Marios Zouridakis, PhD

RESEARCH SCOPE AND EXPERTISE

I am a research fellow at the lab of Molecular Neurobiology and Immunology with research interests in the biochemical, structural and functional studies of pentameric ligand-gated ion channels and especially of the neuronal nicotinic acetylcholine receptors (nAChRs).

Neuronal nAChRs are abundant in the peripheral and central nervous systems, regulating neuronal excitability and neurotransmitter release. They are also present in the immune system and in various peripheral tissues. In humans, the eleven known neuronal nAChR subunits (α2-α7, α9, α10, β2-β4) form either homopentamers (α7 or α9) or heteropentamers (e.g. α4β2, α7β2, α9α10), with each subtype presenting distinct pharmacological and electrophysiological properties. The acetylcholine binding sites of nAChRs are formed between the extracellular domains (ECDs) of adjacent subunits. Neuronal nAChRs are responsible for nicotine addiction, while their dysfunction is related to various neurological and neuropsychiatric diseases, such as Alzheimer's and Parkinson's, autism, schizophrenia, epilepsy, depression, anxiety and attention deficit hyperactivity disorder. They are also implicated in the neuropathic chronic pain, inflammation, lung and breast cancers, and in some autoimmune disorders. Thus, nAChRs are important drug targets for developing modified ligands as efficient drugs, each specific for an individual nAChR subtype. However, high-resolution structures of nAChRs are needed for understanding their operating mechanisms and for accurate drug design.

Towards this aim I am expressing the wild-type and mutated forms of various neuronal nAChR subunits and proceed to their biochemical, pharmacological, structural (X-ray crystallography) and functional characterization (electrophysiology). My expertise is in molecular cloning, protein expression (in higher eukaryotes) and purification, protein crystallization and two-electrode voltage clamp in *Xenopus* oocytes.

PROJECTS

- Expression of wild-type, mutated and chimeric forms of the ECDs of the neuronal α2, α5, α7, α9 and β3 nAChRs
- Protein purification and kinetics studies with use of labeled ligands
- Crystallization and co-crystallization trials of the above ECDs with various ligands
- Two-electrode voltage clamp recordings of neuronal nAChRs

PROFESSIONAL AND RESEARCH EXPERIENCE

January 2009 – present	Research fellow, Hellenic Pasteur Institute
September 2010–February 2014	Scientific Project Manager of EC-FP7 REGPOT-NEUROSIGN program, Hellenic Pasteur Institute

February 2011- July 2011	Temporary Lecturer at School of Life Sciences, Department of Pharmacy, University of Patras
October 2010 – March 2011	Temporary Lecturer at Technological Educational Institute of Athens, Department of Medical Laboratories
May 2004 – August 2008	PhD fellow, School of Life Sciences, Department of Pharmacy, University of Patras
March 2002 - September 2003	MSc research project, School of Life Sciences, Department of Medicine, University of Patras

EDUCATION

INSTITUTION AND LOCATION	DEGREE	MM/YYYY	FIELD OF STUDY
University of Patras, Dept of Pharmacy	PhD	05/2009	Biochemistry and Molecular & Structural Biology
University of Patras, Depts of Pharmacy and Chemistry	MSc	09/2003	Medicinal Chemistry
University of Patras, Dept of Biology	BSc	07/2000	Biology

HONOURS AND AWARDS

2006 Travel grant for UK Circular Dichroism Summer School Course & UK CD Users Meeting, Warwick University, UK, 4-8 September 2006

2005 Travel grant for EMBO lecture course on channels and transporters, 33rd Workshop: Excitability, Secretion and Transport: Molecules to Medication, Ettore Majorana Foundation and Center for Scientific Culture, Erice, Sicily, May 31st–June 6th 2005

2004 Travel grant for FEBS advanced course: Advanced methods in protein crystallization, Academic and University Center at Nove Hrady, Czech Republic, October 2-9, 2004

2004 Travel grant for EMBO practical course in protein expression, purification and crystallization, EMBL outstation in Hambourg, Germany, 11–19 August 2004

2004 Travel grant for DGK/DGKK protein crystallization course, Conventus, Jena, Germany, 11-14 March 2004

MEMBER OF ORGANIZING COMMITTEES

2017: Member of the Organizing Committee of the International Conference on «Nicotinic Acetylcholine Receptors 2017» Chania, Crete, 7-11/05/2017

2013: Member of the Organizing Committee of the International Workshop on "Live Cell Imaging and Electrophysiology" Hellenic Pasteur Institute, 1-4/10/2013

PUBLICATIONS

- Vulfius CA, Kasheverov IE, Kryukova EV, Spirova EN, Shelukhina IV, Starkov VG, Andreeva TV, Faure G, **Zouridakis M**, Tsetlin VI, Utkin YN **(2017)** Pancreatic and snake venom presynaptically active phospholipases A2 inhibit nicotinic acetylcholine receptors. ***PLoS One*** doi: 10.1371/journal.pone.0186206. eCollection 2017

- Giastas P, Zouridakis M, Tzartos SJ **(2017)** Understanding structure-function relationships of the human neuronal acetylcholine receptor: insights from the first crystal structures of neuronal subunits. ***Br J Pharmacol.*** doi: 10.1111/bph.13838
- Lykhmus O, Koval L, Pastuhova D, Zouridakis M, Tzartos S, Komisarenko S & Skok M **(2016)** The role of carbohydrate component of recombinant α7 nicotinic acetylcholine receptor extracellular domain in its immunogenicity and functional effects of resulting antibodies. ***Immunobiology*** doi: 10.1016/j.imbio.2016.07.012
- Lykhmus O, Gergalova G, Zouridakis M, Tzartos S, Komisarenko S & Skok M **(2015)** Inflammation decreases the level of alpha7 nicotinic acetylcholine receptors in the brain mitochondria and makes them more susceptible to apoptosis induction. ***Int Immunopharmacol.*** doi: 10.1016/j.intimp.2015.04.007
- Lykhmus O, Voytenko L, Koval L, Mykhalskiy S, Kholin V, Peschana K, Zouridakis M, Tzartos S, Komisarenko S & Skok M **(2015)** α7 Nicotinic Acetylcholine Receptor-Specific Antibody Induces Inflammation and Amyloid β42 Accumulation in the Mouse Brain to Impair Memory. ***PLoS One*** doi: 10.1371/journal.pone.0122706
- Azam L, Papakyriakou A, Zouridakis M, Giastas P, Tzartos SJ & McIntosh JM **(2015)** Molecular interaction of α-conotoxin RgIA with the rat α9 nAChR. ***Mol Pharm*** doi: 10.1124/mol.114.096511
- Zouridakis M, Giastas P, Zarkadas E, Chroni-Tzartou D, Bregestovski P & Tzartos SJ **(2014)** Crystal structures of free and antagonist-bound states of human α9 nicotinic receptor extracellular domain. ***Nature Struct Mol Biol*** doi: 10.1038/nsmb.2900
- Niarchos A, Zouridakis M, Douris V, Georgostathi A, Kalamida D, Sotiriadis A, Poulas K, Iatrou K & Tzartos SJ **(2013)** Expression of a highly antigenic and native-like folded extracellular domain of the human α1 subunit of muscle nicotinic acetylcholine receptor, suitable for use in antigen specific therapies for Myasthenia Gravis. ***PLoS One*** doi: 10.1371/journal.pone.0084791
- Koval L, Lykhmus O, Kalashnyk O, Bachinskaya N, Kravtsova G, Soldatkina M, Zouridakis M, Stergiou C, Tzartos S, Tsetlin V, Komisarenko S & Skok M **(2011)** The presence and origin of autoantibodies against α4 and α7 nicotinic acetylcholine receptors in the human blood: possible relevance to Alzheimer's pathology. ***J Alzheimers Dis*** doi: 10.3233/JAD-2011-101845
- Lykhmus O, Koval L, Skok M, Zouridakis M, Zisimopoulou P, Tzartos SJ, Tsetlin V, Granon S, Changeux JP, Komisarenko S & Cloëz-Tayarani I **(2011)** Antibodies against extracellular domains of alpha4 and alpha7 subunits alter the levels of nicotinic receptors in the mouse brain and affect memory: possible relevance to Alzheimer's pathology. ***J Alzheimers Dis*** doi: 10.3233/JAD-2011-101842
- Lykhmus O, Koval L, Pavlovych S, Zouridakis M, Zisimopoulou P, Tzartos S, Tsetlin V, Volpina O, Cloëz-Tayarani I, Komisarenko S & Skok M **(2010)** Functional effects of antibodies against non-neuronal nicotinic acetylcholine receptors. ***Immunol Lett.*** doi: 10.1016/j.imlet.2009.11.006
- Zouridakis M, Zisimopoulou P, Poulas K & Tzartos SJ **(2009)** Recent advances in understanding nicotinic acetylcholine receptor structure. ***IUBMB-Life*** doi: 10.1002/iub.170
- Zouridakis M, Zisimopoulou P, Eliopoulos E, Poulas K & Tzartos SJ **(2009)** Design and expression of human α7 nicotinic acetylcholine receptor extracellular domain mutants with enhanced solubility and ligand-binding properties ***Biochim Biophys Acta*** doi: 10.1016/j.bbapap.2008.11.002
- Zouridakis M, Zisimopoulou P, Eliopoulos E, Jacobson L, Poulas K & Tzartos SJ **(2007)** Recombinant extracellular domains of human neuronal nicotinic receptors. Preliminary studies on mutant forms for the improvement of solubility. ***Neurophysiology*** **39** (4/5) 302-306
- Kalamida D, Poulas K, Avramopoulou V, Fostieri E, Lagoumintzis G, Lazaridis K, Sideri A, Zouridakis M & Tzartos SJ **(2007)** Muscle and neuronal nicotinic acetylcholine receptors. Structure, function and pathogenicity. ***FEBS Journal*** 274 (15), 3799-845

- Zouridakis M, Kostelidou K, Sotiriadis A, Stergiou C, Eliopoulos E, Poulas K & Tzartos SJ **(2007)** Circular dichroism studies of extracellular domains of human nicotinic acetylcholine receptors provide an insight into their structure. ***Int Journal of Biological Macromolecules*** 41(4):423-9
- Kostelidou K, Trakas N, Zouridakis M, Bitzopoulou K, Sotiriadis A, Gavra I & Tzartos SJ **(2006)** Expression and characterisation of soluble forms of the extracellular domains of the β, γ and ε subunits of the human muscle acetylcholine receptor. ***FEBS Journal*** 273, 3557-3568