Physiopathology of Sigma-1 Receptors

5th European Symposium/ 1st Meeting of the European Network for Sigma-1 Receptor as a Therapeutic Opportunity (SIGMA-1EUROPE - CA23156)



IN SCIENCE AND TECHNOLOGY

25-27 june 2025

Organizers

Scientific Committee Dr. Tangui MAURICE MMDN, University of Montpellier, EPHE, INSERM, Montpellier, France

> Dr. Liga ZVEJNIECE Latvian Institute of Organic Chemistry, Riga, Latvia

Dr. Carmen ABATE Università degli Studi di Bari Aldo Moro, Bari, Italy

Dr. **Enrique J COBOS** Universidad de Granada, Granada, Spain

Local Organizers

Dr. Francisco R Nieto Dr. Rafael González-Cano Dr. Miguel Ángel Tejada Dr. M Carmen Ruiz-Cantero Dr. Antonia Artacho Cordón Miriam Santos-Caballero Miguel Ángel Huerta Martínez María Robles Funes Amada Puerto Moya Universidad de Granada, Granada, Spain



25th June Wednesday Facultad de Medicina – Faculty of Medicine Salón de Actos - Assembly Hall

8.30 Registration

9.00 Opening ceremony. Enrique Cobos (on the behalf of the scientific committee), Tanqui Maurice (Chair SIGMA-1EUROPE) and Liga Zvejniece (vice Chair SIGMA-1EUROPE), José Juan Jiménez Moleón (Dean of the Faculty of Medicine, University of Granada)

09.30 Opening lecture.

Anti-amnesic and neuroprotective effects of sigma-1 receptor agonists. **Tangui Maurice**, University of Montpellier, Montpellier, France

Chair: Liga Zvejniece, Latvian Institute of Organic Synthesis, Riga, Latvia

10.15 Coffee (with cookies/sandwiches) + posters 1 (odd numbers)

11.00 Medicinal Chemistry 1

Development of sigma-1 receptor ligands: past, present and future perspectives. **Carmen Abate**, Università degli Studi di Bari Aldo Moro, Bari, Italy (25 min)

- Modulation of Sigma-1 receptor and TSPO through bivalent ligands: exploring a new approach against neuroinflammation and neurodegeneration. **Giacomo Rossino**, University of Pavia, Pavia, Italy (10 min)
- Discovery of novel class of multi-target ligands for sigma-1 receptor and selected GPCRs among selenoether derivatives of piperazine. **Patryk Pyka**, Jagiellonian University, Kraków, Poland (10 min)
- Unlocking the Power of Inhibiting Soluble Epoxide Hydrolase and Sigma-1 Receptor Antagonism through Dual Mechanism Analgesic Compounds. **Celia Escriche** Molina, Universitat de Barcelona, Barcelona, Spain (10 min)

Debate and questions: 15 min Chair: Francisco R Nieto, Universidad de Granada, Granada, Spain

12.15 Medicinal Chemistry 2

Development of sigma receptor modulators for the treatment of neuropathic pain. Emanuele Amata, Università degli Studi di Catania, Catania, Italy (25 min)

Sigma-1 receptor fluorescent ligands: development and use of powerful pharmacological tools. **Gabriella Rosanna Musillo**, Università Degli Studi di Bari Aldo Moro, Bari, Italy (10 min)

- Structural and Dynamic Determinants of Sigma-1 Receptor Oligomerization: Insights from Molecular Dynamics Simulations. **Vittoria Nanna**, National Research Council - Institute of Crystallography, Bari, Italy (10 min)
- Tackling Neurodegenerative Diseases by Developing Light-Activated Drugs through an Integrated Multiscale Approach. **Giacomo Salvadori**, Institute for Computational Biomedicine, Jülich,Germany (10 min)

Debate and questions: 15 min

Chair: Rafael González Cano, Universidad de Granada, Granada, Spain

13.30 Lunch (60 min) - Canteen of the PTS

14.30 Coffee + posters 2 (odd numbers)

15.30 Plenary

The Sigma-1 Receptor - Enigmatic? Arnold Ruoho, University of Wisconsin-Madison, Madison, USA

Chair: Carmen Abate, Università degli Studi di Bari Aldo Moro, Bari, Italy

16.15 Neurodegenerative and other neurological diseases

Sigma-1 as a target for antiseizure and disease-modifying effects? Preclinical validation in mouse models of epilepsy. **Eva-Lotta von Rüden**, Ludwig-Maximilians-Universität München, Munich, Germany. (25 min)

Targeting Sigma-1 Receptor for Neurodegenerative Diseases: Insights into Physiopathology and Therapeutic Potential. Kanika Verma, Chulalongkorn University, Bangkok, Thailand (10 min)

Pridopidine, a Sigma-1 Receptor Agonist, Offers Therapeutic Potential for Huntington's Disease and Amyotrophic Lateral Sclerosis. **Andrew Tan**, Prilenia Therapeutics B.V., Naarden, The Netherlands (10 min)

Allosteric positive modulator of Sigma-1 receptor: a new weapon to mitigate disease progression in amyotrophic lateral sclerosis. **Hugo Mourier**, University of Montpellier, INSERM, Montpellier, France (10 min)

Debate and questions: 15 min

Chair: Enrique J Cobos. University of Granada, Granada, Spain

17.30-18.00 Break (coffee)

18.00 Cognition, depression, anxiety and other psychiatric disorders Neuroprotective Potential of 6-Hydroxy-L-Nicotine: Modulating Memory, Oxidative Stress, and Neuroinflammation. Lucian Hritcu, Alexandru Ioan Cuza University of Iasi, Iasi, Romania (25 min) Targeting Sigma-1 Receptors for Improved Executive Flexibility Under Glutamatergic Dysfunction. Kinga Sałaciak, Jagiellonian University, Kraków, Poland (10 min) SIGMA1R play an indispensable role in Th9 differentiation. Michel Mickael, Institute of Genetics and Animal Biotechnology, Garbatka, Poland (10 min)

Reduced levels of the sigma-1 receptor in the brains of Alzheimer's disease patients. **Ruiqing Ni**, University of Zurich, Zurich, Switzerland (10 min)

Debate and questions: 15 min Chair: Tangui Maurice, University of Montpellier, Montpellier, France

19.30-21.00 Welcome reception (same building)

26th June Thursday Facultad de Medicina – Faculty of Medicine Salón de Actos - Assembly Hall

09.00 Plenary

Sigma-1 Receptor Controls Glycolysis via Mitochondrial GRIM19 and Glucose Uptake. **Tsung Ping Su**. National Institute on Drug Abuse, Baltimore, USA *Chair: Tangui Maurice, University of Montpellier, Montpellier, France*

09.45 Coffee (with cookies/sandwiches) + posters 3 (even numbers)

10.30 Sigma-1 receptor biochemistry and cellular biology: structure, protein targets and basic mechanisms

- TIRF Microscopy-Based Assay for Detecting and Colocalizing Membrane Proteins. Ago Rinken, University of Tartu, Tartu, Estonia (25 min)
- Conserved LIR-specific interaction of sigma-1 receptor and GABARAP. Fazilet Bekbulat, Johannes Gutenberg University Mainz, Mainz, Germany (10 min)
- Investigation of σ1 receptor mechanism of activity and identification of novel agonists. **Andrea Ilari**, Institute of Molecular Biology and Pathology (IBPM), National Research Council of Italy (CNR), Rome (10 min)
- Accelerated mutant huntingtin aggregation and reduction of ER stress by the S1R agonist pridopidine. **Gerardo Lederkremer**, Tel Aviv University, Tel Aviv, Israel (10 min)

Debate and questions: 15 min

Chair: Andrea Fekete, Semmelweis University and SigmaDrugs, Budapest, Hungary

11.45 Pain, inflammation and non-central diseases

- Effects of S1RA (E-52862), a selective sigma-1 antagonist, in neuropathic pain: Two randomized, double-blind, phase 2 studies in patients with chronic postsurgical pain and painful diabetic neuropathy. **Víctor Mayoral**, Bellvitge University Hospital, Barcelona, Spain (25 min)
- The application of AI tools in analyzing pain behavior in mice: examples on the study of sigma-1 receptor function. **Rafael Gonzalez-Cano**, University of Granada, Granada, Spain (10 min)
- Dual-Targeting Histamine H3 and Sigma-1 Receptor Ligands as Candidates for the Treatment of Neuropathic Pain. **Katarzyna Szczepańska**, Maj Institute of Pharmacology, Polish Academy of Sciences, Kraków, Poland (10 min)
- Fluvoxamine mitigates bleomycin-induced pulmonary fibrosis in mice. Adam Hosszu, Semmelweis University, Budapest, Hungary (10 min)

Debate and questions: 15 min

Chair: M Carmen Ruiz Cantero, University of Barcelona, Barcelona, Spain

13.00 Lunch (Same building)

14.00 Coffee + posters 4 (even numbers)

15.00 Other diseases and disease models

- Identifying and Characterizing Novel Small Molecule-Sigma-1 Ligands using *Caenorhabditis elegans*. James Brimson, Chulalongkorn University, Bangkok, Thailand (25 min)
- The role of sigma-1 receptor in the anticancer activity of thiosemicarbazones. **Bianca Stiller**, Medical University of Vienna, Vienna, Austria (10 min)
- Regulation of Sigma-1 Receptor in Cancer Progression and Drug Resistance. **Ioannis Trougakos**, National and Kapodistrian University of Athens, Athens, Greece (10 min)
- Fluvoxamine, eyedrop, glaucoma, intraocular pressure, fibrosis. **Judit Hodrea**, Semmelweis University, Budapest, Hungary (10 min)

Debate and questions: 15 min

Chair: Miguel Ángel Tejada, University of Granada, Granada, Spain

16.15 Closing lecture

Sex-Specific Role of Sigma-1 Receptor in Cardiac and Metabolic Function in Mice **Liga Zvejniece**, Latvian Institute of Organic Synthesis, Riga, Latvia *Chair: Enrique J Cobos, University of Granada, Granada, Spain*

17.00 Excursion to the city (<u>GranaDown</u>) – please follow the local committee to the bus

Closing dinner 21.00-23.00 (Carmen de la Victoria)

27th June Friday Facultad de Medicina – Faculty of Medicine Salón de Grados B - Graduation Hall B

9.00-10.30 Management Committee meeting 1

10.30-11.00 Coffee (with cookies/sandwiches)

11.00-12.00 Management Committee meeting 2

12.00-14.00 WG3 (Establishment of SOPs for in-vitro/in-vivo models to assess sigma-1 receptor ligands) meeting

14.00-15.30 Lunch + Coffee (Same building)

15.30-17.30 WG4 (Industry strategies requirements for drug development) meeting

17.30-17.45 Break

17.45-19.45 WG5 (Dissemination, Communication and Outreach) meeting

Poster Presentations - 25th June Wednesday (odd numbers)

Ν		Chemistry enting author name	Title of the communication
1	Ι	Barvik	Design of sigma-1 receptor agonists and antagonists using computer modeling
3	Х	Codony	Innopharma Sigma Chemical Library for hit identification and tool compound discovery
5	G	Cosentino	Design, synthesis, and in silico studies of novel tetrahydropyrrolo[3,4-c]pyrazoles sigma-1 receptor ligands
7	G	Cosentino	Synthesis of new benzylpiperazines as selective sigma-1 receptor ligands with in vitro antiproliferative activity against cancer cells
9	AT	Lisi	Structure-activity relationship studies on phenoxyalkylpiperidines reveal the structural determinants for potent sigmal receptor agonist activity and antineurodegenerative properties.
11	М	Mammone	Exploiting the Therapeutic Potential of Sigma and Cannabinoid subtype 2 Receptors (CB2R) as Dual Targets approach in Inflammatory Diseases
13	S	Obradović Jovčić	Vildagliptin: insight into SIGMA-1 receptor profile
15	С	Rodriguez-Tanty	Amylovis-201 is a potent agonist of the s1 chaperone protein with anti-amylodogenic activity for treatment of Alzheimer's disease
17	J	Sánchez Sánchez- Corral	Targeting Sigma-1 for Pain Relief: Selective Antagonists with Dual Mechanism of Action
Neu	-		hiatric disorders and pain
Ν	Pres	enting author name	Title of the communication
19	Т	Aparicio Mescua	Antagonism of Sigma-1 inhibits binge ethanol drinking in adolescence
21	А	Gazzano	Leveraging Multi-Targeted Direct Ligands To target TSPO and S1R crosstalk in microglia.
23	MA	Huerta	Sigma-1 Receptor Inhibition Reduces Arthritis Progression and Pain
25	KK	Kumaree	Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by dopaminergic neuron loss, oxidative stress, and mitochondrial dysfunction.
27	А	López-Ruiz	Multi-Target Directed Ligands binding the sigma-1 receptor: promising therapeutic strategy for pain management
29	М	Meltzer	Pridopidine exerts neuroprotective effects, via activation of the Sigma-1 receptor (S1R)
31	М	Meltzer	The Phase 3 PROOF-HD Trial Demonstrates Meaningful Benefits of Pridopidine on Function, Cognition, and Motor in Huntington Disease (HD)
33	D	Svob Strac	DHEA(S) in dementia: from cellular and animal models to patients
		ceptor biochemistry ar liseases and disease mo	nd cellular biology: structure, protein targets and basic mechanisms, odels
N		enting author name	Title of the communication
35	AP	Cherciu	The hidden effects of Metformin on oxidative stress
37	J	Jonane	Sigma-1 receptor is associated with tetraspanin-labelled extracellular vesicles: insights from single particle analysis
39	Ι	Pantic	Concept of a random forest machine learning model for detection of chromatin structural rearrangements induced by Sigma-1 receptor ligands
41	А	Rozsahegyi	Sigma-1 receptor agonist fluvoxamine is protective against hyperglycemia-induced fibrosis in human trabecular meshwork cells
43	W	Trein	The interplay of S1R and Wolframin in neuronal autophagy

Poster Presentations - 26th June Thursday (even numbers)

Medicinal Chemistry					
Ν	Pres	enting author name	Title of the communication		
2	D	Arella	Development of Sigma-1 Receptor Photowitchable Ligands as Molecular Tools		
4	V	Cavalloro	Sigma-1 receptor: the hidden target of traditional preparations for neurodegeneration and neuropathic pain		
6	G	Costanzo	Synthesis and biological evaluation of novel S1R ligands		
8	J	Handzlik	In vivo evaluation on antipsychotic-like activity for the first-in-		
-			class arylselenoether-piperazine derivatives targeting sigma- 1/D2/5-HT1A receptors in mice		
10	MC	Lomuscio	SIGMAP: an explainable artificial intelligence tool for SIGMA- 1 receptor affinity prediction		
12	F	Mastropasqua	DEVELOPMENT OF POSITRON EMISSION TOMOGRAPHY RADIOTRACERS FOR IMAGING SIGMA- 1 RECEPTORS IN CNS DISEASES		
14	S	Salvi	RC-106, a promising therapeutic agent against glioblastoma. Scale up synthesis, solid-state characterization and in vivo evaluation		
16	Е	Szymanska	Novel multi-target ligands of sigma-1 receptor as potential agents for treatment of neuropsychiatric disorders		
Neu	urodeg	enerative diseases, ps	sychiatric disorders and pain		
Ν	Pres	enting author name	Title of the communication		
18	F	Bekbulat	ni2n: a networking project to promote progressive, multidimensional research concepts		
20	М	Cagalinec	Endoplasmic reticulum stress, integrity and mitochondrial morphology in a cellular model of Wolfram syndrome		
22	А	Jagielska	HBK-15, a multimodal compound activating sigma-1 receptors,		
		-	reverses memory and executive function deficits in neuropsychiatric disorder models		
24	AM	Jiménez-García	Modulation of Frustration through Sigma-1 Receptors: Effects of PRE-084 and S1RA in Wild-Type and Knockout Rats Using the CSNc Paradigm		
26	М	Meltzer	Pridopidine For the Treatment of ALS (Healey ALS Platform Trial)		
28	MC	Ruiz Cantero	Sigma-1 receptor antagonism and soluble epoxide hydrolase inhibition: synergistic effect in the reduction of capsaicin-		
			induced and surgical incision-induced tactile allodynia		
30	М	Santos	Sigma-1 receptor antagonism enhances endogenous and drug- induced opioid analgesia: promising strategies for postoperative pain treatment		
Sigma-1 receptor biochemistry and cellular biology: structure, protein targets and basic					
mechanisms, and other diseases and disease models					
Ν	Pres	enting author name	Title of the communication		
32	Т	Lakat	Transcriptomic profiling of Sigma-1 receptor agonism in		
			bleomycin-induced pulmonary fibrosis: Insights into therapeutic mechanisms		
34	Т	Medveczki	Age-specific anti-glaucomatous effect of a Fluvoxamine- containing eye drop		
36	K	Palikaras	High-content drug screening for Sigma-1 Receptor activators using the nematode Caenorhabditis elegans		
38	J	Paunovic Pantic	Potential of support vector machine learning in Sigma-1 receptor physiology		
40	А	Toth	Protective effects of a novel Sigma-1 receptor agonist in renal ischemia/reperfusion injury		