6. HRVATSKI KONGRES NEUROZnanosti
S MEĐUNARODnim SUDJELovanJEm
THE 6. CROATIAN NEUROSCIENCE CONGRESS
WITH INTERNATIONAL PARTICIPATION
Osijek, Hrvatska/Croatia

Pozvani predavači Predsjedničkog simpozija/Presidential symposium speakers
Ronald L. Schnaar, Johns Hopkins School of Medicine, Baltimore, USA
Paško Račić, Yale University, New Haven, USA
Nenad Šestan, Yale University, New Haven, USA
Harry Lylings, VU University Medical Center, Amsterdam, Netherlands
Monique Esclapez, Institut de Neurosciences des Systèmes Inserm, Marseille, France
Karlo Mlinic, Munroe-Meyer Institute, University of Nebraska Medical Center, Nebraska, USA
Mladen Roko Rasin, RWJ Medical School, Rutgers University, Piscataway, USA

Pozvani predavači ISN simpozija/ISN Symposium speakers
Dirk Montag, Leibniz Institute for Neurobiology, Magdeburg, Germany
Rodrigo Herrera-Molina, Leibniz Institute for Neurobiology, Magdeburg, Germany
Raquel Marin, Laguna University, Santa Cruz de Tenerife, Spain
Gundela Meyer, Laguna University, Santa Cruz de Tenerife, Spain

Administracija kongresa/Congress administration
conTres projekti d.o.o..
info@contres.hr
https://www.contres.hr/category/6hkr/
ISN Symposium
Frontiers in Neurochemistry: Crosstalk of Membrane Proteins and Lipids in Health and Disease

The Symposium took place on 16th of September 2017, before The 6th Croatian Neuroscience Congress with International Participation at the City of Osijek, capital of Croatian region Slavonia and Baranja. The venue was the new conference hall at Vicary (J. J. Strossmayer street 58, Osijek), technically fully equipped and well managed. The main organizer of Symposium was J. J. Strossmayer University of Osijek Faculty of Medicine and responsible person was prof. Marija Heffer, PhD (Department of Medical Biology and Genetics). The organization was fully supported by Croatian Society for Neuroscience, City Council and Osijek-Baranja County.

The Symposium was advertised as follows;
1. the official page of congress (https://contres.hr/category/6hkn/) - expired after congress
2. the official page of Croatian Institute for Brain Research (http://www.hiim.unizg.hr/)
3. the official page of Faculty of Medicine Osijek (http://www.mefos.unios.hr/index.php/hr/home/novosti/1298-6-hrvatski-kongres-neuroznanosti-2017 )
4. the official poster of manifestation (in att)
5. the local newspapers (Glas Slavonije), radio stations (Gradski radio, Slavonski radio, HRT Radio Osijek) and web page http://www.osijek031.com/osijek.php?najava_id=68817

Symposium had following program:

10.00 - 11.00 REGISTRATION OF PARTICIPANTS
10.30 – Welcome coffee and refreshments
11.00 -11.30 Raquel Marin: “Neuronal lipid homeostasis: A main factor for brain maintenance and neuroprotection”
11.30 -12.00 Dirk Montag: “Neuroplastin ablation causes retrograde amnesia and circuit dependent deficits correlated to loss of neuroplastin PMCA complexes”
12.00 -12.30 Rodrigo Herrera Molina: “Why is neuroplastin essential for circuit activity balance? New interactions with TRAF6 and PMCA”
12.30-13.00 Gundela Meyer: „Cell substrates of Reelin-Lipoprotein receptor signalling in human cerebral cortex development”
19.30 Welcome Cocktail

The symposium was open by Prof. Ronald Schnaar, PhD (Johns Hopkins University, USA). Also, he introduced each speaker and lead discussion after each lecture. The short abstract of lectures were published at book of abstracts (in att). Participants got a chance to continue discussion with speakers after Symposium and during cocktail party held at Gallery of Fine Arts Osijek.

At the work of Symposium were 47 participants (the list of participants is in att).

From ISN budget were covered following expenses:
1. return travel tickets for 4 speakers
2. hotel expenses for 4 speakers
3. registration fees for 4 speakers
Detailed cost spent on each speaker is presented in att excel table as well as proof of payment. The cost of travel expenses from Zagreb to Osijek and back was covered by Faculty of Medicine Osijek. Osijek-Baranja County covered the cost of welcome coffee and refreshments, while City of Osijek covered the cost of welcome cocktail at Gallery of Fine Arts. All published materials (book of abstracts, poster, schedule etc.) were covered by Croatian Society for Neuroscience.

In front of organizers, I would like to take a chance to express my gratitude to International Society of Neurochemistry for granting Faculty of Medicine Osijek possibility to invite the prominent speakers from the field of neurochemistry of lipid rafts. We expect that lectures presented at symposium would motivate further research and collaborations.

President of Organizing Committee

Marija Heffer

In Osijek, 16th October 2017
THE 6. CROATIAN NEUROSCIENCE CONGRESS WITH INTERNATIONAL PARTICIPATION

Osijek, Croatia
September 16-18, 2017

BOOK OF ABSTRACTS
Raquel Marin

Neuronal lipid homeostasis: A main factor for brain maintenance and neuroprotection.

Laboratory of Cellular Neurobiology, Dept. Basic Medical Sciences, School of Medicine, University of La Laguna, Spain

The brain is one of the organs containing the largest amount of different lipid molecular species. In this sense, neurolipidomic studies are crucial to understand the potential changes that may occur during brain ageing progression and age-associated neuropathologies. For more than a decade, our research group has been working in elucidating the potential changes that may occur in lipid raft microdomains which are distinct microstructures present in neuronal plasma membranes with a particular lipid composition. Lipid rafts are considered functional domains where numerous signaling proteins interact, and initiate different signal transduction pathways that ultimately lead to neuroprotection and neuronal survival.

During brain ageing, some subtle differences as compared to normal levels have been observed in the lipid composition of neuronal lipid rafts, in particular in brain regions involved in memory and cognitive processes, such as cortical areas and hippocampus. These changes are exacerbated in age-associated neuropathologies such as synucleopathies, Parkinson’s disease and Alzheimer’s disease, even at early asymptomatic stages, as an indicative of the importance of the maintenance of brain lipid homeostasis in neuronal membranes to preserve against injury. One of the main consequences of these lipid alterations is the enhancement of aberrant protein-lipid and protein-protein associations of the multimolecular interactions occurring in these signaling platforms detecting, among others, an enhancement in the interaction of proteins involved in amyloid beta formation machinery at early stages of Alzheimer’s disease, protein abnormal aggregation and post-transductional modifications in synucleopathies, and toxic intracellular signaling. Interestingly, similar molecular anomalies have been observed in neuronal lipid rafts of, both, cortical areas and hippocampus during menopausal periods where a detriment of steroid hormones is observed, as an indicative of the importance of lipid raft activities in estrogen-related neuroprotection.

The identification of the early events involving the molecular disarrangements in neuronal lipid rafts may be a potential tool for the development of neuronal early diagnostic biomarkers for these neuropathological diseases.

Grants: SAF2014-52582-R.
Dirk Montag

Neuroplastin ablation causes retrograde amnesia and circuit dependent deficits correlated to loss of neuroplastin PMCA complexes

Leibniz Institute for Neurobiology, Magdeburg, Germany

Memory acquisition, consolidation, storage and retrieval are critical processes affected in numerous psychopathological disorders, but mechanistically sparingly understood. Polymorphisms in the human neuroplastin (NPTN) gene were linked to cortical thickness and adolescent intellectual ability and to schizophrenia. Neuropilin-deficient mice reveal profound physiological and behavioral deficits, some related to depression and schizophrenia. Associative learning in conditioning paradigms (two-way active avoidance and fear conditioning) requires neuroplastin cell recognition molecules. Inducible neuron-specific ablation of neuroplastin gene expression in adult mice elicits retrograde amnesia specifically of learned associative memories and proving neuroplastins as indispensable for access and retrieval of previously acquired associative memories. Glutamatergic neuron-selective lack of neuroplastin resulted in behavioral deficits indicating hippocampal, striatal, and sensorimotor dysfunction paralleled by highly altered brain activities in hippocampal CA1 area, sensorimotor cortex layers I-III/IV, and the striatal sensorimotor domain detected by SPECT-imaging. Using this technique in awake mice, we have begun to map brain structures activated during memory recall. Neuroplastin expression in glutamatergic neurons commands particular behaviors, whereas neuroplastin expression by GABAergic interneurons appears necessary for fear memories requiring disinhibition of cortical interneurons. Neuroplastin-Plasmin Membrane Ca\(^{2+}\) ATPase (PMCA) complexes are strongly related to regulation of intracellular Ca\(^{2+}\)-homeostasis in many tissues. Reduced PMCA levels in neuroplastin-mutant mice may increase [iCa2+] altering neuronal activities. Neuro-type-specific neuroplastin ablation empowers the investigation of circuit-coded learning and memory and its relation to cognitive deterioration. The inducible neuroplastin-deficient mouse model, achieving experimental induction of retrograde amnesia genetically, provides new means to analyze the molecular and cellular mechanisms underlying retrograde amnesia and memory.

Rodrigo Herrera-Molina  

*Why is Neuroplastin Essential for Circuit Activity Balance? - New interactions with TRAF6 and PMCA*

Leibniz Institute for Neurobiology, Magdeburg, Germany

The importance of the cell adhesion molecules neuroplastin 55/65 for brain architecture and function has been demonstrated by studies on humans and rodents. Indeed, our recently published findings reveal that neuroplastin expression in distinct neuronal sub-types and circuits commands particular behaviors. Neuroplastins are present in synapses regulating synapse plasticity and protein levels of the Plasma Membrane Calcium ATPases (PMCAS). Thus, we aim to identify neuron type- and circuit-specific functions of the Np-PMCA association. We identified PMCA isoforms as prevalent Np partners in rodent synaptic membranes. Analysis showing stoichiometrically-linked Np-PMCA native complexes in wild type and drastically reduced PMCA levels in synaptic membranes from Nptn<sup>−/−</sup> and Nptn<sup>loxploxCrelox1</sup> mice indicate a close physical coupling. *In vitro* experimentation confirmed that the transmembrane region of Np is sufficient to promote PMCA membrane localization and PMCA-mediated Ca<sup>2+ </sup>-clearance. As second important feature, Np regulates the number and structural stability of hippocampal excitatory synapses and Np mice display reduced number of excitatory synapses. Because Np cytoplasmic domain contains a tumor necrosis factor receptor-associated factor 6 (TRAF6) motif, we also evaluate the role Np-TRAF6 interaction in synapse formation/stabilization in CA1 pyramidal neurons. Np-deficient hippocampal neurons form less and shorter dendritic protrusions during synaptogenesis. Rescue of dendritic protrusion formation by Np expression did not occur in mutant neurons co-transfected with TRAF6 siRNA. Np mutants in the TRAF6 binding site failed to promote dendritic protrusion formation in wild type and Np-deficient neurons. Np-TRAF6 direct interaction was confirmed using molecule docking modelling *in silico*, surface plasmon resonance, pulldown and immunoprecipitation assays and a series of negative dominant and mutant constructs. Over-expressing different Nps tagged with fluorescent proteins, we observed multimerization of Nps (FRET experiments), recruitment of cytosolic TRAF6 and robust Np-TRAF6 co-localization (confocal imaging) in the cell plasma membrane. Examination of downstream signaling cascades lead us to identify a role for NF-kB and PI3K/Akt/WASP pathways in Np-TRAF6-induced formation of dendritic protrusions in neurons. Our data support the existence of a new synaptogenic interaction between Np and TRAF6 as well as a novel and tight association between Np and PMCA participating in distinct calcium regulation in particular neuronal types.
Gundela Meyer

Cell substrates of Reelin-Receptor signalling in human cerebral cortex development

Department of Basic Medical Science, Faculty of Medicine, University of La Laguna, Tenerife, Spain

In the developing cerebral cortex, pyramidal neurons migrate along radial glia fibers from their birth place in the periventricular proliferation zones to their destination in the cortical plate. This radial migration is under the control of the Reelin-Disabled 1 (Dab1) signalling pathway. The large glycoprotein Reelin is secreted by the Cajal-Retzius cells in the marginal zone below the pial surface, and is the main ligand in the brain for Very Low Density Lipoprotein Receptor (VLDLR) and Apolipoprotein E Receptor 2 (ApoER2), expressed in the target cells of the Reelin signal. Both receptors interact, through their NPXY domains, with the adaptor protein Dab1 and induce reciprocal phosphorylation of Dab1 and the Src family kinases. Phosphorylation of Dab1 leads to its degradation by ubiquitination. Disturbances of this canonical signalling pathway (loss of Reelin or Dab1, or deletion of both lipoprotein receptors) give rise to the reeler phenotype, characterized by a severely disrupted architecture of the cerebral cortex and cerebellum. Single ApoER2 or VLDLR knockout mice present distinct cortical phenotypes which are less severe than the reeler cortex. In humans, loss-of-function mutations of REELIN lead to lissencephaly and cerebellar hypoplasia, whereas mutations of VLDLR present a less severe cortical phenotype but a similar severe hypoplasia of the cerebellum. The two receptors have been proposed to play different roles in radial migration; ApoER2 would be more implicated in the stability of the cytoskeleton of the neurons migrating along the radial glia, whereas VLDLR would act principally at the end of migration near the marginal zone. In fact, the expression patterns of ApoER2 and VLDLR in the developing human cortex are different, although both reach their highest expression levels around midgestation. Despite the differential expression of both receptors, the activity of the signalling pathway depends also on the presence of Dab1 in migrating neurons. Dab1 in the fetal human cortex follows a dynamic and distinct expression pattern, with highest levels at the top of the cortical plate, near the Reelin signal, but also in the intermediate zone and the proliferating periventricular zones. The identification of the cellular substrates of the different components of the Reelin-Dab1 pathway is thus critical to understand normal cortex development, and the resulting malformations if one of the key players is disrupted. An important difference between cortex development in mouse and human is the expression of all the components in subsets of Cajal-Retzius cells of the latter. These neurons are particularly prominent in the human brain; similarly, they show high complexity in their expression of Reelin (which is always present), together with the less consistent presence of Dab1, ApoER2 and VLDLR. It is thus possible that Reelin/Lipoprotein Receptors/Dab1 signalling regulates the positioning of the Cajal-Retzius cells, which are the very origin of the Reelin signal during fetal life.
HIGHLIGHTS OF THE SYMPOSIUM SUPPORTED BY INTERNATIONAL SOCIETY FOR NEUROCHEMISTRY

Frontiers in neurochemistry - Crosstalk of membrane proteins and lipids in health and disease

The moderator of the Symposium was prof. Ronald L. Schnaar coming from Johns Hopkins University School of Medicine, Baltimore, Maryland, USA. After welcoming auditorium, prof. Schnaar presented speakers and invited them to hold the talk. The discussions followed each talk led by prof. Schnaar.

First talk was held by prof. Raquel Marin coming from Laboratory of Cellular Neurobiology, Dept. Basic Medical Sciences, School of Medicine, University of La Laguna, Spain. It was titled “Neuronal lipid homeostasis: A main factor for brain maintenance and neuroprotection”. She stressed the fact that the brain is one of the organs containing the largest amount of different lipid molecular species from which some of them are organizing functional membrane subdomains - lipid rafts. Since subtle changes in composition of lipid rafts were observed during ageing and age-related neuropathologies (such as Parkinson’s or Alzheimer’s disease), it is important to clarify these changes by neurolipidomic studies. Prof. Marin has presented numerous results from her research group which elucidated two effects caused by modified lipid raft composition: (1) changes in the physicochemical properties and (2) impairment of raft protein interactions and promotion of toxic signal transduction. It was also highlighted that menopausal women are susceptible to the age-related diseases because signalosome of estrogen receptor is altered in lipid rafts. Prof. Marin concluded that identification of the early events involving modifications of neuronal lipid rafts may be a potential tool for the development of neuronal early diagnostic biomarkers for age-related neuropathological diseases. In the end prof. Marin also noted that modern diet rich in additional calories affects neuronal lipid rafts which may contribute to acceleration of neuronal lipid raft aging.

Prof. Dirk Montag, coming from Leibniz Institute for Neurobiology, Magdeburg, Germany, held the second talk titled “Neuroplastin ablation causes retrograde amnesia and circuit dependent deficits correlated to loss of neuroplastin PMCA complexes”. Prof. Montag stressed the role of neuroplastin in the human brain as an indispensible molecule for access and retrieval of previously acquired associative memories. He presented results of his research group from studies involving mouse models for inducible neuron-specific ablation of neuroplastin gene. Prof. Montag concluded that inducible neuroplastin-deficient mouse model
provides new means to analyze the molecular and cellular mechanisms underlying retrograde amnesia and memory.

The next talk held **prof. Rodrigo Herrera-Molina** also coming from Leibniz Institute for Neurobiology, Magdeburg, Germany. The title of the talk was “Why is Neuroplastin Essential for Circuit Activity Balance? - New interactions with TRAF6 and PMCA”. Prof. Herrera-Molina continued the story about neuroplastin presenting the most important findings of his research group: (1) they count a number of robust models for the study of neuroplastin functions in vivo and in vitro, (2) they have defined functions of neuroplastin in both inhibitory and excitatory synapses. These functions may contribute differentially, and importantly, the balance of E/I in the hippocampal circuit, (3) they confirmed interaction between Np and TRAF6 that results in a cascade of intrinsic mechanisms able to coordinate gene transcription and actin cytoskeleton organization during early formation and stabilization of spines, and (4) the observation of this research group that neuroplastins are localized in GM1-containing nanodomains (lipid rafts) opens new possibilities for the identification of regulatory mechanisms underlaying the function of the CAM and their interaction partners.

The last talk was held by **prof. Gundela Meyer** coming from Department of Basic Medical Science, Faculty of Medicine, University of La Laguna, Tenerife, Spain. Her talk was titled “Cell substrates of Reelin-Receptor signalling in human cerebral cortex development”. Prof. Meyer has showed the importance of the Reelin pathway during cortical development. It involves glycoprotein reelin and its receptors Very Low Density Lipoprotein Receptor (VLDLR) and Apolipoprotein E Receptor 2 (ApoER2), as well as adaptor protein Dab1. The source of reelin are Cajal-Retzius cells in the marginal zone of the developing cortex. Any loss of the key players in Reelin pathway results in reeler phenotype. Prof. Meyer has shown cortical distribution of reelin in the cortex of different age, the histology of the reeler cortex, Dab1, VLDLR and ApoER2 cortical distribution, as well as the VLDLR-/- and ApoER2-/- phenotypes. She concluded that identification of the cellular substrates of the different components of the Reelin-Dab1 pathway is critical to understand normal cortex development, and the resulting malformations if the pathway is disrupted.

The speakers gave us insights into their research activities from the the field of neurochemistry, cellular and molecular neuroscience that resulted and will result in further understanding of nervous system on molecular, cellular and biochemical aspect and in novel biomarkers of the development of neurological diseases.
Comment for ISN symposium

I: Comment on quality and content of lectures:

As a participant, I attended all lectures, held by: Raquel Marin, Dirk Montag, Rodrigo Herrera Molina and Gundela Meyer.

All lectures were focused, very interesting and clear. I would particularly stress out that lectures were interesting for specialists in the field, but have been also been structured so they can be followed and interesting to a wider audience.

I would recommend all speakers for future meetings.

II. Comment on organization

The symposium has been excellently announced, and from my perspective, had a surprisingly high number of participants. The location and lecture hall was excellent, and all technical equipment was of high quality.

The registration was easy, a sufficient amount of informative materials was available, and accompanying events were organized in a way to allow high interaction among participants and speakers. I wish to applaud the possibility to interact with speakers not only after lectures, but also during breaks and poster presentations.

III: The symposium and congress fulfilled all my expectations and allowed me interactions with experienced researchers, as well as young colleagues, to reach new ideas and collaborations for future work.

I found the organization very professional, but also very gracefull, and would certainly give the highest grade to organizers.

Zdravko Petanjek, MD, PhD
Full Professor of Human Anatomy and Neuroscience, tenured
Department of Anatomy, Croatian Institute for Brain Research,
School of Medicine, University of Zagreb,
Zagreb, Croatia
Telephone: +385 1 459 6803, +385 98 9043 144
E-mail: zdravko.petanjek@mef.hr
Comment for ISN symposium

ISN SYMPOSIUM – Frontiers in Neurochemistry Crosstalk of Membrane Proteins and Lipids in Health and Disease

I. Comment on quality and content of lectures:

As a participant, I attended the following lectures: Raquel Marin – “Neuronal lipid homeostasis: A main factor for brain maintenance and neuroprotection”; Dirk Montag – “Neuropilin ablation causes retrograde amnesia and circuit dependent deficits correlated to loss of neuropilin PMCA complexes”; Rodrigo Herrera Molina – “Why is neuropilin essential for circuit activity balance? New interactions with TRAF6 and PMCA”; Gundela Meyer – „Cell substrates of Reelin-Lipoprotein receptor signalling in human cerebral cortex development“. All lectures were brief, clear, informative, extremely interesting and valuable. I would definitely recommend all 4 speakers for future symposiums.

II. Comment on organization

Symposium was well advertised but that might be due to my membership in Croatian society for neuroscience which was the part of organization committee and which send the invitations and reminders.
The registration process was easy and clear, as well as all steps that precede the symposium itself (such as abstract submission).
The location of symposium was amazing and the lecture hall was fully equipped and very cozy. Organizers provided informative backing materials such as book of abstracts, fliers for future congress etc.). Accompanying events such as welcome reception was well placed and organized so that all participants can get a chance to meet the speakers and colleague scientists. That was also possible during coffee breaks. The minor objection was that to short time was planned for lunch break since the lunch wasn’t provided on the spot.

III. Since my main goal of attending symposiums and congresses’ is to meet new ideas and experts in my field of work, I’m always glad to participate in such events. This symposium left an impression of well organized, professional, very informative and friendly event.

Anja Bukovac, mag. oecol. et prot. nat.

Assistant at the Laboratory of Neurooncology, Croatian Institute for Brain Research, Department of biology, School of Medicine University of Zagreb, Šalata 12, 10 000 Zagreb, Croatia; e-mail: anja.bukovac@mef.hr
1. Comment on quality and content of lecture:

The most interesting and useful lecture for me personally, were following:
Raquel Marin: “Neuronal lipid homeostasis: A main factor for brain maintenance and neuroprotection”. The lecture was clear and innovative. Since our lab group does a similar research it was very interesting to see a different view on the similar research area. Prof. Marin is an excellent speaker, so it was easy to follow her lecture.

Dirk Montag: “Neuroplastin ablation causes retrograde amnesia and circuit dependent deficits correlated to loss of neuroplastin PMCA complexes”, Rodrigo Herrera Molina: “Why is neuroplastin essential for circuit activity balance? New interactions with TRAF6 and PMCA”. I would like to comment these two lectures in parallel, since the topic is similar. Both lecturers gave very interesting overview of novel roles discovered for neuroplastin. They both gave very detailed insight into their results and explained in details the animal procedure which I find very useful for my own research.

Gundela Meyer: „Cell substrates of Reelin-Lipoprotein receptor signaling in human cerebral cortex development”. Prof. Meyer showed an important role of Reelin receptor in human cortex development. The lecture was very detailed, informative and specifically useful for students.

2. Comment on organization:

Advertising of the Symposium was very well organized. I got all of the info from the Croatian Society for Neuroscience. Registration procedure was very simple and clear. The Symposium venue was very nice and the main lecture hall was fully equipped and spacious. Additional materials were provided by organizers and were very useful. Welcome reception was very well organized and it was a nice chance to get to know many of the main speakers.
3. My opinion on attending similar events:

I am always glad to attend scientific Symposiums since it is a great opportunity to get to know the similar work of other scientists. It is also a great way to get to know other scientists of the same field and learn a better way to do an experiment or get a great insight in novel findings which is useful in designing our own experiments.

Marta Balog, MSc in Biology
J. J. Strossmayer University of Osijek
Faculty of Medicine
Laboratory for Neurobiology
Department of Medical Biology and Genetics
### Expenses per person

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### TOTAL

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### EXCHANGE RATE

- 1 EUR = 7,48 kn
- 1 USD = 6,23 kn

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**ISN SYMPOSIUM: “FRONTIERS IN NEUROCHEMISTRY - CROSSTALK OF MEMBRANE PROTEINS AND LIPIDS IN HEALTH AND DISEASE”**

**HELD IN OSIJEK, CROATIA, 16TH SEPTEMBER 2017,**

**WITHIN 6th CROATIAN NEUROSCIENCE CONFERENCE (16.09.-18.09.2017.)**
ISN SYMPOSIUM: Frontiers in Neurochemistry Crosstalk of Membrane Proteins and Lipids in Health and Disease, Osijek, September 16th, 2017
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