

Maria Koufaki

PhD/Research Director
Institute of Biology, Medicinal Chemistry and Biotechnology

Phone: +30 2107273818

Fax: +30 2107273831

E-mail: mkoufa@eie.gr

Website: www.eie.gr



Appointments

- 2007-present: Research Director, Institute of Biology, Medicinal Chemistry and Biotechnology, NHRF
- 2002-2007: Senior Researcher, (IOPC) NHRF
- 1994-2002: Functional Scientist, (IOPC) NHRF
- 1989-1994: Research Associate, Institute of Organic and Pharmaceutical Chemistry, (IOPC) NHRF
- 1983-1988: Teaching Assistant, University of Geneva, Switzerland

Current Research interests

Research interests are focused on the design and synthesis of *bioactive heterocyclic molecules*. In particular:

- Multifunctional antioxidants bearing five-membered heterocycles, such as oxadiazoles, 1,2,3-triazole, tetrazole and isoxazole. These heterocycles are potential pharmacophores and have been utilized as ester or amide bioisosteres in the search for compounds with superior pharmacokinetic profiles.
- Purine and adenosine analogues bearing nitrate esters, mimicking and/or enhancing endogenous cardioprotective mechanisms *in vivo*,
- Purine analogues as BRAF^{V600E} inhibitors for the development of agents against colorectal cancer.
- Chroman/hydroxytyrosol hybrids as proteasome activators, against ageing.

Research activities also involve:

- Design and synthesis of new inhibitors of inflammasome activation.
- Synthesis of heterocycles using microwave or ultrasound irradiation.

Education

1988: PhD, University of Geneva, Faculty of Sciences, Switzerland. Supervisor J.M.J Tronchet. Title "Désoxyhydroxyaminosucres par cyclisation ou réduction des nitrones et radicaux libres correspondants. Nouvelles voies de synthèse d'oligosaccharides"

1983: BSc, in Chemistry, National University of Athens, Greece

Foreign languages

French (excellent), English (excellent), German (basic knowledge)

Honours, awards, distinctions

November 2006: 5th International Congress of Cardiology, Thessaloniki, Greece,
1st Prize of 3000 €

2005-2011: Member of Editorial Advisory Board of *Current Topics in Medicinal Chemistry*

7-12/1991: Fulbright Research Fellow, University of Connecticut, USA

Teaching experience

1993-present: Supervisor of post-graduate and diploma students, 6 MSc, 4 PhD and 2 post doctoral fellows (NHRF)

1983-1988: Teaching Assistant and trainer of technical personnel (apprentis), University of Geneva

Masters

1. A. Roditis "Novel antioxidants against reperfusion arrhythmias" University of Athens, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, December 2001
2. E. Theodorou "Synthesis of cytoprotective chroman/catechol hybrids" University of Athens, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, April 2005
3. C. Kiziridi "Synthesis of new 5-substituted benzopyran analogues bearing class III antiarrhythmic pharmacophores" University of Athens, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, April 2005
4. T. Fotopoulou "Design and synthesis nitrate esters of aromatic heterocyclic compounds as pharmacological preconditioning agents: New ischemic

- preconditioning mimics" University of Athens, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, March 2007
5. A. Tsatsaroni "Design and synthesis of neuroprotective benzopyran analogues" University of Athens, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, November 2010
 6. E. Charalambous "Synthesis of new phospholipase A₂ inhibitors bearing antioxidant pharmacophores" University of Athens, Department of Chemistry, December 2013

Doctoral Theses

1. E. Theodorou "Neuroprotective compounds possessing antioxidant and iron chelating properties" University of Athens, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, October 2008
2. C. Kiziridi "Design and synthesis of novel neuroprotective 1,2-dithiolane analogues" University of Athens, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, October 2008
3. T. Fotopoulou "Design, synthesis and pharmacological study of new cardioprotective purine and adenosine analogues" University of Athens, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, November 2011
4. D. Pournara "Design and synthesis of inhibitors of inflammasome activation with potential cardioprotective activity" University of Athens, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, *in progress*

Professional activities

- 1993-present: Member of the Organizing Committee of 13 Greek and 6 International Symposia
- 1998-present: Reviewer in peer-reviewed international journals: *Journal of Medicinal Chemistry*, *European Journal of Medicinal Chemistry*, *Bioorganic & Medicinal Chemistry*, *Bioorganic & Medicinal Chemistry Letters*, *Synthetic Communications*, etc.
- 1998-2001: Treasurer of the board of Fulbright alumni
- 1995-1998: Member of the board of Fulbright alumni
- 1993-1998: Member of the board of Greek Chemical Society, Pharmaceutical Chemistry Division
- 2004-2014: Vice President of the board of Greek Chemical Society, Organic and Medicinal Chemistry Division
- 2002-2003: Guest Editor of *Current Topics in Medicinal Chemistry* (Bentham Science Publishers Ltd. USA) Title of the issue: "Therapeutic strategies against HIV infection"

Significant research achievements

- One of the first groups worldwide to introduce the concept of hybrid multifunctional antioxidants.
- Pioneer in Greece in the synthesis of compounds providing cardioprotection after myocardial infarction.

Funded Programs

- *PENED 99 181* (2000-01) "Development of novel biochemical methods for the evaluation of compounds possessing antioxidant properties"
- *Excellence in the Research Institutes* (2002-05) "Novel strategies against neurodegeneration"
- *Univ. Connecticut PSA No 2328* (1998-99) "Novel antiarrhythmics and anticancer ether lipids" *PSA No 3324* (2001-02) "Biologically active ether phospholipids" *PSA No 3680* (2002-03) "Novel Antioxidants" *PSA No 4505* (2004-05) "Novel Antioxidants and Bioactive ether phospholipids"
- *GSRT programme Location and use of research results by the creation of new enterprises (Spin-off, 2003-05)* "New ether phospholipids as ultrasound contrast agents"
- *Operational Programme for Competitiveness, GSRT YB/39* (2004-07) "Therapeutic Interventions Against Protozoan Infections"
- *Bilateral Collaboration of Greece-Hungary* (2003-06) "Synthesis of novel antiarrhythmics and study of their electrophysiological effects"
- *Northeastern Univ. Boston, Center for Drug Discovery* (2006-07) "Synthesis of tropolone derivatives"
- *E2050-4/2 Greek Ministry of Development* (2006-09) "Design and Synthesis of Bioactive Molecules"
- *EU MARIE CURIE EARLY STAGE TRAINING (EST)* (2006-10) "A European Research Training Site for the Design and Synthesis of Novel Neuroprotective and Hypoglycaemic Agents through a Multi-disciplinary approach"
- *HELLENIC SOCIETY OF CARDIOLOGY* (2007-10) "Synthesis of nicorandil and adenosine derivatives as triggers of pharmacological preconditioning" (2010-12) "Development of agents mimicking postconditioning"
- *REGPOT-2009-1/ARCADE 245866* (2010-2013) "Advancement of Research Capability for the Development of New Functional Compounds" WP leader
- *Research Funding Program KRIPIS: (2013-2015) Project STHENOS: "Targeted therapeutic approaches against ageing and degenerative diseases, cancer in particular"*

Publications

1. Tronchet J.M.J., Bizzozero N., Koufaki M., Habashi F., Geoffroy M. Analogs of blocked disaccharides bearing a N-hydroxyimino bridge and nitroxyl free radicals thereof. *J. Chem. Research* **1989** (M) 2601 *J. Chem. Research* **1989** (S) 334
2. Tronchet J.M.J., Koufaki M., Zosimo- Ladolfo G. Spacer arms bearing two N-hydroxyimino groups and nitroxyl free radicals thereof. *Carbohydr. Res.* **1991** *209*, 299
3. Tronchet J.M.J., Koufaki M., Zosimo-Ladolfo G., Bernardinelli G. Spiro naphthoxazine derivatives of furanose sugars. *J. Chem. Research* **1992** (M) 2501, *J. Chem. Research* **1992** (S) 293
4. Calogeropoulou T., Koufaki M., Tsotinis A., Balzarini J., De Clercq E., Makriyannis A. Synthesis and anti-HIV evaluation of alkyl and alkoxyethyl phosphodiester AZT derivatives. *Antiv. Chem. Chemother.* **1995**, *6*, 43-49.
5. Tsotinis A., Calogeropoulou T., Koufaki M., Souli Ch., Balzarini J., De Clercq E., Makriyannis A. Synthesis and Antiretroviral Evaluation of New Alkoxy and Aryloxy Phosphate Derivatives of AZT. *J. Med. Chem.* **1996**, *39*, 3418-3422.
6. Koufaki M.*, Calogeropoulou T., Mavromoustakos T., Theodoropoulou E., Tsotinis. A., Makriyannis A. Synthesis of 2H-Labelled Alkoxyethyl Phosphodiester AZT Derivatives for Solid-State 2H-NMR Studies. *J. Het. Chem.* **1996**, *33*, 619-622.
7. Koufaki M., Polychroniou V., Calogeropoulou T., Tsotinis A., Drees M., Fiebig H.H., LeClerc S., Hendriks H.R., Makriyannis A. Alkyl and alkoxyethyl antineoplastic phospholipids. *J. Med. Chem.* **1996**, *39*, 2609-2614
8. Mavromoustakos T., Theodoropoulou E., Yang D.P., Lin S.Y., Koufaki M., Makriyannis A. The conformational properties of the antineoplastic ether lipid 1-thiohexyl-2-O-methyl-S-glycero-3-phosphocholine. *Chem. Phys. Lipids* **1996**, *84*, 21-34
9. Tronchet J.M.J., Koufaki M., Barbalat F., Geoffroy M. Blocked Sugar Analogues Bearing two or three N(sp³)-O Bonds. *Carbohydr. Lett.* **1999**, *3*, 255-262
10. Mavromoustakos T., Calogeropoulou T., Koufaki M., Kolocouris A., Demetzos K., Meng Z., Makriyannis A., Balzarini J., De Clercq E. Ether phospholipid-AZT conjugates possessing anti-HIV and anti-tumor cell activity. Synthesis, conformational analysis and study of their thermal effects on membrane bilayers. *J. Med. Chem.* **2001**, *44*, 1702-1709
11. Koufaki M.*, Calogeropoulou T., Detsi A., Roditis A., Kourounakis A., Papazafiri P., Tsiakitzis K., Gaitanaki C., Beis I., Kourounakis P. Novel potent inhibitors of lipid peroxidation with protective effects against reperfusion arrhythmias. *J. Med. Chem.* **2001**, *44*, 4300-4303

12. Detsi A., Koufaki M., Calogeropoulou T. Synthesis of (*Z*)-4-hydroxytamoxifen and (*Z*)-2-(4-[1-(*p*-hydroxyphenyl)-2-phenyl]-1-butenyl)phenoxyacetic acid. *J. Org. Chem.* **2002**, *67*, 4608-4611
13. Avlonitis N., Lekka E., Detsi A., Koufaki M., Calogeropoulou T., Skoulica E., Siapi E., Kyrikou I., Mavromoustakos T., Tsotinis A., Golic Grdadolnik S., Makriyannis A. Antileishmanial Ring-Substituted Ether Phospholipids. *J. Med. Chem.* **2003**, *46*, 755-767
14. Koufaki M.*, Calogeropoulou T., Rekkas E., Chryselis M., Papazafiri P., Gaitanaki C., Makriyannis A. Bifunctional Agents for Reperfusion Arrhythmias. Novel Hybrid Vitamin E/Class I Antiarrhythmics. *Bioorg. Med. Chem.* **2003**, *11*, 5209-5219
15. Calogeropoulou T., Detsi A., Lekkas E., Koufaki M. Strategies in the design of prodrugs of anti HIV agents. *Curr. Top. Med. Chem.*, **2003**, *3*, 1467-1495
16. Koufaki M.*, Detsi A., Theodorou E., Kiziridi C., Calogeropoulou T., Vassilopoulos A., Kourounakis A., Rekkas E., Kourounakis P., Gaitanaki C., Papazafiri P. Synthesis of Chroman Analogues of Lipoic Acid and Evaluation of their Activity against Reperfusion Arrhythmias. *Bioorg. Med. Chem.* **2004**, *12*, 4835-4841
17. Papazafiri P., Avlonitis N., Angelou A., Calogeropoulou T., Koufaki M., Skoulica E., Fragiadaki I. Structure-activity relationships of antineoplastic ring-substituted ether phospholipid derivatives. *Cancer Chemother. Pharmacol.* **2005**, *56*, 261-270
18. Koufaki M.*, Theodorou E., Galaris D., Nouis L., Katsanou E. S., Alexis M.N. Chroman/catechol hybrids: Synthesis and evaluation of their activity against oxidative stress induced cellular damage. *J. Med. Chem.* **2006**, *49*, 300-306
19. Koufaki M.*, Kiziridi C., Papazafiri P., Vassilopoulos A., Varró A., Nagy Z., Farkas A., Makriyannis A. Synthesis and biological evaluation of benzopyran analogues bearing class III antiarrhythmic pharmacophores. *Bioorg. Med. Chem.* **2006**, *14*, 6666-6678
20. Detsi A., Bouloumbasi D., Prousis K.C., Koufaki M., Athanasellis G., Melagraki G., Afantitis A., Igglessi-Markopoulou O., Kontogiorgis C., Hadjipavlou-Litina D.J. Design and synthesis of novel quinolinone-3-aminoamides and their α -lipoic acid adducts as antioxidant and anti-inflammatory agents. *J. Med. Chem.* **2007**, *50*, 2450-2458
21. Kapou A., Avlonitis N., Detsi A., Koufaki M., Calogeropoulou T., Benetis N.P., Nikolaropoulos S., Mavromoustakos T. CoMFA and CoMSIA 3D Quantitative Structure-Activity Relationships of New Flexible Antileishmanial Ether Phospholipids. *Bioorg. Med. Chem.* **2007**, *15*, 1252-1265
22. Koufaki M.*, Kiziridi C., Nikoloudaki F., Alexis M.N. Design and synthesis of 1,2-dithiolane derivatives and evaluation of their neuroprotective activity. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 4223-4227

23. Fotopoulou T., Iliodromitis E. K., Koufaki M.*, Tsotinis A., Zoga A., Gizas V., Pyriochou A., Papapetropoulos A., Andreadou I., Kremastinos D.Th. Design and synthesis of nitrate esters of aromatic heterocyclic compounds as pharmacological preconditioning agents. *Bioorg. Med. Chem.* **2008**, *16*, 4523-4531
24. Andreadou I., Koufaki M., Iliodromitis E., Kremastinos D.Th. Pharmacological pre- and post-conditioning agents: reperfusion-injury of the heart revisited. *Mini Rev. Med. Chem.* **2008**, *8*, 952-959
25. Andreadou I., Iliodromitis E.K., Farmakis D., Koufaki M., Tsotinis A., Kremastinos D.Th. Alternative pharmacological interventions that limit myocardial infarction *Curr. Med. Chem.* **2008**, *15*, 3204-3213
26. Koufaki M.*, Detsi A.; Kiziridi C. Multifunctional lipoic acid conjugates. *Curr. Med. Chem.* **2009**, *16*, 4728-4742
27. Koini E.N., Papazafiri P., Vassilopoulos A., Koufaki M., Horváth Z., Koncz I., Virág L., Papp G.J., Varró A., Calogeropoulou T. 5,7,8-trimethyl-benzopyran and 5,7,8-trimethyl-1,4-benzoxazine aminoamide derivatives as novel antiarrhythmics against ischemia-reperfusion injury. *J. Med. Chem.* **2009**, *52*, 2328-2340
28. Melagraki G., Afantitis A., Igglessi-Markopoulou O., Detsi A., Koufaki M., Kontogiorgis C., Hadjipavlou-Litina D.J. Synthesis and evaluation of the antioxidant and anti-inflammatory activity of novel coumarin-3-aminoamides and their alpha-lipoic acid adducts. *Eur. J. Med. Chem.* **2009**, *44*, 3020-3026
29. Koufaki M.*, Kiziridi C., Alexi X., Alexis M.N. Design and synthesis of novel neuroprotective 1,2-dithiolane/chroman hybrids. *Bioorg. Med. Chem.*, **2009**, *17*, 6432-6441
30. Koufaki M.*, Theodorou E., Alexi X., Nikoloudaki F., Alexis M.N. Synthesis of tropolone derivatives and evaluation of their *in vitro* neuroprotective activity. *Eur. J. Med. Chem.* **2010**, *45*, 1107-1112
31. Koufaki M.*, Theodorou E., Alexi X., Alexis M.N. Synthesis of a second generation chroman/catechol hybrids and evaluation of their activity in protecting neuronal cells from oxidative stress-induced cell death. *Bioorg. Med. Chem.* **2010**, *18*, 3898-3909
32. Koufaki M.*, Tsatsaroni A., Alexi X., Guerrand H., Zerva S., Alexis M.N. Isoxazole substituted chromans against oxidative stress-induced neuronal damage. *Bioorg. Med. Chem.* **2011**, *19*, 4841-4850
33. Koufaki M.*, Fotopoulou T., Iliodromitis E. K., Bibli S. I., Zoga A., Kremastinos D.Th., Andreadou I. Discovery of 6-[4-(6-nitroxyhexanoyl)piperazin-1-yl]-9H-purine, as pharmacological post-conditioning agent. *Bioorg. Med. Chem.* **2012**, *20*, 5948-5956

34. Koufaki M.*, Fotopoulou T., Heropoulos G.A. Synergistic effect of dual-frequency ultrasound irradiation in the one-pot synthesis of 3,5-disubstituted isoxazoles. *Ultrason. Sonochem* **2014**, *21*, 35-39
35. Maugé L., Fotopoulou T., Delemasure S., Dutartre P., Koufaki M., Connat J.-L. *In vitro* inflammatory/anti-inflammatory effects of nitrate esters of purines. *Eur. J. Pharmacol.* **2014**, *730*, 148–156
36. Koufaki M.*, Fotopoulou T., Kapetanou M., Heropoulos G.A., Gonos E.S., Chondrogianni N. Microwave-assisted synthesis of 3,5-disubstituted isoxazoles and evaluation of their anti-ageing activity. *Eur. J. Med. Chem.* **2014**, *83*, 508–515
37. Koufaki M. Therapeutic applications of lipoic acid: a patent review (2011-2014) *Expert Opin. Ther. Pat.* **2014**, *24*, 993–1005
38. Koufaki M. Vitamin E derivatives: a patent review (2010-2015). *Expert Opin. Ther. Pat.* **2016**, *26*, 35–47
39. Fotopoulou, T., Ćirić, A., Kritsi, E., Calhella, R.C., Ferreira, I.C.F.R., Soković, M., Zoumpoulakis, P., Koufaki, M. Antimicrobial/Antibiofilm Activity and Cytotoxic Studies of β -Thujaplicin Derivatives. *Archiv. Pharm.* **2016**, 698-709

Meeting abstracts

1. Andreadou I., Fotopoulou T., Koufaki M., Tsotinis A., Zoga A., Gizas V., Iliodromitis E., Kremastinos D.Th. Novel pharmacological compounds as triggers of ischemic preconditioning *in vivo*. *J. Mol. Cell. Cardiol.* **2007**, *42*, *S1*, S178
2. Andreadou I., Fotopoulou T., Koufaki M., Tsotinis A., Zoga A., Papapetropoulos A., Iliodromitis E.K., Kremastinos, D.Th. Development of novel pharmacological agents that precondition the ischemic heart *in vivo* through parallel and combined molecular mechanisms *Eur. Heart J.* **2008**, *29*, *Suppl. 1*, 110-111
3. Andreadou I., Fotopoulou T., Koufaki M., Tsotinis A., Zoga A., Pyriochou A., Farmakis D., Iliodromitis E.K., Kremastinos D.Th. Novel pharmacological compounds as triggers of preconditioning *in vivo*. *J. Am. Coll. Cardiol.* **2008**, *51*, *Suppl. A*, A183
4. Andreadou I., Fotopoulou T., Georgakopoulos A., Zoga A., Koufaki M., Kremastinos D.Th., Iliodromitis E.K., Anastasiou-Nana M. Nitric oxide donors as pharmacological postconditioning agents: the formation of peroxynitrite during reperfusion plays a critical role. *Eur. Heart J.* **2011**, *32S1*, 331-332
5. Andreadou I., Bibli S.I., Zhou Z., Fotopoulou T., Koufaki M., Anastasiou-Nana M., Papapetropoulos A., Iliodromitis E.K. Pharmacological characterization and elucidation of the molecular mechanism of action of a novel purine analogue which has superior effects to ischemic postconditioning. *Eur. Heart J.* **2014**, *35S1*, 386-387

Patents

1. Koufaki M., Calogeropoulou T., Makriyannis A. Applicant: UNI-PHARMA SA "Bifunctional agents possessing antioxidant and antiarrhythmic activity" WO0204438. US2004259763, CA2415523, EP1301504, DE60106922T, ES231514T
2. Calogeropoulou T., Koufaki M., Avlonitis N., Makriyannis A. "Antiprotozoal ring-substituted phospholipids" US2003/34225, WO2004041167, CN1742017, CA2503058, AU2003285071, EP1578754, US2006105998
3. Calogeropoulou T., Koufaki M. "Ultrasound contrast agents containing anticancer ether phospholipids" GR20050100100

Chapter in book

Maria Koufaki and Anastasia Detsi. Design and Synthesis of Antioxidant α -Lipoic Acid Hybrids. Advanced Protocols for Oxidative Stress II Series: *Methods in Molecular Biology*, Vol. 594, Armstrong, Donald (Ed.) **2010**, p. 297-309

Reviews

1. Buchholzer F.J., Koufaki M., Tronchet J.M.J. La spectrométrie de masse: Une excellente méthode quantitative très utile en pharmacologie. *Epitheor. Klin. Pharmacol. Farmakokinet. Int. Ed.* **1987**, 1, 119
2. Koufaki M., Buchholzer F.J. Les liposomes comme transporteurs de médicaments. *Epitheor. Klin. Pharmacol. Farmakokinet. Int. Ed.* **1990**, 4, 12-23

42 Presentations in International Symposia

41 Presentations in National Symposia