

Research Group of Structural Neurobiology

CV of the PI

NAME: MARIOS ZOURIDAKIS

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POSITION TITLE: Principal Research Staff Scientist (Grade B)

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
University of Patras, Dep. of Biology	BSc	06/2000	Biology
University of Patras, Deps of Chemistry and Pharmacy	MSc	10/2003	Medicinal Chemistry
University of Patras, Dep. of Pharmacy	PhD	09/2009	Structural Biochemistry
Hellenic Pasteur Institute	Post-doc	08/2021	Structural and functional Neurobiology

A) Personal Statement

Despite recently appointed as a Research Staff Scientist to the Hellenic Pasteur Institute (Sep. 2021), I had actually been a post-doctoral researcher at the same Institute for more than a decade (2009-Aug. 2021). During my post-doctoral research in the lab of Molecular Neurobiology and Immunology, I gained strong background in Biochemistry, molecular biology and protein crystallography. I have also obtained high experience in *a*) guiding the research of undergraduate and post-graduate students (co-supervised two PhD students, two MSc and one undergraduate, and supervised three internship students from National and International Institutes), *b*) conducting independent research (corresponding author in two recent articles) and *c*) publishing the results (author and co-author of 19 peer-reviewed papers). I have strong experience in the implementation of research grants as having been a co-investigator in 8 National and International-funded research programmes (contributed to proposal writing and submission in two; work package leader in four) and I have also served as Scientific Manager in a EC-funded programme. My main research interests deal with the biochemical, structural and functional studies of pentameric ligand-gated ion channels and especially of the neuronal nicotinic acetylcholine receptors (nAChRs). During the last couple of years I have expanded my interests to the structural studies of the COVID-19 key proteins (region binding domains of variants and the human ACE2 receptor). My expertise is in heterologous expression and purification of proteins and in their functional (ligand-binding and electrophysiology) and structural (dynamic light scattering, circular dichroism and crystallography) studies.

B) Positions and Honors

Positions and Employment

2004 – 2009	PhD candidate, Department of Pharmacy, University of Patras
2009 – Aug 2021	Post-doctoral fellow, Hellenic Pasteur Institute
Sep 2010 – Feb. 2014	Scientific Manager of EC-FP7-REGPOT-2010 Neurosign programme, Hellenic Pasteur Institute
Oct. 2010 – Feb. 2011	Temporary Lecturer, Technological Educational Institute of Athens, Department of Medical Laboratories
Mar. 2011 - May 2011	Temporary Lecturer, Department of Pharmacy, University of Patras
Sep. 2021-	Research Staff Scientist, Grade B, Hellenic Pasteur Institute

Professional Memberships

- 2002 – Member, Hellenic Society of Biochemistry and Molecular Biology
2013 – Member, Hellenic Crystallographic Association

Honors

- 2003 Scholarship for outstanding performance in the MSc class 2003 of Medicinal Chemistry; University of Patras
2004 EMBO travel grant for participation in Practical Course in Protein expression, purification and crystallization; EMBL, Hambourg
2004 FEBS travel grant for participation in Advanced Methods In Protein Crystallization; Academic and University Center at Nove Hradý, Czech
2005 EMBO travel grant for participation in EMBO lecture courses on channels and transporters, Ettore Majorana Foundation, Erice, Italy

Organization of Scientific Meetings/Advanced Courses

- 2013 Co-organizer of the International Workshop “*Live Cell Imaging and Electrophysiology*”, HPI, Athens
2017 Co-organizer of the 4th International Conference “*Nicotinic Acetylcholine Receptors*”, Chania-Crete

C) Contributions to Science

1. I have been studying pentameric-ligand gated receptors for more than a decade with emphasis on nicotinic acetylcholine receptors (nAChRs) implicated in several neurological diseases (e.g. schizophrenia, autism, epilepsy) and in addiction to smoking. My long-lasting research goal is the elucidation of the structure of the ligand-binding sites of nAChRs in order to facilitate rational drug design and understand the molecular mechanisms underlying their function and pharmacology. Towards this end, a major scientific achievement was the X-ray crystal structure of the ligand-binding domain of the human $\alpha 9$ nAChR in the Apo and ligand-bound forms. This was the first crystal structure reported for any neuronal nAChR at that time, published in *Nature Struct and Mol Biol* (2014). The study was complemented by mutational and electrophysiological analysis shedding light on the structural rearrangements upon ligand binding leading to channel opening.
2. A more recent achievement was the co-crystallization of $\alpha 9$ nAChR with α -conotoxin (α -Ctx) RgIA, a potent drug for the neuropathic chronic pain, targeting $\alpha 9$ -containing nAChRs published in *Frontiers in Pharmacology* (2019). The interactions of α -Ctx RgIA with the ligand-binding site of $\alpha 9$ nAChR were revealed in full detail and are expected to be useful for the rational design of improved RgIA analogs with enhanced potency and selectivity for $\alpha 9$ -containing nAChRs.

Selected relevant publications:

1. **Zouridakis M[#]**, Papakyriakou A, Ivanov IA, Kasheverov IE, Tsetlin V, Tzartos SJ, and Giastas P[#] Crystal structure of the extracellular domain of the $\alpha 9$ nicotinic receptor subunit in complex with α -conotoxin RgIA: Insights into RgIA binding to $\alpha 9 \alpha 10$ nicotinic receptors *Front Pharmacol* 10:474. (2019) doi:10.3389/fphar.2019.00474 [#]*Corresponding authors*
2. Azam, L., Papakyriakou, A., **Zouridakis M**, Giastas P, Tzartos SJ, and McIntosh JM. Molecular interaction of alpha-conotoxin RgIA with the rat alpha9alpha10 nicotinic acetylcholine receptor *Mol Pharmacol* 87(5), 855-864 (2015) doi: 10.1124/mol.114.096511
3. **Zouridakis M**, Giastas P, Zarkadas E, Chroni-Tzartou D, Bregestovski P and Tzartos SJ. Crystal structures of free and antagonist-bound states of human alpha9 nicotinic receptor extracellular domain *Nature Struct Mol Biol* 21(11), 976-980 (2014) doi: 10.1038/nsmb.2900

Full list of publications:

<https://pubmed.ncbi.nlm.nih.gov/?term=Zouridakis+M&sort=date>

D) Research Support

Ongoing Research Support

Project Title	Funding source	Duration	Role of PI
Development of innovative biological products and services for infectious and neurodegenerative diseases	Stavros Niarchos Foundation	Jan. 2017- Dec. 2021	Co- investigator
Structural and functional studies of nicotinic acetylcholine receptors	HFRI	Nov. 2018- Mar. 2022	Co- investigator
High Technology Infrastructure for Preclinical Studies and Provision of Specialized Services for Infectious and Neurodegenerative Diseases	NSFR	July 2021- Dec. 2023	Co- investigator

Completed Research Support

Project Title	Funding source	Duration	Role of PI
Biomarkers in autoimmune neurological diseases	NSFR, EC	Sep. 2018 – Nov. 2021	Co- investigator
Research infrastructure on biotechnology and structural biology: INSPIRED-Node HPI	NSFR, EPaNEK	2018 –2021	Co- investigator
Antigen-specific therapeutic auto-antibody depletion in Myasthenia gravis	MDA	Oct. 2015 - Dec. 2016	Co- investigator
Development of assays for tracing antibodies based on cells, RIPA and ELISA	GSRT	June 2014 – Nov. 2015	Co- investigator
NEUROSIGN: Expression of membrane proteins followed by biochemical and biophysical studies	EC FP7	Oct. 2010 – Feb. 2014	Co- investigator
NEUROCYPRES: Expression and study of domains of the acetylcholine receptor	EC FP7	May 2009 – Dec. 2010	Co- investigator