Action Plan for Rare Diseases.

Since 2017, in his function as the coordinator of ERN-RND, he is a member of the Rare Disease Task Force of the European Academy of Neurology. In the Coordinator's Group of the European Reference Networks, he leads the cross-border healthcare working group.

MAURIZIO LEONE
ITALY

Maurizio A. LEONE, MD, is Director of the Neurology Unit at the Clinical Research Institute IRCCS "Casa Sollievo della Sofferenza" in San Giovanni Rotondo, Italy. He was born in Torino, Italy, 3-11-1955 and took his medical degree at the University of Torino in 1980 and the Board Certification in Neurology in 1984. He was Guest Researcher at the Neuroepidemiology, Branch, NINCDS, NIH, Bethesda, USA (1986-7). From 1987 to 2014 he has worked in the Departments of Neurology at the Ivrea and Aosta hospitals, and at the University Hospital in Novara, where he was head of the Multiple Sclerosis Centre. He was Consultant at the Laboratorio di Neurologia, "Mario Negri" Pharmacological Institute in Milan (1998-2012). Within the European Academy of Neurology he is Chair of the Scientific Panel "Neurotoxicology", member of the Scientific Committee and of the guideline production group, and member of the assembly of delegates. He was President of the Italian Society of Neuroepidemiology in 2012-4, is currently member of the Italian Society of Neurology, and honorary member of the Moldovan Society of Neurologists. He serves as Associate Editor for the European Journal of Neurology since 2006 and is referee for many neurological journals. Dr. Leone authored 157 papers in peer-reviewed journals in the area of neuroepidemiology –including amyotrophic lateral sclerosis, multiple sclerosis, alcohol-related neurological diseases- and of evidence-based Neurology.

ALBERT LUDOLPH
GERMANY

PROFESSIONAL EXPERIENCE:

1979 - 1984	Resident, Board Neurology and Psychiatry (Department of Neurology and Psychiatry, University of Münster FRG (Prof. G. Brune, Prof. R. Tölle)
1984 - 1985	Stipend, Deutsche Forschungsgemeinschaft: Institute of Neurotoxicology, Albert Einstein College of Medicine, Bronx, New York (Prof. P.S. Spencer,

	Prof. H.H. Schaumburg)
1985 - 1989	Staff, Department of Neurology, University of Münster (Prof. G. Brune)
1987	Habilitation, Faculty of Medicine, University of Münster, C2 Professor of Neurology
1990 - 1992	Staff Scientist, Visit. Assoc. Prof., Center for Research on Occupational and Environmental Toxicology and the Department of Neurology, Portland (Oregon)
1992	Staff, Department of Epileptology, University of Bonn (Prof. C.E. Elger)
1993 - 1996	C3 Professor of Neurology, Vice Chairman, Department of Neurology, Humboldt University Berlin (Prof. K.-M. Einhäupl)
1996	C4 Professor of Neurology, Chair, Department of Neurology, University of Ulm
2003 -	Chair (elected) Academic Neuroscience Center, University of Ulm
2005 - 2009	Deputy Chair and Chair (elected), European ALS-MND-Group
2007 -	Chair (elected) ALS panel of the EFNS and EAN (since 2014, together with Prof. Vincenzo Silani)
2008 -	Scientific Advisory Board Thierry Latran Foundation
2008 - 2010	Chair, Scientific Council of Deutsche Stiftung Querschnittlähmung (DSQ)
2008 -	Chair Scientific Council Deutsche Gesellschaft für Muskelkranke
2009 -	Scientific Advisory Board Member of the Stifterverband der Schilling-Research-Groups for Translational Neuroscience
2009 -	Chair (elected), World Federation of Neurology, ALS Research Group
2009 - 2016	Reviewer for Neuroscience Board of the German Research Foundation (DFG)
2010 -	Vice Dean of the Medical Faculty of Ulm

2013 -	Chair (elected), World Federation of Neurology, ALS Research Group
2014 -	Delegate of the German Society of Neurology at the World Federation of Neurology
2015 - 2017	Speaker (elected), Clinical Neurosciences Neurowissenschaftliche Gesellschaft

PRIZES AND AWARDS (recent)

2013	Honorary Member of the Mongolian Society of Neurology
2015	Erb-Gedenkmünze of the German Society of Neurology (DGN)

10 IMPORTANT PUBLICATIONS (last 2 years)

1. Braak H, Ludolph AC, Neumann M, Ravits J, Del Tredici K. Pathological TDP-43 changes in Betz cells differ from those in bulbar and spinal α-motoneurons in sporadic amyotrophic lateral sclerosis. Acta Neuropathol. 2016 Oct 18.

2. Brenner D, Müller K, Wieland T, Weydt P, Böhm S, Lulé D, Hübers A, Neuwirth C, Weber M, Borck G, Wahlqvist M, Danzer KM, Volk AE, Meitinger T, Strom TM, Otto M, Kassubek J, Ludolph AC, Andersen PM, Weishaupt JH. NEK1 mutations in familial amyotrophic lateral sclerosis. Brain. 2016 May;139(Pt 5):e28.

3. Vercruysse P, Sinniger J, El Oussini H, Scekic-Zahirovic J, Dieterlé S, Dengler R, Meyer T, Zierz S, Kassubek J, Fischer W, Dreyhaupt J, Grehl T, Hermann A, Grosskreutz J, Witting A, Van Den Bosch L, Spreux-Varoquaux O; GERP ALS Study Group, Ludolph AC, Dupuis L. Alterations in the hypothalamic melanocortin pathway in amyotrophic lateral sclerosis. Brain. 2016 Apr; 139:1106-22.

4. Weydt P, Sagnelli A, Rosenbohm A, Fratta P, Pradat PF, Ludolph AC, Pareyson D. Clinical Trials in Spinal and Bulbar Muscular Atrophy-Past, Present, and Future. J Mol Neurosci. (2016) 58:379-387.

5. Freischmidt A, Müller K, Zondler L, Weydt P, Volk AE, Božič AL, Walter M, Bonin M, Mayer B, von Arnim CA, Otto M, Dieterich C, Holzmann K, Andersen PM, Ludolph AC, Danzer KM, Weishaupt JH. Serum microRNAs in patients with genetic amyotrophic lateral sclerosis and pre-manifest mutation carriers. Brain 2014;137(Pt 11):2938-50

6. Brettschneider J, Del Tredici K, Irwin DJ, Grossman M, Robinson JL, Toledo JB, Fang L, Van Deerlin VM, Ludolph AC, Lee VM, Braak H, Trojanowski JQ. Sequential distribution of pTDP-

43 pathology in behavioral variant frontotemporal dementia (bvFTD). Acta Neuropathol 2014;127(3):423-39

7. Kassubek J, Müller HP, Del Tredici K, Brettschneider J, Pinkhardt EH,
Lulé D, Böhm S, Braak H, Ludolph AC. Diffusion tensor imaging analysis of sequential spreading of disease in amyotrophic lateral sclerosis confirms patterns of TDP-43 pathology. Brain 2014;137(Pt 6):1733-40

8. Storch A, Kassubek J, Tumani H, Vladimirtsev VA, Hermann A, Osakovsky VL, Baranov VA, Krivoshapkin VG, Ludolph AC. Communicating hydrocephalus following eosinophilic meningitis is pathogenic for chronic Viliuisk encephalomyelitis in Northeastern Siberia. PLoS One. 2014 28;9(2):e84670

9. Brettschneider J, Del Tredici K, Toledo JB, Robinson JL, Irwin DJ, Grossman M, Suh E, Van Deerlin VM, Wood EM, Baek Y, Kwong L, Lee EB, Elman L, McCluskey L, Fang L, Feldengut S, Ludolph AC, Lee VM, Braak H, Trojanowski JQ. Stages of pTDP-43 pathology in amyotrophic lateral sclerosis. Ann Neurol 2013;74:20-38

10. Braak H, Brettschneider J, Ludolph AC, Lee VM, Trojanowski JQ, Tredici KD. Amyotrophic lateral sclerosis - a model of corticofugal axonal spread. Nat Rev Neurol 2013;9(12):708-714

MARIA JUDIT MOLNAR
HUNGARY

Maria Judit Molnar MD, PhD, Professor of Neurology, Psychiatry, Clinical Genetics, and Clinico-pharmacology, Doctor of the Hungarian Academy of Sciences is the director of Semmelweis University's Institute of Genomic Medicine and Rare Disorders. Among others president of the Hungarian Medical College of Clinical Genetics, past president of the Hungarian Society of Clinical Neurogenetics, secretary of the Hungarian Society of Personalized Medicine, board member of the Neurogenetic and Neuromuscular Committee of the European Academy of Neurology, president of the Advisory Board of the Hungarian Insurance Company for Rare Disorders. She was the vice-rector for Scientific Affairs at Semmelweis University (Budapest, Hungary) between 2012 and 2015, where she was also responsible for International Affairs. She has been adjunct professor at the Montreal

Neurological Institute, McGill University between 1999 and 2012. Dr. Molnar is the Facilitator of a Challenge Group of the International Consortia of Personalized Medicine initiated by the European Commission. She has a country coordinator role in the European Rare Disease Joint Action Program ('Promoting Implementation of Recommendations on Policy, Information and Data for Rare Diseases — RD-ACTION'). She is the leader of the WP for Education and Training of the European Reference Network (ERN) for Rare Neurological Diseases. She is the representative of Hungary in the Rare disease EJP established by the European Commission. She is the member of the steering committee of the Association of Academic Health Centres International.

Dr. Molnar is recognized as a leading experts on the diagnosis and treatment of rare neurological disorders. The Institute of Genomic Medicine and Rare Disorders lead by her offers a comprehensive state of the art, patient-centered care for patients with rare neurological disorders including genetic testing, neuropathological investigations and genetic counselling as well. Dr. Molnar's research covers a broad range of basic and clinical studies on rare neurological disorders, utilizing a broad spectrum of technologies in the development of improved diagnostics and therapeutics using molecular approaches
She plays important role in the organization of rare disease management in Hungary and acts as an ambassador promoting the personalized healthcare.

She published 1 book, 20 book chapters, 137 papers with cumulative impact factors 175, Hirsch index: 19 and more than 1250 citations. She owns 2 patents.

DAFIN F. MUREȘANU
ROMANIA

Professor of Neurology, Senior Neurologist, Chairman of the Neurosciences Department, Faculty of Medicine, University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca, President of the Romanian Society of Neurology, President of the Society for the Study of Neuroprotection and Neuroplasticity (SSNN), member of the Academy of Medical Sciences, Romania, secretary of its Cluj Branch. He is member of 16 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 a specialist in Leadership and Management of Research and Health Care Systems (specialization in Management and Leadership, Arthur Anderson Institute, Illinois, USA, 1998 and several international courses and training

stages in Neurology, research, management and leadership). 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 300 scientific participations as "invited speaker" in national and international scientific events, a significant portfolio of scientific articles (146 papers indexed on Web of Science-ISI, H-index: 16) as well as contributions in monographs and books published by prestigious international publishing houses. Prof. Dr. Dafin F. Muresanu has been honoured with: the University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca, Faculty of Medicine, "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, 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 "Gheorghe Marinescu Award" for advanced contributions in Neuroprotection and Neuroplasticity.

ALESSANDRA RUFA

ITALY

Dr Alessandra Rufa MD and Phd in Neurometabolic Diseases is a Neurologist and Ophthalmologist at the University of Siena. Her medical position is currently of Neurologist and Neurophthalmologist at the Neurometabolic Unit of the University of Siena. Her main research interest is on eye movement analysis for clinical and basic research. She

developed an eye tracking Lab with clinical and diagnostic applications. Dr Rufa established an international collaboration with other experts in the field of Neuroscience of Vision and eye movements.

JOHANN SELLNER
AUSTRIA

Johann Sellner is a neurologist who specializes in CNS inflammation, cerebrovascular disorders and non-compressive myelopathies. He graduated from the Medical University Graz in 2001and received post-graduate training in Heidelberg, DE (Prof. W. Hacke, 2001-2004), Bern, CH (Prof. Ch. Hess, 2005-2007) and Munich, DE (Prof. B. Hemmer, 2008-2010). He held fellowship positions in Bern, CH (2004-2005), San Francisco, USA (2006) and London, UK (2009). In 2013 he moved to the Paracelsus Medical University where he heads the centers for Multiple Sclerosis and Primary Stroke Prevention at the Department of Neurology.

ANTONIO TOSCANO
ITALY

Antonio Toscano is Professor of Neurology, since 2009, at the Department of Clinical and Experimental Medicine of the University of Messina, Italy.

He is responsible of a ERN Reference Center for Rare Neuromuscular disorders at the

University Hospital of Messina, Italy.
He received his MD "cum laude" in 1981 and, then, he specialized in Neurology in 1985 in the University of Messina.

From 1986 to 1987, he attended as a fellow "The National Hospital for Nervous Diseases, London, UK, under the guide of dr. John Morgan-Hughes, studying Mitochondrial Disorders. His main research interests are focused on Neuromuscular and Neurodegenerative Disorders with particular attention to Metabolic Myopathies and, more specifically, to pathogenic, clinical and therapeutic aspects of muscle glycogenoses (i.e. Pompe disease), lipid storage myopathies and mitochondrial encephalo-myopathies or other rare neurodegenerative disorders.

In these fields, he has published over 180 papers.

He has been President of the Italian Association of Myology (AIM)

Since 2015, he is member of the Scientific Committee of the European Academy of Neurology (EAN)

Since 2016, he is Chairman of the EAN Panel for Muscle and Neuromuscular Junction Disorders,

He is also member of: a) National Board of the Italian Neurological Society (SIN), b) Board of the European Consortium for Pompe Disease (EPOC), c) international board of the Pompe registry, d) several other National and International Scientific Societies and Groups

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