COST Action
CA18133

ERNEST
European Research
Network on Signal
Transduction

Horizon 2020
Programme

cost
EUROPEAN COOPERATION
IN SCIENCE & TECHNOLOGY

BOĞAZİÇİ ÜNİVERSİTESİ
1863

2nd ERNEST Online Meeting
New Perspectives in Signal Transduction: GPCRs and Beyond

28-30 March, 2020

Abstract Book

Greetings!

It is our pleasure to host you **online** for Second Meeting of the European Research Network on Signal Transduction (**ERNEST** COST Action CA18133) with the theme of ***New Perspectives in Signal Transduction: GPCRs and Beyond*** March 28-30, 2020.

The main scientific objective of **ERNEST** is to develop a common, comprehensive and holistic map of signal transduction that will advance development of pathway-specific chemical modulators. This unique and innovative goal will be realized by linking diverse research groups in the field through the networking activities.

In line with the scientific objectives of the ERNEST, the program of the meeting will cover different aspects of signal transduction involving, but not limited to, GPCRs: Macromolecular interactions in signaling pathways, biological roles of signal transduction, molecular modulators of signal transduction, advances in methodologies and technologies and public web resources.

This 3-day event will bring together internationally renowned scientists as well as early career researchers from all around Europe and nearby countries. It will serve as an excellent global platform for researchers from industry and academia to interact and discuss the latest scientific findings, innovations and technologies in the field of cellular signalling. We believe that the meeting will also be an exceptional stage for *virtual* congregation, *streaming* of ideas and establishing new *Skype-enabled* collaborations.

We are excited to be part of this event, and we hope that you will be able to participate and join us in this effort.

Organizing Committee

İbrahim Yaman (Local Organizer, Boğaziçi University)
Necla Birgül (Local Organizer, Boğaziçi University)
Martha Sommer (Chair of ERNEST, Charité and MDC Berlin)
Jana Selent (Vice-chair of ERNEST, Pompeu Fabra University)

COST Action
CA18133

ERNEST
European Research
Network on Signal
Transduction

2nd ERNEST Meeting: Online program		
Time (CET)	**Day 1: Saturday, 28 March 2020**	Abstract page #
9:00-9:45	**Opening and Announcements** **Ibrahim Yaman, Necla Birgul, Martha Sommer**	
10:00-10:45	**Keynote talk** **Michel Bouvier** (University of Montreal) *Detecting and analyzing functional selectivity and biased signalling, historical perspective and potential for drug discovery*	6
10:45-11:15	**BREAK (30 min)**	
11:15-12:05	**SESSION 1 WG1** (chair: **Milka Vrecl**) 11:15-11:35 **Martha Sommer** (Charité Medical University Berlin) *Dynamic versatility of arrestin in GPCR and membrane binding* **Short talks** (selected from abstracts) 11:35 - 11:50 **Daniel Hilger** (Philipps-University Marburg) *Structural insights into differences in G protein activation by Family A and Family B GPCRs* 11:50 - 12:05 **Gemma Navarro** (University of Barcelona) *Functional pre-coupled complexes of receptor heteromers and adenylyl-cyclase*	7 8 9
12:05-12:30	**BREAK (25 min)**	
12:30-13:00	**SESSION 2** **Poster Flash Talks 1 to 10** (10 x 3 min)	10-19
13:00-14:30	**BREAK (90 min)**	
14:30-15:30	**SESSION 3 Short Talks** (chair: **Fabrizio Fierro**) 14:30 - 14:45 **Johanna K. S. Tiemann** (University of Copenhagen) *Formation of a β2AR*-GsGDP intermediate complex* 14:45 - 15:00 **Thor Moller** (University of Copenhagen) *Dissecting the roles of GRK2 and GRK3 in µ-opioid receptor internalization and b-arrestin2 recruitment using CRISPR/Cas9-edited HEK293 cells* 15:00 - 15:15 **Aleksandra Luginina** (Moscow Inst. Physics&Technology) *δ-branch of class A GPCRs: structural aspects of activation* 15:15 - 15:30 **Pedard Martin** (Normandie University) *The urotensin II G protein-coupled receptor relays key neurobiological mechanisms in subarachnoid hemorrhage through a Gq-dependent pathway*	20 21 22 23
15:30-15:45	**BREAK (15 min)**	
15:45-17:15	**SESSION 4 GPCRdb / GPCRmd satellite meeting** (organizers: Jana Selent and David Gloriam) 15:45 - 16:30 GPCRdb (**Albert Kooistra & Christian Munk**) · Demo-session (www.gpcrdb.org) · Questions and user-implementation wishes 16:30 - 17:15 GPCRmd (**Jana Selent**) · Demo-session (www.gpcrmd.org) · Updates on objectives and call for contributions	24
17:15-18:00	**BREAK (45 min)**	
18:00-20:00	**SESSION 5** **Social event - meeting up in virtual rooms**	25

COST Action
CA18133

ERNEST
European Research
Network on Signal
Transduction

Time (CET)	2nd ERNEST Meeting: Online program	
	Day 2: Sunday, 29 March 2020	Abstract page #
9:00-10:30	**SESSION 6 WG2** (chair: **Necla Birgul & Nina Vardjan**)	
	9:00-09:20 **Miriam Stoeber** (University of Geneva) *Biosensors reveal ligand-selective patterns of opioid receptor activation*	26
	9:20-9:40 **Graham Ladds** (University of Cambridge) *Systems analysis of G protein-coupled receptor pharmacology*	27
	9:40-10:00 **Ines Liebscher** (University of Leipzig) *The force within – Mechano-sensitive adhesion GPCR shape physiology*	28
	Short talks (selected from abstracts) 10:00-10:15 **Hélène Castel** (Normandie University) *Chemokine GPCRs function with different G proteins or anchoring partners to control glioma invasiveness*	29
	10:15-10:30 **Aida Shahrakia** (Bogazici University) *In silico and in vitro Approaches to Characterize a Novel G-Protein Coupled Receptor in Thaumetopoea pityocampa*	30
10:30-11:20	**BREAK (50 min)**	
11:20-12:45	**SESSION 7 WG3** (chair: **Masha Niv & Fabrizio Fierro**)	
	11:20-11:40 **Christa Müller** (University of Bonn) *Tools and drugs for G proteins and G protein-coupled receptors*	31
	11:40-12:00 **Leigh Stoddart** (University of Nottingham) *Ligand-directed affinity labelling - a new approach to visualise GPCRs*	33
	Short talks (selected from abstracts) 12:00 - 12:15 **Giulia Morra** (Ist di Scienze e Tecnologie Chimiche) *Investigating functional selectivity in and around GPCRs with Molecular Dynamics*	34
	12:15 - 12:30 **Pierre Matricon** (Uppsala University) *Design of a GPCR agonist by Targeting a Binding Site Water Network*	35
	12:30 - 12:45 **Vigneshwaran Namasivayam** (University of Bonn) *Computational approaches for the proinflammatory lipid-activated G protein-coupled receptor GPR84 providing structural insights*	36
12:45-13:30	**BREAK (45 min)**	
13:30-14:00	**SESSION 9** **Poster Flash Talks 11 to 19** (9 x 3 min)	37-45
POSTPONED	**SESSION 8** Academia-Industry Cooperation	
POSTPONED	**SESSION 10** Management Committee Meeting	

COST Action
CA18133

ERNEST
European Research
Network on Signal
Transduction

4

Time (CET)	2nd ERNEST Meeting: Online program	
	Day 3: Monday, 30 March 2020	Abstract page #
9:00-10:40	**SESSION 12 WG4** (chair: **Nuska Tschammer & Eddy Sotelo**)	
	9:00-9:50 **Martin J. Lohse** (MDC, Berlin; ISAR Bioscience Institute, Munich)	46
	Watching receptors at work – using the microscope to study GPCRs	
	9:50-10:10 **Bence Szalai** (University of Semmelweis)	47
	Gene expression signatures - footprints of GPCR signalling pathway activity	
	Short talks (selected from abstracts)	
	10:10-10:25 **Adrian Morales-Pastor** (Pompeu Fabra University)	48
	Exploration of allosteric communication networks that underlie GPCR functionality	
	10:25-10:40 **Tõnis Laasfeld** (University of Tartu)	49
	Novel fluorescence ligands for the characterization of muscarinic acetylcholine receptors	
10:40-11:15	**BREAK (35 min)**	
11:20-12:30	**SESSION 13 WG5** (chair: **Jana Selent**)	
	11:15-11:45 **Vassiliki Iconomidou** & **Avgi-Elena Apostolakou** (University of Athens)	50
	hGPCRnet: A tool for Cell-Type Specifc Analysis of GPCR Signaling Pathways	
	11:45-12:10 GPCRdb update (**David Gloriam**)	51
	12:10-12:30 GPCRmd update (**Mariona Torrens**)	52
12:30-12:45	**BREAK (15 min)**	
12:45-13:45	**SESSION 14 Short talks** (chair: **David Gloriam**)	
	12:45-13:00 **Alexey Bondar** (Augusta University)	53
	Membrane domain localization and mobility of Gs signaling cascade components	
	13:00-13:15 **Marcel Bermudez** (Freie Universität Berlin)	54
	Pharmacological approaches to decipher the signaling networks of GPCR of the reproductive axis	
	13:15-13:30 **Pascale Crépieux** (Université de Tours)	55
	Pharmacological approaches to decipher the signaling networks of GPCR of the reproductive axis	
	13:30-13:45 **Shannon O'Brien** (University of Birmingham)	56
	Hydroxy-carboxylic acid receptor 2 signalling at endosomal compartments	
13:45-14:00	**BREAK (15 min)**	
14:00	**SESSION 15** **Meeting Closure** (chair: Martha Sommer)	57
POSTPONED	**Focus Group on Functional Selectivity** (by invitation only) Organizer: Peter Kolb	

COST Action
CA18133
ERNEST
European Research
Network on Signal
Transduction

Combined ligand-based and structure-based approaches in rational drug design of novel 5-HT$_{2A}$ receptor antagonists #1

Milica Radan, Dusan Ruzic, Mirjana Antonijevic, Teodora Djikic, and Katarina Nikolic[*]

Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Belgrade, Vojvode Stepe 450, 11000 Belgrade, Serbia.

Section:
1. Macromolecular Interactions in Signalling Pathways,
2. Biological Roles of Signal Transduction,
3. Molecular Modulators of Signal Transduction,
4. Advanced Methodologies and Technologies
5. Public Web Resources

Position of the presenter: Group Leader
Email address of the presenter: knikolic@pharmacy.bg.ac.rs

The serotonin 5-HT$_{2A}$ receptor plays an important role in many physiological functions.[1] Various neurological and psychiatric disorders are associated with certain imbalances in 5-HT neurotransmission.[2] Therefore, antagonists of these receptors are efficient as antipsychotics but also have a significant role in the treatment of depression, anxiety, and Parkinson disease. In order to find crucial structural features responsible for high binding affinity of 5-HT$_{2A}$ antagonists, we have combined structure based and ligand based drug design methods. This study was performed on wide range of structurally diverse antagonists. Based on their chemical structures they were divided into three different clusters: clozapine, ziprasidone, and CHEMBL240876 derivatives. Each cluster representative in complex with 5-HT$_{2A}$ receptor was submitted to 50ns long molecular dynamics (MD) simulation in order to obtain their inactive, antagonist-bound, conformations. Subsequently, these conformations were used as templates for docking studies in order to generate virtually bioactive conformations of studied ligands. Selected conformers were used for calculation of specific molecular descriptors (Grid Independent Descriptors- GRIND) and three-dimensional quantitative structure-activity relationship (3D-QSAR) model building. The 3D-QSAR approach helps us to identify the most important structural determinants responsible for the antagonistic activity and to propose structural modification for novel antagonists of serotonin 5-HT$_{2A}$ receptors. Furthermore, the reliability and predictive potential of the created model was evaluated using an external test set compounds. Results obtained from performed 3D-QSAR, MD and molecular docking studies were analysed and used for rational drug design of novel 5-HT$_{2A}$ receptor antagonists.

References

1. A. Frazer, J.G. Hensler, Basic Neurochem. Mol. Cell. Med. Asp. 1999, 6th
2. Lin, S.-H., Lee, L.-T., Yang, Y.K., 2014. Serotonin and Mental Disorders: A Concise Review on Molecular Neuroimaging Evidence. Clin. Psychopharmacol. Neurosci. **12**:196–202

COST Action
CA18133
ERNEST
European Research
Network on Signal
Transduction