

# Alexios N. Matralis

## OBJECTIVE

Design, Synthesis and Pharmacological Evaluation of Bioactive Molecules against the Pathogenesis of Human Diseases



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## EXPERIENCE

April 2018 to date

Researcher • Bioinnovation Institute, Biomedical Sciences Research Center “Alexander Fleming” • Vari, Athens, Greece

January 2017 to January 2018

Senior Researcher • Drug Development Department against Neglected Tropical Diseases, GlaxoSmithKline • Madrid, Spain

September 2013– December 2016

Postdoctoral Research Fellow • Department of Chemistry, McGill University • Montreal, Canada

## EDUCATION

January 2008– April 2013

PhD in Medicinal Chemistry • Department of Medicinal Chemistry, School of Pharmacy, University of Athens • Athens, Greece

November 2005– January 2008

MSc in Medicinal Chemistry • Department of Medicinal Chemistry, School of Pharmacy, University of Athens • Athens, Greece

November 2003– July 2005

MSc in Science and Technology of Polymers • Department of Chemical Engineering, University of Patras • Patra, Greece

October 1999– November 2003

BSc in Chemistry • Department of Chemistry, University of Patras • Patra, Greece

## RESEARCH FUNDING

- 1) Hellenic Society of Atherosclerosis (2008-2011)
- 2) Group de Recherche Axè sur la Structure des Protèines (GRASP), Canada (2014-2016)
- 3) “Stavros Niarchos” Foundation (2018-2021)
- 4) European Union and Greek national funds through the

- Operational Program Competitiveness, Entrepreneurship and Innovation, under the call Research – Create – Innovate (Grant ID: T2EΔK-01076) (2020-2023)
- 5) Hellenic Foundation for Research and Innovation (Grant ID: HFRI 7337) (2022-2025)

## PUBLICATIIONS

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- 1) Water-soluble Stoichiometric Polyelectrolyte Complexes Based on Cationic Comb-Type Copolymers. Alexios Matralis, Maria Sotiropoulou, George Bokias and George Staikos. *Macromol. Chem. Phys.*, **2006**, *207*, 1018-1025 ([onlinelibrary.wiley.com/doi/10.1002/macp.200600083/full](https://onlinelibrary.wiley.com/doi/10.1002/macp.200600083/full)).
- 2) Hypolipidemic and Antioxidant Properties of Novel Squalene Synthase Inhibitors. Alexios Matralis and Angeliki Kourounakis. *Clinical Pharmacology and Pharmacokinetics*, **2008**, *22*, 238-240.
- 3) Antioxidant Activity of Newly Synthesized 2,7-Diazaphenothiazines. Beata Morak-Miodawska, Krystian Pluta, Alexios N. Matralis and Angeliki P. Kourounakis. *Arch. Pharm. Chem. Life Sci.*, **2010**, *343*, 268-273 ([onlinelibrary.wiley.com/doi/10.1002/ardp.200900253/abstract](https://onlinelibrary.wiley.com/doi/10.1002/ardp.200900253/abstract)).
- 4) Design of More Potent Squalene Synthase Inhibitors with Multiple Activities. Angeliki P. Kourounakis, Alexios N. Matralis, Anastasios Nikitakis. *Bioorg. Med. Chem.*, **2010**, *18*, 7402-7412 ([www.sciencedirect.com/science/article/pii/S0968089610008230](http://www.sciencedirect.com/science/article/pii/S0968089610008230)).
- 5) Novel Benzoxazine and Benzothiazine Derivatives as Multifunctional Anti-hyperlipidemic Agents. Alexios N. Matralis, Maria G. Katselou, Anastasios Nikitakis and Angeliki P. Kourounakis. *J. Med. Chem.*, **2011**, *54*, 5583-5591 ([pubs.acs.org/doi/abs/10.1021/jm200763k](https://pubs.acs.org/doi/abs/10.1021/jm200763k)).
- 6) Squalene Synthase Inhibitors: An Update on the Search for New Antihyperlipidemic and Antiatherosclerotic Agents. Angeliki P. Kourounakis, Maria G. Katselou, Alexios N. Matralis, Eleni M. Ladopoulou and Eugenia Bavavea. *Curr. Med. Chem.*, **2011**, *18*, 4418-4439. ([www.eurekaselect.com/75134/article](http://www.eurekaselect.com/75134/article)).
- 7) New Multifunctional di-*tert*-butyl-phenol-octahydro(pyrido/benz)oxazine Derivatives with Antioxidant, Antihyperlipidemic and Antidiabetic Action. Eleni M. Ladopoulou, Alexios N. Matralis and Angeliki P. Kourounakis. *J. Med. Chem.*, **2013**, *56*, 3330-3338 ([pubs.acs.org/doi/abs/10.1021/jm400101e?journalCode=jmcmr](https://pubs.acs.org/doi/abs/10.1021/jm400101e?journalCode=jmcmr)).
- 8) Design of Novel Potent Antihyperlipidemic Agents with Antioxidant/Anti-inflammatory Properties. Exploiting Phenothiazine's Strong Antioxidant Activity. Alexios N. Matralis and Angeliki P. Kourounakis. *J. Med. Chem.*, **2014**, *57*, 2568-2581. **Highlighted by SciBX** (March **2014**, vol. 7, issue 11)

([pubs.acs.org/doi/abs/10.1021/jm401842e](https://pubs.acs.org/doi/abs/10.1021/jm401842e)).

9) Multi-targeted Drug Design Approaches for Multifactorial Diseases: from Neurodegenerative to Cardiovascular Applications. Maria Katselou, Alexios N. Matralis and Angeliki P. Kourounakis. *Curr. Med. Chem.*, **2014**, *21*, 2743-2787 ([www.eurekaselect.com/120679/article](http://www.eurekaselect.com/120679/article)).

10) Human Isoprenoid Synthase Enzymes as Therapeutic Targets. Jaeok Park, Alexios N. Matralis, Albert M. Berghuis and Youla S. Tsantrizos. *Frontiers in Chemistry*, **2014**, *2*, 1-21 ([journal.frontiersin.org/article/10.3389/fchem.2014.00050/full](http://journal.frontiersin.org/article/10.3389/fchem.2014.00050/full)).

11) Evaluation of two Novel Antioxidants with Differential Effects on Curcumin-induced Apoptosis in C2 Skeletal Myoblasts; Involvement of JNKs. Maria Peleli, Ioanna-Katerina Aggeli, Alexios N. Matralis,<sup>#</sup> Angeliki P. Kourounakis, Isidoros Beis and Catherine Gaitanaki. *Bioorg. Med. Chem.*, **2015**, *23*, 390-400 (<sup>#</sup> second author due to equal contribution of the first two authors), ([www.sciencedirect.com/science/article/pii/S0968089614009043?via%3Dihub](http://www.sciencedirect.com/science/article/pii/S0968089614009043?via%3Dihub)).

12) Antihyperlipidemic Morpholine Derivatives with Antioxidant Activity: An Investigation of the Aromatic Substitution. Eleni M. Ladopoulou, Alexios N. Matralis, Anastasios Nikitakis and Angeliki P. Kourounakis. *Bioorg. Med. Chem.*, **2015**, *23*, 7015-7023 ([www.sciencedirect.com/science/article/pii/S0968089615300602](http://www.sciencedirect.com/science/article/pii/S0968089615300602)).

13) Synthesis of Benzothiophene-containing 10- and 11-Member Cyclic Phosphonates. Alexios N. Matralis and Youla S. Tsantrizos. *Eur. J. Org. Chem.*, **2016** (22), 3728-3736 ([onlinelibrary.wiley.com/doi/10.1002/ejoc.201600333/abstract](http://onlinelibrary.wiley.com/doi/10.1002/ejoc.201600333/abstract)).

14) Balancing Antioxidant, Hypolipidemic and Anti-inflammatory Activity in a Single Agent: The Example of 2-Hydroxy-2-Substituted Morpholine, 1,4-Benzoxazine and 1,4-Benzothiazine Derivatives as a Potential Therapeutic Approach against Atherosclerosis. Alexios N. Matralis, Eugenia-Ismini Bavavea, Sandra Incerpi, Jens Z. Pedersen and Angeliki P. Kourounakis. *Curr. Med. Chem.*, **2017**, *24*, 1214-1227 ([www.eurekaselect.com/144805/article](http://www.eurekaselect.com/144805/article)).

15) Pharmacophore Mapping of Thienopyrimidine-Based Monophosphonate (ThP-MP) Inhibitors of the Human Farnesyl Pyrophosphate Synthase. Jaeok Park, Chun Y. Leung, Alexios N. Matralis,<sup>#</sup> Cyrus Lacbay, Michail Tsakos, Guillermo Fernandez De Troconiz, Albert Berghuis and Youla S. Tsantrizos. *J. Med. Chem.*, **2017**, *60*, 2119-2134 (<sup>#</sup> second author due to equal contribution of the first two authors), ([pubs.acs.org/doi/abs/10.1021/acs.jmedchem.6b01888](https://pubs.acs.org/doi/abs/10.1021/acs.jmedchem.6b01888)).

16) Developing Potential Agents against Atherosclerosis: Design, Synthesis and Pharmacological Evaluation of Novel Dual Inhibitors of Oxidative Stress and Squalene Synthase Activity. Maria Katselou, Alexios N. Matralis and Angeliki P. Kourounakis. *Eur. J. Med. Chem.*, **2017**, *138*, 748-760 ([www.sciencedirect.com/science/article/pii/S0223523417304890](http://www.sciencedirect.com/science/article/pii/S0223523417304890)).

17) Molecular Tools that Block Maturation of the Nuclear Lamin A and Decelerate Cancer Cell Migration. Alexios N. Matralis, Dimitrios Xanthopoulos, Geneviève Huot, Stéphane Lopes-Paciencia, Charles Cole, Hugo de Vries, Gerardo Ferbeyre and Youla S. Tsantrizos. *Bioorg. Med. Chem.*, **2018**, *26*, 5547-5554 ([www.sciencedirect.com/science/article/pii/S0968089618315049](http://www.sciencedirect.com/science/article/pii/S0968089618315049)).

18) Development and Therapeutic Potential of Autotaxin Small Molecule Inhibitors. From Bench to Advanced Clinical Trials. Alexios N. Matralis,\* Antreas Afantitis and Vassilis Aidinis.\* In Press, *Med. Res. Rev.*, **2018** (\* corresponding authors), (<https://doi.org/10.1002/med.21551>).

19) Optimization of the Pharmacological Profile of Bifunctional Antihyperlipidemic/Antioxidant Morpholine Derivatives by Focusing on the Squalene Synthase Inhibitory Activity. Alexios N. Matralis and Angeliki P. Kourounakis. *Med. Chem. Lett.*, **2019**, *10*, 98-104 (<https://pubs.acs.org/doi/10.1021/acsmchemlett.8b00469>).

20) Development of Chemical Entities Endowed with Potent Fast-killing Properties against *Plasmodium falciparum* Malaria Parasites. Alexios N. Matralis,\* Adnan Malik, Maria Penzo, Inmaculada Moreno, Maria J. Almela, Isabel Camino, Begnino Crespo, Anas Saadeddin, Sonja Ghidelli-Disse, Lurdes Rueda, Félix Calderón, Simon A. Osborne, Gerald Drewes, Markus Böesche, Elena Fernández-Álvaro, José Ignacio Martín Hernando, David A. Baker.\* *J. Med. Chem.*, **2019**, *62*, 9217-9235 (\* corresponding authors), (<https://pubs.acs.org/doi/10.1021/acs.jmedchem.9b01099>).

21) Structure-Based Discovery of Novel Chemical Classes of Autotaxin Inhibitors. Christiana Magkrioti, Eleanna Kaffe, Elli-Anna Stylianaki, Camelia Sidahmet, Georgia Melagraki, Antreas Afantitis, Alexios N. Matralis,\* Vassilis Aidinis.\* *Int. J. Mol. Sci.*, **2020**, *21*, 7002-7018 (\* corresponding authors), (<https://www.mdpi.com/1422-0067/21/19/7002/xml>).

22) Targeting Malaria Parasite cGMP Signalling to Develop New Drugs. David A. Baker, Alexios N. Matralis, Simon A. Osborne, Jonathan M. Large, Maria Penzo. *Front. Microbiol.*, **2020**, *11*, article 602803, (<https://www.frontiersin.org/articles/10.3389/fmicb.2020.602803/full>).

23) Commonalities between ARDS, Pulmonary Fibrosis and COVID-19: The Potential of Autotaxin as a Therapeutic Target. Konstantinos Ntatsoulis, Theodoros Karampitsakos, Eliza Tsitoura, Elli-Anna Stylianaki, Alexios N. Matralis, Argyrios Tzouvelekis, Katerina Antoniou, Vassilis Aidinis. *Front. Immunol.*, **2021**, *12*, article 687397, (<https://www.frontiersin.org/articles/10.3389/fimmu.2021.687397/full>).

24) Synthesis and Evaluation of Structurally Diverse C-2-Substituted Thienopyrimidine-Based Inhibitors of the Human Geranylgeranyl Pyrophosphate Synthase. Hiu-Fang Lee, Cyrus M. Lachbay, Rebecca Boutin, Alexios N. Matralis, Jaeok Park, Daniel D. Waller, Tian Lai Guan, Michael Sebag and Youla S. Tsantrizos. *J. Med. Chem.*, **2022**, *65*, 2471-2496, (<https://pubs.acs.org/doi/10.1021/acs.jmedchem.1c01913>).

25) “Hit” to lead optimization and chemoinformatic studies for a new series of Autotaxin inhibitors. Elli-Anna Stylianaki, Christiana Magkrioti, Eleni M. Ladopoulou, Konstantinos D. Papavasileiou, Panagiotis Lagarias, Georgia Melagraki, Martina Samiotaki, George Panayotou, Skarlatos G. Dedos, Antreas Afantitis, Vassilis Aidinis,\* Alexios N. Matralis.\* (\*corresponding authors), *Eur. J. Med. Chem.*, **2022**, *249*, article 115130, (<https://www.sciencedirect.com/science/article/pii/S0223523423000454>).

26) Repurposing the antipsychotic drug Amisulpride for targeting synovial fibroblast activation in arthritis. Dimitra Papadopoulou, Fani Roumelioti, Christos Tzaferis, Panagiotis Chouvardas, Anna-Kathrine Pedersen, Filippou Charalampous, Eleni Christodoulou-Vafeiadou, Lydia Ntari, Niki Karagianni, Maria C. Denis, Jesper V. Olsen, Alexios N. Matralis and George Kollias. *JCI Insight*, **2023**, *8*, article e165024 (<https://insight.jci.org/articles/view/165024>).

27) Effect of a new Squalene Synthase inhibitor on an ApoE<sup>-/-</sup> mouse model of atherosclerosis. Alexios N. Matralis,\* Loukas Kaklamanis, Despina Perrea, Angeliki Kourounakis.\* (\*corresponding authors), *Bioorg. Med. Chem.*, **2023**, *90*, article 117378 (<https://www.sciencedirect.com/science/article/pii/S0968089623002262>).

28) Discovery of the First-in-Class Inhibitors of Hypoxia Up-regulated Protein 1 (HYOU1) Suppressing Pathogenic Fibroblast Activation. Dimitra Papadopoulou, Vasiliki Mavrikaki, Filippou Charalampous, Christos Tzaferis, Martina Samiotaki, Konstantinos D. Papavasileiou, Antreas Afantitis, Niki Karagianni, Maria C. Denis, Julie Sanchez, J. Robert Lane, Zacharias Faidon Brotzakis, Georgios Skretas, Dimitris Georgiadis, Alexios N. Matralis,\* George Kollias.\* *Angew. Chem. Int. Ed.* (IF: 16.6), **2024**, article e202319157 (\* corresponding authors) (<https://onlinelibrary.wiley.com/doi/10.1002/anie.202319157>).

29) Identification of Two Novel Chemical Classes of Autotaxin (ATX) Inhibitors Using Enalos Asclepios KNIME Nodes. Elli-Anna Stylianaki, Varnavas D. Mouchlis, Christiana Magkrioti, Konstantinos Papavasileiou, Antreas Afantitis, Alexios N. Matralis,\* Vassilis Aidinis.\* *Bioorg. Med. Chem. Lett.*, **2024**, *103*, article 129690 (\* corresponding authors) (<https://www.sciencedirect.com/science/article/pii/S09680894X24000921#ab010>).

## PATENTS

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- 1) Thieno[3,4-c]pyrazol-3-yl acetamides as novel Autotaxin inhibitors. Vassilios Aidinis and Alexios Matralis. Patent No: WO2022/003377 A1.
- 2) Anti-inflammatory Carboxamide Derivatives. George Kollias,

Niki Karagianni, Maria Denis, Alexios N. Matralis, Dimitra Papadopoulou, Eleni Karkoulia. Patent No: WO2022/189636 A1.

- 3) 4-(2-(4-((2,4-Dioxothiazolidin-5-yl)methyl)phenoxy) Derivatives Having Inhibitory Activity on Autotaxin. Alexios N. Matralis and Vassilis Aidinis. This patent was initially submitted to and accepted by the Hellenic Industrial Property Organization (Patent No: GR1010570B.