

Socrates Tzartos

Emeritus Professor, Department of Pharmacy, University of Patras,

Emeritus researcher, group of Molecular Neurobiology and Immunology, Hellenic Pasteur Institute

EDUCATION

INSTITUTION	DEGREE	YEARS	FIELD OF STUDY
Univ. of Athens, Athens, Greece	B.Sci	1970	Natural Sciences
Univ. of Athens, Athens, Greece	Ph.D.	1976	Biology

POSITIONS AND EMPLOYMENT

1976-1978 Post-doctoral researcher, Physiological laboratory, Univ. of Cambridge, Cambridge, U.K

1978-81 Research associate, The Salk Institute, San Diego, California

1981-83 Research associate, Institut Pasteur Paris, France

1983 - 2016: Head of the Biochemistry Laboratory, later renamed: Laboratory of Molecular Neurobiology and Immunology, Hellenic Pasteur Institute, Athens, Greece.

1996-1997: Interim Acting General Director of the Hellenic Pasteur Institute.

2001-2012: Professor of Immunobiology, Dep. of Pharmacy, Univ. of Patras, Greece,

2003-2005: Deputy Chairman of the Department of Pharmacy, University of Patras

2012-present: Emeritus Professor, Dep. of Pharmacy, Univ. of Patras,

2016-present: Emeritus researcher, Molecular Neurobiology and Immunology group, Hellenic Pasteur Institute, Athens, Greece

HONORS, AWARDS, PROFESSIONAL ACTIVITIES

1972-76: Four pre-doctoral fellowships from the Natl. Hellenic Research Foundation.

1976-78: Two long-term Post-doctoral EMBO fellowships.

1979-81: Two Post-doctoral fellowships from the Muscular Dystrophy Association of America.

1981-83: Two long-term Post-doctoral EMBO fellowships.

1988-1990, 1998, 2003: 4 awards of the 14th and 16th, 24th και 29th Panhellenic Medical Symposia.

1993: Short-term (3-month) EMBO fellowship.

1994: **Full member of EMBO** (European Molecular Biology Organization).

2000-present: Member of the Advisory Board of the Myasthenia Gravis Foundation of America

2001-2004: Associate member of the Greek National Research and Technology Council

2003-2004: Member of the Advisory Group on "Life Sciences, Genomics and Biotechnology for Health" FP6 of the European Commission.

2010-present: Member of the Scientific Committee of the Hellenic Myasthenia Gravis Association

2012-2011: Program Director of Graduate Studies, Department of Pharmacy, University of Patras

2013 and 2015: Two Awards of the American Academy of Neurology annual Conferences, USA

SUPERVISION OF GRADUATE STUDENTS AND POSTDOCTORAL FELLOWS

16 Postdocs (5 current),

28 PhD students (23 degrees awarded from the Univ. of Athens, Patras and Ioannina, and 5 are in progress

9 MSc students (9 degrees from the University of Patras, Greece)

INVITED SPEAKER AND TEACHING ACTIVITIES

- Delivered invited lectures in >45 International and >32 Greek Conferences, in >25 international Universities and Institutes and several Greek Universities and Institutes.
- 2001- 2012: Professor of Immunobiology. Undergraduate and postgraduate courses in Immunology, Biochemistry and Molecular Biology. Dep. of Pharmacy, Univ. of Patras, Greece

PUBLIC HEALTH

Introduced in Greece the radioimmunoassays for the diagnosis of myasthenia gravis and performed it at the HPI from 1983 to 2013. In 2013 I founded the diagnostic and research laboratory Tzartos NeuroDiagnostics, specialized in neuroimmune diseases, which collaborates with our HPI laboratory. We offered strong support to the MG patients of Greece for the creation and development of their Association (H-MGA; <http://www.myasthenia.gr/>), whose office is hosted in our laboratory at the HPI, and we interact in various ways.

RESEARCH GRANTS

Total of **59** grants as **coordinator or PI**: 17 from European Commission (6 as coordinator), 28 from other international sources (most from muscular dystrophy organizations) and 13 from Greek sources.

The most recent grants are listed below:

- Stavros Niarchos Foundation. Development of innovative biological products and services for infectious and neurodegenerative diseases: “Structural and functional studies of nAChRs” (2016-2019)
- Toleranzia. Treatment of experimental autoimmune MG (2016-2017)
- Hellenic Neuroimmunology Society. Antibodies to Aquaporin-1 in neuromyelitis optica (2016-2017)
- Muscular Dystrophy Association of America. Diagnosis and characterization of LRP4-MG, a novel myasthenia gravis subtype (2013-2016)
- GSRT Greek-Israeli bilateral Program: Development of tools for the understanding and diagnosis of neurological diseases (2013-2015)
- GSRT-Program Thalys: “Autoimmunity” (University of Patras, coordinator S. Tzartos) in collaboration with Prof. A. Tzioufa (University of Athens) and Prof. A. Germeni (University of Thessaly) 2012-2015
- GSRT-Program Excellence: Myasthenia Gravis (2012-2015)
- Association Francaises des Myopathies (AFM) Diagnosis, prevalence and characterization of a novel myasthenia gravis subtype, LRP4-MG (2012-2014)
- FP7-Regpot “Neurosign”. Development of a center of excellence in Neurosignaling. With the labs of R. Matsas and L. Probert (coordinator: S. Tzartos) 2010-2014
- FP7 Fight-MG. Myasthenias, a group of immune mediated neurolog. diseases (2009-2014)
- Muscular Dystrophy Association of America (MDA). Antigen-specific therapeutic autoantibody depletion in myasthenia gravis (MDA158763) 2010-2012
- FP7 Fight-MG. Myasthenias, a group of immune mediated neurological diseases: from etiology to therapy (2009-2013)
- FP7-Neurocyprus. Neurotransmitter Cys-loop receptors: structure, function and disease (2008-2012)
- Association Francaises des Myopathies (AFM), Pentameric AChR extracellular domain for efficient autoantibody depletion in myasthenia gravis (2009-2011)
- FP6-STREP-Myastaid. Development of models to improve management of myasthenia gravis: From basic knowledge to clinical application (2006-2010)

- FP6- Public Health. European Myasthenia Gravis Network (EuroMyasthenia) 2006-2009

PUBLICATIONS AND CITATIONS

290 scientific papers (187 original papers in refereed international journals, 80 reviews (most peer reviewed), 23 papers in Greek journals). Total impact factor: >**1076**. Citations:>**7189**(up to 7/2016). H-factor: **42**(up to 7/2016).

PUBLICATIONS

2017

Hong Y, Zisimopoulou P, Trakas N, Karagiorgou K, Stergiou C, Skeie GO, Hao HJ, Gao X, Owe JF, Zhang X, Yue YX, Romi F, Wang Q, Li HF, Gilhus NE, Tzartos SJ. Multiple antibody detection in 'seronegative' myasthenia gravis patients. *Eur J Neurol*. 2017 Jun;24(6):844-850. doi: 10.1111/ene.13300.

Giastas P, Zouridakis M, Tzartos SJ. Understanding structure-function relationships of the human neuronal acetylcholine receptor: insights from the first crystal structures of neuronal subunits. *Br J Pharmacol*. 2017 Apr 27. doi: 10.1111/bph.13838. [Epub ahead of print] Review.

Lazaridis K, Baltatzidi V, Trakas N, Koutroumpi E, Karandreas N, Tzartos SJ. Characterization of a reproducible rat EAMG model induced with various human acetylcholine receptor domains. *J Neuroimmunol*. 2017 Feb 15;303:13-21. doi: 10.1016/j.jneuroim.2016.12.011.

Koneczny I, Stevens JA, De Rosa A, Huda S, Huijbers MG, Saxena A, Maestri M, Lazaridis K, Zisimopoulou P, Tzartos S, Verschuuren J, van der Maarel SM, van Damme P, De Baets MH, Molenaar PC, Vincent A, Ricciardi R, Martinez-Martinez P, Losen M. IgG4 autoantibodies against muscle-specific kinase undergo Fab-arm exchange in myasthenia gravis patients. *J Autoimmun*. 2017 Feb;77:104-115. doi: 10.1016/j.jaut.2016.11.005.

Türkoğlu R, Lassmann H, Aker FV, Tzartos J, Tzartos S, Tüzün E. Recurrent tumefactive demyelinating lesions: a pathological study. *Clin Neuropathol*. 2017 Feb 17. doi: 10.5414/NP301005.

Hong Y, Skeie GO, Zisimopoulou P, Karagiorgou K, Tzartos SJ, Gao X, Yue YX, Romi F, Zhang X, Li HF, Gilhus NE. Juvenile-onset myasthenia gravis: autoantibody status, clinical characteristics and genetic polymorphisms. *J Neurol*. 2017 May;264(5):955-962. doi: 10.1007/s00415-017-8478-z.

2016

Lykhmus O, Koval L, Pastuhova D, Zouridakis M, Tzartos S, Komisarenko S, Skok M. The role of carbohydrate component of recombinant $\alpha 7$ nicotinic acetylcholine receptor extracellular domain in its immunogenicity and functional effects of resulting antibodies. *2016 Immunobiology*;221(12):1355-1361. doi: 10.1016/j.imbio.2016.07.012.

Kouvatsos N, Giastas P, Chroni-Tzartou D, Pouloupoulou C, Tzartos SJ. Crystal structure of a human neuronal nAChR extracellular domain in pentameric assembly: Ligand-bound $\alpha 2$ homopentamer. *Proc Natl Acad Sci U S A*. 2016 Aug 23;113(34):9635-40. doi: 10.1073/pnas.1602619113.

Gilhus NE, Skeie GO, Romi F, Lazaridis K, Zisimopoulou P, and Tzartos S. Myasthenia gravis-autoantibody characteristics and their implications for therapy. *Nat. Rev. Neurol*. 2016; 12(5):259-68. doi: 10.1038/nrneurol.2016.44. Epub 2016 Apr 22. Review

Küçükerden M, Huda R, Tüzün E, Yılmaz A, Skriapa L, Trakas N, T. Strait R, Finkelman FD, Kabadayı S, Zisimopoulou P, Tzartos S, Christadoss P. MuSK induced experimental autoimmune myasthenia gravis does not require IgG1 antibody to MuSK. *J. Neuroimmunol.* 2016. Jun 15;295-296:84-92. doi: 10.1016/j.jneuroim.2016.04.003.

Stergiou C, Lazaridis K, Zouvelou V, Tzartos J, Mantegazza R, Antozzi C, Andreetta F, Evoli A, Deymeer F, Saruhan-Direskeneli G, Durmus H, Brenner T, Vaknin A, Berrih-Aknin S, Behin A, Sharshar T, De Baets M, Losen M, Martinez-Martinez P, Kleopa KA, Zamba-Papanicolaou E, Kyriakides T, Kostera-Pruszczyk A, Szczudlik P, Szyluk B, Lavrnica D, Basta I, Peric S, Tallaksen C, Maniaol A, Gilhus NE, Casasnovas Pons C, Pitha J, Jakubikova M, Hanisch F, Bogomolovas J, Labeit D, Labeit S, Tzartos SJ. Titin antibodies in “seronegative” myasthenia gravis – A new role for an old antigen. *J. Neuroimmunology*, 2016. 292: 108-115. doi: 10.1016/j.jneuroim.2016.01.018.

2015

Lykhmus O, Voytenko L, Koval L, Mykhalskiy S, Cholin V, Peschana K, Zouridakis M, Tzartos S, Komisarenko S and Skok M. $\alpha 7$ Nicotinic Acetylcholine Receptor-Specific Antibody Induces Inflammation And Amyloid $\beta 42$ Accumulation In The Mouse Brain To Impair Memory. *Plos-1*, 2015 Mar 27;10(3):e0122706. doi: 10.1371/journal.pone.0122706.

Maurer M, Bougoin S, Feferman T, Frenkian M, Bismuth J, Mouly V, Clairac G, Tzartos S, Fadel E, Eymard B, Fuchs S, Souroujon MC, Berrih-Aknin S. IL-6 and Akt are involved in muscular pathogenesis in myasthenia gravis. *Acta Neuropathol Commun.* 2015 Jan 15;3(1):1. doi: 10.1186/s40478-014-0179-6.

Azam L, Papakyriakou A, Zouridakis M, Giastas P, Tzartos SJ, McIntosh JM. Molecular Interaction of α -Conotoxin RgIA with the Rat $\alpha 9\alpha 10$ Nicotinic Acetylcholine Receptor. *Mol Pharmacol.* 2015 May;87(5):855-64. doi: 10.1124/mol.114.096511. Epub 2015 Mar 4. PMID:25740413

Arnautouli S, Giastas P, Andreou A, Tzanodaskalaki M, Aldridge C, Tzartos SJ, Vollmer W, Eliopoulos E, Bouriotis V. Two putative polysaccharide deacetylases are required for osmotic stability and cell shape maintenance in *Bacillus anthracis*. *J Biol Chem.* 2015 Mar 30. pii: jbc.M115.640029. [Epub ahead of print] PMID:25825488

Yılmaz V, Oflazer P, Aysa F, Durmus H, Poulas K, Parman Y, Tzartos S, Tuzun E, Deymeer F, Saruhan-Direskeneli G. Differential cytokine changes in patients with myasthenia gravis with antibodies against AChR and MuSK. *PLOS-1.* 2015; 10(4):e0123546. doi: 10.1371/journal.pone.0123546

Özkök E, Durmus H, Yetimler B, Taslı H, Trakas N, Ulusoy C, Lagoumintzis G, Tzartos S, and Tüzün E: Reduced muscle mitochondrial enzyme activity in MuSK-immunized mice. *Clinical Neuropathology.* 2015 Nov-Dec;34(6):359-63. doi: 10.5414/NP300875.

Ulusoy C, Zibandeh N, Yıldırım S, Trakas N, Zisimopoulou P, Küçükerden M, Taşlı H, Tzartos S, Göker K, Tüzün E, Akkoç T. Dental follicle mesenchymal stem cell administration ameliorates muscle weakness in MuSK-immunized mice. *J Neuroinflammation.* 2015 Dec 9;12(1):231. doi: 10.1186/s12974-015-0451-0.

Tsonis AI, Zisimopoulou P, Lazaridis K, Tzartos J, Matsigkou E, Zouvelou V, Mantegazza R, Antozzi C, Andreetta F, Evoli A, Deymeer F, Saruhan-Direskeneli G, Durmus H, Brenner T, Vaknin A, Berrih-Aknin S, Behin A, Sharshar T, De Baets M, Losen M, Martinez-Martinez P, Kleopa KA, Zamba-Papanicolaou E, Kyriakides T, Kostera-Pruszczyk A, Szczudlik P, Szyluk B, Lavrnica D, Basta I, Peric S, Tallaksen C, Maniaol A, Casasnovas Pons C, Pitha J, Jakubikova M, Hanisch F, Tzartos SJ. MuSK

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Lykhmus O, Gergalova G, Zouridakis M, Tzartos S, Komisarenko S, Skok M. Inflammation decreases the level of alpha7 nicotinic acetylcholine receptors in the brain mitochondria and makes them more susceptible to apoptosis induction. *Int Immunopharmacol.* 2015 Nov;29(1):148-51. doi: 10.1016/j.intimp.2015.04.007.

Tuzun E, Berrih-Aknin S, Brenner T, Kusner LL, Le Panse R, Yang H, Tzartos S, Christadoss P. Guidelines for standard preclinical experiments in the mouse model of myasthenia gravis induced by acetylcholine receptor immunization. *Exp Neurol.* 2015 Feb 16. pii: S0014-4886(15)00032-1. doi: 10.1016/j.expneurol.2015.02.009.

Kusner LL, Losen M, Vincent A, Lindstrom J, Tzartos S, Lazaridis K, Martinez-Martinez P. Guidelines for pre-clinical assessment of the acetylcholine receptor-specific passive transfer myasthenia gravis model-Recommendations for methods and experimental designs. *Exp Neurol.* 2015 Mar 3.pii: S0014-4886(15)00055-2. doi: 10.1016/j.expneurol.2015.02.025.

Losen M, Martinez-Martinez P, Molenaar PC, Lazaridis K, Tzartos S, Brenner T, Duan RS, Luo J, Lindstrom J, Kusner L. Standardization of the experimental autoimmune myasthenia gravis (EAMG) model by immunization of rats with Torpedo californica acetylcholine receptors – Recommendations for methods and experimental designs. *Exp Neurol.* 2015 Mar 18.pii: S0014-4886(15)00078-3. doi: 10.1016/j.expneurol.2015.03.010.

2014

Zouvelou V, Zisimopoulou P, Psimenou E, Matsigkou E, Stamboulis E, Tzartos SJ. AChR-myasthenia gravis switching to double-seropositive several years after the onset.*J. Neuroimmunol.* 2014 Feb 15;267(1-2):111-2. doi: 10.1016/j.jneuroim.2013.12.012.

Tsivgoulis G, Dervenoulas G, Tzartos SJ, Zompola C, Papageorgiou SG, Voumvourakis K. Double seropositive myasthenia gravis with acetylcholine receptor and lipoprotein receptor-related protein 4 antibodies. *Muscle and Nerve.*2014 Jan 7.doi: 10.1002/mus.24166.

Zis P, Argiriadou V, Temperikidis PP, Zikou L, Tzartos SJ, Tavernarakis A. Parkinson's disease associated with myasthenia gravis and rheumatoid arthritis. *Neurol. Sci.*(Letter to the Editor). Published on line 2-7-2014. DOI 10.1007/s10072-014-1660-5

Marino M, Maiuri MT, Di Sante G, Scuderi F, La Carpia F, Trakas N, Provenzano C, Zisimopoulou P, Ria F, Tzartos SJ, Evoli A, Bartoccioni E. T cell repertoire in DQ5-positive MuSK-positive myasthenia gravis patients. *J Autoimmun.* 2014 Jan 4.pii: S0896-8411(13)00154-6. doi: 10.1016/j.jaut.2013.12.007.

Avidan N, Le Panse R; Harbo H, Bernasconi P, Poulas K, Ginzburg E; Cavalcante P, Colleoni L; Baggi F, Antozzi C, Truffault F, Horn-Saban S, Pöschel S, Zagoriti Z, Maniaol A, Lie B; Bernard I, Saoudi A, Illes Z, Casasnovas C, Melms A, Tzartos S; Willcox N, Kostera-Pruszczyk A, Tallaksen C, Mantegazza R, Berrih-Aknin S, Miller A. VAV1 and BAFF, via NFκB pathway, are genetic risk factors for Myasthenia Gravis. 2014 *Annals of Clinical and Translational Neurology*,1(5):329-39. doi: 10.1002/acn3.51

Ulusoy C, Kim E, Tüzün E, Huda R, Yılmaz V, Poulas K, Trakas N, Skriapa L, Niarchos A, Strait RT, Finkelman FD, Turan S, Zisimopoulou P, Tzartos S, Saruhan-Direskeneli G, Christadoss P. Preferential

production of IgG1, IL-4 and IL-10 in MuSK-immunized mice. *Clin Immunol.* 2014 Feb 28;pii: S1521-6616(14)00049-7. doi: 10.1016/j.clim.2014.02.012.

Tuzun E., Tzartos J., Ekizoglu E., Stergiou C., Zisimopoulou P., Çoban A., Shugaiv E., Türkoglu R., Kürtüncü M., Baykan B., Tzartos S. Title: Aquaporin-1 Antibody in Neuromyelitis Optica Patients. *European Neurology*, 2014. *Eur Neurol.* 2014 Sep 27;72(5-6):271-272.

Kouvatsos N, Niarchos A, Zisimopoulou P, Eliopoulos E, Poulas K, and Tzartos S. Purification and functional characterization of a truncated human $\alpha 4\beta 2$ nicotinic acetylcholine receptor. *Int. J Biol Macromol*, 2014 Jul 8. pii: S0141-8130(14)00441-3. doi: 10.1016/j.ijbiomac.2014.06.058.

Boltsis I, Lagoumintzis G, Chatzileontiadou DSM, Giastas P, Tzartos SJ, Leonidas DD, and Poulas K. Non-contact Current Transfer Induces the Formation and Improves the X-ray Diffraction Quality of Protein Crystals. 2014 *Cryst.Growth Des.* DOI: 10.1021/cg5004098

Zouridakis M, Giastas P, Zarkadas E, Chroni-Tzartou D, Bregestovski P and Tzartos SJ. Crystal structures of the free and antagonist-bound states of the extracellular domain of human $\alpha 9$ nicotinic receptor. 2014. *Nat. Struct & Mol. Biol.* doi:10.1038/nsmb.2900.

Tsivgoulis G, Dervenoulas G, Kokotis P, Zompola C, Tzartos J, Tzartos SJ, Voumvourakis KI. Double seronegative myasthenia gravis with low density lipoprotein-4 (LRP4) antibodies presenting with isolated ocular symptoms. 2014. *J. Neurol. Sci.* doi: 10.1016/j.jns.2014.09.013.

Kordas G, Lagoumintzis G, Sideris S, Poulas K and Tzartos SJ. Direct proof of the in vivo pathogenic role of the AChR autoantibodies from myasthenia gravis patients. *PLOS-1.* 2014. Sep 26;9(9):e108327. doi: 10.1371/journal.pone.0108327.

Skriapa L, Zisimopoulou P, Trakas N, Grapsa E, Tzartos SJ. Expression of extracellular domains of Muscle Specific Kinase (MuSK) and use as immunoadsorbents for the development of an antigen specific therapy. 2014. *J. Neuroimmunol.* DOI: 10.1016/j.jneuroim.2014.09.013

Lazaridis K, Evaggelakou P, Bendenidi E, Sideri A, Grapsa E and Tzartos S.J. Specific adsorbents for myasthenia gravis autoantibodies using mutants of the muscle nicotinic acetylcholine receptor extracellular domains. *J. Neuroimmunol.* 2015 Jan 15;278:19-25. doi: 10.1016/j.jneuroim.2014.12.001.

2013

Zouvelou V, Stamboulis E, Skriapa L, Tzartos SJ. MuSK-Ab positive myasthenia: Not always grave. *J Neurol Sci.* 2013, 15;331(1-2):150-1.

Zouvelou V, Kyriazi S, Rentzos M, Belimezi M, Micheli MA, Tzartos SJ, Stamboulis E. Double-seropositive myasthenia gravis. *Muscle Nerve.* 2013, 47(3):465-6.

Zouvelou V, Zisimopoulou P, Rentzos M, Karandreas N, Evangelakou P, Stamboulis E, Tzartos SJ. Double seronegative myasthenia gravis with anti-LRP 4 antibodies. *Neuromuscul Disord.* 2013 Jul;23(7):568-70.

Tzartos JS, Stergiou Ch, Kilidireas K, Zisimopoulou P, Thomaidis T, and Tzartos SJ, Aquaporin-1 autoantibodies in patients with neuromyelitis optica spectrum disorders. *PLOS-1*, 2013. doi: 10.1371/journal.pone.0074773.

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Niarchos A, Zouridakis M, Douris V, Georgostathi A, Kalamida D, Sotiriadis A, Poulas K, Iatrou K., Tzartos SJ. Expression of a highly antigenic and native-like folded extracellular domain of the human $\alpha 1$ subunit of muscle nicotinic acetylcholine receptor, suitable for use in antigen specific therapies for Myasthenia Gravis. 2013 *PLOS-1*; 8(12):e84791. doi: 10.1371/journal.pone.0084791

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2012

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Zhang, B., J.S. Tzartos, M. Belimezi, S. Ragheb, B. Bealmear, R.A. Lewis, W.C. Xiong, R.P. Lisak, S.J. Tzartos, and L. Mei, (2012) Autoantibodies to Lipoprotein-Related Protein 4 in Patients With Double-Seronegative Myasthenia Gravis. *Archives of Neurology*. 69(4): p. 445-451.

2011

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