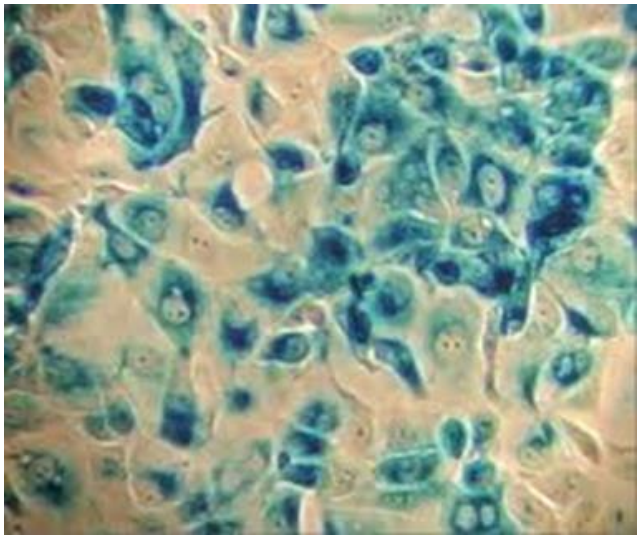
NATIONAL CENTRE FOR
SCIENTIFIC RESEARCH "DEMOKRITOS"

INSTITUTE OF BIOSCIENCES & APPLICATIONS

IB-A
NCSR Demokritos

ANNUAL REPORT 2017



DECEMBER 2018

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ANNUAL REPORT

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ORGANISATION CHART

DIRECTOR'S OFFICE
Director: D. KLETSAS

SCIENTIFIC ADVISORY BOARD
President: A. PROMBONA

ADMINISTRATIVE SERVICES
SECRETARIAT: M. Papadaki
ACCOUNTING & MANAGEMENT OFFICE:
A. Kostakou

GRADUATE STUDENT CONSELOR:
A.CHRONI

SCIENTIFIC UNITS

PROGRAMME A
REGULATION OF CELL FUNCTION – AGED-RELATED DISEASES (6 LABS)

- **Cellular Signalling and Molecular Pharmacology of G Protein – Coupled Receptors**
  In Charge: *Z. Georgoussi*
- **Regulation of Kinase Function and Role of the Heat Shock Proteins (HSPs) in Signal Transduction**
  In charge: *N. Grammatikakis*
- **Mechanisms of Cell Proliferation and Ageing**
  In charge: *D. Kletsas*
  H. Pratsinis
- **Nuclear Proteins and Chromatin Function**
  In charge: *Th. Sourlingas*
- **Cell and Matrix Pathobiology**
  In charge: *A. Chroni*
  P. Kitsiou, A. Tzinia, A. Chroni, G. Drossopoulou
- **Environmental Mutagenesis-Carcinogenesis**
  In charge: *M. Voutsinas*

PROGRAMME B
MODELS SYSTEMS FOR THE STUDY OF CELL FUNCTION (4 LABS)

- **Molecular Genetics of Insects and Biotechnology**
  In charge: *L. Swevers, V. Labropoulou*
- **Chronobiology**
  In charge: *A. Prombona*
- **Microbial Molecular Genetics**
  In charge: *V. Sophianopoulou*
- **Biophysics and Biotechnology of Membranes**
  In charge: *K. Stamatakis*

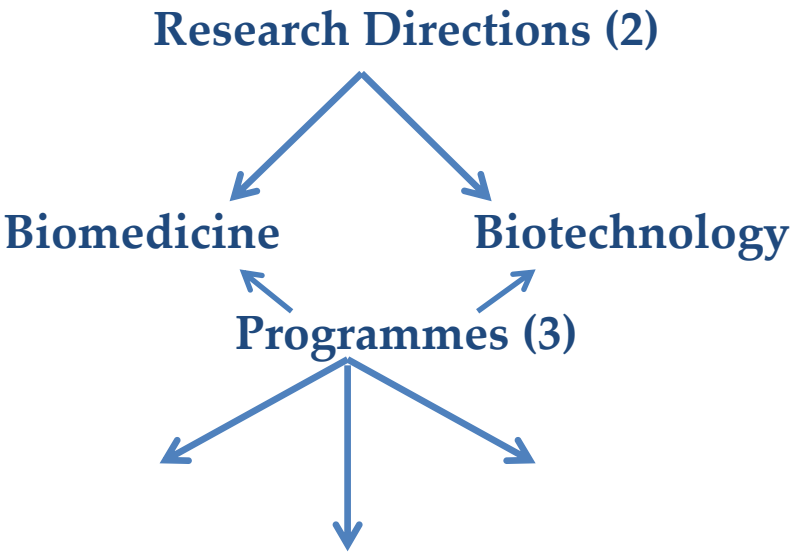
PROGRAMME CΓ
STRUCTURAL AND COMPUTATIONAL BIOLOGY (3 LABS)

- **Theoretical Biology and Computational Genomics**
  In charge: *Y. Almirantis*
- **NMR Studies of Biomolecules and Pharmaceuticals**
  In charge: *M. Pelecanou*
  M. Sagnou
- **Protein Structure and Molecular Modeling**
  In charge: *M. Vlassi*

SERVICE UNITS

- **EXPERIMENTAL ANIMAL COLONY**
  In charge: *D. Kletsas*
- **HUMAN TISSUE LABORATORY/BANK**
  In charge: *H. Vavouraki*
- **LASER CONFOCAL MICROSCOPY**
  Admin. Responsible: D. Kletsas, Director IBA
- **CIRCULAR DICHROISM (CD) LABORATORY**
  In charge: *M. Vlassi – M. Pelecanou*
- **LABORATORY OF CELL & MATRIX PATHOBIOLGY**
  In charge: *P. Kitsiou*
- **LABORATORY OF MOLECULAR DIAGNOSIS OF GENETIC DISEASE**
  In charge: *G. Voutsinas*
- **LABORATORY OF CELL-BASED ASSAY SYSTEMS AND BIOACTIVE COMPOUNDS**
  In charge: *D. Kletsas – H. Pratsinis*

Institute of Biosciences & Applications



Regulation of Cell Function/ Aged- related Diseases

Models Systems for the Study of Cell Function

Structural and Computational Biology

P E R S O N N E L

DIRECTOR

Dimitris Kletsas	Dr. Biologist

SCIENTIFIC STAFF

Research Directors

Almirantis Yannis	Dr. Chemist
Chroni Angeliki	Dr. Chemist
Georgoussi Zafiroula-Iro	Dr. Biochemist
Kletsas Dimitris	Dr. Biologist
Pelecanou Maria	Dr. Pharmacist
Sophianopoulou Vassiliki	Dr. Biologist
Swevers Luc	Dr. Biologist
Vlassi Metaxia	Dr. Physicist-Chrystallographer
Voutsinas Gerassimos	Dr. Biologist

Senior Researchers

Grammatikakis Nikolaos	Dr. Cell Biologist
Kitsiou Paraskevi	Dr. Biologist
Konstantopoulou Maria	Dr. Biologist
Labropoulou Vassiliki	Dr. Biochemist
Prombona Anastasia	Dr. Biologist
Sourlingas Thomae	Dr. Biologist
Stamatakis Konstantinos	Dr. Biologist
Tzinia Athina	Dr. Biochemist
Vavouraki Helen	Dr. Radiopharmacist

Researchers

Drossopoulou Garifallia	Dr. Biologist
Pratsinis Haris	Dr. Chemist
Sagnou Marina	Dr. Biologist/ Chemist

Functional Scientific Personnel

Angeliki Panagiotopoulou	Dr. Biochemist

Technical Specialists

Stefanou Dimitra	Agronomist

RESEARCH TECHNICIANS

Avgeris Socratis
Doulgeridis George
Giannakas Nikolaos
Zachariadis Michalis *(PhD)*
Zafiropoulos Ioannis

ADMINISTRATIVE & TECHNICAL STAFF

Kostakou Athanassia	Accountant
Papadaki Margarita	Secretary
Lionis Ioannis	Technician for electronic equipment & maintenance of equipment
Vlachos Panagiotis	Administrator

COLLABORATING SCIENTISTS

Scientists	**Laboratory**
Iatrou Kostas (Dr. Biochemist & Molecular Biologist)	Georgoussi Z.
Ignatiadou Lydia (Dr. Hydrobiologist)	Georgoussi Z.
Kottakis Christos (Dr. Biologist)	Stamatakis K.
Papageorgiou George (Dr. Biophysicist)	Stamatakis K.
Papageorgiou Spyros (Dr. Physicist)	Almirantis I.
Sekeri Kalliope (Dr. Biochemist)	Sourlingas Th.
Tsimilli – Michael Meropi (Dr. Biologist)	Stamatakis K.

POSTDOCTORAL FELLOWS

Fellow	**Supervisor**
Athanassopoulos Alexandros	Sophianopoulou V.
Dafnis Ioannis	Chroni A.
Mavrogonatou Eleni	Kletsas D.
Mavroidi Barbara	Pelecanou M.
Papadopoulou Adamantia	Kletsas D.
Tsitoura Panagiota	Iatrou K.
Trohatou Ourania	Drossopoulou G.

GRADUATE STUDENTS

Student	**Supervisor**
Angelopoulou Maria	Kletsas D.
Biratsi Alda	Sophianopoulou V.
Galeou Aggeliki	Prombona A.
Gkolfinopoulou Christina	Chroni A.
Kaminari Archontia	Tzinia A. *–PhD obtained*
Karoussiotis Christos	Georgoussi Z
Katrini Konstantina *(MSc)*	Chroni A.
Kouroumalis Anastasios	Kletsas D.
Koutloglou Sofia	Georgoussi Z.
Pallaki Paschalina	Georgoussi Z
Vayenos Dimitris	Stamatakis K.

GRADUATE RESEARCH ASSOCIATES

Fellow	**Supervisor**
Katopodi Annita	Chroni A.
Klamarias Lykourgos (Veterinarian)	Kletsas D.
Ninios Ioannis *(PhD)*	Vavouraki E.
Raptopoulos Dimitris (Dr. Biologist)	Konstantopoulou M.
Sdralia Konstantia	Iatrou K.

Theophanidi Eleni	Drossopoulou G.

COLLABORATING GRADUATE STUDENTS

Student (University)	**Supervisor**
Chaldaiopoulou Georgia (Univ. of Athens, *MSc*)	Kletsas D. - *MSc obtained*
Delimitsou Aggeliki (Univ. of Athens)	Voutsinas G.
Grammatikaki Stefania Diana (Univ. of Athens, *MSc*)	Kletsas D. - *MSc obtained*
Kikidou Eleni (Univ. of Athens, *MSc*)	Voutsinas G..
Konstantinou Angeliki (Univ. of Athens, *MSc*)	Kletsas D. - *MSc obtained*
Lesgidou Nastazia (Univ. of Athens, *MSc*)	Vlassi M.
Manikas Neoklis (Agricultural Univ. of Athens)	Konstantopoulou M.
Mountaki Christina (Univ. of Athens, *MSc*)	Chroni A. - *MSc obtained*
Nikopoulou Despoina (Univ. of Athens, *MSc*)	Kletsas D. - *MSc obtained*
Pateraki Eva (Univ. of Athens, *MSc*)	Kletsas D.
Tsimelis Efstathios (Univ. of Athens, *MSc*)	Kletsas D.
Tsourou Olga (Univ. of Athens, *MSc*)	Kletsas D. - *MSc obtained*
Yongchao Zhao (South China Agricultural University)	Swevers L.

UNDERGRADUATE STUDENTS AND OTHER IN TRAINING

Student (University)	**Supervisor**
Amoiradaki Konstantina (Univ. of York, UK)	Georgoussi Z.
Apostolidou Myrto (Univ. of Thessaloniki)	Georgoussi Z.
Arfara Maria (Technical Univ. of Athens)	Pelecanou M.
Broussos Panagiotis (Agricultural Univ. of Athens)	Stamatakis K.
Charikleous Myrsini (Univ. of Athens)	Sophianopoulou V.
Christodouloy Eleni Anna (Univ. of Athens)	Swevers L.
Dedemadi Anastasia Georgia (Univ. of Athens)	Sourlingas Th.
Dimopoulou Sofia (Univ. of Thessaly)	Pelecanou M.
Georga Maria (Agricultural Univ. of Athens)	Prombona A.
Giannakoulis George (Univ. of Kent, UK)	Georgoussi Z.
Kazantzis Konstantinos (Technical Univ. of Athens)	Georgoussi Z.
Kaplani Eleni (TEI of Larissa)	Kletsas D. - *undergraduate dissertation completed*
Kafetzopoulos Grigoris (Univ. of Athens)	Georgoussi Z.
Koutrouli Isis (Univ. of Athens)	Georgoussi Z.
Moutzouvi Christina (Univ. of Athens)	Chroni A.
Papavranoussi – Daponte Danae (Univ. of Athens)	Georgoussi Z.
Papasakellariou Kostis (Agricultural Univ. of Athens)	Prombona A. .
Salazar Arias Loudes (Foundacion Ceimar, Madrid, Spain)	Sophianopoulou V.
Vidali Nikolina (Agricultural Univ. of Athens)	Stamatakis K.
Zerva Maria Christina (Agricultural Univ. of Athens)	Sophianopoulou V.

INTRODUCTION

The Institute of Biosciences and Applications (IBA) is one of the five Institute of the National Centre for Scientific Research (NCSR) "Demokritos". The Centre, among the best in Greece and in Europe, is characterized by multidisciplinarity and the unique coexistence of different fields of science, as well as the collaboration among scientists of different disciplines, towards the promotion of science and innovation. Within this framework, the IBA focuses its research and developmental activities on the study of cellular function, with an emphasis to age-related diseases, on biotechnology and the environment, as well as on structural and computational biology. Despite the adverse financial environment, the 22 faculty members of the IBA and the total 97 members (scientific, technical and administrative personnel) contributed to the upgrading of the research and the developmental work produced in the Institute. They all deserve congratulations for their efforts!

I wish to thank the Vice Director Dr. V. Sophianopoulou and the members of the Scientific Committee of the IBA Dr. A. Prombona (President), Drs. A. Chroni, M. Konstantopoulou, K. Stamatakis and L. Swevers (Members) Drs. A. Tzinia and H. Vavouraki (Alternate Members) and A. Kostakou and S. Avgeris (Representatives of the administrative and technical personnel), as well as the Responsible of the Educational Committee Dr. A. Chroni and the Deputy Dr. M. Sagnou for the orderly function of the Institute within 2017. In this effort contributed also all the colleagues of the Institute that were members of various committees of NCSR "Demokritos". A special reference is needed to those colleague who worked, in collaboration with all the members of the Institute, for the implementation of important projects for the function and upgrading of the infrastructure of the IBA, namely OPENSCREEN-GR (Drs. K. Iatrou, A. Chroni, H. Pratsinis and Z. Georgoussi), BIOIMAGING-GR (Drs. V. Labropoulou, H. Pratsinis, and M. Sagnou), INSTRUCT (Drs. A. Chroni, A. Panagiotopoulou, M. Pelecanou and M. Vlassi) and SANITURA (Drs. V. Labropoulou and H. Pratsinis). The successful implementation of these projects will support considerably the development of the Institute and will attract a significant number of young researchers.

During 2017 Dr. G. Voutsinas was promoted to the level of Researcher A' and Dr. H. Pratsinis to the level of Researcher B'. Congratulations to both! The Institute welcomes with great pleasure the newly elected researcher Dr. A. Papakyriakou (at the level of Researcher B') and wishes every success in his new position.

Finally, I wish to thank the IBA accountat Mrs. A. Kostakou and the IBA secretary Mrs. M. Papadaki for their significant contribution to the orderly function of the Institute.

Dimitris Kletsas, PhD
Director of the IBA
December 2018

PROGRAMME A:

REGULATION OF CELL FUNCTION

AGED-RELATED DISEASES

Research Group: Cellular Signalling and Molecular Pharmacology

Research Staff
Iro Georgoussi, Research Director
Paschalina Pallaki, Graduate Student
Christos Karoussiotis, Graduate Student
Sofia Koutloglou, Graduate Student
Alexandra Simeonof, Undergraduate Student
Isis-Anzel Koutrouli, Undergraduate Student
Danae Papavranousi-Daponte, Undergraduate Student
Myrto Apostolidou, Training Student
Gregory Kafetzopoulos Training Student
Konstantina Amiraraki, Training Student
George Giannakoulis, Training Student

Kostas Iatrou, Collaborating Former Staff Scientist
Lydia Ignatiades, Collaborating Former Staff Scientist
Panagiota Tsitoura, Postdoctoral Fellow
Konstantia Sdralia, Graduate Research Associate

Research Interests

The research activities of the laboratory of Cellular Signaling and Molecular Pharmacology are focused on the elucidation of the regulatory mechanisms governing the heptahelical G protein-coupled receptor family (GPCRs) with emphasis on the protein players (Gαβγ, RGS, spinophilin, arrestin and others), as molecular machines or switches modulating signaling upon receptor activation.

As a model we use the three opioid receptor subtypes (δ, μ and κ) due to their involvement in downstream signaling affecting neurotransmission, neurogenesis and endogenous synaptic alterations, responsible for various pathological conditions ranging from pain perception, tolerance and dependence upon prolonged drug administration, to inflammation and regulation of emotional responses such as anxiety and stress.

More specifically our objectives are composed of four major areas which are thematically interrelated such as the :

- Identification of the role of G protein coupled receptors (GPCRs) signaling molecules, such as G and RGS proteins, in pathological conditions and receptor-mediated behaviors
- Elucidation of novel signaling pathways mediated upon activation of the three opioid receptors (δ.μ,κ) in an attempt to define new pharmacological targets
- Identification of new transcription factors and genes which action is altered upon opioid administration with selective agonists, *bias signalling,* implicated in neuronal differentiation and,
- Characterization of new bioactive compounds for opioid or other GPCRs using cell based assays in an attempt to identify "*smart drugs*" to alleviate pain or other diseases of the central nervous system.

2017 Findings

Alternative signal transduction pathways mediated upon opioid receptor activation

Role of RGS4 protein: Previous observations from our lab have shown that the C-terminal region of the δ-opioid receptor (δ-OR) serves as a platform for the formation of a multiprotein complex (signalosome) composed of Gi/o proteins, the RGS4, the transcription factor STAT5B, spinophilin and the c-Src kinase that leads to neurite outgrowth and differentiation upon opioid receptor activation with selective agonists (Georganta et al., 2010, 2013; Fourla et al., 2012; Georgoussi et al., 2015). Based on these observations we found that RGS4 couples directly with STAT5B and blocks its transcriptional activation an effect that results in alterations in neuronal outgrowth and differentiation. Moreover we demonstrated that lysates from RGS4$^{-/-}$ mice, that lack a functional RGS4, the levels of the *SNX9* and

FAK2 gene expression implicated in axonogenesis and neurite growth are altered suggesting for the first time a novel functional role of RGS4 in regulating STAT5B-inducible genes during neurogenesis.

Parallel studies and under the auspices of the COST-Action-GLISTEN *(GPCR Ligand Interactions, Structures and Transmembrane Signaling)* in collaboration with Jana Selent, Pompeu Fabra University, Barcelona, we identified with molecular dynamics the structural determinants and the critical amino-acids residues responsible for RGS4 and δ-OR interaction.

Role of spinophilin: Spinophilin is a neuronal scaffold protein that interacts with the δ- and μ- opioid receptors (Fourla et al., 2012, Georgoussi et al., 2013). We found that δ-OR activation leads to tyrosine phosphorylation of spinophilin. Site-directed mutagenesis of tyrosines 398 and 483 of spinophilin revealed the critical phosphorylation sites. Further studies determined that spinophilin is involved in the internalization and desensitization of the δ-opioid receptor (δ-OR) and that the aforementioned spinophilin's mutants alter its ability to stabilize the receptor in the plasma membrane, suggesting its role in the regulation and function of the δ-OR desensitisation.

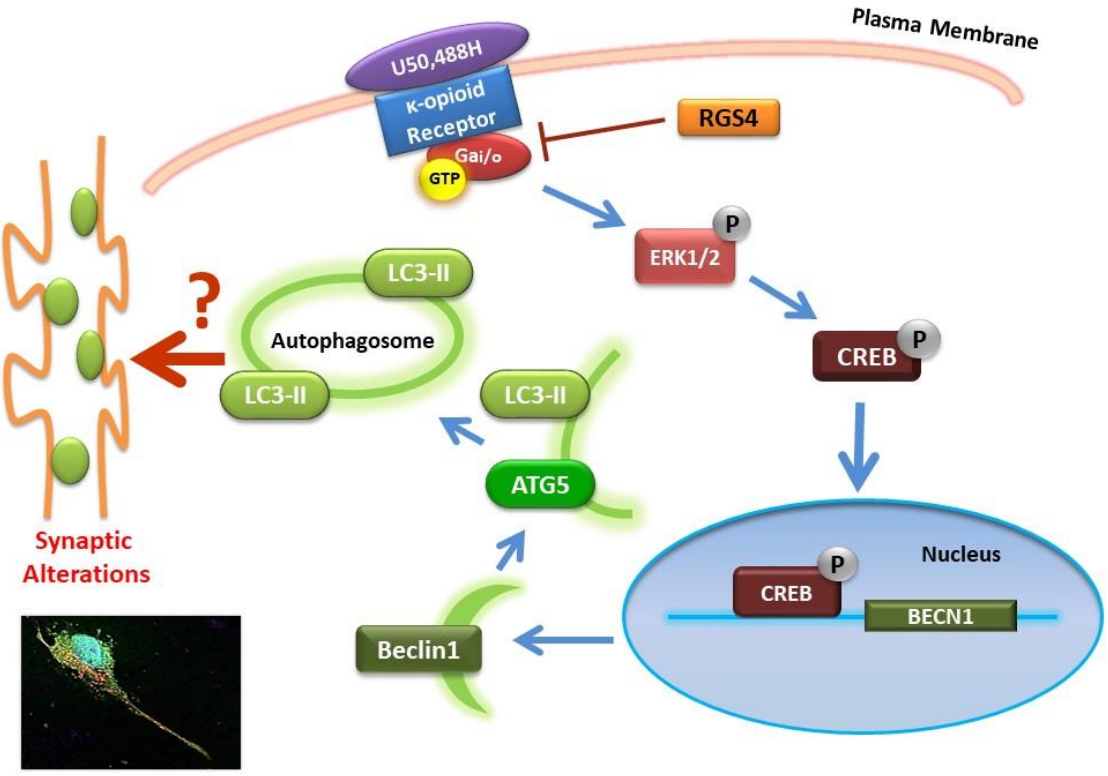


Figure 1: Putative model of the molecular signaling pathway via which the κ-opioid receptor may modulates cell death and autophagy.

Autophagy mediated by κ-opioid receptor analogs: Observations have shown that opioids exert a neuroprotective role and modulate neurogenesis and neuronal plasticity. We found that activation of the κ-opioid receptor (κ-OR) with selective agonists results in increased accumulation of two specific markers of autophagy LC3II and Beclin1 in neuronal cells, suggesting the role of κ-OR in the autophagic machinery. This κ-OR induced autophagic death is mediated via Gαi/o proteins and ERK1,2 kinases that in turn phosphorylate CREB with subsequent activation of *beclin1* gene (Fig. 1). Moreover, the levels of LC3 from primary cortical neuronal cultures of RGS4$^{-/-}$ mice were reduced compared with those of wild type, suggesting the involvement of RGS4 in autophagy mediated effects.

Pharmacological characterization of new bioactive compounds in cell based throughput platforms: Through participation in the EU consortium «*NORMOLIFE NETWORK*» (collaboration with Profs L. Pasquinucci & G. Ronsisvalle, University of Catania) and using the facilities of the Research

Infrastructure OPENSCREEN-GR (coordinated by IBA) our group characterized the affinity of newly synthesized compounds that exert both agonistic and antagonistic properties for the three opioid receptor subtypes (δ, μ and κ), thus providing new perspectives for the use of opioid analogs with dual effects for pain management.

Publications

Pallaki P, Georganta EM, Serafimidis I, Papakonstantinou MP, Papanikolaou V, Koutloglou S, Papadimitriou E, Agalou A, Tserga A, Simeonof A, Thomaidou D, Gaitanou M, Georgoussi Z (2017) «*A novel regulatory role of RGS4 in STAT5B activation, cell proliferation and neurite outgrowth*» *Neuropharmacology* 1, 117: 408-421.

Pasquinucci L. Turnaturi R., Prezzavento O., Arena E., Aricò G., Georgoussi Z**.** and Parenti C. (2017) *Development of novel LP1-based analogues with enhanced delta opioid receptor profile J. Biorg. Med. Chem.* Sep 1; 25(17): 4745-4752.

Articles in Books and Conference Proceedings

Z. Georgoussi, P.Pallaki, I. Serafimidis, A. Symeonof, S. Koutloglou , M. Papakonstantinou, E. Georganta, D. Thomaidou and M. Gaitanou (2017). *"A novel regulatory role of RGS4 in δ-opioid receptor mediated neuronal outgrowth and differentiation".* FASEB Journal, 31:992.6

Articles in Press

Turnaturi R, Parenti C, Prezzavento O, Marrazzo A, Pallaki P, Georgoussi Z, Amata E, Pasquinucci L. (2018). "*Synthesis and Structure-Activity Relationships of LP1 Derivatives: N-Methyl-N-phenylethylamino Analogues as Novel MOR Agonists"*. *Molecules.* 16; 23(3). (IF: 2.861)

L.Pasquinucci, C.Parenti, E. Amata, Z. Georgoussi, P. Pallaki, V. Camarda, G. Calò, E. Arena, L. Montenegro, R. Turnaturi (2018) *" Synthesis and structure-activity relationships of (−)-cis-N-normetazocine-based LP1 derivatives" Pharmaceuticals* 11(2), 40 (IF: 4.90)

Turnaturi R, Parenti C, Prezzavento O, Marrazzo A, Pallaki P, Georgoussi Z, Amata E, Pasquinucci L. (2018). "*Synthesis and Structure-Activity Relationships of LP1 Derivatives: N-Methyl-N-phenylethylamino Analogues as Novel MOR Agonists"*. *Molecules.* 16; 23(3). (IF: 2.861)

L.Pasquinucci, C.Parenti, E. Amata, Z. Georgoussi, P. Pallaki, V. Camarda, G. Calò, E. Arena, L. Montenegro, R. Turnaturi (2018) *" Synthesis and structure-activity relationships of (−)-cis-N-normetazocine-based LP1 derivatives" Pharmaceuticals* 11(2), 40 (IF: 4.90)

Presentations at Scientific Conferences

C. Karoussiotis, M. Marti-Solano, J. Selent and Z. Georgoussi (2017)." *Identification of a specific region of δ-opioid receptor critical for RGS4 recruitment"*. COST-GLISTEN meeting, March 29-31, 2017 Porto, Portugal.

Z. Georgoussi, P. Pallaki, I. Serafimidis, A. Symeonof, S. Koutloglou, M. Papakonstantinou, E. Georganta, D. Thomaidou, M. Gaitanou. *"A Novel Regulatory Role of RGS4 in δ-Opioid Receptor Mediated Neuronal Outgrowth and Differentiation"* (2017) Experimental Biology-2017, April 22-26, 2017 Chicago, USA.

P. Pallaki, I. Serafimidis, E. Papadimitriou, M. P. Papakonstantinou, I.R.A. Koutrouli, D. Thomaidou, M. Gaitanou, Z. Georgoussi. (2017). *"A novel regulatory role of RGS4 in STAT5B transcriptional responses and cell proliferation*." 68th Congress of the Hellenic Society for Biochemistry and Molecular Biology, November 10-12, 2017, Athens, Greece.

C. Karoussiotis, A. Sotiriou and Z. Georgoussi. (2017). *"Activation of the κ-opioid receptor by U-50,488H induces autophagy in neuronal cells"*. 68th Congress of the Hellenic Society for Biochemistry and Molecular Biology, November 10-12, 2017, Athens, Greece.

P. Pallaki, I. Serafimidis, E. Papadimitriou, M. P. Papakonstantinou[1], I.R.A. Koutrouli, D. Thomaidou, M. Gaitanou, Z. Georgoussi. (2017). *"A novel regulatory role of RGS4 in neurite outgrowth and cell proliferation mediated by STAT5B transcriptional responses upon δ-opioid receptor activation".* 27th Meeting of the Hellenic Society for Neuroscience, December 8-10, 2017, Athens, Greece.

C. Karoussiotis, A. Sotiriou and Z. Georgoussi. (2017) *"Selective κ-opioid receptor ligands exert a neuroprotective role through induction of autophagy".* 27th Meeting of the Hellenic Society for Neuroscience, December 8-10, 2017, Athens, Greece.

S. Koutloglou and Z. Georgoussi (2017). *"Activation of the δ-opioid receptor phosphorylates the neuronal protein spinophilin implicated in receptor endocytosis".* 27th Meeting of the Hellenic Neuroscience Society, December 8-10, 2017, Athens, Greece.

Educational Activities

- Member of the organizing committee for the establishment of a new international Masters course in Neurosciences entitled "*Athens International Master's Programme for Neurosciences*" together with the Kapodistrian University of Athens, the NHRF, BRFAA the Institute Pasteur, and EIE.
- Co-corganizer of the course «*Cellular and Molecular Neurosciences*» of Athens International Master's Programme in Neurosciences, 40 hours
- Teaching responsibilities in the Master Course program Biochemistry, Division of Biochemistry and Molecular Biology, Department of Biology, Kapodistrian University of Athens, 4 hours, 25 students.
- Teaching in the Master Course program of Medical School, Kapodistrian University of Athens. "*Molecular and Applied Physiology*", 4 hours, 72 students.
- Teaching in the Interdepartmental Master Course program of Kapodistrian University of Athens, Department of Biochemistry and Molecular Biology "*Molecular basis of Human Disease"* 6 hours, 30 students.
- Teaching in the Athens "*International Master's Programme in Neurosciences*" National Kapodistrian University, Department of Biology (16 hrs, 15 students)
- Supervisor of PhD dissertation of postgraduate students: Paschalina Pallaki, Sofia Koutloglou and Christos Karoussiotis
- Supervisor of BSc dissertation of undergraduate students: D. Papavranousi-Daponte, I. Koutrouli, A. Symeonof, Department of Biology, Kapodistrian University of Athens.
- Supervisor of Internship of undergraduate student: M. Apostolidou, Aristotle University of Thessaloniki, G. Kafetzopoulos Department of Biology, Kapodistrian University of Athens. K. Amiraraki, University of Bath, G. Giannakoulis, University of Sussex, UK
- Member of the Advisory Committee in the Department of Biology of the Kapodistrian University in Athens for the Ph.D students P. Pallaki, S. Koutloglou and C. Karoussiotis

Distinctions and Awards

Sofia Koutloglou: ELIDEK scholarship for PHD students (18-08-2017/31-08-2018) entitled "*Regulation of opioid receptor function by protein-protein interactions*"

Christos Karoussiotis: Scholarship for participating in the COST1207 meeting GLISTEN in Porto, Portugal April 2017

Other Activities for the Institute of Biosciences & Applications and NCSR "Demokritos"

- Member of the working group for the establishment and funding of the National Roadmap Research Infrastructure "OPENSCREEN-GR: *An Open – Access Research Infrastructure of Target-Based Screening Technologies and Chemical Biology for Human and Animal Health, Agriculture and the Environment"* coordinated by Prof. K. Iatrou in the Institute of Biosciences and Applications.

- Member of the evaluation and promotion committee for selection of research personnel of IBA, NCSRD.
- Member of the laboratory entitled: "*Biotechnological Products and Services"* for the provision of specialized scientific and technological services and products.
- Responsible scientist for the ultracentrifuges Beckman Coulter OPTIMA-MAX και L8-8OM and the Speed Vac, Savant.

Impact factor (for 4 publications): 15,703

Citations for 2017 (without self-citations): 23

Citations for 2013-2017 (without self-citations): 170

h-factor: 17 (Scopus), 18 (Google Scholar)

Current external funding

Programme GLISTEN entitled *GPCR Ligand Interactions, Structures and Transmembrane Signalling*, funded by the EU–COST Action with Dr. Z. Georgoussi as Member and National Representative of the Management Committee
Duration: 04/2013- 03/2017

ELIDEK Scholarship for PhD candidates (funding S. Koutloglou) entitled *Regulation of opioid receptors by protein interactions*
Duration: 08/2017-08/2018
Total budget: 11.150 €

Kostas Iatrou: Insect Physiology and Ethology and Applications

Research Interests

(1) Control of olfactory functions in the malaria mosquito vector *Anopheles gambiae*.
(2) Oogenesis in lepidopteran insects as a model of terminal differentiation induced by ecdysteroids.
(3) Genetically modified nuclear polyhedrosis viruses as tools for genetic transformation of insect and mammalian cells.
(4) Production of recombinant proteins in insect cell cultures.
(5) Development of cell-based assays for fast screening of natural and synthetic collections of small molecule and discovery of novel regulators of cellular functions.

2017 Findings

Our research activities focused on the study of insect olfactory function with special emphasis on the identification of novel agonists or antagonists of olfactory receptors of the African malaria mosquito vector *Anopheles gambiae*. Based on our previous findings, which had shown that ORco, the common subunit of mosquito ORx/ORco odorant receptor heteromers (cation channels) represents a target for small molecules, which cause either significant inhibition or significant enhancement of the olfactory capacity of mosquitoes, we designed a novel cell-based screening platform for fast identification of new olfactory regulators. This platform, which was based on the expression of ORco and an appropriate luminescence-producing reporter gene in lepidopteran insect cells under the control of proprietary expression elements, was initially tested and proven to be functional as predicted using as test molecules known ORco agonists. Subsequent screening of a small collection of natural volatile organic compounds (VOCs; bacterial, plant and insect origin) resulted in the identification of three putative ORco antagonists. Further examination of these putative antagonists for *in vivo* bioactivity showed one of them to be as strong a repellent as DEET, the most powerful repellent in current use, for laboratory populations of the Asian tiger mosquito *Aedes albopictus* that can vector pathogens such as the yellow fever, dengue fever, Chikungunya fever, Saint Louis and Japanese encephalitis, West Nile,

and Zika viruses (work carried out by Dr. Antonios Michaelakis, Benaki Phytopathological Institute). Our studies on the determination of the minimal doses that offer the desired level of protection of humans against *A. albopictus* and other mosquito species are in progress together with the parallel screening of additional natural VOCs for discovery of new olfaction-relevant bioactive compounds.

Publications

Ignatiades L. (2017). Size scaling patterns of species richness and carbon biomass for marine phytoplankton functional groups. Marine Ecology, 38: 1-9.

Articles in Press

Kröber, T., Koussis, K., Bourquin, M., Tsitoura, P., Konstantopoulou, M., Awolola, T.S., Dani, F.R., Pelosi, P., Iatrou, K. and Guerin, P.M. (2018). Odorant-binding protein-based identification of natural spatial repellents for the African malaria mosquito, Anopheles gambiae. Insect Biochem Mol Biol. 96:36-50. doi: 10.1016/j.ibmb.2018.03.008 (Impact Factor 3.756)

Thireou, T, Kythreoti, G, Tsitsanou, KE, Drakou, CE, Koussis, K, Kinnersley, J, Kröber, T, Guerin, PM, Zhou, JJ, Iatrou, K, Eliopoulos, E, Zographos, SE (2018) Identification of novel bioinspired synthetic repellents by combined ligand-based screening and OBP-structure-based molecular docking. Insect Biochem Mol Biol. In Press. doi: 10.1016/j.ibmb.2018.05.001. [Epub ahead of print] (Impact Factor 3.756)

Presentations at Scientific Conferences

K Iatrou, P Tsitoura, M Konstantopoulou (2017) Distracting the Hungry: Mosquito Anosmia-Inducing and Odor Perception-Enhancing Compounds of Natural Origin Targeting ORco Function for Control of Transmission of Malaria and Other Mosquito-Borne Infectious Diseases. Annual Experimental Biology meeting (EB 2017), April 21-25, 2018, Chicago, IL, USA

Other Scientific Activities

Participation in editorial boards of scientific journals:

Subject editor, "The Journal of Insect Science".

Member, Editorial Boards for "Sericologia", "Insect Biochemistry and Molecular Biology", "Archives of Insect Biochemistry and Physiology", "The Open Biotechnology Journal" και "BioMed Research International" (formerly Journal of Biomedicine and Biotechnology).

Organization of scientific conferences or participation in conference organizing committees:

Co-Organizer (with Dr. Marian Goldsmith, University of Rhode Island, USA), 10th International Workshop on "the Molecular Biology and Genetics of Lepidoptera", Kolymbari, Crete, Greece, August 19-25, 2018.

Reviewing of funding applications:

Review of funding application for the French National Research Agency (ANR), section "CE20 Animal biology, plant biology, and micro-organism biology/Biotechnologies".

Reviews of scientific publications:

Reviewer of scientific manuscripts for "Insect Biochemistry and Molecular Biology", "Journal of Insect Physiology", "BioMed Research International", "The Open Biotechnology Journal", "Insect Science", "Journal of Insect Science", "Archives of Insect Biochemistry and Physiology", "Journal of Biological Chemistry", "Cellular and Molecular Life Sciences", "PNAS Plus", "British Journal of Pharmacology".

Member, Management Committee of the European Joint Doctorate Programme on *"High Performance Computing in Life Sciences Engineering and Physics (HPC-LEAP)"*, Marie Sklodowska-Curie Innovative Training Network Programme.

Impact factor (for 1 publication): 1,177

Citations for 2017 (without self citations):
Iatrou K: 176
Ignatiades L: 100

Citations for 2013-2017 (without self citations):
Iatrou K: 902
Ignatiades L: 491

h-factor:
Iatrou K: 32 (Scopus), 39 (Google Scholar)
Ignatiades L: 21 (Scopus), 25 (Google Scholar)

Current external funding

Marie Sklodowska-Curie Innovative Training Network entitled *High Performance Computing in Life Sciences, Engineering and Physics (HPC-LEA*P) funded by EE with Coordinator of the Greek (NCSR "D") research group, Dr. K. Iatrou
Duration: 2015-2018
Total programme funding: 3.723.916, 32 €
Funding of the lab for 2017: 0€.

Program entitled *Identification of new insect olfactory and taste enhancers of natural or synthetic origin* funded by Inscent, Inc., USA with Coordinator of the Greek (NCSR" D") research group, Dr. K. Iatrou.
Duration: 2017-2018
Total program funding: 40.000€
Funding of the lab for 2017: 30.000€.

Program entitled *OPENSCREEN-GR: An Open-Access Research Infrastructure of Target-Based Screening Technologies and Chemical Biology for Human and Animal Health, Agriculture and the Environment",funded by* GSRT (*Action on Support of Research and Innovation Infrastructures, "Competitiveness, Business and Innovation", 2014-2020)* with Program Coordinator (until September 2017) Dr. K. Iatrou
Duration: 2017-2020
Total program funding: 3.025.090€
Total funding for IBA: 899.600 €
Funding for IB-A in 2017: 0 €

Programme GLISTEN entitled *GPCR Ligand Interactions, Structures and Transmembrane Signalling*, funded by the EU–COST Action with Dr. K. Iatrou as Member and National Representative of the Management Committee
Duration: 04/2013- 03/2017

Research Group: Regulation of Kinase Function and Role of the Heat Shock Proteins (HSPs) in Signal Transduction

Research Staff
Nikos Grammatikakis, Senior Researcher

Research Interests

A) Cell Signaling

- Mechanisms of mammalian kinase regulation during normal differentiation and disease
- Chemotherapeutical inhibition of oncogenic kinase activity

B) Cellular Responses to Stress and Nutrition

- Regulation of Chaperone Protein Activity
- Identification of Signaling Mediators (including kinases and transcriptional factors) which are modulated by the Chaperone Machinery in response to Stress and Dietary Factors

C) Cell Cycle Regulation

- The Chaperone Machinery as an effector of cellular Stress in cell cycle progression

D) Novel Molecular Chaperones

- Characterization and study of a group of novel Molecular Chaperones identified in our lab and their potential role as mediators of the assembly and activity of ErbB2, Raf, Akt, Cdk4 and I-kappaB kinases (IKK) in cell proliferation and cell cycle progression. Our study extends to learning how the activity of these novel signal modulators is regulated by Growth conditions and Stress (Radiation and chemotherapeutic drugs).

Research Group: Mechanisms of Cell Proliferation and Ageing

Research Staff
Dimitris Kletsas, Research Director
Harris Pratsinis, Researcher
Eleni Mavrogonatou, Postdoctoral Fellow
Adamantia Papadopoulou, Postdoctoral Fellow
Maria Angelopoulou, Graduate Student
Anastasios Kouroumalis, Graduate Student
Angeliki Konstantinou, Collaborating Graduate Student *(MSc) - MSc obtained in 2017*
Olga Tsourou, Collaborating Graduate Student *(MSc) - MSc obtained in 2017*
Georgia Chaldaiopoulou, Collaborating Graduate Student *(MSc) - MSc obtained in 2017*
Stefania-Diana Grammatikaki, Collaborating Graduate Student *(MSc) - MSc obtained in 2017*
Despoina Nikopoulou, Collaborating Graduate Student *(MSc) - MSc obtained in 2017*
Eleni Kikidou, Collaborating Graduate Student *(MSc)*
Eva Pateraki, Collaborating Graduate Student *(MSc)*
Efstathios Tsimelis, Collaborating Graduate Student *(MSc)*
Eleni Kaplani, Training Student - *BSc obtained in 2017*

Research Interests

The Laboratory is focusing on tissue repair during development and ageing with an emphasis on the role of growth factors, and especially that of TGF-β. The action of growth factors on cell proliferation and extracellular matrix production, as well as the responsible signaling pathways are investigated. Alternative mechanisms of cell proliferation and differentiation, such as autocrine regulation, cell-matrix interactions, exogenous stresses and the effect of mechanical forces are also studied.

Main goal of the Laboratory is the investigation of the mechanisms of ageing and longevity. The structural and functional characteristics of the senescent cell - as a result of successive duplications or of exogenous stresses - in comparison to that of the young or the cancer cell are investigated. Especially, we are interested in the role of the senescent - somatic and stem - cell in the process of ageing and the development of age-related diseases, including cancer. In this direction, we study the interaction between senescent stromal fibroblasts and adjacent cancer cells. Emphasis is given on tissues, such as the intervertebral disc, the degeneration of which provokes severe dysfunctions during ageing.

Aim of our studies is the elucidation of the mechanisms underlying the regulation of tissue homeostasis, especially during ageing, and furthermore the contribution, through research networks, in the development of cell replacement therapies. Finally, we study natural products and new synthetic compounds with putative anti-cancer, anti-ageing/anti-oxidant and wound healing action, as well as their mode of action.

2017 Findings

In our laboratory the role of growth factors in tissue repair is being studied with a special emphasis on the action of TGF-β. We showed that TGF-β has differential effects in human fibroblasts regarding their proliferative potential, depending on the tissue, the developmental stage and the presence of extracellular matrix components, such as collagen and hyaluronic acid.

Main goal of the laboratory is the study of the functional features of senescent cells, as well as their role in the development of age-related diseases including cancer. We have observed that various known anti-cancer drugs induce premature senescence of the stromal cells, which in turn favours the growth of cancer cells. Furthermore, a new marker for the identification of senescent cells *in vitro* and *in vivo* was developed in collaboration with other research groups.

In addition, we continued our research on the cellular physiology of intervertebral disc degeneration, and especially the cellular responses to various stresses, such as hyperosmolality, oxidative stress, and

cyclic mechanical stretching. It was observed that these stresses stimulate intracellular signalling pathways leading to the regulation of cell proliferation and to premature senescence. In parallel, bioinformatics' analysis of cDNA microarray experiments in intervertebral disc cells treated with high osmolality revealed the differential expression of numerous genes, the role of which is currently under investigation.

A further goal of our work is the use of cell therapies in age-related degenerative disorders, by employing either autologous somatic cells or mesenchymal stem cells (MSCs). We have shown that MSCs that have reached replicative senescence or senescence induced by the use of anti-cancer treatments possess a diminished differentiation capacity. This finding was also observed in fibroblasts of the periodontal ligament, which lose their differentiation capacity towards osteoblasts during senescence due to down-regulation of the relative transcription factors.

Finally, we identified a significant number of plant extracts and of their fractions with anti-oxidant activity and a capacity to protect human skin fibroblasts from the cytotoxic effects of UVB-radiation.

Main goal of the Laboratory is the study of the mechanisms implicated in cellular senescence and of the role of senescent cells in tissue homeostasis. Cellular senescence is known to be a major anti-cancer mechanism, but senescent cells can also create a permissive environment for tumor growth. We have shown previously that ionizing radiation, a classical anti-cancer treatment, leads stromal fibroblasts to senescence *in vitro* and *in vivo*, and these senescent cells can promote tumor growth through the overexpression of metalloproteases or of proteoglycan syndecan 1 (SDC1). We have recently shown that senescent fibroblasts downregulate proteoglycan decorin, which plays an anti-cancer role by inhibiting paracrine interactions between stromal and cancer cells, reinforced by the action of cancer cells (Figure 1). These findings indicate a side effect of radiotherapy, which can promote carcinogenesis through the induction of premature senescence of stromal fibroblasts.

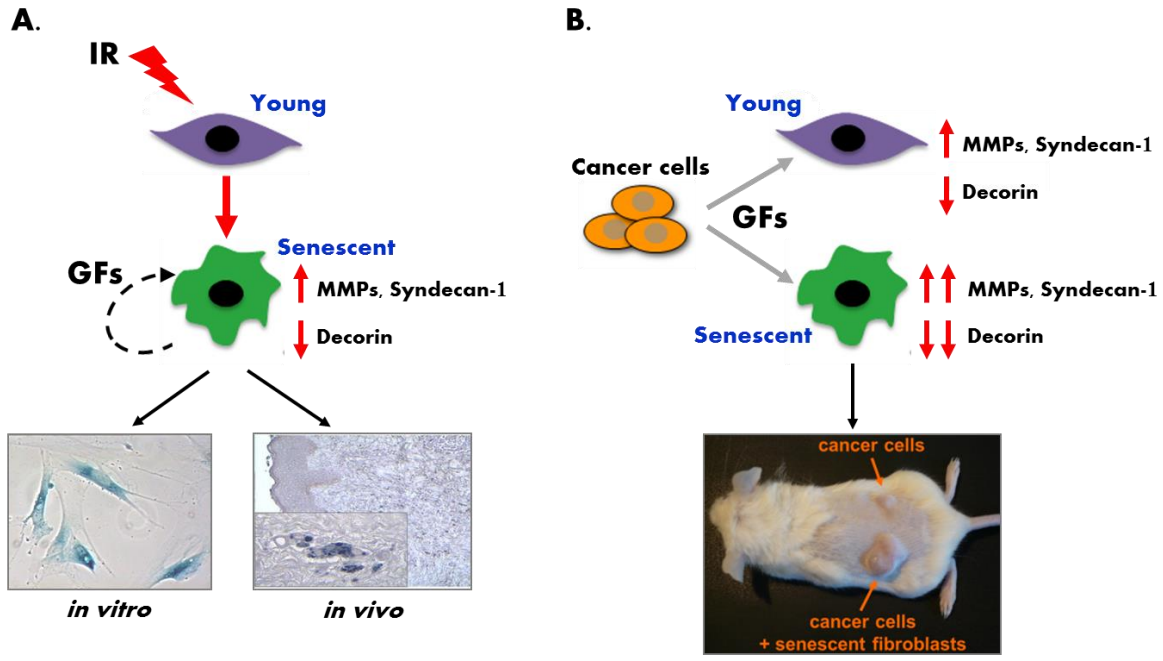


*Figure 1. Model representing the creation of a permissive environment for cancer development as a consequence of stromal fibroblasts' premature senescence induced by ionizing radiation (A) and their interaction with cancer cells (B). Adapted from Papadopoulou and Kletsas (2011) Int J Oncol.**39,** 989, Liakou et al. (2016) Aging (Albany NY) **8**, 1650 and unpublished data.*

In addition, we continued our research on intervertebral disc cells' senescence and we showed that several stimuli like successive duplications, ionizing radiation, oxidative stress or cell cycle inhibitors'

overexpression lead intervertebral disc cells to premature senescence; these senescent cells display a similar inflammatory/catabolic phenotype, which remains generally unaltered under the harsh environmental conditions prevailing in the disc characterized by nutrient and growth factor deprivation, hyperosmolality and hypoxia.
We also demonstrated that inflammatory cytokine TNF-α, found in high concentrations in chronic ulcers, may lead dermal fibroblasts to premature senescence through the activation of p38 MAPK and through reactive oxygen speceies' accumulation. In parallel, we continued our research on the study of cytoprotective mechanisms towards UV radiation.

Finally, we continued our research on the investigation of natural products and novel synthetic compounds with anti-cancer, anti-oxidant and cosmetic applications.

Publications

Evangelou, K., Lougiakis, N., Rizou, S.V., Kotsinas, A., Kletsas, D., Muñoz-Espín, D,, Kastrinakis, N.G., Pouli, N., Marakos, P., Townsend, P., Serrano, M., Bartek, J., Gorgoulis, V.G. (2017) Robust, universal biomarker assay to detect senescent cells in biological specimens. Aging Cell 16, 192-197.

Papadopoulou, A., Iliadi, A., Eliades, T., Kletsas, D. (2017). Early responses of human periodontal ligament fibroblasts to cyclic and static mechanical stretching. Eur. J. Orthod. 39, 258-263.

Gavriil, E.S., Lougiakis, N., Pouli, N., Marakos, P., Skaltsounis, A.L., Nam, S., Jove, R., Horne, D., Gioti, K., Pratsinis, H., Kletsas, D., Tenta, R. (2017). Synthesis and antiproliferative activity of new pyrazolo[3,4-c]pyridines. Med. Chem. 13, 365-374.

Antonopoulou, I., Leonov, L., Jütten, P., Cerullo, G., Faraco, V., Papadopoulou, A., Kletsas, D., Ralli, M., Rova, U., Christakopoulos, P. (2017) Optimized synthesis of novel prenylferulate performed by feruloylesterases from *Myceliophthora thermophila* in microemulsions. Appl. Microbiol. Biotechnol. 101, 3213-3226.

Metwally, K., Pratsinis, H., Kletsas, D. (2017). Novel 2,4- thiazolidinediones: Synthesis, *in vitro* cytotoxic activity, and mechanistic investigation. Eur. J. Med. Chem. 133, 340-350.

Souli, M.P., Klonos, P., Fragopoulou, A.F., Mavragani, I.V., Pateras, I.S., Kostomitsopoulos, N., Margaritis, L.H., Zoumpoulis, P., Kaklamanis, L., Kletsas, D., Gorgoulis, V.G., Kyritsis, A., Pissis, P., Georgakilas, A.G. (2017). Applying broadband dielectric spectroscopy (BDS) for the biophysical characterization of mammalian tissues under a variety of cellular stresses. Int. J. Mol. Sci. 18, 838.

Ågren, M.S., Danielsen, P.L., Gottrup, F., Kletsas, D., Eming, S.A., Volk, S., Gould, L. (2017). From bed to bench: 7th Joint meeting of European Tissue Repair Society (ETRS) with the Wound Healing Society (WHS) and the 25th Annual Meeting of ETRS in Copenhagen, Denmark. Wound Repair Regen. 25, 341-346.

Santarmaki, V., Kourkoutas, Y., Zoumpopoulou, G., Mavrogonatou, E., Kiourtzidis, M., Chorianopoulos, N., Tassou, C., Tsakalidou, E., Simopoulos, C., Ypsilantis, P. (2017). Survival, intestinal mucosa adhesion and immunomodulatory potential of Lactobacillus plantarum strains. Curr. Microbiol. 74, 1061-1067.

Vamvakas*, S.-S., Mavrogonatou*, E., Kletsas, D. (2017). Human nucleus pulposus intervertebral disc cells becoming senescent by using different treatments exhibit a similar transcriptional profile of catabolic and inflammatory genes. Eur. Spine J. 26, 2063-2071 [* *equal contribution*].

Tenta, R., Fragopoulou, E., Tsoukala, M., Xanthopoulou, M., Skyrianou, M., Pratsinis, H., Kletsas, D. (2017).Antiproliferative effects of red and white wine extracts in PC-3 prostate cancer cells. Nutr. Cancer 69, 952-961.

Havaki, S., Vlachou, V., Zampetidis, C.P., Selemenakis, P., Kotsinas, A., Mavrogonatou, E., Rizou, S.V., Kyrodimos, E., Evangelou, K., Kletsas, D., Giatromanolaki, A., Gorgoulis, V.G. (2017). Monitoring autophagy immunohistochemically and ultrastructurally during human head and neck carcinogenesis. Relationship with the DNA damage response pathway. Int. J. Mol. Sci. 18, E1920.

Metwally, K., Pratsinis, H., Kletsas, D., Quattrini, L., Coviello, V., Motta, C., El-Rashedy, A.A., Soliman, M.E. (2017). Novel quinazolinone-based 2,4-thiazolidinedione-3-acetic acid derivatives as potent aldose reductase inhibitors. Future Med. Chem. 9, 2147-2166.

El-Sayed, S., Metwally, K., El-Shanawani, A.A., Abdel-Aziz, L.M., Pratsinis, H., Kletsas, D. (2017). Synthesis and anticancer activity of novel quinazolinone-based rhodanines. Chem. Cent. J. 11, 102.

Krokidis, M.G., Terzidis, M.A., Efthimiadou, E., Zervou, S.K., Kordas, G., Papadopoulos, K., Hiskia, A., Kletsas, D., Chatgilialoglu, C. (2017). Purine 5',8-cyclo-2'-deoxynucleoside lesions: formation by radical stress and repair in human breast epithelial cancer cells. Free Radic. Res. 51, 470-482.

Georgalaki, M., Zoumpopoulou, G., Mavrogonatou, E., Van Driessche, G., Alexandraki, V., Anastasiou, R., Papadelli, M., Kazou, M., Manolopoulou, E., Kletsas, D., Devreese, B., Papadimitriou, K., Tsakalidou, E. (2017). Evaluation of the antihypertensive angiotensin-converting enzyme inhibitory (ACE-I) activity and other probiotic properties of lactic acid bacteria isolated from traditional Greek dairy products. Int. Dairy J. 75, 10-21.

Articles in Press

Baltzis, D., Meimeti, E., Grammatikopoulou, M.G., Roustit, M., Mavrogonatou, E., Kletsas, D., Efraimidou, S., Manes, C., Nikolouzakis, T.K., Tsiaoussis, J., Tsatsakis, A.M., Spandidos, D.A., Trakatelli, C.-M., Drakoulis, N. (2018). Assessment of telomerase activity in leukocytes of type 2 diabetes mellitus patients having or not foot ulcer: Possible correlation with other clinical parameters. Exp. Ther. Med. 15, 3420-3424. (IF: 1,410)

Apostolou, K.G., Papanikolaou, I.G., Katselis, C., Feretis, T., Kletsas, D., Konstadoulakis, M.M., Lymperi, M., Saetta, A.A., Tsikalakis, S., Agrogiannis, G., Patsouris, E., Zografos, G.C., Papalois, A.E. (2018). Undifferentiated Adipose Tissue Stem Cell Transplantation Promotes Hepatic Regeneration, Ameliorates Histopathologic Damage of the Liver, and Upregulates the Expression of Liver Regeneration- and Liver-Specific Genes in a Rat Model of Partial Hepatectomy. Stem Cells Int. 2018, 1393607. (IF: 3,989)

Antonopoulou, I., Papadopoulou, A., Iancu, L., Cerullo, G., Ralli, M., Jütten, P., Piechot, A., Faraco, V., Kletsas, D., Rovaa, U., Christakopoulos, P. (2018). Optimization of enzymatic synthesis of l-arabinose ferulate catalyzed by feruloylesterases from *Myceliophthora thermophila* in detergentless microemulsions and assessment of its antioxidant and cytotoxicity activities. Process Biochem. 65, 100-108. (IF: 2,616)

Mavrogonatou, E., Pratsinis, H., Papadopoulou, A., Karamanos, N.K., Kletsas, D. (2017). Extracellular matrix alterations in senescent cells and their significance in tissue homeostasis. Matrix Biol. (in press). (IF: 8,136)

Zoumpopoulou, G., Tzouvanou, A., Mavrogonatou, E., Alexandraki, V., Georgalaki, M., Anastasiou, R., Papadelli, M., Manolopoulou, E., Kazou, M., Kletsas, D., Papadimitriou, K., Tsakalidou, E. (2017). Probiotic Features of Lactic Acid Bacteria Isolated from a Diverse Pool of Traditional Greek Dairy Products Regarding Specific Strain-Host Interactions. Probiotics Antimicrob. Proteins 10, 313-322. (IF: 2,345)

Mavrogonatou, E., Konstantinou, A., Kletsas, D. (2017) Long-term exposure to TNF-α leads human skin fibroblasts to a p38 MAPK- and ROS-mediated premature senescence. Biogerontology 19, 237-249. (IF: 3,702)

Bonatsou, S., Karamouza, M., Zoumpopoulou, G., Mavrogonatou, E., Kletsas, D., Papadimitriou, K., Tsakalidou, E., Nychas, G.E., Panagou, E.Z. (2018) Evaluating the probiotic potential and technological characteristics of yeasts implicated in cv. Kalamata natural black olive fermentation. Int. J. Food Microbiol. 271, 48-59. (IF: 3,451)

Crespo, I., Giménez, J., Porté, S., Cousido-Siah, A., Mitschler, A., Podjarny, A., Pratsinis, H., Kletsas, D., Parés, X., Ruiz, F.X., Metwally, K., Farrés, J. (2018) Design, synthesis, structure-activity

relationships and X-ray structural studies of novel 1-oxo-pyrimido[4,5-c]quinoline-2-acetic acid derivatives as selective and potent inhibitors of human aldose reductase. Eur. J. Med. Chem. 152, 160-174. (IF: 4,816)

Al Naqbi S.R., Pratsinis H., Kletsas D., Eliades T., Athanasiou A.E. (2018). Cytotoxicity and estrogenicity of Vivera® retainers. J. Contemp. Dent.Pract. (in press). (IF: -)

Theochari I., Papadimitriou V., Papahatjis D., Assimomytis N., Pappou E., Pratsinis H., Xenakis A., Pletsa V.(2018). Oil-in-water microemulsions as hosts for benzothiophene-based cytotoxic compounds: an effective combination. Biomimetics (in press). (IF: -)

Pratsinis, H., Mavrogonatou, E., Kletsas, D. (2018). Scarless wound healing: From development to senescence. Adv. Drug Deliv. Rev. (in press) (IF: 13,660)

Hiebert P., Wietecha M.S., Cangkrama M., Haertel E., Mavrogonatou E., Stumpe M., Steenbock H., Grossi S., Beer H.D., Angel P., Brinckmann J., Kletsas D., Dengjel J., Werner S. (2018). Nrf2-mediated fibroblast reprogramming drives cellular senescence by targeting the matrisome. Dev Cell. 46,145-161.e10. (IF: 9,616)

Articles in Books and Conference Proceedings

Pratsinis, H., Mavrogonatou, E., Kletsas, D. TGF-β in development and ageing. In "Hormones in Ageing and Longevity" (S. Rattan, and R. Sharma, eds.) pp. 127-148, Springer-Verlag Berlin Heidelberg, 2017.

Basu, A., Singh, K., Kletsas, D., Schumacher, B., Scharffetter-Kochanek, K. (2017). UVA irradiation of Senescence fibroblasts epigenetically unlock anti-apoptotic GDF15 expression via interleukin-6 mediated promoter demethylation in melanoma cells. Exp. Dermatol. 26, E77.

Presentations at Scientific Conferences

D. Kletsas (2017). Irradiadion-mediated premature senescence of stromal fibroblasts: implications in tumor development. 7 Lakes Proteoglycans conference, September 10-14, 2017, Varese, Italy (invited speaker).

D. Kletsas (2017). Senescent human stromal fibroblasts after exposure to ionizing radiation have an altered proteoglycan expression facilitating tumour progression. The IUBMB Focused Meeting on "Molecular aspects of Aging and Longevity", October 16-19, 2017, Athens, Greece (invited speaker).

D. Kletsas (2017). Cellular Senescence: Implications and Interventions. OPTIBIOCAT Final Conference "Mining enzymes for green products", November 7, 2017, Rimini, Italy (invited speaker).

D. Kletsas (2017). Cellular Senescence: Implications and Interventions. RADIOMAG TRAINING SCHOOL, "Multifunctional Nanoparticles for Magnetic Hyperthermia: and Indirect Radiation Therapy", November 21-24, 2017, Athens, Greece (invited speaker).

A. Papadopoulou, E. Mavrogonatou, E. Liakou, H. Pratsinis, P. Panagiotou, V. Gorgoulis, N. Karamanos, D. Kletsas (2017). Senescent human breast fibroblasts after exposure to ionizing radiation have an altered proteoglycan expression facilitating tumor progression. The International Cell Senescence Association (ICSA) Conference, May 16-19, 2017, Paris, France.

A. Papadopoulou, E. Liakou, E. Mavrogonatou, H. Pratsinis, P. Panayotou, V. Gorgoulis, N. Karamanos, D. Kletsas (2017). Altered metalloprotease and proteoglycan expression in senescent human breast stromal fibroblasts: implications in tumour progression. 6th FEBS Advanced Lecture Course "Matrix Pathobiology, Signaling and Molecular Targets", May 25-30, 2017, Spetses, Greece.

H. Pratsinis, A. Papadopoulou, C. Neidlinger-Wilke, M. Brayda-Bruno, H.-J. Wilke, D. Kletsas (2017). Cyclic tensile stress stimulates mitogen-activated protein kinases in human annulus fibrosus cells inducing the expression of proinflammatory genes. 6th FEBS Advanced Lecture Course "Matrix Pathobiology, Signaling and Molecular Targets", May 25-30, 2017, Spetses, Greece.

S.S. Vamvakas, E. Mavrogonatou, D. Kletsas (2017). Different types of senescence lead to a similar transcriptional regulation of catabolic and inflammatory genes in human intervertebral disc cells. The 44th ISSLS (International Society for the Study of the Lumbar Spine) Annual Meeting, May 29-June 2, 2017, Athens, Greece.

A. Kouroumalis, E. Mavrogonatou, H. Pratsinis, O.D. Savvidou, P.J. Papagelopoulos, D. Kletsas (2017). The effect of the intervertebral disc environment on the specific phenotype of senescent nucleus pulposus cells. The 44th ISSLS (International Society for the Study of the Lumbar Spine) Annual Meeting, May 29-June 2, 2017, Athens, Greece.

H. Pratsinis, A. Papadopoulou, C. Neidlinger-Wilke, M. Brayda-Bruno, H.-J. Wilke, D. Kletsas (2017). Stimulation of mitogen-activated protein kinases by cyclic tensile stress in human annulus fibrosus cells induces the expression of pro-inflammatory genes. The 44th ISSLS (International Society for the Study of the Lumbar Spine) Annual Meeting, May 29-June 2, 2017, Athens, Greece.

D. Kletsas (2017). Biomedical Research in NCSR "Demokritos". 3rd conference of the Hellenic Society of Pharmaceutical Medicine "Biomedical Research: Targeting Innovation", June 16-17, 2017, Athens, Greece (invited speaker).

D. Kletsas (2017). Life sciences in Greece of the economic crisis. 4th Scientific Forum "Life Sciences and Cancer: From Prevention to Treatment", October 13-14, 2017, Athens, Greece (invited speaker).

D. Kletsas (2017). Genotoxic stresses and cell senescence. Thematic Meeting of the Hellenic Society of Biochemistry and Molecular Biology "Biochemistry and Health: From the Cell to Therapy" Faculty of Health Sciences of the University of Thessaly, May 5, 2017, Larissa, Greece (invited speaker).

M.G. Krokidis, M.A. Terzidis, E. Efthimiadou, S.-K.Zervou, E. Mavrogonatou, K. Papadopoulos, A. Hiskia, D. Kletsas, C. Chatgilialoglu (2017). Purine 5',8-cyclo-2'-deoxynucleoside lesions: formation by radical stress and repair in human breast epithelial cancer cells. 68th Congress of the Hellenic Society of Biochemistry and Molecular Biology, November 10-12, 2017, Athens, Greece.

A. Kouroumalis, E. Mavrogonatou, H. Pratsinis, O.D. Savvidou, P.J. Papagelopoulos, D. Kletsas (2017). The phenotype of senescent nucleus pulposus cells is retained under the harsh physicochemical conditions of the intervertebral disc environment. 68th Congress of the Hellenic Society of Biochemistry and Molecular Biology, November 10-12, 2017, Athens, Greece.

E. Mavrogonatou, A. Konstantinou, D. Kletsas (2017). TNF-α-induced premature senescence of human skin fibroblasts *in vitro* is p38 MAPK- and ROS-mediated. 68th Congress of the Hellenic Society of Biochemistry and Molecular Biology, November 10-12, 2017, Athens, Greece.

E. Mavrogonatou, A. Papadopoulou, H. Pratsinis, E.Liakou, S. Rizou, K. Evangelou, P.N. Panagiotou, N.K. Karamanos, V.G. Gorgoulis, D. Kletsas (2017). Ionizing radiation-induced senescent human breast stromal fibroblasts display alterations in metalloprotease and proteoglycan expression creating a permissive environment for tumor growth. 68th Congress of the Hellenic Society of Biochemistry and Molecular Biology, November 10-12, 2017, Athens, Greece.

E. Roupou, I. Chatziandreou, M. Michelli, N.V. Michalopoulos, H. Pratsinis, S. Tsikalakis, E. Patsouris, A.A. Saetta (2017). Expression of TNF-related apoptosis-inducing ligand (TRAIL) apoptotic pathway in breast carcinogenesis. 68th Congress of the Hellenic Society of Biochemistry and Molecular Biology, November 10-12, 2017, Athens, Greece.

D. Manou, P. Bouris, D. Kletsas, T.M. Reine, S.O. Kolset, N.K. Karamanos, A.D. Theocharis (2017).The emerging role of serglycin as a regulator of glioblastoma cell aggressiveness. 68th Congress of the Hellenic Society of Biochemistry and Molecular Biology, November 10-12, 2017, Athens, Greece.

H. Pratsinis, K. Metwally, D. Kletsas (2017). Synthesis and *in vitro* studies of novel 2,4-thiazolidinediones. 68th Congress of the Hellenic Society of Biochemistry and Molecular Biology, November 10-12, 2017, Athens, Greece.

A. Papadopoulou, A. Kanioura, P. Argitis, S. Kakabakos, D. Kletsas (2017). Changes in cell shape is not the cause of functional alterations in senescent cells. 68th Congress of the Hellenic Society of Biochemistry and Molecular Biology, November 10-12, 2017, Athens, Greece.

Educational Activities

Supervision of the Ph.D. theses of Eleni Liakou, Maria Angelopoulou and Anastasios Kouroumalis (D. Kletsas)

Supervision of the theses for the acquisition of a Master's degree of Angeliki Konstantinou, Olga Tsourou, Georgia Chaldaiopoulou, Despoina Nikopoulou and Stefania-Diana Grammatikaki (D. Kletsas)

"Cell senescence: the Janus' s faces of tissue homeostasis" Open Educational Program "Molecular Medicine", Medical School of the University of Thessaly, 26 January 2017, Larissa, 50 students) (D. Kletsas)

"Cell senescence and tissue homeostasis", NCSR "Demokritos" Summer School, 1 hour, 100 students (D. Kletsas)

"*In vitro* studies of natural and synthetic bioactive products", NCSR "Demokritos" Summer School, 1 hour, 100 students (H. Pratsinis)

"Cell senescence and carcinogenesis" Lecture in the framework of the class entitled "Thoracic oncology", Medical School of the University of Athens, 1 hour, 50 students (D. Kletsas)

"Cell senescence and tissue homeostasis" Post-graduate Master's Degree in Physiology, Medical School of the University of Athens, 2 hours, 30 students (D. Kletsas)

"Cell proliferation and tissue homeostasis. Growth factors: Structure, receptors and signal transduction. Cell senescence and tissue homeostasis. Methodologies for the study of cell proliferation", Post-graduate Master's Degree "Applications of Biology in Medicine", Department of Biology of the University of Athens, 6 hours, 20 students (D. Kletsas, H. Pratsinis and E. Mavrogonatou)

"Cell senescence", Post-graduate Master's Degree "Clinical Chemistry", Department of Chemistry of the University of Athens, 2 hours, 6 students (H. Pratsinis)

"Cell systems in the research of carcinogenesis" Post-graduate Master's Degree "Neoplastic Disease in Humans: Diagnosis, Modern Treatment and Research", Medical School of the University of Athens, 2 hours, 20 students (H. Pratsinis)

Member of examination committees for Ph.D. and MSc theses:
Nikolaos G. Margetis, Ph.D. thesis, "Study of K-RAS mutations at all stages of colon cancer development" (Medical School, University of Athens) (D. Kletsas)

Mohamed Hosney Abdel Naby Hassan, Ph.D. thesis, "Studying the role of Leptin in breast cancer sub-types" (Zoology Department, Faculty of Science, Cairo University) (D. Kletsas)

Angeliki Konstantinou concluded her M.Sc. thesis entitled "Comparative study of the regulation of fibroblast cells' proliferation and senescence after exposure to oxidative stress and cytokines" in the framework of the Master's Degree Program of the Biology Department of the University of Athens "Clinical Biochemistry-Molecular Diagnosis". The thesis was unanimously accepted and awarded the degree "Excellent" (Scientific Supervisor D. Kletsas)

Olga Tsourou concluded her M.Sc. thesis entitled "Study of the effect of bacterial toxins on the physiology of human dermal fibroblasts" in the framework of the Master's Degree Program of the Medical School of the University of Athens "Molecular and Applied Physiology". The thesis was unanimously accepted and awarded the degree "Excellent" (Scientific Supervisor D. Kletsas)

Georgia Chaldaiopoulou concluded her M.Sc. thesis entitled "The role of cytokines in the aging of intervertebral disc" in the framework of the Master's Degree Program of the Biology Department of the University of Athens "Applications of Biology in Medicine". The thesis was unanimously accepted and awarded the degree "Excellent" (Scientific Supervisor D. Kletsas)

Despoina Nikopoulou concluded her M.Sc. thesis entitled "Study of the putative healing effect of extracts of the marine arthropod *Ceratothoaoestroides*" in the framework of the Master's Degree Program of the Pharmacy Department of the University of Athens "Cosmetology-Dermatopharmacology". The thesis was unanimously accepted and awarded the degree "Excellent" (Scientific Supervisor D. Kletsas)

Stefania-Diana Grammatikaki concluded her M.Sc. thesis entitled "Peptides with possible healing action" in the framework of the Master's Degree Program of the Pharmacy Department of the University of Athens "Cosmetology-Dermatopharmacology". The thesis was unanimously accepted and awarded the degree "Excellent" (Scientific Supervisor D. Kletsas)

Other Scientific Activities

Participation in Greek and international scientific bodies and organizations:

President of the Hellenic Society for Biochemistry and Molecular Biology (2014-2017) (D. Kletsas)

Member (Secretary General) of the Research Club for Connective Tissue and Matrix Biology of the Hellenic Society for Biochemistry and Molecular Biology (D. Kletsas)

Member of the Attica Region Research and Innovation Council (PSEK) (D. Kletsas)

Secretary of the Biology Section (Europe) of the International Association of Gerontology and Geriatrics (IAGG) (D. Kletsas)

Member of the Committee for the election of an Associate Professor of "Cell Biology" in the University of Thessaloniki (D. Kletsas)

Participation in editorial boards of scientific journals:
Editorial board member of the scientific journals "Biogerontology", "Mechanisms of Ageing and Development", "Experimental Gerontology", "European Spine Journal", "PLoS ONE", "Fibrogenesis and Tissue Repair", "Open Longevity Science", "Open Spine Journal" and "Journal of Dental Biomechanics" (D. Kletsas)

Organization of scientific conferences or participation in organizing committees of conferences:
6th FEBS Advanced Lecture Course "Matrix Pathobiology, Signaling and Molecular Targets", May 25-30, 2017, Spetses, Greece. Member of the Scientific Committee (D. Kletsas)

44th Annual Meeting of the International Society for the study of the Lumbar Spine (ISSLS) May 29-June 2 2017, Athens. President of the Organizing Committee (Co-organization with Dr. Dino Samartzis) (D. Kletsas)

7 Lakes Proteoglycans Conference, 10-14 September 2017, Varese, Italy. Member of the Scientific Committee (D. Kletsas)

5th Hellenic Forum for Science, Technology and Innovation, 5-7 July 2017, Athens. Organization of the Workshop "Ageing and Age-Related Diseases" (D. Kletsas)

Participation in committees for the reviewing of research proposals:
Research Grants Council of Hong-Kong (D. Kletsas)

Research projects of the Hellenic Foundation for Research and Innovation (HFRI) for the support of post-doctoral researchers (D. Kletsas, H. Pratsinis)

Reviewing of manuscripts in scientific journals:
Matrix Biology, Experimental Gerontology, Scientific Reports, Aging Cell, AGE, PLoS ONE, Wound Repair and Regeneration Molecular Pain, Mechanisms of Ageing and Development, Acta

Odontologica Scandinavica, European Spine Journal, Journal of Cellular Physiology, Computational Biology and Chemistry, Dental Materials, Genes & Comput. Endocrin., Journal of Cellular and Molecular Medicine, Osteoarthritis and Cartilage, Biogerontology (D. Kletsas)

BioMed Research International, Molecules (2), Pharmacological Reports, PLoS ONE (3), Wound Repair and Regeneration (2) (H. Pratsinis)

PLoS ONE, American Journal of Orthodontics & Dentofacial Orthopedics (6), iMedPub (2), Evidence-Based Complementary and Alternative Medicine, Biomedicine & Pharmacotherapy (3), Journal of Clinical, Medical and Experimental Images, BAOJ Pathology, International Journal of Molecular Sciences (2), Materials (2), Nutrients, Toxics (E. Mavrogonatou)

Other lectures or presentations of scientific content:
H. Pratsinis (2017). Cellular senescence and its role *in vivo*. Educational Seminar "Current developments and trends in natural sciences" organized by the Administration of Secondary Education of Athens, February 22, 2017, Athens, Greece (invited speaker)

Other Activities in the Institute of Biosciences & Applications

D. Kletsas:
Director of IBA & Member of the Administrative Board of NCSR "Demokritos"
Supervisor of the Ethics Committee of NCSR "Demokritos"
Member of the Hygiene and Security Committee of NCSR "Demokritos"
Scientific Supervisor of the Experimental Animal Colony
Supervisor of the Fluorescence Activated Cell Sorting Facility

H. Pratsinis:
Responsible for the conducted tours in the Institute of Biosciences and Applications of NCSR "Demokritos"

Impact Factors:
D. Kletsas (for 14 publications): 46,935
H. Pratsinis (for 5 publications): 16,147

Citations 2017 (without self-citations):
D. Kletsas: 605
H. Pratsinis: 173

Total Citations 2013-2017 (without self-citations):
D. Kletsas: 2780
H. Pratsinis: 794

h-factor:
D. Kletsas: 39 (Scopus), 47 (Google Scholar)
H. Pratsinis: 27 (Scopus), 29 (Google Scholar)

Current External Funding

Project entitled *Matrix glycans as multifunctional pathogenesis factors and therapeutic targets in cancer (GLYCANC),* EU-funded (*MSCA-RISE-2014)* and Scientific Supervisor Dr. D. Kletsas.
Duration: 2015-2019
Total program funding: 567.000 €
Funding of the lab for 2017: 0 €.

Project entitled *Effect of TNF-α and glucose on the response of human PDL fibroblasts to mechanical stretching*, funded by the University of Zurich and Scientific Supervisor Dr. D. Kletsas.
Duration: 2016-2018
Total program funding: 14.928,34 €
Funding of the lab for 2017: 8.000€.

Current External Funding IBA

Project entitled *SANITURA (TARGET IDENTIFICATION AND DEVELOPMENT OF NOVEL APPROACHES FOR HEALTH AND ENVIRONMENTAL APPLICATIONS), funded by the General Secretariat for Research and Technology* (*Action for the Strategic Development on the Research and Technological Sectors, Operational Programme "Competitiveness, Entrepreneurship and Innovation", NSRF 2014-2020)* and Scientific Supervisor Dr. D. Kletsas.
Duration: 2017-2020
Total program funding: 740.000 €
Funding of the IBA for 2017: 74.000 €.

Project entitled *OPENSCREEN-GR: An Open-Access Research Infrastructure of Chemical Biology and Target-Based Screening Technologies for Human and Animal Health, Agriculture and the Environment*, funded by the General Secretariat for Research and Technology (*Action "Reinforcement of the Research and Innovation Infrastructure", Operational Programme "Competitiveness, Entrepreneurship and Innovation", NSRF 2014-2020)* and Scientific Supervisor Dr. D. Kletsas (since September 2017).
Duration: 2017-2020
Total program funding: 899.600 €
Funding of the IBA for 2017: 0 €.

Project entitled *BIOIMAGING-GR: A Greek Research Infrastructure for visualizing and monitoring fundamental biological processes*, funded by the General Secretariat for Research and Technology (*Action "Reinforcement of the Research and Innovation Infrastructure", Operational Programme "Competitiveness, Entrepreneurship and Innovation", NSRF 2014-2020)* and Scientific Supervisor Dr. D. Kletsas.
Duration: 2017-2020
Total program funding: 211.250 €
Funding of the IBA for 2017: 0 €.

Research Group: Nuclear Proteins and Chromatin Function

Research Staff
Thomae Sourlingas, Senior Researcher
Kalliope Sekeri, Collaborating Former Scientific Scientist
Anastasia- Georgia Dedemadi, Undergraduate Student

Research Interests

Basic factors that affect chromatin remodeling and thus gene expression and cellular function are the histone subtype constitution of nucleosomes and histone post translational epigenetic modifications. Changes in the subtype constitution and in histone modifications can active or inactive genes that are involved in biological processes and pathological states. Based on the aforementioned, the lab's present research interests are focused on:

1. Cancer: We are studying changes in the histone subtype constitution and in histone post translational modifications in age-related cancers, as well as in other cancer cell types. Observed differences in histone subtype levels or differences in epigenetic modifications of these cancer cell types with respect to normal controls may possibly be used as biomarkers for the specific cancer cell type or as targets for future intervention. Within this framework, the efficiency of histone deascetylase inhibitors (HDACIs) as proapoptotic anticancer agents will also be studied.
2. Aging/Senescence: We are studying the relationship amongst the expression profiles of the histone subtypes and their epigenetic modifications during aging and the role that histone epigenetic modifications play in gene-expression changes of age-related genes.
3. Psychotic Disorders: We are investigating how changes in the chromatin constitution and the expression profiles of the histone H1 subtypes and histone post translational epigenetic modifications are associated with observed chromatin remodeling events (conformational changes) in chromatin of human peripheral blood leucocytes from individuals with psychiatric disorders.
4. Chromatin and the Mammalian Biological Clock: We are investigating the role of chromatin conformational changes that are brought about by changes in the levels of histone post translational epigenetic modifications, such as histone acetylation and methylation in the regulation of the mammalian biological clock.

2017 Findings

Investigation of the effect of sodium butyrate (HDACI) on the levels of histone H1 subtypes and histone post translational epigenetic modifications in leukemic cell types

In the present work, we studied the protein and mRNA levels of three H1 subtypes (H1.0, H1.3, H1.5) and three epigenetic modifications of histone H3 (acetylation, trimethylation dimethylation) in the absence and presence of sodium butyrate in three leukemic cell types (K562, NB4, Molt4) in comparison with normal lymphocytes. The results showed: (1) H1.0 levels increase after sodium butyrate treatment in the NB4 and Molt4 cell lines, which also have the highest mortality rates in the presence of this agent. (2) The histone acetylation levels increase in all cell lines in the presence of butyrate. The highest acetylation levels were observed in the NB4 cells, where increases in the trimethylation and dimethylation levels were also observed. From these results it can be concluded that certain subtypes and/or histone modifications may be useful biomarkers for the ascertainment of the degree of sensitivity of cancer cell types to the effects of HDACIs. This work was part of the pre graduate diplome thesis of Anastasia-Georgia Dedemadi (BS).

Investigation of the histone H1 subtype levels in human peripheral blood leucocytes of individuals with schizophrenia

Given that data has shown that the H1 histones play a significant role in chromatin conformational changes, we chose to investigate the protein levels of specific H1 subtypes. We observed that there is a significant decrease in the H1.0 subtype in the leucocytes of patients as compared to controls, a result that indicates a decrease in inactive, condensed chromatin in the schizophrenic patients.

The decrease of H1.0 suggests that there may be a conformational reorganization of hetero- and euchromatin regions in the leucocytes of patients as compared to controls. This study constitutes a significant first step in the analysis of the changes of the H1 subtypes in this pathological condition, since for the first time an H1 subtype, H1.0, is associated with schizophrenia and the conformational changes of chromatin that may take place in the leucocytes of individuals with psychotic disorders. Part of this project was in collaboration with Dr. A. Prombona and also part of the Masters' thesis diplome work of Christina Panagiotopoulou (MSc).

Presentations at Scientific Conferences

A-G. Dedemadi, T. G. Sourlingas (2017). Effect of the histone deacetylase inhibitor, sodium butyrate on histone H1 subtype levels and histone epigenetic modifications in human leukemic cells as compared to normal lymphocytes. 68th Panhellenic Conference of the Hellenic Society of Biochemistry and Molecular Biology, 10-12 November, 2017, Athens.

A-G. Dedemadi, T. G. Sourlingas (2017). Effect of the histone deacetylase inhibitor, sodium butyrate on histone H1 subtype levels and histone epigenetic modifications in human leukemic cells as compared to normal lymphocytes. 6th Workshop of Young Scientists of HSBMB, November 9, 2017, Athens.

Educational Activities

Seminar: "Cell Cycle: Checkpoints and Consequences for Normal Cellular Function when Cell Cycle Progress Dysfunctions" within the framework of the course "Ageing and Age-Related Diseases" of the Graduate Masters' Program: Applications of Biology in Medicine, Dept. of Biology and Medical School of the University of Athens (6 hours, 20 students).

Supervision of the pre-graduate diplome thesis work of Anastasia-Georgia Dedemadi. Title of thesis work: "Study of the effect of sodium butyrate on histone H1 subtype levels and on histone epigenetic modifications in the leukemic cell lines K562, NB4 and Molt4 as compared to normal peripheral blood lymphocyte".

Other Activities for the Institute of Biosciences & Applications

Responsible for the organization of bibliographic seminars of the graduate students (doctoral candidates) of IBA.

Member of the IB-A committee for the receipt of new materials and services and for the examination and characterization of materials unsuitable for use and to be destroyed that have been acquired by funds from the Demokritos budget.

Other Scientific Activities

*R*eviewer of scientific publications: Biochemistry and Cell Biology, Apoptosis, Leukemia Research, Life Sciences, Acta BB Sinica, J Pharmaceutical Sci Exp Pharmacology

Scientific collaborations:

- With Dr. A. Prombona (Laboratory of Chronobiology), Institute of Biosciences and Applications, NCSR "D". This research collaboration involves the study of the effects of histone modifications on genes that regulate the mammalian biological clock (circadian rhythm) and the potential consequences to cellular function and carcinogenesis.
- With the Neurobiology Research Institute of the Th. Th. Cozzika Foundation (Dr. Margarita Chrysanthou-Piterou). Within the framework of this program we are studying changes in the expression levels of histone genes in leucocytes of patients with bipolar disorder and schizophrenia.
- With the Assistant Professor of Psychiatry K. Kollias, University of Athens, Medical School, 1st Department of Psychiatry, Eginition Hospital.
- With the Professor of Psychiatry V. Kontaxakis, University of Athens, Medical School, 1st Department of Psychiatry, Eginition Hospital.

- With the Professor I. Angelopoulos, University of Athens, Medical School, 1st Department of Psychiatry, Eginition Hospital.

Citations 2017 (without self-citations): 26

Total Citations 2013-2017 (without self-citations): 126

h-factor: 10 (Scopus), 12 (Google Scholar)

Research Group: Cell & Matrix Biochemistry/Pathobiology

Research Staff
Angeliki Chroni, Research Director
Athina Tzinia, Senior Researcher
Paraskevi Kitsiou, Senior Researcher
Garyfalia Drossopoulou, Researcher
Ioannis Dafnis, Postdoctoral Fellow
Ourania Trohatou, Postdoctoral Fellow
Archontia Kaminari, Graduate Student - *PhD obtained in 2017*
Christina Gkolfinopoulou, Graduate Student
Christina Mountaki, Collaborating Graduate Student - *MSc obtained in 2017*
Konstantina Katrini, Graduate Student *(MSc)*
Christianna Moutzouvi, Undergraduate Student
Annita Katopodi, Graduate Research Associate
Eleni Theofanidi, Graduate Research Associate
Nikolaos Giannakas, Technical Specialist

Research Interests

1. **Neurodegenerative Disorders:**

A) Study of cell survival mechanisms in age-related diseases like Alzheimer Disease and type II Diabetes; the role of MMP-9 in the insulin-dependent survival pathway in Alzheimer's disease
B) Analysis of the structure-function relationship of apoE4, the major risk factor for Alzheimer's disease, and its role in the mechanism of disease pathogenesis.

2. **Diabetes mellitus:**

A) Cross talk between nephrin and survival signaling pathways in mouse pancreatic insulin-producing beta cells (βTC-6 cells).
B) Effect of liraglutide on nephrin signaling and islet β-cell survival in db/db lepr−/− type 2 diabetic mice.
C) Kidney function: Regulation of gene expression and epigenetic mechanisms in glomerular podocytes.
D) Analysis of the insulin-mediated survival pathway in isolated rat glomeruli and animal modes of Type2 Diabetes. Role in prevention and/ or treatment of diabetic nephropathy.
E) Identification of lncRNA targets in renal podocytes as potential markers for Diabetic Nephropathy progression. Investigation of the mode of action of liraglutide on the process of regeneration of β-cells from mesenchymal stem cells (MSCs). Renoprotective role of VitaminD3 on glomerular kidney function, using animal models of Type2 Diabetes.

3. **Molecular mechanisms of dyslipidemias and atherosclerosis**

A) Elucidation of disorders of high density lipoprotein (HDL) metabolism that affect the HDL atheroprotective properties. Specific (dys)functions and compositional changes of HDL could be targeted as biomarkers for the assessment of cardiovascular risk and/or effects exerted by HDL modifying therapies.

B) Analysis of structure-function relationship of apoA-I and apoE and their role in atherosclerosis.

2017 Findings

1. **Neurodegenerative Disorders:**

A) Studying the role of MMP-9 in the insulin-dependent survival pathway in Alzheimer's disease it was shown that overexpression of MMP-9 prevents, at least in part, the impairment of the insulin survival pathway in vitro in primary hippocampal cell cultures of 5XFAD animals, as well as in vivo in

young animals of the same genotype. More specifically, MMP-9 is directly involved in inhibiting the formation of Aβ oligomers and hence reducing the rate of cellular apoptosis, whilst restoring the levels of neurotrophic factor BDNF.

B) ApoE isoforms were found to induce distinct significant changes in the organization of the membrane fatty acids of human neuroblastoma SK-N-SH cells, which predominantly influence membrane properties and peroxidation susceptibility. These findings may be related to the different effect of apoE isoforms in brain pathophysiological processes.

2. Diabetes mellitus:

A-B) In mouse pancreatic insulin-producing beta cells (βTC-6 cells). nephrin signaling promotes cell survival by inhibiting apoptosis. Immunohistochemical studies with nephrin and insulin in pancreatic islets of type 2 diabetic *(db/db lepr−/−)* mice revealed an *in vivo* reduction of both nephrin expression and islet size. Decreased islet size was attributed to increased β-cell apoptosis. However, treatment of *lepr−/−* diabetic animals with liraglutide resulted in a) re-establishment of both nephrin expression and islet size and b) inhibition of islet beta-cell apoptosis. The mechanism of action of liraglutide involves Akt activation which in turn promotes β-cell survival by inhibiting cell stress-induced apoptosis.

C-E) In diabetic nephropathy (DN), podocytes become structurally and functionally compromised. In our ex-vivo model, glomeruli exhibited high-glucose-mediated downregulation of podocalyxin, and nephrin, while vitaminD3 reversed the high glucose-induced decrease of nephrin and podocalyxin expression. Hyperglycemia impaired survival of cultured glomeruli. The implemented nephrin downregulation was reversed by vitaminD3 treatment, initiating Akt signal transduction and promoting glomerular survival. Our findings were further verified in vivo. In the STZ-diabetic animal model, vitaminD3 treatment resulted in significant amelioration of hyperglycemia and restoration of nephrin signaling, suggesting that vitaminD3 may provide molecular bases for protection against loss of the permselective renal barrier in DN.

3. Dyslipidemia and atherosclerosis

Heritable point mutations in apoA-I (the major protein component of HDL) are associated with low HDL cholesterol (HDLc) levels and/or increased risk of cardiovascular disease (CAD). However, a new mutation in apoA-I, V19L, was associated with increased HDLc and reduced CAD risk. Our analyses showed that the increased thermodynamic stability of apoA-I [V19L] in lipoprotein particles combined with increased SR-BI-mediated cholesterol efflux capacity could a) lead to increased HDLc levels and b) support a atheroprotective role for apoA-I[V19L], since the cholesterol efflux by SR-BI can protect the arterial wall macrophages from cholesterol accumulation.

Publications

Kostomoiri M, Fragkouli A, Sagnou M, Skaltsounis LA, Pelecanou M, Tsilibary EC, Tzinia AK. Bouras, K., Kopsidas, K., Bariotakis, M., Kitsiou, P., Kapodistria K., Agrogiannis, G., Vergados, I., Theodossiadis, P., Perrea, D. (2017). Effects of Dietary Supplementation with Sea Buckthorn (*Hippophae rhamnoides* L.) Seed Oil on an Experimental Model of Hypertensive Retinopathy in Wistar Rats. Biomed Hub 2 (DOI: 10.1159/000456704)

Kaminari A, Giannakas N, Tzinia A, Tsilibary EC. (2017). Overexpression of matrix metalloproteinase-9 (MMP-9) rescues insulin-mediated impairment in the 5XFAD model of Alzheimer's disease. Sci Rep.7 (1):683

Kavetsou E., Gkionis L., Galani G., Gkolfinopoulou C., Argyri L., Pontiki E., Chroni A., Hadjipavlou-Litina D. and Detsi A. Synthesis of prenyloxy coumarin analogues and evaluation of their antioxidant, lipoxygenase (LOX) inhibitory and cytotoxic activity. Med. Chem. Res., 26, 856–866 (2017)

Prasinou P., Dafnis I., Giacometti G., Ferreri C., Chroni A. and Chatgilialoglu C. Fatty acid-based lipidomics and membrane remodeling induced by apoE3 and apoE4 in human neuroblastoma cells. Biochim. Biophys. Acta, 1859, 1967-1973 (2017)

Trohatou O, Tsilibary EF, Charonis A, Iatrou C, Drossopoulou G. (2017). Vitamin D3 ameliorates podocyte injury through the nephrin signalling pathway. J Cell Mol Med. doi: 10.1111/jcmm.13180.

Articles in Press

Barbara Pijet, Marzena Stefaniuk, Agnieszka Kostrzewska, Photini-Effie Tsilibary, Athina Tzinia, Leszek Kaczmarek (2018). Increased MMP-9 activity promotes epileptogenesis after traumatic brain injury. Molecular Neurobiology (IF: 6.190)

Chroni A. and Kardassis D. (2018) HDL dysfunction caused by mutations in apoA-I and other genes that are critical for HDL biogenesis and remodelling. Curr. Med. Chem. (IF 3.249)

Hatziioanou D., Barkas G., Critselis E., Zoidakis J., Gakiopoulou H-H., Androutsou M-E., Drossopoulou G., Charonis A., Vlahakos D. (2018). Chloride Intracellular Channel 4 Overexpression in the Proximal Tubules of Kidneys from the Spontaneously Hypertensive Rat: Insight from Proteomic Analysis. Nephron (IF: 2.03)

Kaminari A, Tsilibary EC, Tzinia A (2018). A New Perspective in Utilizing MMP-9 as a Therapeutic Target for Alzheimer's Disease and Type 2 Diabetes Mellitus. J Alzheimers Dis. (IF: 3.73)

Kapodistria, K., Tsilibary, E., Kotsopoulou E., Moustardas, P., Kitsiou, P. (2018). Liraglutide, a human glucagon-like peptide-1 analogue, stimulates AKT-dependent survival signaling and inhibits pancreatic β-cell apoptosis. J. Cell. Mol. Med. 22 (6), 2970-2980 (IF: 4.499).

Dafnis I., Raftopoulou C., Mountaki C., Megalou E., Zannis V. I. and Chroni A. (2018) ApoE isoforms and carboxyl-terminal-truncated apoE4 forms affect neuronal BACE1 levels and Aβ production independently of their cholesterol efflux capacity. Biochem J. 31;475(10):1839-1859 (IF: 3.857)

Articles in Books and Conference Proceedings

Gkolfinopoulou C., Soukou F., Stratikos E. and Chroni A. Natural human apoA-I mutations L144R, A164S and L178P alter apoA-I and HDL structure and functionality. Atherosclerosis, 263:e95-e96 (2017).

Presentations at Scientific Conferences

Gkolfinopoulou C., Soukou F., Stratikos E. and Chroni A. Natural human apoA-I mutations L144R, A164S and L178P alter apoA-I and HDL structure and functionality. 85th European Atherosclerosis Society Congress, 23-26 April 2017, Prague, Czech Republic (moderated poster)

Dafnis I., Raftopoulou C., Megalou E. and Chroni A. Effect of apoE4 and apoE4 carboxyl-terminal truncations on BACE-1 levels and Aβ production in neuronal cells. "Lipids and Brain IV" conference. Lipids in Alzheimer's disease. 8-11 October 2017, Nancy, France (poster)

Chroni A. "HDL-cholesterol: reappraisal of its clinical significance." 7th Meeting of the working groups of the Hellenic Atherosclerosis Society, 1-2 December 2017, Athens (invited speaker)

Gkolfinopoulou C., Soukou F., Stratikos E. And Chroni A. Analysis of the effect of inherited mutations on human apolipoprotein A-I on the structure of the protein and atheroprotective functions of HDL. 20th Meeting of the Hellenic Society of Lipidology, Atherosclerosis and Vascular Disease, 2-4 November 2017, Athens (poster)

Gkolfinopoulou C. and Chroni A. Effect of a new apoA-I mutation associated with high HDL levels on protein structure and function. 68th Congress of the Hellenic Society of Biochemistry and Molecular Biology, 10-12 November 2017, Athens (oral presentation)

Mountaki C, Dafnis I and Chroni A. Role of apolipoprotein E isoforms in regulation of neuronal cholesterol efflux and amyloid-beta peptide generation. 68th Congress of the Hellenic Society of Biochemistry and Molecular Biology, 10-12 November 2017, Athens (poster)

Gkolfinopoulou C. and Chroni A. Effect of a new mutation in apolipoprotein A-I, associated with high levels of HDL, in the structure and functions of the protein. 7th Meeting of the working groups of the Hellenic Atherosclerosis Society, 1-2 December 2017, Athens (oral presentation)

Other Scientific Activities

A. Chroni:
Participation in Greek and international scientific bodies and organizations (except of the participation as a member in scientific societies and organizations):
Member of the Coordinating Committee of the Working Group "Study of Pathophysiology of Atherosclerosis" of the Hellenic Atherosclerosis Society

Organization of scientific meetings or participation in meeting organizing committees:
Member of the Organizing Committee of the 68th Congress of the Hellenic Society of Biochemistry and Molecular Biology, 10-12 November 2017, Athens

Participation in research panels of research proposals:
Evaluator of proposals submitted under the Call for "Support of Researchers with Emphasis to Young Researchers" under the code ΕΔΜΜ34 of the Operational Program "Human Resources Development, Education and Lifelong Learning" (NSRF 2014-2020)

Scientific publications reviewer:
A. Chroni: BBA - General Subjects, BBA - Molecular Basis of Disease, PLOS ONE, Computational and Structural Biotechnology Journal, Journal of Functional Foods
A. Tzinia: PLoS ONE, Cellular Physiology and Biochemistry, Neural Regeneration Research
P. Kitsiou: Current Diabetes Reviews, PLoS ONE, Recent Patents on Endocrine, Metabolic & Immune Drug Discovery
G. Drossopoulou: Current Diabetes Reviews, Journal of Nephrology, PLoS ONE, Nutrients, International Journal of Environmental Research and Public Health.

Other Distinctions and Awards

A. Chroni:
Best poster presentation award
Gkolfinopoulou C., Soukou F., Stratikos E. And Chroni A. Analysis of the effect of inherited mutations on human apolipoprotein A-I on the structure of the protein and atheroprotective functions of HDL. 20th Meeting of the Hellenic Society of Lipidology, Atherosclerosis and Vascular Disease, 2-4 November 2017, Athens

Educational Activities

Archontia Kaminari presented her doctoral thesis entitled "Study of the effect of metalloproteinase-9 (MMP-9) on the insulin-dependent survival pathway in Alzheimer's disease" at the Department of Biology of the University of Athens and received her Ph.D. with grade "Excellent"

Christina Mountaki presented her MSc thesis entitled "Role of apolipoprotein E isoforms in regulation of neuronal cholesterol efflux and amyloid-beta peptide generation" at the Department of Chemistry, University of Athens. Grade: Excellent

A. Chroni:
1) Visiting Professor at the Department of Chemistry, University of Athens.
Main Instructor of the undergraduate course "Biochemistry I" (6th semester), 26h of lectures, 180 students
2) Guest lecturer in graduate course "Clinical Chemistry II", Clinical Chemistry Graduate Program, Department of Chemistry, University of Athens
Title of lecture: "Lipids and apolipoproteins: from atherosclerosis to Alzheimer's disease" (2 h lecture – 5 students)
3) PhD supervisor of C. Gkolfinopoulou and C. Mountaki, MSc supervisor of C. Mountaki and K. Katrini and diploma thesis supervisor of C. Moutzouvi

4) Member of PhD Advisory Committee of C. Gkolfinopoulou and C. Mountaki at the Department of Chemistry, University of Athens and E. Valanti at the School of Medicine, University of Athens
5) Lecture entitled «"Good" cholesterol HDL: understanding its biological role and evaluation of its clinical use for diagnosis and treatment of human diseases», Summer School NCSR Demokritos, 3-14 July 2017, (1 h lecture, 250 students)
6) Presentation of "IBA Research Activities and Educational Opportunities", Summer School NCSR Demokritos, 3-14 July 2017, (30 min, 250 students)

G.Drossopoulou:
1) Lecture entitled "Age-Related Diseases: Can regenerative medicine contribute in therapeutic approaches?" Summer School NCSR Demokritos, 3-14 July 2017, (1 h lecture, 250 students)
2) Guest lecturer in graduate course "Molecular and Applied Physiology" Graduate Program Medical School, University of Athens «Regulation of Apoptosis in disease progression: Is it desirable or must be avoided?» October 2017 (3 hours lecture - 22 students)

Other Activities for the Institute of Biosciences & Applications

A. Chroni:
1) Member of the Scientific Board of IBA.
2) Person in charge for education issues in the Institute of Biosciences and Applications (IBA). Representative of IBA in the Education Committee of NCSR Demokritos.

Impact Factors (for 5 publications): 14,121

Citations 2017 (without self-citations): A. Chroni: 158, A. Tzinia: 71, P. Kitsiou: 25, G. Drossopoulou: 76. Total: 330

Total Citations 2013-2017 (without self-citations): A. Chroni: 761, A. Tzinia: 290, P. Kitsiou: 119, G. Drossopoulou: 337. Total: 1170

h-factor: A. Tzinia: 16 (Scopus), 19 (Google Scholar), P. Kitsiou: 9, A. Chroni: 21 (Scopus), 24 (Google Scholar) G. Drossopoulou: 13 (Scopus), 13 (Google Scholar)

Current External Funding

Project entitled *Prognostic value of HDL function in patients with acute ischemic stroke,* funded by Hellenic Atherosclerosis Society with Principal Investigator for NCSR "Demokritos"Dr. A. Chroni.
Duration: 1/10/2016-30/9/2018
Total funding (lab): €3.000
Funding of the lab for 2017: 0€

Project entitled entitled *Modulating neoantigen epitope generation for melanoma immunotherapy* funded by Harry J. Lloyd Charitable Trust with Principal Investigator for NCSR "Demokritos"Dr. E. Stratikos (INRASTES).
Duration: 2016-2018
Funding of the lab for 2017: 0€

Project entitled *Investigation of the mechanism of action of the carboxy-terminal deficient form of apoE4 apoE4[Δ(166-299)] in the pathogenesis of Alzheimer's disease* funded by the State Scholarships Foundation (Fellowships of Excellence for Postdoctoral Research - Siemens Program) with Postdoctoral fellow Dr. Ioannis Dafnis and Principal Investigator Dr. A. Chroni
Duration: 2016-2017
Funding of the lab for 2017: 30.000€

Project entitled *Podocyte and β-cell survival in diabetes mellitus: The role of Liraglutide* (Industrial Postdoc Researcher Program) funded by Stavros Niarchos Foundation/NCSR "Demokritos" and NOVO NORDISK HELLAS
Duration: 2017-2020

Funding of the lab for 2017: 27.650€

Project entitled *Nephroprotective role of VitaminD3,* funded by AENORASIS SA with Principal Investigator Dr. G. Drossopoulou
Duration: 2017-2020
Funding of the lab for 2017: 13.825€

Research Group: Environmental Mutagenesis -Carcinogenesis

Research Staff

Gerassimos Voutsinas, Research Director

Angeliki Delimitsou, Collaborating Graduate Student

Sokratis Avgeris, Research Technician

Research Interests

1. Identification and validation of drug targets for cancer therapy
2. Development and evaluation of biomarkers for diagnosis, prognosis and response to treatment in human diseases
3. Development of genetic testing protocols for molecular diagnosis of human genetic diseases

2017 Findings

1. Deep-proteome mapping of WM-266-4 human metastatic melanoma cells: From oncogenic addiction to druggable targets
2. Unraveling the human protein atlas of metastatic melanoma in the course of ultraviolet radiation-derived photo-therapy
3. Mutational analysis of TSC1 and TSC2 genes in Tuberous Sclerosis Complex patients from Greece

Publications

Konstantakou E.G., A.D. Velentzas, A.K. Anagnostopoulos, Z.I. Litou, O.A. Konstandi, A.F. Giannopoulou, E. Anastasiadou, G.E. Voutsinas, G.Th. Tsangaris, D.J. Stravopodis (2017) Deep-proteome mapping of WM-266-4 human metastatic melanoma cells: From oncogenic addiction to druggable targets, PLoS ONE 12(2): e0171512.

Konstantakou, E.G., A.D. Velentzas, A.K. Anagnostopoulos, A.F. Giannopoulou, E. Anastasiadou, I.S. Papassideri, G.E. Voutsinas, G.Th. Tsangaris, D.J. Stravopodis (2017) Unraveling the human protein atlas of metastatic melanoma in the course of ultraviolet radiation-derived photo-therapy, J Proteomics S1874-3919(17), 30395-0.

Avgeris, S., F. Fostira, A. Vagena, Y. Ninios, A. Delimitsou, R. Vodicka, R. Vrtel, S. Youroukos, D.J. Stravopodis, M. Vlassi, A. Astrinidis, D. Yannoukakos, G.E. Voutsinas (2017) Mutational analysis of TSC1 and TSC2 genes in Tuberous Sclerosis Complex patients from Greece, Sci Rep. 7(1):16697.

Presentations at Scientific Conferences

Giannopoulou A.F., E.G. Konstantakou, A.D. Velentzas, I.S. Papassideri, G.E. Voutsinas and D.J. Stravopodis (2017) The role of epithelial-to-mesenchymal transition (EMT) phenomenon in human cancer urothelium, 39th Meeting of the Hellenic Society of Biological Sciences, May 25-27, 2017, Lamia, Greece.

Educational Activities

3 Semester Courses: "Introduction to Molecular Biology", including 16 hours of practical laboratory exercises, American College of Greece (Deree), Aghia Paraskevi Attikis, Greece.

One Semester Course: "Environmental Health", American College of Greece (Deree), Aghia Paraskevi Attikis, Greece.

Lecture (3 hours): "Research on Rare Diseases", in the course for "Molecular Biology – Systemic and in silico approaches", in the frame of the Post-Graduate Specialization Diploma "Biological Applications in Medicine" of the Departments of Biology and Medicine of the National Kapodistrian University of Athens (NKUA), Athens, May 31, 2017.

Distinctions and Awards

Best Poster Prize:

Giannopoulou A.F., E.G. Konstantakou, A.D. Velentzas, I.S. Papassideri, G.E. Voutsinas and D.J. Stravopodis (2017) The role of epithelial-to-mesenchymal transition (EMT) phenomenon in human cancer urothelium, 39th Meeting of the Hellenic Society of Biological Sciences, May 25-27, 2017, Lamia, Greece.

Other Scientific Activities

Head of the Laboratory for "Molecular Diagnosis of Genetic Diseases" (E1609), rendering genetic testing services for Tuberous Sclerosis Complex and Neurofibromatosis type I.

Participation in Greek and International scientific bodies and organizations:

1. Reviewer of research articles for Molecular Carcinogenesis, FEBS Open Bio, European Spine Journal, Cancer Medicine, και Balkan Medical Journal.
2. Reviewer for the Union for International Cancer Control.
3. Reviewer of research proposals for the Swiss National Science Foundation.
4. Association of Medical Geneticists of Greece (SIGE).
5. Greek Alliance for Rare Diseases (PESPA) (Treasurer).
6. Greek Alliance for Rare Diseases (Member of the Scientific Committee).
7. Tuberous Sclerosis Association of Greece (EEOS) (Member of the Scientific Committee).

Other Activities for the Institute of Biosciences and Applications

1. In charge for the operation of ABI Prism 310 Genetic Analyzer (Applied Biosystems), Mx3000P QPCR system (Stratagene), Image Analysis System (Vilber Lourmat), LAS-4000 Luminescent Image Analyzer (Fuji-Film) and FLA-7000 Fluorescent Image Analyzing System (Fuji-Film) of the Institute of Biosciences and Applications, NCSR "Demokritos".
2. Member of the Research Committee of NCSR "Demokritos" (May 8, 2017 – December 31, 2017).
3. Member of the Research Council of the Institute (ESI) (June 21, 2017 – December 31, 2017).
4. Member of the Objections Committee of NCSR "Demokritos" (June 8, 2017 – December 31, 2017).
5. Member of 2 Reviewer Committees for hiring new research personnel at the IBA.
6. Member of a Proposition Committee for hiring research personnel at the IBA.
7. Member of an Election Committee at the Institute of Nuclear Technology (INT).

Impact factors (for 3 publications): 10,979

Number of citations for 2017 (without self-citations): 61

Number of citations 2013-2017 (without self-citations): 387

h-factor: 18

Current External Funding

Project entitled *Genetic Analysis of Tuberous Sclerosis,* financed by the company Novartis Hellas with with Principal Investigator for NCSR "Demokritos"Dr. G. Voutsinas.
Duration: 2017-2018
Total Funding: 16.000€
Funding of the laboratory for 2017: 8.000€

PROGRAMME B:

MODEL SYSTEMS FOR THE STUDY OF CELL FUNCTION

Research Group: Molecular Genetics of Insects and Biotechnology

Research Staff
Luc Swevers, Research Director
Vassiliki Labropoulou, Senior Researcher
Yongchao Zhao, Collaborating Graduate Student
Eleanna Christodoulou, Undergraduate Student
Dimitra Stefanou, Technical Specialist
Dimitris Kopanelis, Research Technician *(retired)*

Research Interests

(1) Analysis of small RNA (miRNA, siRNA) pathways in Lepidoptera. Development of methods for improvement of RNAi efficiency in lepidopteran insects.
(2) Immune response and innate immunity against virus infections in insects. Analysis of the immune response against RNA virus infections in lepidopteran insects: small RNAs and "cytokines".
(3) Study of antimicrobial peptides (AMPs) that are produced during the immune response of insects against pathogen infections and their role in antiviral defense.
(4) Parasitism of insects by hymenopterans and endo-parasitic viruses. Mechanisms of inhibition of innate immune response in lepidopteran insects. Functional role of the interactions between endosymbiotic viruses of hymenopterans and their lepidopteran hosts. Interference with immune signaling pathways of lepidopterans by proteins from PDV viruses.
(5) Development of methods for insect pest control: development of nuclear polyhedrosis viruses as transformation vectors, exploration of the use of transposable elements for insect transformation, environmental RNAi, insect growth regulators.
(6) Functional genomics: development of high-throughput screening systems for the detection of biologically active compounds (ecdysone agonists), functional expression of metabolic enzymes that are involved in insecticide resistance.

2017 Findings

Viral mechanisms of inhibition of RNAi in insects
A role for the RNAi machinery was demonstrated to control both persistent and pathogenic infections of RNA viruses in lepidopteran cell lines. More specifically, it was shown that over-expression of Dicer-2 (Dcr-2) and Argonaute-2 (Ago-2) provides protection against pathogenic infection by Cricket paralysis virus (CrPV; Dicistroviridae). On the other hand, knock-down of Dcr-2 and Ago-2 increases the replication of Macula-like latent virus (MLV; related to Tymoviridae). The production of viral small interfering RNAs was demonstrated during persistent infections of rhabdovirus, iflavirus and MLV (collaboration with Dr. Dulce Santos and Dr. J. Vanden Broeck, KULeuven, Belgium).

Functional expression of metabolic enzymes that are involved in insecticide resistance
The baculovirus expression system was used for the production of UDP-glucosyltransferases (UGTs) and the sensory appendage protein 2 (SAP-2) which are both involved in the insecticide resistance mechanism in mosquitoes (*Aedes aegypti* and *A. albopictus*; *Anopheles gambiae*). The purification and functional characterization of the proteins is in progress (collaboration with Dr. E. Morou and Dr. J. Vontas, Agricultural University of Athens).

Expression and functional analysis of immune factors against viral infections in insects.
Two recombinant AcMNPV viruses were constructed that express two molecules with an important role in the innate immune response of insects: BmSpätzle, the ligand of the Toll receptor, and the homolog of the factor Vago of *Drosophila* in the silkworm *B. mori* (SVWC).
In parallel was extended the study of the anti-microbial peptides (AMPs) with functional assays of inhibition of infection of cells by AcMNPV-YFP virus. The experiments indicate that Attacin and the insulin-binding protein (IBP2) show inhibitory activity with respect to viral infection.

Pubications

Kontogiannatos, D., Swevers, L., and Kourti, A. (2017). Abnormal development in larvae of *Sesamia nonagrioides* (Lepidoptera: Noctuidae) resulting from baculovirus-mediated overexpression of a JHE-related gene (*SnJHER*). Eur. J. Entomol. 114, 7-15.

Kolliopoulou, A., Taning. C.N.T., Smagghe, G., and Swevers, L. (2017). Viral Delivery of dsRNA for Control of Insect Agricultural Pests and Vectors of Human Disease: Prospects and Challenges. Front. Physiol. 8, 399.

Articles in press

Santos, D., Wynant, N., Van den Brande, S., Verdonckt, T.-W., Mingels, L., Peeters, P., Kolliopoulou, A., Swevers, L., and Vanden Broeck, J. (2018). Insights into RNAi-based antiviral immunity in Lepidoptera: acute and persistent infections in *Bombyx mori* and *Trichoplusia ni* cell lines. Sci. Rep. 8, 2423. (IF = 4.259)

Hu, X., Yin, B., Cappelle, K., Swevers, L., Smagghe, G., Yang, X., and Zhang, L. (2018). Identification of novel agonists and antagonists of the ecdysone receptor by virtual screening. J. Mol. Graph. Model. 81, 77-85. (IF = 1.754)

Articles in books and conference proceedings

Kourti, A., Swevers, L., and Kontogiannatos, D. (2017). In search of new methodologies for efficient insect pest control: the RNAi "movement". In "Entomology", InTech Open, Edited by V. Shields, ISBN 978-953-51-5041-1, pp 71-95.

Presentations at Scientific Conferences

Swevers, L., Vontas, J., and Kalantidis, K. (2017). Plant viruses for delivery of RNAi triggers for pest control: possibilities and obstacles. 1st COST iPlanta Conference: Creating the plant RNAi research network (CA15223), 15-17 February, Rome, Italy.

Pinto, C.P.G., Rickes, L.N., Penteado, F., Cappelle, K., Thurow, S., Swevers, L., Zotti, M.J., Smagghe, G., Lenardão, E.J., and Grutzmacher, A.D. (2017). Organochalcogen-containing compounds demonstrate antagonistic activity towards insect EcR. The 3rd International Insect Hormone Workshop, 9-14 July , Nasu Highland, Japan.

Swevers, L., Kolliopoulou, A., Zhao, Y., Taning, C.N.T., Smagghe, G., and Sun, J.-C. (2017). Delivery of RNAi triggers in insects by viruses and virus-like particles. International Symposium for New Technology in Arthropods Pest Management, 16-18 November, Chongqing, People's Republic of China.

Kontogiannatos, D., Swevers, L., Hatzopoulos, P., and Kourti, A. (2017). Genetic therapy and synthetic biology technologies in the construction of gene silencing pesticides. 17th Panhellenic Entomological Congress, September 19-22, Athens, Greece.

Other Scientific Activities

Participation in editorial boards of scientific journals:
Member of the editorial board of the scientific journals: «Archives of Insect Biochemistry and "Physiology" and "Journal of Insect Science" (L. Swevers).

Participation in committees for evaluation of research projects:
Member of the committee of experts of the Funds of Scientific Research FWO-Vlaanderen (Belgium) «Bio2» (Functional Biology) for the evaluation of research proposals (PhD and postdoc scholarships, national research programs) (L. Swevers).
Expert in the thematic committee "Agricultural Sciences", 1st announcement of research projects ELIDEK for the support of postdoctoral researchers (2 proposals) (L. Swevers).

Reviewer of research articles:

Reviewer for the journals «Archives of Insect Biochemistry and Physiology» (3x), «BMC Genomics» (2x), «Comparative Biochemistry and Physiology B» (2x), «European Journal of Entomology», «Frontiers in Physiology», «General and Comparative Endocrinology» (2x), «Genes» (2x), « Insect Biochemistry and Molecular Biology» (8x), « International Journal of Molecular Sciences» (2x), «Insect Molecular Biology», «In Vitro Animal», «Journal of Invertebrate Pathology», «Journal of Insect Physiology», «Journal of Insect Science», «Molecules», «Pest Management Science» (3x), «Phytoparasitica», «PLoS ONE» (3x), «Scientific Reports» (5x), «Toxins» (3x) (L. Swevers).
"Publons" Award: Top 1% in Field (Biochemistry, Genetics and Molecular Biology). For the most pre-publication peer-reviews (L. Swevers).

Educational Activities

One hour-lecture with title «The democratization of genome editing: from zinc fingers to CRISPR/Cas» at the Summer School of NCSR "Demokritos" (L. Swevers).

Participation in the lesson: «Molecular Biology: Systemic and *in silico* approaches», Bi-institutional postgraduate diploma of specialization, Department of Biology and Medical School, National and Kapodistrian University of Athens, coordinator: Dr. D. Stravopodis. Title: "RNA-mediated gene silencing: pathways and applications in medicine and agriculture" (3 hours) (L. Swevers).

Member of PhD evaluation committee (external examiner): «Virus infection and host antiviral defense, a story between Israeli acute paralysis virus (IAPV) and bumblebees (Bombus terrestris)», Haidong Wang, Faculty of Bioscience Engineering, Department Crop Protection, Ghent University, Ghent, Belgium (L. Swevers).

Other activities for the Institute of Biosciences & Applications

Member of the management committee for the project INFRASTRUCTURES "Biomaging" of IB-A (V. Labropoulou).

Member of the committee of IB-A for the management, monitoring and receipt of the project "Target identification and development of innovative approaches for health and environmental applications (SANITURA)" (MIS 5002514) in the framework of EPAnEK (V. Labropoulou).

Member of the scientific board of the institute (L. Swevers).

Responsible for the following instruments: Fluostar Microplate Fluorometer, HPLC Hewlett Packard, microplate reader for luminescence and fluorescence TECAN InfiniTE M-200 (L. Swevers).

Impact Factor (for 2 publications): 6,478

Citations for 2017 (without self-citations)
Swevers L: 227
Labropoulou V.: 40

Total Citations 2013-2017 (without self-citations)
Swevers L: 937
Labropoulou V.: 238

h-factor:
L. Swevers: 26 (Scopus), 28 (Google Scholar)
V. Labropoulou: 12 (Scopus), 13 (Google Scholar)

Current External Funding

Project FWO–Vlaanderen (Belgium) entitled *Optimizing RNA interference for insect pest control* with coordinator for the Greek participation Dr. L. Swevers.
Duration: 1/2016-12/2019
Total Program Funding: 800.000€
Total funding of the laboratory: 0€
Funding of the laboratory for 2017: 0€.

COST Action CA15223 entitled *Modifying plants to produce interfering RNA (iPlanta),* with national delegate Dr. Luc Swevers, funded by the EU.
Duration: 10/2016-4/2020
Total funding (for the period 11/16-4/17): 106.230€
Funding of the laboratory for 2017: 0 €.

Project entitled *Functional expression of Cytochrome P450s that are involved in insecticide resistance,* financed by the company SYNGENTA in collaboration with the Agricultural University of Athens and with coordinator Dr. J. Vontas.
Duration: 9/2017-8/2018
Funding of the laboratory for 2017: 2.500€

Scholarship (*Graduate Student Overseas Study Program)* from South China Agricultural University (Guangzhou, People's Republic of China) for graduate student Yongchao Zhao, 18.000€.
Duration: 9/2017-8/2018

Research Group: Chemical Ecology and Natural Products, *in collaboration with the Laboratory of* Insect Molecular Genetics and Biotechnology

Research Staff

Maria Konstantopoulou, Senior Researcher

Dimitris Raptopoulos, Graduate Research Associate

Neoklis Manikas, Collaborating Graduate Student

Research Interests

- Chemical ecology: isolation and identification of biologically active compounds, relating to insect chemical communication and plant – insect interactions (pheromones, volatile compounds of plant origin etc.) that may be used in integrated pest management programs.
- Isolation and identification of secondary metabolites (mainly of plant origin) acting on insect physiology and/or behavior (behavior modifying agents - infochemicals). Laboratory and field evaluation of bioactivity of the isolated metabolites; study of their mode of action. Chemical synthesis of semiochemicals (infochemicals).
- Development of specialized dispensers for chemical attractants/repellants for insects and technologies for their application in pest population control. Biodegradable materials endowed with controlled- release rate and UV protection properties.
- Development of biocides of biological origin (Biological Control Agents. BCAs) and of methods/technologies of application aiming to incorporate them in integrated management methods for pest of agricultural and urban environment but also for pests of public health concern such as mosquitoes.
- Biochemistry of insect olfactory receptors with emphasis on the localization and isolation of protein receptors for semiochemicals.
- Microorganisms and Biotechnology: Isolation of naturally occurring microorganisms and their biologically active secondary metabolites (toxins) aiming to their incorporation in insect population management.

2017 Findings

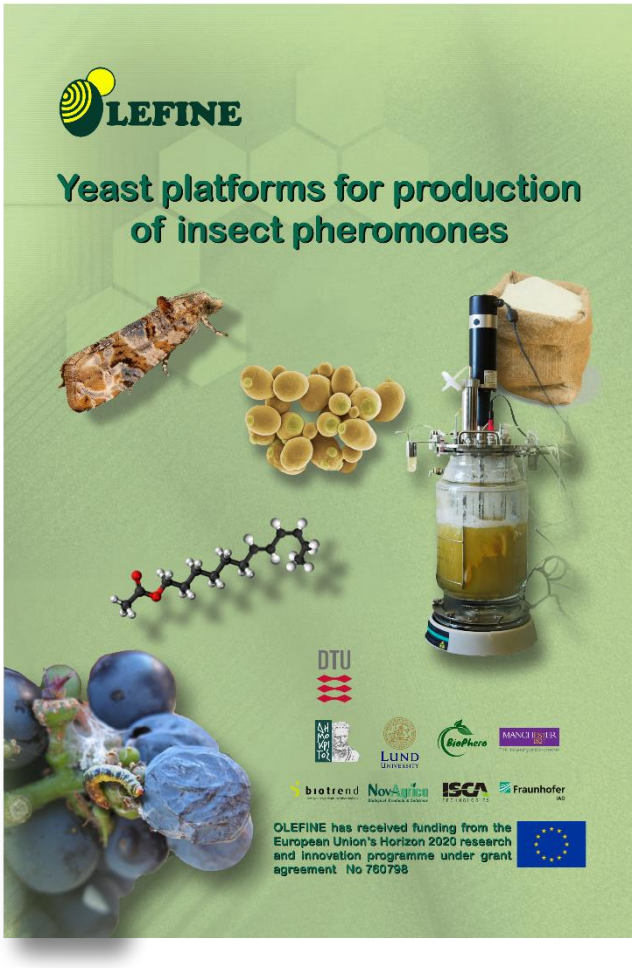
Participation in the OLEFINE consortium (OLEaginous yeast platforms for FINE chemicals) HORIZON 2020 (Grant Agreement No. 760798). OLEFINE (http://olefine.eu) aims to produce insect sex pheromones through biotechnological methods using yeasts to allow pheromone production at low cost so they may be used in mating disruption methods as an economic and effective alternative to chemical insecticides (Figure 1). In the framework of the project new colonies of insect pests of high value crops have been established, as the European grapevine moth (*Lobesia botrana*), and the European corn borer (*Ostrinia nubilalis*) for electrophysiological and behavioural assays.

Isolation and identification of semiochemicals (infochemicals) and other bioactive metabolites of biocides of biological origin (Biological Control Agents. BCAs) as "smart" insecticides and of methods/technologies of application aiming to incorporate them in integrated management methods for pest of agricultural and urban environment but also for pests of public health concern. In the framework of the given research activity a memorandum of collaboration has been signed between the NCSR "D" (Laboratory of Chemical Ecology & Natural products), the University of Thessaly and the Benaki Phytopathological Institute. The memorandum refers to the collaboration of the parties in issues of recording, studying and managing populations of spatial species of mosquitos in the prefecture of Chania/Crete.

In the framework of development and application of methods for the control of insect pests *de novo* synthesis of sex pheromones of click beetles of the genus *Agriotes* and of the vine mealybug (*Planococcus ficus*) has been done.

The research on development of semiochemicals release systems endowed with slow-release rate and UV protection properties in non-toxic, biodegradable and environmentally-friendly polymerization products was continued. As well as the study of release rate of the semiochemicals from such polymers under laboratory conditions (including aging).

The study of olfactory functions of *Anopheles gambiae* (in collaboration with Prof. K. Iatrou) was continued. A number of extracts aromatic plants and their fractions from the collection held at the Laboratory was tested for identification of agonists showing action similar to that of special agonist OrcoRAM2.



Publications

Kikionis S., Ioannou E., Konstantopoulou M., Roussis V. (2017). Electrospun micro/nanofibers as controlled release systems for pheromones of *Bactrocera oleae* and *Prays oleae*. Journal of Chemical Ecology 43: 254-262.

Kröber T., Koussis K., Bourquin M., Tsitoura M., Konstantopoulou M., Awolola T.S., Dani F., Qiao H., Pelosi P., Iatrou K., Guerin P. (2017). Odorant-binding protein-based identification of natural spatial repellents for the African malaria mosquito *Anopheles gambiae.* Insect Biochemistry and Molecular Biology (accepted for publication).

Presentations at Scientific Conferences

Iatrou, K., Tsitoura, P. and Konstantopoulou, M. (2017) Distracting the hungry: mosquito anosmia inducing and odor perception enhancing compounds of natural origin targeting ORco function for control of transmission of malaria and other mosquito borne infectious diseases. Experimental Biology Chicago, USA, 22-26 April. *The FASEB Journal vol. 31 no. 1 Supplement 766.4*

Patents

Iatrou, K., Guerin P.M., Kröber, T. and Konstantopoulou, M. (2017). Methods, compounds and compositions for repelling insects and/or arachnids. USA Patent No. 9615585 (from PCT/EP2014/055170), Date of Patent: April 11, 2017.

Iatrou, K., Guerin P.M., Kröber, T. and Konstantopoulou, M. (2017). Methods, compounds and compositions for repelling insects and/or arachnids. European Patent Publication No. 20170231221 (from PCT/EP2014/055170) filed 27/02/2017. Publication date: August 17, 2017.

Other Scientific Activities

Member of the Attica Region Research and Innovation Council (PSEK) 2017-2021

Coordinator in the session "Digital transformation in the agro-nutritional sector" at Athens Innovation Festival, 20-22/11 Zappeion, Athens

Member of the international committee of the 10th International workshop of Molecular Biology and Genetics of the Lepidoptera, 19-25/8/2018, Kolymbari, Crete

Reviewer of the following international scientific journals: Chemosphere, Journal of Agricultural and Food chemistry, Entomologia Experimentalis et Applicata, Bulletin of Insectology, Journal of Applied Entomology, Crop Protection, Insect Science, Journal of Pest Science, Bulletin of Entomological Research, Pest Management Science, Journal of Chromatography B, PLoS-One, Journal of Chemistry, Journal of Medicinal Plant Research, Research in Veterinary science, Journal of essential oil bearing plants.

Member of the evaluation committee for recruitment of seventeen (17) external co-workers for the Institute of Informatics and Telecommunications in the framework of an international project funded by the European Commission.

Other activities for the Institute of Biosciences & Applications

Member of the Scientific Advisory Board of the Institute

Signor of the Memorandum of cooperation between NCSR "D" the University of Thessaly and the Benaki Phytopathological Institute. The memorandum refers to the collaboration of the parties in issues of recording, studying and managing populations of spatial species of mosquitoes in the prefecture of Chania/Crete.

Participation as full member in the project "Administration of the research infrastructure and materialization of programs of identification of bioactive compounds in NCSR D" of the Action {OPENSCREEN-GR: Research infrastructure of open access for targeted screening technologies and detection of bioactive molecules to protect Health, Livestock, Agriculture and the Environment"

Coordinator of three-membered opinion committee of the research personnel (Researchers-ELE) for the evaluation of the candidates for the position of the Director of IBE.

Lecture under the title "Chemical Ecology and Natural Products", 52nd Summer School of NCSR "D"

Responsible for radioprotection of the radioactive source Co-60, with activity 5470 Ci (March 2004-).

Impact Factors (for 2 publications): 5,981

Citations 2017 (without self-citations): 42

Total Citations 2013- 2017 (without self-citations): 228

h-factor: 12 (Scopus), 14 (Google Scholar)

Current External Funding

Project entitled *Oleaginous yeast platforms for Fine chemicals* (Horizon 2020, Call: H2020-NMBP-2016-2017/H2020-NMBP-BIO-2017, GRANT AGREEMENT 760798) funded by EU, and Scientific responsible Dr. M. Konstantopoulou.
Duration: 1/1/2018 – 31/12/2021
Total program funding: 441.311 €

Research Group: Chronobiology

Research Staff
Anastassia Prombona, Senior Researcher
Aggeliki Galeou, Graduate Student
Kostis Papasakellariou, Training Student
Maria Georga, Training Student

Research Interests

The research interests of our laboratory are focused on the study of the circadian oscillator function in *Phaseolus vulgaris* and in mammalian cell culture systems.

The circadian clock of plants
This project deals with the study of the expression of rhythmic genes in *P. vulgaris* primary leaves during the synchronization of the circadian clock by different photoperiods and by the application of light at night. In addition, we investigate the molecular mechanisms involved in the regulation of clock gene expression by implementation of an *in vitro* protoplast system from *P. vulgaris* leaves.

The circadian clock of mammals-correlation with pathological conditions
This project concentrates on the study of the role of the biological circadian clock in carcinogenesis, more specifically in the regulation by the circadian clock of the expression of the oncogene *c-MYC* and the interaction of the oncoprotein with components of the circadian clock. We are also interested in the regulation of gene expression related to chromatin remodelling at the promoter of clock genes under physiological and pathological conditions. The effect of bioactive and pharmaceutical compounds on the clock function is also investigated.

2017 Findings

Investigation of the biological clock function in plants
With the aim to explore the function of central oscillator elements in *P. vulgaris*, A. Galeou has implemented the *P. vulgaris* protoplast system to investigate the effect of the overexpression of three putative clock components PvLHY, PvTOC1 and PvELF4 on the promoter region of the respective genes. Using the firefly luciferase (*Luc*) as a reporter gene driven by each of the circadian promoters *PvLHY, PvTOC1 and PvELF4*, we were able to show that the *PvLHY* promoter, despite its very low expression level, is repressed by the PvTOC1 protein. This finding is similar to results from equivalent experiments in the plant *Arabidopsis thaliana*. *PvELF4* promoter activity, on the other hand, is not influenced by the overexpression of any of the three examined proteins. Finally, the *PvTOC1* promoter was found to be repressed by the PvTOC1 protein. As this is a novel finding regarding the plant circadian clock mechanism, the region involved in this auto-repression was explored. The study with deletion mutants showed that the presence of the C-terminal CCT (CONSTANS, CO-like and TOC1) domain is necessary for the repressive effect of the PvTOC1 protein on its own gene promoter. This result adds a new feedback regulatory step regarding the loops of the plant circadian clock mechanism. Additional efforts in our laboratory have succeeded to show that the *P. vulgaris* protoplast system is suitable for the *in vivo* recording of promoter activity of clock genes. These results are accepted for publication in the Journal of Plant Physiology (2018).

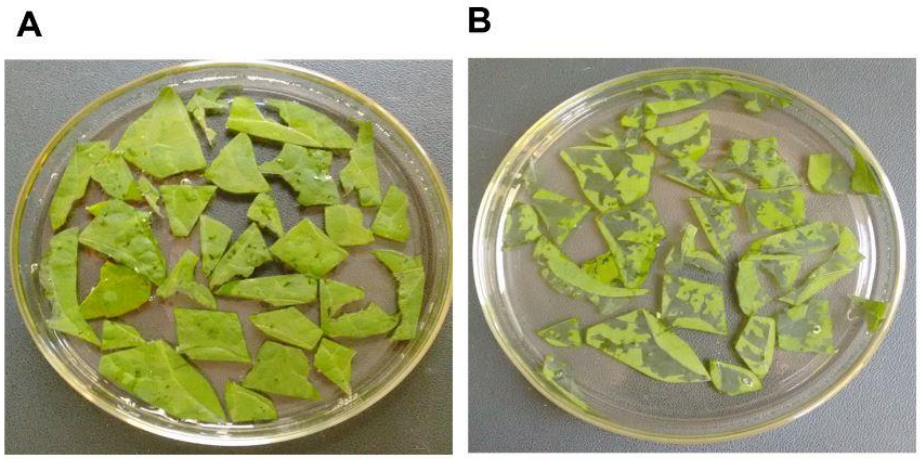


Figure. 1. (A) Pieces of *P. vulgaris* fully developed primary leaves, cut with a razor-blade, in digestion medium. The mid-rib and the lower epidermis of the leaves have been removed. (B) The leaves' pieces following a 2-hour digestion at 22°C, which serve for the isolation of protoplasts.

Investigation of protein levels of H1 histone subtypes in peripheral blood cells of psychotic patients

We investigated the protein levels of histone H1 subtypes in leukocytes and neutrophils of schizophrenic patients, as there are strong indications that under psychotic conditions the histone levels can change. Our results show a statistically significant reduction in patients, in comparison with healthy persons, of the H1.0 subtype, which may be related to conformational changes in the heterochromatic regions. No statistically significant differences could be detected regarding the subtypes H1.3 and H1.5. Thus, for the first time schizophrenia is correlated with chromatin remodeling that may result in differences in gene expression. The potential changes in clock gene expression levels in this psychotic disorder will also be investigated. This project is performed in collaboration with Dr. T. Sourlingas.

Articles in Press

Galeou, A., Roussis, A., Prombona, A. (2018) Investigation of the Phaseolus vulgaris circadian clock and the repressive role of the PvTOC1 factor by a newly established in vitro system. J. Plant Physiol. 222, 79-85 (IF: 3.121)

Presentations at Scientific Conferences

S. Mamoucha, V. Liapis, A. Prombona (2017) Plant biodiversity of Greece: Utilization of aromatic and medicinal plants' essential oils and extracts for their antimicrobial activity. 15th Congress of the Greek Botanical Society, 14-17 September 2017, Chania, Crete, oral presentation 13 - 16.9/12.15

S. Mamoucha, V. Liapis, A. Prombona (2017) Antifungal activity of plants essential oils and extracts against *Candida albicans.* 7th Panhellenic Congress of the Hellenic Society of Medical Mycology, 3-5 November, Athens, Greece, oral presentation EA 1

A. Galeou, A. Prombona (2017) The repressive role of the PvTOC1 factor in the *Phaseolus vulgaris* circadian clock. 68th Congress of the Hellenic Society of Biochemistry and Molecular Biology, 10-12 November, Athens, Greece, Poster no 56

Educational Activities

Supervision of PhD work of the graduate student A. Galeou

Member of the scientific committee for the supervision of the PhD thesis of A. Galeou in the Department of Biology of the National Kapodistrian University of Athens.

Other Activities for the Institute of Biosciences & Applications

President of the Scientific Council of IBA

Member in charge for the presentation of IBA activities to schools.

Person in charge for the safety and removal of chemical waste.

Citations 2017 (without self-citations): 28

Total Citations 2013-2017 (without self-citations): 60

h-factor: 8

Research Group: Microbial Molecular Genetics

Research Staff
Vassiliki Sophianopoulou, Research Director
Alexandros Athanassopoulos, Postdoctoral Fellow
Alda Biratsi, Postgraduate Graduate Student
Myrsini Charicleous, Undergraduate Student
Maria Christina Zerba, Training Student
Loudes Arias Salazar, Training Student (Erasmus Student)

Research Interests

Our group is primarily interested in the regulation, organization and function of the fungal plasma membrane. The plasma membrane, as the boundary between the cell and its environment, is a platform for selective nutrient exchange, signaling events, and cell-cell interactions. A major challenge is to elucidate the mechanisms coordinating these numerous functions of the plasma membrane. The general concept of our work is to understand how specific compartments/domains of the plasma membrane regulate the activity and /or trafficking of transporters and efflux pumps, the survival of cells under stress conditions, and how these cellular processes are related to fungal pathogenicity (*I. Vangelatos et al., 2010; C. Scazzocchio et al., 2011; A. Athanasopoulos et al., 2013, 2015*).

Our group has involved to the understanding of the above processes, mainly in two subjects:
A) Regulation of expression, structure-function relationships, specificity, trafficking and evolution of amino acid transporter proteins
B) The organization of the lateral compartmentalization of the fungal plasma membrane.
Long-term objectives: identification of new pharmaceutical targets and future development of highly-targeted antifungals/vaccines.

Our model of choice is a genetically tractable microorganism, the opportunistic pathogen ascomycetes *Aspergillus nidulans*, a soil fungus that has been extensively exploited for the discovery of a plethora of the molecular mechanisms underlay cellular processes and for which state of the art genetic tools are available.

In addition, our group is interested in elucidate the molecular mechanisms underlie detoxification of toxic amino acid analogues. L-Azetidine-2-Carboxylic Acid (AZC) is a toxic analogue of proline, produced by the flowering plant *Convallaria majalis* (valley lily), certain species of the genus *Polygonatum* and beets (*Beta vulgaris*). In nature, AZC has a protective role for the plants that produce it, and at the same time is a toxic substance for a multitude of organisms, including various bacteria, fungi and even mammals. Our studies targeted to understanding the molecular mechanism(s) underlie detoxification and catabolism of AZC in soil fungi.

Medium and long-term objectives: design new and specialized antifungal substances to protect crops of nutritional and economic significance.

2017 Findings

In the context of the study of the specificity of the main proline transporter PrnB, *A. nidulans* was found to be resistant to L-Azetidine-2-carboxylic acid (AZC), a toxic chemical analogue of proline, which can utilize as a sole nitrogen source. In particular, our results have shown that two enzymes, AZC hydrolase (AzhA) and AZC acetyltransferase (Ngn2), are responsible for the detoxification and the catabolism of AZC in *A. nidulans*. Heterologous expression of azhA hydrolase gene in *Saccharomyces cerevisiae* yeast strain S1278b, having the MPR1 AZC acetyltransferase (an orthologue of Ngn2), gives the strain the ability to use AZC as a sole nitrogen source, indicating that AZC hydrolysis is necessary and sufficient for ACZ catabolism.

In the context of the study of structure-function analysis of amino acid transporters and based on recent *in silico* studies (https://www.ncbi.nlm.nih.gov/pubmed/28196534), we have identified that the gene named AN8816 in AspGD data base (http://www.aspergillusgenome.org/), encodes a secondary aspartate / glutamate transporter in *A. nidulans*.

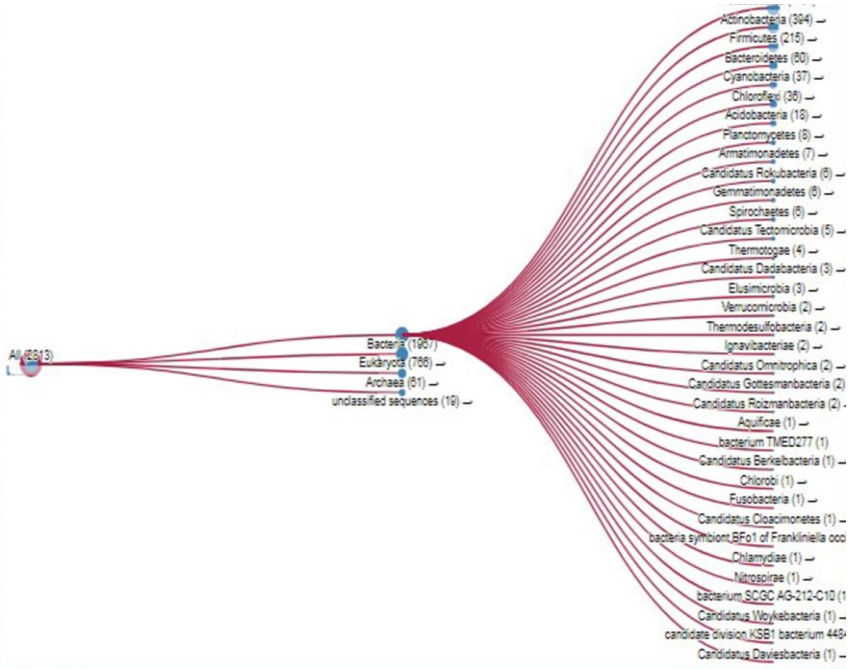


Figure 1: *Phylogenetic analysis of A. nidulans AzhA hydrolase using the HMMER web platform. The results demonstrate the existence of possible homologous sequences in bacteria, eukaryotic organisms and archea.*

In the context of the study of the biological role of lateral fungal plasma membrane organization, we have shown that PilA and AnNce102 eisosomal proteins are directly involved in the response of fungal cells to oxidative stress -as *Annce102Δ* and / or *pilAΔ* strains are sensitive to hydrogen peroxide (H_2O_2) and paraquat and resistant to menadione (https://www.ncbi.nlm.nih.gov/pubmed/26468899). Moreover, we have investigated the possible correlation of SngA protein, *S. cerevisiae* SNG1 orthologue, in the response of *A. nidulans* cells in oxidative stress, based on recent data showing genetic interaction of Nce102 with SNG1 https://www.ncbi.nlm.nih.gov/pubmed/27033517. Our results have shown that SngA is a protein with 6 transmembrane domains, and that deletion of the gene encoding it confers on *A. nidulans* cells sensitivity to the oxidizing agent, menadione. Functional characterization of SngA is under investigation.

Publications

Ronald Peter de Vries …Ch. Gournas….V.Sophianopoulou….I. Grigoriev (2017). Comparative genomics reveals high biological diversity and specific adaptations in the industrially and medically important fungal genus *Aspergillus*. Genome Biol. 14; 18:28, 1-45.

Articles in Press

Ch. Gournas A. Athanasopoulos and V. Sophianopoulou (2018). On the Evolution of Specificity in members of the Yeast Amino Acid Transporter family as Parts of Specific Metabolic Pathways. Int. J. Mol. Sci. (Invited review article: Biochemistry, Molecular and Cellular Biology, Special Issue "Amino Acids Transport and Metabolism" (IF 3,226).

Articles in Books and Conference Proceedings

A. Biratsi, Ch. Gournas and V. Sophianopoulou (2017). Abstract: "A toxic analogue of proline, L-Azetidine-2-carboxylic acid, is detoxified and catabolized by the filamentous fungus *Aspergillus nidulans*" Section: Biotechnology of plants and microorganisms. 68th Congress of the Hellenic Society of Biochemistry and Molecular Biology, 10-12 November 2017 at the Eugenides Foundation, Athens, page 31, P43, http://eebmb2017.gr/wp-content/uploads/2017/11/FINAL-PROGRAM-.pdf.

M. Charikleous and V. Sophianopoulou (2017). Abstract: "Identification of the genes encoding secondary proline and aspartate/glutamate transporters in the filamentous fungus *Aspergillus nidulans*». Section: Cell organization and Function. 68th Congress of the Hellenic Society of Biochemistry and Molecular Biology, 10-12 November 2017 at the Eugenides Foundation, Athens, page 36, P82, http://eebmb2017.gr/wp-content/uploads/2017/11/FINAL-PROGRAM-.pdf

Educational activities

- Post-graduate Education Courses on "Molecular Biology: Systemic and *in silico* Approaches", a Graduate Mandatory Course of the Interdisciplinary (Faculty of Biology and Medical School, National and Kapodistrian University of Athens. Two - Years Graduate Program "Applications of Biology in Medicine" (20 students 4 hours) (V. Sophianopoulou).
- Supervisor of Loudes Arias Salazar Fundacion Ceimar, Department of Sciences, Madrid, Spain, in the context of Erasmus+ Student Mobility for Traineeships
- Supervisor of A. Biratsi, PhD candidate at the Department of Biology, National and Kapodistrian University of Athens (V. Sophianopoulou).
- Supervisor of Mirsini Charicleous, Diploma student at the Department of Biology, University of Crete (V. Sophianopoulou).
- Supervisor of Iliana Theodorou, Diploma student at the Department of Molecular Biology, University of Thrace (V. Sophianopoulou).
- Member of the Advisory Committee for the PhD thesis of A. Biratsi, Department of Biology, National and Kapodistrian University of Athens.
- Member of the Advisory Committee for the diploma thesis of M. Charicleous, University of Crete
- Member of the Advisory Committee for the diploma thesis of I. Theodorou University of Thrace.

Other Administrative and Scientific Activities

- Deputy President of the Protocols Evaluation Committee of the Experimental Animal Colony of IB-A (01/2017-07/2017) (ΠΔ 56/2013)
- Member of the Advisory Committee on Scientific Issues of NCSR "D" (03/2017 - 03/2019).
- Member of the executive body for the the recruitment of faculty members in the field of Molecular Microbiology, Aristotle University Thessaloniki.
- Substitute member of the executive body for the the recruitment of faculty members in the field of Microbial Genetics, University of Ioannina (2017).
- Substitute member of the executive body for the the recruitment of faculty members in the field of Molecular Microbiology in agriculture, Agricultural University of Athens.
- Co-chair of the "Functional genomics and proteomics" session of the 68th Conference of EEBMB, Athens (2017).
- Member of the Organizing and Scientific Committee of the European Biotechnology Congress, Athens (2018).
- Member of the Evaluation Committee for the recruitment of graduate students and post-doctorates at IB-A within the Industrial Scholarship Programme of Stavros Niarchos and NCSR Demokritos.
- Member of the Complaints Assessment Committee in the framework of the Industrial Scholarship Program of Stavros Niarchos and NCSR Demokritos.

Other Distinctions and Awards

- FEBS Scholarship for participation and presentation of work at the 43rd Febs Congress "Biochemistry forever" Prague 2018 (A. Biratsi).
- Member of the EUFGEN EUrotialles Functional GENomics Consortium (V. Sophianopoulou).

Other Scientific activities

- Member of the editorial board of *Scientific Reports* (Published by Springer Nature)
- Referee of peer-review articles published in International Journals
- Evaluator of Competitive National GSRT Grants

Other Activities for the Institute of Biosciences & Applications

V. Sophianopoulou:

- Member of the Board of Directors of NCSR "D" (10/2016-07/2017)
- Acting Vice Director of IB-A (10/2016-07/2017)
- Vice Director of IB-A (07/2017-07/2018)
- Head of the Microbial Molecular Genetics lab of IB-A (2004-today)
- President of the Evaluation Committee for the recruitment and/or deployment of Researchers B and A at the IB-A (2017).

Impact Factor (for 1 publication): 11,313

Citations 2017 (without self-citations): 49

Total Citations 2013-2017 (without self-citations): 229

h-factor: 17

Research Group: Biophysics and Biotechnology of Membranes

Research Staff
Kostas Stamatakis, Senior Researcher
George Papageorgiou, Collaborating Former Staff Scientist
Meropi Tsimilli – Michael, Collaborating Scientist
Christos Kottakis, Collaborating Scientist
Dimitris Vayenos, Graduate Student
Panagiotis Broussos, Undergraduate Student
Nikolina Vidali, Training Student
Eufrosini Karayianni, Training Student

Research Interests

Photosynthetic cyanobacteria are preferable candidates for the sequestration of large quantities CO_2 from the atmosphere because they can grow in extreme or/and specified environmental conditions (temperature, pressure, salinity, pH, chemical composition) and are capable of binding CO_2 to produce high energy chemical compounds using sunlight. The rapidly growing cyanobacteria constitutes a very promising and CO_2 emission-free source for biofuels production which can substitute for other carbon-dependent natural sources of energy. The production and accumulation of sucrose in cyanobacteria is connected to their adaptation to extreme environmental conditions. Our research addresses the following themes:
(a) We investigate the production of hydrogen (H_2) production by cyanobacteria through the process of anaerobic "dark fermentation" of the sucrose they accumulated under salinity stress.
(b) We study, also, the time dependent changes of chlorophyll *a* fluorescence ($\mathbf{F}_{Chla}$), or fluorescence induction, in cyanobacteria, giving emphasis to the distribution of the electronic excitation to the reaction centers of photosystem I (PSI) and photosystem II (PSII), as an indicator of protective mechanism against the destructive effects of the reactive oxygen species (ROS) that are produced during photosynthesis.
(c) In co-operation with a research group at the Oceanographic Institution at Woods Hole, MA, USA, we study the photosynthetic apparatus of the haptophyte *Phaeocystis antarctica* and of a novel Ross Sea dinoflagellate (RSD) that hosts *P. Antarctica* chloroplasts as kleptoplasts. Both algae are dominant in the phytoplankton of Ross Sea in Antarctica. Our research led to the discovery of the mechanism by which these two algae maximize, in the light-poor Ross Sea, the amount of light they absorb for photosynthesis.
(d) We have developed a new method for the evaluation and assessment of antibacterial properties of materials and surfaces by means of time-dependent changes of F_{Chla} (Patent No. OBI 20140100263/02.05.2014). Specifically, the method relates F_0, the initial value of F_{Chla} kinetic trace (OJIP), upon a transition from darkness to continuous light of cyanobacteria. Since cyanobacteria are gram negative, we can use them as a guide for antibacterial assay.

2017 Findings

The haptophyte *P. antarctica* and the novel Ross Sea dinoflagellate hosting kleptoplasts derived from *P. antarctica* (RSD; R.J. Gast et al., 2006, J. Phycol. 42 233–242) were compared for photosynthetic light harvesting and O_2 evolution activity. Both chloroplasts and kleptoplasts emit F_{Chla} peaking at 683 nm (F683) at 277 K and at 689 (F689) at 77 K. Second derivative analysis of the F689 band at 77 K revealed two individual contributions centered at 683 nm (Fi-683) and at 689 (Fi-689). Using the p-nitrothiophenol (p-NTP) treatment of Kobayashi et al. (Biochim. Biophys. Acta 423 (1976) 80–90) to differentiate between Photosystem(PS) II and I fluorescence emissions, we could identify PSII as the origin of Fi-683 and PSI as the origin of Fi-689. Both emissions could be excited not only by Chl a-selective light (436 nm) but also by mycosporine-like amino acids (MAAs)-selective light (345 nm). This suggests that a fraction of MAAs must be proximal to Chls a and, therefore, they must be located within the plastids. On the basis of second derivative fluorescence spectra at 77 K, of p-NTP resolved fluorescence spectra, as well as of PSII-driven oxygen evolution activities, PS II appears substantially

less active (~1/5) in dinoflagellate kleptoplasts than in *P. antarctica* chloroplasts. Therefore, we proposed a diminished role for PS II, a known source of reactive oxygen species and for the nucleus-encoded light-harvesting proteins thanks to the supplementary light-harvesting by the MAAs. These properties may account for the extraordinary longevity of RSD kleptoplasts.

The realization of antibacterial surfaces is an important scientific problem, which may be addressed by the use of superhydrophobic surfaces, reducing bacterial adhesion. However, there are several limitations and contradicting reports on the antibacterial efficacy of such surfaces. Moreover, achieving antibacterial action through minimization of adhesion does not ensure complete protection against bacteria. Here, we identify the important factors affecting antibacterial action on superhydrophobic surfaces, emphasizing the role of bacterial concentration, and observing an upper concentration threshold above which antibacterial action of any surface is compromised. Finally, we propose metal enriched, superhydrophobic surfaces, as the "ultimate" "hybrid" antibacterial surfaces for in vitro applications.

Publications

Stamatakis, K., Vayenos, D., Kotakis, Ch., Gast, R.J., Papageorgiou, G.C. (2017) The extraordinary longevity of kleptoplasts derived from the Ross Sea haptophyte *Phaeocystis antarctica* within dinoflagellate host cells relates to the diminished role of the oxygen-evolving Photosystem II and to supplementary light harvesting by mycosporine-like amino acid/s. Biochim. Biophys. Acta (Bioenergetics) 1858: 189–195

Ellinas, K., Kefallinou, D., Stamatakis, K., Gogolides, E., Tserepi· A. (2017) Is there a threshold in the antibacterial action of superhydrophobic surfaces? ACS Applied Materials & Interfaces 9: 39781–39789

Articles in books and Conference Proceedings

Stamatakis, K., Broussos P.-I., Gast, R.J., Papageorgiou, G.C. (2017) The Ross Sea haptophyte *Phaeocystis antarctica* and dinoflagellate cells hosting kleptoplasts derived from it are both capable of light state transitions» στο Photosynthesis Research for Sustainability-2017, Hyderabad, India, 30 October-3 November 2017.

Impact Factor (for 2 publications): 12,368

Citations 2017 (without self-citations): 44

Total citations 2013-2017 (without self-citations): 187

h-factor: 11(Scopus),15 (Google Scholar)

PROGRAMME C:

STRUCTURAL AND COMPUTATIONAL BIOLOGY

Research Group: Theoretical Biology and Computational Genomics

Research Staff
Yannis Almirantis, Research Director
Spyros Papageorgiou, Collaborating Former Staff Scientist

Research Interests

Probabilistic and statistical aspects in genome organization – Non-randomness at several length scales.

- Deviations from randomness at the level of nucleotide n-tuplets. Patterns related to the functionality of genomic regions and to the global genome structure.
- Deviations from randomness at the "middle" length scale, expressed as clustering of similar nucleotides. Use of such approaches for the distinction of coding and non-coding segments.
- Long range correlations and Zipf laws in the genome structure. Power laws in the distribution of exons, transposable elements, CpG-islands, CNEs and of other genomic localizations.
- DNA sequences seen as genomic text – Linguistic features in the genome: redundancy – multiple coding – asymmetry etc.
- "Conservation laws" at the genome structure. The case of "Chargaff's 2nd parity rule". The use of deviations from this law in the study of genomic dynamics and evolution.
- Evolution at the genomic level. Formulation of minimal evolutionary scenarios compatible with the observed probabilistic features of genomes. Interpretation of the above mentioned probabilistic features either by selectionist or mutationist causality.

Pattern formation in biological systems – Self-organization and evolution.

- Early development – Left-right asymmetries – Mechanisms of activation of Hox genes during limb development.
- Reaction-diffusion systems – Spontaneous symmetry breaking and pattern-formation in systems with feedbacks.
- Prebiotic and early evolution as a complex self-organization procedure.

2017 Findings

Analysis of DNA composition at several length scales constitutes the bulk of many early studies aimed at unravelling the complexity of the organization and functionality of genomes. Dinucleotide relative abundances are considered an idiosyncratic feature of genomes, regarded as a 'genomic signature'. Motivated by this finding, we introduce the 'Generalized Genomic Signatures' (GGSs), composed of over- and under-abundances of all oligonucleotides of a given length, thus filtering out compositional trends and neighbour preferences at any shorter range. Previous works on alignment-free genomic comparisons mostly rely on k-mer frequencies and not on distance-dependent neighbour preferences. Therein, nucleotide composition and proximity preferences are combined, while in the present work they are strictly separated, focusing uniquely on neighbour relationships. GGSs retain the potential or even outperform genomic signatures defined at the dinucleotide level in distinguishing between taxonomic subdivisions of bacteria, and can be more effectively implemented in microbial phylogenetic reconstruction. Moreover, we compare DNA sequences from the human genome corresponding to protein coding segments, conserved non-coding elements and non-functional DNA stretches. These classes of sequences have distinctive GGSs according to their genomic role and degree of conservation. Overall, GGSs constitute a trait characteristic of the evolutionary origin and functionality of different genomic segments.

Publications

Almirantis Y., Charalampopoulos P., Gao J., Iliopoulos C.S., Mohamed M., Pissis S.P., Polychronopoulos D. (2017). On avoided words, absent words, and their application to biological sequence analysis. Algorithms Mol. Biol. 12. DOI 10.1186/s13015-017-0094-z.

Articles in Press

Almirantis Y., Tsitinidis K. (2018). Ultra-high dilutions and homeopathy: can they be explained without non-local theory? *Homeopathy* 107, pp. (I.F. 1.16)

Articles in Books and Conference Proceedings

Almirantis, Y., Charalampopoulos, P., Gao, J., Iliopoulos, CS., Mohamed, M., Pissis SP., Polychronopoulos. D. (2016). Optimal computation of Avoided Words. *Lecture Notes in Computer Science* 9838, 1-13.

Other Scientific Activities

Reviewer of scientific papers for: Computational Biology and Chemistry, Oncotarget, Journal of Theoretical Biology, Gene, Austin Journal of Analytical & Pharmaceutical Chemistry, PLoS1, Royal Society Open Science. (Y. Almirantis).

Educational Activities

- Teaching (15h) of the course "An Introduction to Computational Genomics" in the framework of the "Post Graduate Specialisation Diploma" in Bioinformatics, Biology *Department, U.O.A.*

- Teaching (3h) of the course "An Introduction to Computational Genomics" in the framework of the Post Graduate Specialisation Diploma in Clinical Biochemistry and Molecular Diagnostics, Biology Department, U.O.A.

Impact Factor (for 1 publication): 1,79

Citations 2017 (without self- citations): 37

Total Citations 2013-2017 (without self- citations): 164

h-factor: 13 (Scopus), 15 (Google Scholar)

Research Group: Structural Studies of Biomolecules and Pharmaceuticals with NMR

Research Staff
Maria Pelecanou, Research Director
Marina Sagnou, Researcher
Angeliki Panagiotopoulou, Functional Scientific Personnel B
Barbara Mavroidi, Postdoctoral Fellow
Constantinos – Thomas Kazantzis, Undergraduate Student
Maria Arfara, Undergraduate Student
Sophia Dimopoulou, Training Student

Research Interests

Development (design, synthesis, characterization, structural analysis, evaluation) of new compounds/agents of pharmacological interest for the diagnosis and/or treatment of diseases as well as for biotechnological and nanotechnological applications. Our main fields of research are Alzheimer's disease and cancer, and our tools are **NMR** and **CD spectroscopies** for structural studies, combined with methodologies of **organic synthesis**, **complexation/labeling** and **biological evaluation** of the new compounds/agents in appropriate systems. Biological evaluation includes studies - mainly by CD – of interactions with biomolecules, biochemical, microscopic and cellular assays in cancer and primary cell lines, as well as *in vivo* evaluation in experimental animals in collaboration with INRASTES.
Recently, our research activity focuses on:

- pharmacophore molecules/bioactive natural products and derivatives with improved pharmacological properties (with typical examples 2- (4'-aminophenyl)benzothiazole, curcumin, isatin, crocine, acteoside, quercetin, etc.) as well as nanostructures (nanoparticles, liposomes) that contain them
- complexes of rhenium and radioactive technetium-99m, with appropriate ligands, designed for targeted action for diagnosis with SPECT and/or treatment of widespread diseases, in collaboration with INRASTES. In addition, anticancer complexes of copper, platinum and palladium designed as anticancer complexes that target DNA, with dual action from the metal and the pharmacophore ligand.
- bioactive peptides with focus on the β-amyloid peptide (Aβ) of Alzheimer's disease and the search of inhibitors of its aggregation to toxic oligomeric and polymeric forms. The effect of potential inhibitors (natural products, synthetic organic molecules, neuroprotective peptides, biosynthetic cyclic peptides) on the aggregation process of Aβ is studied mainly with Circular Dichroism (CD) but also through the reduction of its toxicity in primary neurons (rescue effect).

2017 Findings

In 2017, the synthesis and evaluation of new complexes of benzothiazole and benzimidazole with radioactive ^{99m}Tc were completed in collaboration with INRASTES. The complexes show high permeability of the blood-brain-barrier and high affinity for β-amyloid (Aβ) fibrils and plaques of Alzheimer's disease (AD), while the corresponding stable Re complexes inhibit the aggregation of Aβ to toxic fibrils. The complexes form an ideal pair for diagnosis (^{99m}Tc) and therapy (Re) of AD, and a related patent application has been filed with OBI (22-3-18). In the same field of AD, the study of biosynthetically produced cyclic peptides as inhibitors of Aβ toxicity with *in vitro* and *in vivo* assays, within the framework of Thalis and Aristeia II (NHRF, G. Skretas) programs, was completed and published. At the stage of manuscript preparation is the evaluation of synthetic derivatives of the natural indole isatin through CD, cellular assays and electron microscopy, as well as analogous studies with the natural products of curcumin, quercetin, and their derivatives. In the field of anticancer

agents, the synthesis and evaluation of new curcuminoids as potential photosensitizers in the photodynamic treatment of cancer was completed in collaboration with NTUA, and new complexes of Re with DNA-intercalators were designed and evaluated as multipotent agents.

Furthermore, the team is actively involved in the *in vitro* and *in vivo* biological evaluation of silicon/magnetic nanoparticles and liposomes as carriers of bioactive compounds (benzothiazole, quercetin and chrysine) in collaboration with the University of Patras and the Aristotle University of Thessaloniki. Our activity is also expanding to new collaborations taking advantage of the IB-A infrastructure with characteristic examples: the CD study of live photosynthetic cells (Dr. K. Stamatakis, IB-A), NMR study of commercial agents for dental use (Prof. G. Eliades, School of Dentistry, UOA), the development of a protocol for imaging with Confocal Microscopy of nasal epithelia of patients with chronic sinusitis (Prof. E. Kirodimos, Medical School, UOA).

Publications

Matis, I., Delivoria, D. C., Mavroidi, B., Papaevgeniou, N., Panoutsou, S., Bellou, S., Papavasileiou, K. D., Linardaki, Z. I., Stavropoulou, A. V., Vekrellis, K., Boukos, N., Kolisis, F. N., Gonos, E. S., Margarity, M., Papadopoulos, M. G.., Efthimiopoulos, S., Pelecanou, M., Chondrogianni, N., Skretas, G. (2017). An integrated bacterial system for the discovery of chemical rescuers of disease-associated protein misfolding. Nat. Biomed. Eng. 1, 838–852

Kiritsis, C., Mavroidi, B., Shegani, A., Palamaris, L., Loudos, G., Sagnou, M., Pirmettis, I., Papadopoulos, M., Pelecanou, M. (2017). 2-(4′-Aminophenyl)benzothiazole labeled with ^{99m}Tc-cyclopentadienyl for imaging β-amyloid plaques. ACS Med. Chem. Lett. 8, 1089–1092

Fernández-Luna, V.G., Mallinson, D., Alexiou, P., Khadra, I., Mullen, A.B., Pelecanou, M., Sagnou, M., Lamprou, D.A. (2017). Isatin thiosemicarbazones promote honeycomb structure formation in spin-coated polymer films: concentration effect and release studies. RSC Advances, 7, 12945-12952.

Dimopoulou, A., Kollatos, N., Manta, S., Panagiotopoulou, A., Karastergiou, A., Kontopoulou, F., Schols, D., Komiotis, D. (2017). Facile microwave-assisted synthesis of various C5-modified pyrimidine pyranonucleosides as potential cytotoxic antitumor agents. Curr. Micr. Chem. 4, 1-15

Articles in Press

Xidaki D., Agrafioti P., Diomatari D., Kaminari A., Tsalavoutas-Psarras E., Alexiou P., Psycharis V., Tsilibary E. C., Silvestros S., Sagnou M. (2018) Synthesis and characterization of Hydroxyapatite, β-tricalcium phosphate and biphasic calcium phosphates particles to act as a local delivery carriers of Curcumin: loading, release and in vitro studies, Materials, 11, 595 (I.F. 2.654)

Manta, S., Tzioumaki, N., Kollatos, N., Andrea, P., Margaritouli, M., Panagiotopoulou, A., Papanastasiou, I., Mitsos, C., Tsotinis, A., Schols, D., Komiotis, D. (2018). Polyfunctionalized pyrrole derivatives: Easy three-component microwave-assisted synthesis, cytostatic and antiviral evaluation. Curr. Micr. Chem. 5, 23-31 (I.F. not available)

Sevastos, A., Kalampokis, I.F., Panagiotopoulou, A., Pelecanou. M., Aliferis, K.A. (2018). Implication of fusarium graminearum primary metabolism in its resistance to benzimidazole fungicides as revealed by ^{1}H NMR metabolomics. Pestic. Biochem. Physiol. (I.F. 2.590)

Dimitriadi, M., Panagiotopoulou, A., Pelecanou, M., Yannakopoulou, K., Eliades, G. (2018). Stability and reactivity of γ-MPTMS silane in some commercial primer and adhesive formulations. Dent. Mater. (I.F. 4.070)

Liargkova, T., Eleftheriadis, N., Dekker, F., Voulgari, E., Avgoustakis, C., Sagnou, M., Mavroidi, B., Pelecanou, M., Hadjipavlou-Litina, D. (2018). Small multi-target molecules incorporating the enone moiety Molecules (I.F. 2.988)

Presentations at Scientific Conferences

B. Mavroidi, C. Kyritsis, A. Shegani, A. Stouraitis, C. Triantis, M. Paravatou-Petsotas, M. Sagnou, I. Pirmettis, M. Papadopoulos, M. Pelecanou (2017). Biological evaluation of mixed pharmacophore *fac*-[M(OO)(isc)$(CO)_3$] and *fac*-[M(NO)(isc)$(CO)_3$] (M = Re, ^{99m}Tc) complexes bearing 2-(4'-aminophenyl)benzothiazole for tumor diagnosis. 22nd International Symposium on Radiopharmaceutical Sciences (ISRS 2017), May 17-19, 2017, Dresden, Germany

S. Mourtas, B. Mavroidi, M. Pelecanou, S. G. Antimisiaris (2017). Benzothiazole-decorated liposomes with affinity for amyloid peptides. ILS Liposome Advances and Liposome Research Days, Combined Conference, September 16-18, 2017, Athens, Greece

C. Kiritsis, A. Lazopoulos, A. Shegani, M. Ischyropoulou, E. Papadopoulou, M. Paravatou-Petsotas, M. Pelecanou, M. Papadopoulos, I. Pirmettis (2017). Novel cyclopentadienyl complexes of rhenium and technetium-99m bearing a quinazoline-derivative as a potential ^{99m}Tc biomarker for EGFR-TK imaging. 22nd International Symposium on Radiopharmaceutical Sciences, May 14-19, 2017, Dresden-Germany

I. Roupa, B. Mavroidi, C. Kiritsis, A. Shegani, D. Papagiannopoulou, C. Raptopoulou, V. Psycharis, C. Methenitis, M. Pelecanou, I. Pirmettis, M. Papadopoulos (2017). Complexes of $ReO(V)^{3+}$ with polycyclic aromatic ligands as anticancer agents. 22nd International Symposium on Radiopharmaceutical Sciences, May 14-19, 2017, Dresden-Germany

A. Shegani, M. Ischyropoulou, A. Papasavva, C. Kiritsis, C. Raptopoulou, V. Psycharis, M. Pelecanou, I. Pirmettis, M. Papadopoulos (2017). Synthesis and evaluation of a new "2+1" Re and ^{99m}Tc tricarbonyl dithiocarbamate complexes with various monodentate ligands. 22nd International Symposium on Radiopharmaceutical Sciences, May 14-19, 2017, Dresden-Germany

E. Papadopoulou, A. Papasavva, A. Shegani, C. Kiritsis, P. Kyprianidou, M. Pelecanou, M. Papadopoulos, I. Pirmettis (2017). *fac*-[^{99m}Tc$(CO)_3$(CCS2)(P)] complexes bearing ciprofloxacin dithiocarbamate: A [2+1] concept for potential infection imaging agents. 22nd International Symposium on Radiopharmaceutical Sciences, May 14-19, 2017, Dresden-Germany

M. Ischyropoulou, A. Shegani, C. Triantis, C. Kiritsis, I. Roupa, A. Papasavva, M. Pelecanou, I. Pirmettis, M. Papadopoulos (2017). Synthesis and comparative biological evaluation of *fac*-[^{99m}Tc(Quin)(Cisc)$(CO)_3$], trans-cis-[^{99m}Tc(Quin)$(Cisc)_2(CO)_2$] and [^{99m}Tc(Quin)$(Cisc)_3$(CO)]. 22nd International Symposium on Radiopharmaceutical Sciences, May 14-19, 2017, Dresden-Germany

A. Shegani, C. Kiritsis, I. Roupa, M. Pelecanou, I. Pirmettis, M. Papadopoulos (2017). Novel phenylboranate rhenium and technetium-99m cyclopentadienyl complexes for molecular recognition of overexpressed sialic acid on tumor cells. 24th Young Researcher Fellow Meeting, School of Pharmacy Châtenay-Malabry, February 8-10, 2017, France

M. Dimitriadi, A. Panagiotopoulou, M. Pelecanou, K .Yannakopoulou, G. Eliades (2017). Stability of dental silane coupling agents. 19th International Conference on Dental Medicine and Tools, June 21-22, 2017, Vienna, Austria.

A. Alexopoulos, E. Kakoulides, A. Panagiotopoulou (2017). qNMR spectroscopy as an innovative and powerful technique for the determination of purity of organic compounds. 10th International Conference on Instrumental Methods of Analysis, September 17-21, 2017, Heraklion, Greece.

A. Shegani, A. Papasavva, I. Roupa, C. Karachaliou, L. Palamaris, C. Kiritsis, C. Tsoukalas, C. Triantis, G. Loudos, P. Kyprianidou, P. Bouziotis, M. Pelecanou, M. Papadopoulos, I. Pirmettis (2017). Development of multimodal mannosylated dextran for sentinel lymph node detection with SPECT/ PET and optical imaging. Annual Congress of the European Association of Nuclear Medicine, October 21 – 25, 2017, Vienna, Austria

I. Matis, D. C. Delivoria, B. Mavroidi, N. Papaevgeniou, S. Panoutsou, S. Bellou, N. Boukos, M. Pelecanou, N. Chondrogianni, G. Skretas (2017). Molecular evolution of macrocyclic rescuers of disease-associated protein misfolding. 68th Congress of the Hellenic Society of Biochemistry and Molecular Biology, November 10-12, 2017, Eugenides Foundation, Athens, Greece

M. Sagnou, B. Mavroidi, A. Kaminari, D. Hadjipavlou – Litina, M. Pelecanou (2017). Novel isatin thiosemicarbazone derivatives as potent inhibitors of β-amyloid peptide (Aβ) aggregation and toxicity. 68th Congress of the Hellenic Society of Biochemistry and Molecular Biology, November 10-12, 2017, Eugenides Foundation, Athens, Greece

B. Mavroidi, C. Kiritsis, A. Shegani, A. Stouraitis, C. Triantis, M. Paravatou-Petsotas, M. Sagnou, I. Pirmettis ,M. Papadopoulos, M. Pelecanou (2017). 2-(4'-Aminophenyl)benzothiazole as pharmacophore in tricarbonyl *fac*-$[M(CO)_3]^+$ (M = Re, ^{99m}Tc) complexes for diagnostic/therapeutic applications in breast cancer. 17th Hellenic Symposium on Medicinal Chemistry, June 1-3, 2017, Thessaloniki, Greece

C. Kiritsis, B. Mavroidi, A. Shegani, A. Stouraitis, M. Sagnou, I. Pirmettis, M. Papadopoulos, M. Pelecanou, (2017). Synthesis and biological evaluation of 2-(4′-aminophenyl)benzothiazole labeled with ^{99m}Tc-cyclopentadienyl as potential imaging probe for β-amyloid plaques. 10th Panhellenic Conference on Alzheimer's Disease and Related Disorders and 2nd Mediterranean Conference on Neurodegenerative Diseases, February 2-5, 2017, Thessaloniki, Greece

I. Roupa, B. Mavroidi, C. Kiritsis, A. Shegani, D. Papagiannopoulou, C. Raptopoulou, V. Psycharis, C. Methenitis, M. Pelecanou, I. Pirmettis, M. Papadopoulos (2017). Synthesis of mixed "3+2" ReO complexes as novel anticancer agents. 17th Hellenic Symposium on Medicinal Chemistry, June 1-3, 2017, Thessaloniki, Greece

M. Vlastara, M. Ischyropoulou, I. Roupa, A. Shegani, C. Kiritsis, M. Pelecanou, I. Pirmettis, M. Papadopoulos (2017). Neutral "2+1" mixed ligand complexes with Schiff base (SalH) as bidentate ligand. 17th Hellenic Symposium on Medicinal Chemistry, June 1-3, 2017, Thessaloniki, Greece

A. Shegani, I. Roupa, C. Kiritsis, C. Tsoukalas, M. Paravatou-Petsotas, P. Bouziotis, M. Pelecanou, I. Pirmettis, M. Papadopoulos (2017). A ^{99m}Tc-Labeled cyclopentadienyl phenylboronic acid derivative for in vivo imaging of overexpressed sialic acid on tumor cells. 17th Hellenic Symposium on Medicinal Chemistry, June 1-3, 2017, Thessaloniki, Greece

C. Chatzopoulou, I. Roupa, A. Shegani, E. Marra, C. Kiritsis, M. Pelecanou, I. Pirmettis, M. Papadopoulos (2017). Novel rhenium (I) and technetium (I) complexes with an NO ligand. 17th Hellenic Symposium on Medicinal Chemistry, June 1-3, 2017, Thessaloniki, Greece

V. Sofokleous, M. Zachariadis, E. Kirodimos, M. Sagnou, M. Kotomichelakis, M. Riga, i. Giotakis, V. Daniilidis (2017). Documentation of the existence of bacterial biofilms in the nasal mucosa of patients with chronic rhinosinusitis, using laser confocal microscopy. 17ο Hellenic Seminar of Rhinology, 12-14 May, 2017, Fougaro, Nafplio.

M. Tsoka, M. Sagnou, M. Zachariadis, K. Papadokostaki, M. Sanopoulou (2017). Biphasic elastomer-hydrophilic polymer systems for biomedical applications. 11ο Hellenic Scientific Conference in Chemical Engineering, 25 - 27 May 2017, Thessaloniki Concert Hall Conference centre, Thessaloniki

V. Sofokleous, M. Zachariadis, E. Kirodimos, M. Sagnou, M. Kotomichelakis, M. Riga, i. Giotakis, V. Daniilidis (2017). Correlation between bacterial biofilms and the clinical characteristics of the disease in patience of chronic rhinosinusitis: a pilot study. 19ο Hellenic Otorhinolaryngologyconference, Head and Neck Surgery, 2–5 November 2017, Hilton Hotel, Athens

Educational Activities

Participation in the Summer School 2017: Presentation of the NMR Spectroscopy Laboratory of Liquid Specimens, Principles and Applications of NMR Spectroscopy (A. Panagiotopoulou)

Member of the three-member committee of the PhD Candidate Timotheos Konstantopoulos with Scientific Coordinator Prof. C. Methenitis, Department of Chemistry, University of Athens. Title of thesis "Synthesis and characterization of magnetic nanoparticles as drug transport agents. *In vitro* study of biological activity" (M. Pelecanou)

Oct 2017 - April 2018: Organization and supervision of the educational program "Observing Science", for the two last classes of elementary schools in Attica. The program was held every Thursday and Friday at NCSR "Demokritos" library, with a maximum of 60 students at a time and included actions such as: "Hang your.……DNA" (Figure 1) and "Microscopic Observation of Biological Preparations" (M. Sagnou)

Figure 1. Images from the "Hang Your.……DNA" activity where students make with simple materials (paper or beads) DNA models specifically designed to demonstrate the basic characteristics of the double helix in an easily comprehensible way.

November 2017 - May 2018: Participation every Wednesday in the educational program for high school students named "How well do you know your brain?" and "Discover what neurosciences have taught us about brain functions and the action of addictive substances through ...games and quizes! " (M. Sagnou)

Other Scientific Activities

Participation in editorial boards of scientific journals:
Journal Dialogues in Clinical Neuroscience & Mental Health - Assistant Editor (M. Sagnou)

Review of scientific publications:
Applied Organometallic Chemistry, Inorganic Chemistry (M. Pelecanou)
Letters in Drug Design & Discovery, Bioorganic Medicinal Chemistry Letters, PLOS ONE, Asian Journal of Pharmaceutical and Clinical Research (M. Sagnou)

Other Activities for the Institute of Biosciences & Applications

M Pelecanou:

- Co-responsible (with M. Vlassi) for the operation of the circular dichroism spectrometer (CD) at IB-A.
- Co-responsible for the operation of the NMR Laboratory of NCSR "Demokritos" (Internal Project 949, Provincial Council No. 305 / Issue 18)

M. Sagnou:

- Member of the BIOIMAGING-GR monitoring group within the framework of the Infrastructure Roadmap together with H. Pratsinis, V. Lambropoulou
- Participation in the action "Mind the Lab" (Feb 2017), which was organized for the first time in Greece, an all-day campaign conducted simultaneously in 12 selected Metro stations in Athens, aiming at raising public awareness on issues of everyday life that are related to science and technology.

- Participation in the pre-event of NCSR "Demokritos" organized as part of "Researchers' Night" 2017 with interactive activities, hands-on experiments and games for children and teenagers. Characteristic titles of the 2017 activities include "Treasure hunt", "Silicone and the crazy balls", "colors got mixed-up", "painting with Chemistry" and were carried out with the participation of all members of our Lab.

A. Panagiotopoulou

- Responsible for the Blood Bank of NCSR "Demokritos"
- Functional support of the CD spectropolarimeter and the 250 MHz and 500 MHz NMR spectrometers.

Impact Factors (for 2 -out of the total 4- publications): 7,586

Citations 2017 (without self-citations):

M. Pelecanou: 75
M. Sagnou: 55
A. Panagiotopoulou: 2

Total Citations 2013-2017 (without self-citations):
M. Pelecanou: 386
M. Sagnou: 198
A. Panagiotopoulou: 16

h-factor:
M. Pelecanou: 20 (Scopus)
M. Sagnou: 11 (Scopus), 10 (Google Scholar)
A. Panagiotopoulou: 4 (Scopus)

Current External Funding

Project entitled *Development of a radiodiagnostic agent for breast cancer*, funded by Stavros Niarchos Foundation and Biokosmos SA with Dr M. Pelecanou as scientific coordinator.
Duration: 2017-2020
Total Program Funding: 65.459,88 €
Funding of the lab for 2017: 10.909,98 €

Program entitled Evaluation of compounds as diagnostic agents for cancer , funded by Hygeia Foundation with Dr M. Pelecanou as scientific coordinator.
Duration: 2017-2020
Total Program Funding: 10.000 €
Funding of the lab for 2017: 5.000 €

Note: *Programs to be funded by the team in 2017 - early 2018*

EREVNO-DIMIOURGO-KENOTOMO

Innovative Radiopharmaceuticals with Fluoride-18: Research, Development and Introduction to the Greek Market for Diagnosis / Progression of Major Diseases with PET (INRASTES, NCSR "D", Sc. Res.: I. Pirmettis, responsible for IB-A M. Pelecanou), 2017, **approved**

Stavros Niarchos Foundation, Industrial Research Fellowships 2017-2020

"Nature-loaded" Targeted Nanoparticles for Prostate Cancer Therapy, (Industry: Biohellenika S.A - IB-A, NCSR "D", Sc. Res.: M. Sagnou), 2018, **approved**

Research Group: Protein Structure and Molecular Modeling

Research Staff
Metaxia Vlassi, Research Director
Nastazia Lesgidou, Collaborating Graduate Sudent *(MSc)*

Research Interests

- Protein folding
- Sequence/structure relationships of amino-acid repeats/Role in protein-protein interactions
- Molecular dynamics of proteins
- Molecular dynamics simulations & development of related tools
- Phosphorylation and conformational changes
- Protein interactions
- Intrinsically disordered proteins
- Structure & dynamics of enzymes as potential therapeutic targets

The approach we follow includes mainly *in silico* techniques such as homology/comparative modeling and threading, molecular dynamics simulations, molecular docking etc.

2017 Findings

- In the framework of our studies regarding sequence/structure relationships of amino-acid repeats and their role in protein-protein interactions, in 2017 we elucidated (see ***Publication 1***) the role of **tandem glutamine repeats (PolyQ)** located at the non-TPR N-terminal tail of the previously studied TPR-repeat protein, Ssn6. More specifically, using first, a combination of size exclusion chromatography and circular dichroism, we found that, truncation/deletion of this glutamine-rich domain results in non-physiological self associations of Ssn6 that may prevent its interaction with the Tup1 protein and therefore the formation of the global transcriptional co-repressor, Ssn6-Tup1. Yeast-two hybrid experiments (D. Tzamarias, ITE-Crete) confirmed this prediction. Subsequently, using *in silico* techniques, such as ***ab-initio* folding** by **replica exchange molecular dynamics (REMD) simulations**, we showed that this Ssn6 domain is structurally flexible (disordered) and capable to adopt at least two alternative conformations relative to the TPR super-helix of Ssn6 (**Figure**). Based on our data we propose the following mechanism for the modulation of the formation of the Ssn6-Tup1 complex and therefore of its transcriptional activity: in the absence of Tup1, through transient interactions with its TPR super-helix, the N-terminal polyQ tail of Ssn6 protects its Tup1-binding site from non-physiological TPR-mediated self-associations, and/or stabilizes the Ssn6 TPR structure, which is essential for Tup1 interaction and function. Such modulation mechanism(s) may apply to other glutamine-rich protein complexes involved in transcription.
- In the framework of our studies towards the elucidation of structure/function relationships of proteins linked to diseases, we carried out *in silico* structural studies of two proteins, TSC1 and TSC2 and of their variants (R246K and I1648F, respectively) identified (M. Voutsinas' group) in tuberous sclerosis complex patients from Greece.More precisely, using *in silico* techniques (*in silico* mutagenesis and molecular dynamics simulations), we showed that: a) the R246K change does not affect the structure of TSC1 suggesting that the loss-of-function of this TSC1 variant reported in the literature, is more likely a result of alternative splicing of the related gene and b) the I1648F change affects the structural integrity of the catalytic domain of TSC2 and therefore it is predicted to result in loss of function (see ***Publication 2***).
- In addition, in 2017 we studied *in silico* the role of various cysteine residues in the activity of SRPK1, a kinase that we have studied in the past and its function was found to be regulated through the formation of several disulfide bonds. More specifically, our *in silico* analysis predicted

that the experimentally observed disulfide bonds involve only cysteine residues located outside the catalytic domain of SRPK1 (see ***Publication 3***).

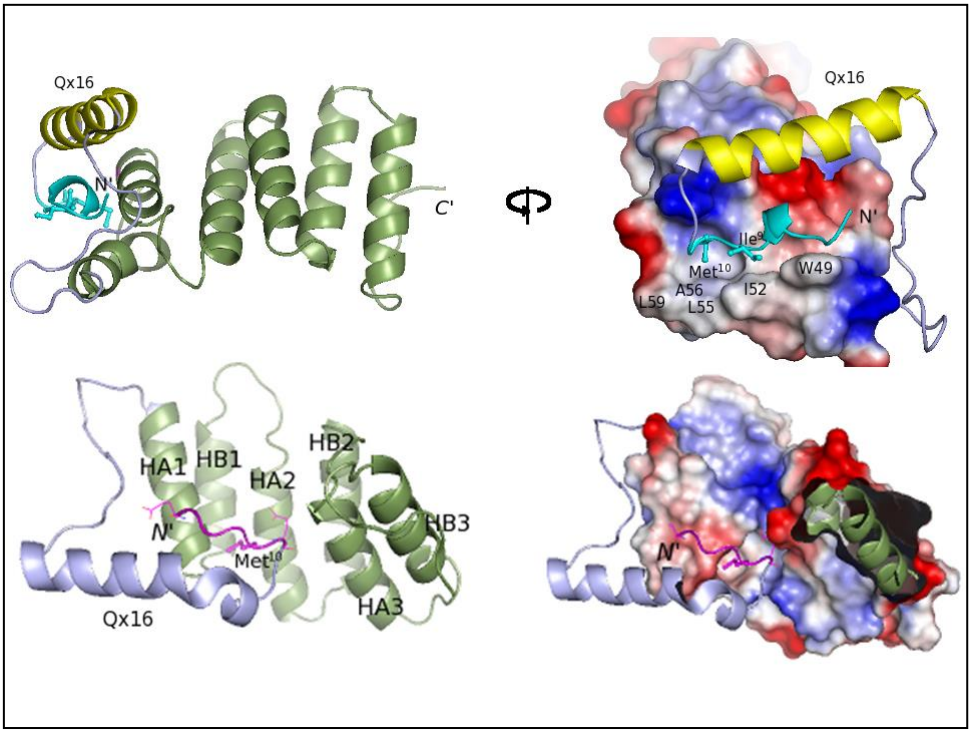


Figure. *In silico ab- initio folding via REMD simulations revealed at least two alternative conformations of the glutamine rich (QX16) N-terminal tail of Ssn6 that, in combination with experimental data suggest a crucial role of this region of Ssn6 in the formation of the general transcriptional co-repressor, Ssn6-Tup1 (see* ***Publication 1****) and therefore its function. Regulation of gene expression through alternative conformations of structurally flexible glutamine-rich domains may not be specific to the Ssn6-Tup1 complex but may apply to other polyQ-containing transcription factors, in general.*

- Finally, in 2017 several potential users have registered to obtain access to updated versions of the **GROMITA-GUI** we have developed in the lab (***http://gromita.bio.demokritos.gr***).

Publications

Tartas, A, Zarkadas, C, Palaiomylitou, M, Gounalaki, N, Tzamarias, D., Vlassi, M. (2017). Ssn6-Tup1 global transcriptional co-repressor: Role of the N-terminal glutamine-rich region of Ssn6. PLoS ONE 12(10): e0186363. (https://doi.org/10.1371/journal.pone.0186363)

Avgeris, S, Fostira, F, Vagena, A, Ninios, Y, Delimitsou, A, Vodicka, R, Vrtel, R, Youroukos, S, Stravopodis, DJ, Vlassi, M, Astrinidis, A, Yannoukakos, D, Voutsinas, GE (2017). Mutational analysis of TSC1 and TSC2 genes in tuberous sclerosis complex patients from Greece. Scientific Reports |7: 16697. (https://doi.org/10.1038/s41598-017-16988-w)

Koutroumani M, Papadopoulos GE, Vlassi M, Nikolakaki E, Giannakouros T (2017) Evidence for disulfide bonds in SR Protein Kinase 1 (SRPK1) that are required for activity and nuclear localization. PLoS ONE 12(2): e0171328. (https://doi.org/10.1371/journal.pone.0171328)

Other Scientific Activities

- Member of the European Network **INSTRUCT-ERIC** (INSTRUCT: An integrated Structural Biology Infrastructure for Europe)
- Member of the related National Research Infrastructure project: "INSTRUCT-EL, an initiative of Greek Researchers related to Structural Biology". A related proposal entitled "***INSPIRED: The***

National RIs on Integrated Structural Biology, Drug Screening efforts and Drug-target functional characterization" *was* included in the National Roadmap for Research Infrastructures in 2014 and a related grant application in the framework of the call for National RIs was submitted to GSRT in October 2016, is currently under "curation".

- Member of the national network BE/OPT-XFEL (Network to Optimize use of the European X-FEL by the Greek Research Community)

Educational Activities

Supervisor of the Masters Thesis of N. Lesgidou (National & Kapodistrian UoA) in collaboration with Prof. E. Eliopoulos (AUoA)

Lectures on "Principles of X-Ray Crystallography: Applications in Structural Biology" in the framework of the post-graduate programs (towards a Masters degree): 1) "Clinical Biochemistry – Molecular Diagnosis" (Depts. of Biology/Chemistry/Nursing, National & Kapodistrian University of Athens) and 2) "Clinical Chemistry" (Dept of Chemistry, National & Kapodistrian University of Athens).

Other Activities for the Institute of Biosciences & Applications

In charge (with Dr. M. Pelecanou) of the Circular Dichroism (CD) service unit of IBA.

Member of various committees of NCSR "D"

Responsible for the operation of various common equipment of the IBA

Impact Factors (for 3 publications): 9,871

Citations 2017 (without self- citations): 15

Total Citations 2013-2017 (without self- citations): 103

h-factor: 14 (Scopus/ISI)

S E R V I C E U N I T S

- ***HUMAN TISSUE LABORATORY/ BANK***
- ***EXPERIMENTAL ANIMAL COLONY***
- ***LASER CONFOCAL MICROSCORY***
- ***CIRCULAR DICHROISM (CD) LABORATORY***
- ***LABORATORY OF CELL & MATRIX PATHOBIOLOGY***
- ***LABORATORY OF MOLECULAR DIAGNOSIS OF GENETIC DISEASES***
- ***LABORATORY OF CELL-BASED ASSAY SYSTEMS AND BIOACTIVE COMPOUNDS***

HUMAN TISSUE BANK

Research Staff
Helen Vavouraki, Researcher
Yannis Ninios, Graduate Research Associate (PhD)

Laboratory Description – Research Interests

The Human Tissue Bank of NCSR "DEMOKRITOS" is one of the first legislated laboratories of the Center, always mentioned in the laws of the Ministry of Health regarding transplantations. The main objective of the Bank includes the collection of various human tissues, their processing and the production of grafts to be used in Regenerative Medicine and Reconstructive Surgery. It is conforming to the European Directives 23/2004, 17/2006 and 86/2006 concerning human tissues and cells, as they were implemented in Greece by the 26/2008 Law, as well as, to the recommendations of IAEA.

Member of the European Association of Tissue Banks, it is the only bank of its kind in Greece, applying its "knowhow" in the processing of a great variety of human tissues and its expertise that has gradually developed in each procedure (procurement, tissue processing, irradiation sterilization and disposal of tissue grafts). In over 45 years of continuous functioning, it has delivered more than 50.000 tissue preparations without any quality-related problems. All procedures taking place in the Bank are fully computerized and accredited according to ISO 9001/2015. It is of main concern for us to constantly be updated in quality control topics and to ensure our compliance with the Greek and European Standards.

The grafts' preparations are delivered to hospitals, health clinics, medical and dental laboratories, all over the country.

The Tissue Bank's research interests are mainly focused on the study of the activity of the produced grafts, the optimization of the production methods, the introduction of new techniques, the process of new types of tissues and the development of new grafts.

Its research activities are therefore based on collaborations with hospitals and university medical and other departments, in order to promote Public Health by launching improved products, publishing original papers and participating in doctorate degrees (Ph.D. theses).

Our research interests and activities have been resulted in and founded by:

a) A Technological Research Project – Research, Development and Delivery of Tissue grafts -products of Tissue Repair-, and

b) A Research Project for the development of a new, specially designed bone graft to accompany the EPO patented TALOS, used in Neurosurgery.

2017 Findings

In 2017, we have collected tissues following the established tissue procurement regulations of the National and European Legislation. We have processed femur heads from living donors and we have prepared and delivered 487 preparations of bone grafts to be used in Dentistry and Orthopedic Surgery. Moreover, we have delivered over 30 various other tissue graft preparations for Medical use.

Scientific collaboration with hospitals, University labs, etc., has resulted in the preparation and study of new optimized products, as well as customized ones e.g. for child facial Surgery.

Other Activities for the Institute of Biosciences & Applications

Scientific Responsible of Human Tissue Bank.

Quality Manager of Human Tissue Bank (ISO 9001/2008 - ISO 9001/2015)

Alternate member of the Scientific Counsil of IBA (Institute of Biosciences & Applications) Member of drafting research proposal committee of IBA (KRIPIS II)

Other Scientific Activities:

Reviewer in the scientific Journals: Platelets, Cell and Tissue Banking

Member of European Committee for the establishment of unique nomenclature of human tissues and cells

Member of European auditors-net of human tissue and cells banks

Expert of National Transplant Organization and Ministry of Health in the field of Human Tissue Banking

Member of Organizing Committee of 28th Congress of European Biomaterials Association Athens, 9/2017.

Research Proposals Assessor

Other Activities at the NSCR "Demokritos"

Member of the Health and Safety Committee of NCSR "D"

Member of Ethics Committee of NCSR "D"

Citations 2017 (without self- citations): 8

Total Citations 2013-2017 (without self- citations): 53

h-factor: 7 (Scopus)

EXPERIMENTAL ANIMAL COLONY

Research Staff

Dimitris Kletsas, Research Director, Scientific and Administrative Responsible

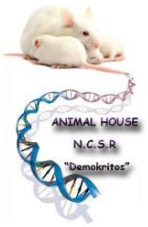
Ioannis Zafiropoulos, Research Technician

George Doulgeridis, Research Technician

Lykourgos Klamarias, Veterinarian

Laboratory Description

The animal facility during 2017 maintained and reproduced inbred strains of experimental animals. The following strains are currently available:



- Mice, strain CFW SWISS ALBINO
- Mice SCID (immunocompromised)
- Mice SKH1 (hairless)
- Mice C57Bl/6 (wild type and transgenic)
- Rats, WISTAR ALBINO
- Rats, FISCHER (CDF)
- Rabbits, NZW ALBINO

During 2017 the Animal Facility provided the following animals:

Users	*Rats* **WISTAR**	*Mice* **SKH1**	*Mice* **CFW**	*Mice* **C57Bl/6J**	*Rabbits* **NZW**	*Rats* **FISCHER**	*Mice* **SCID**	**Total**
Institute of Biosciences and Applications	77	5	0	47	0	0	3	**132**
Institute of Nuclear & Radiological Sciences and Technology, Energy & Safety	0	0	186	52	4	0	114	**356**
Institute of Nanosciences and Nanotechnology	0	0	0	0	0	0	6	**6**
External Users	129	8	10	16	0	36	20	**219**
Total	**206**	**13**	**196**	**115**	**4**	**36**	**143**	**713**

The certification according to ISO 9001:2008 has been renewed.

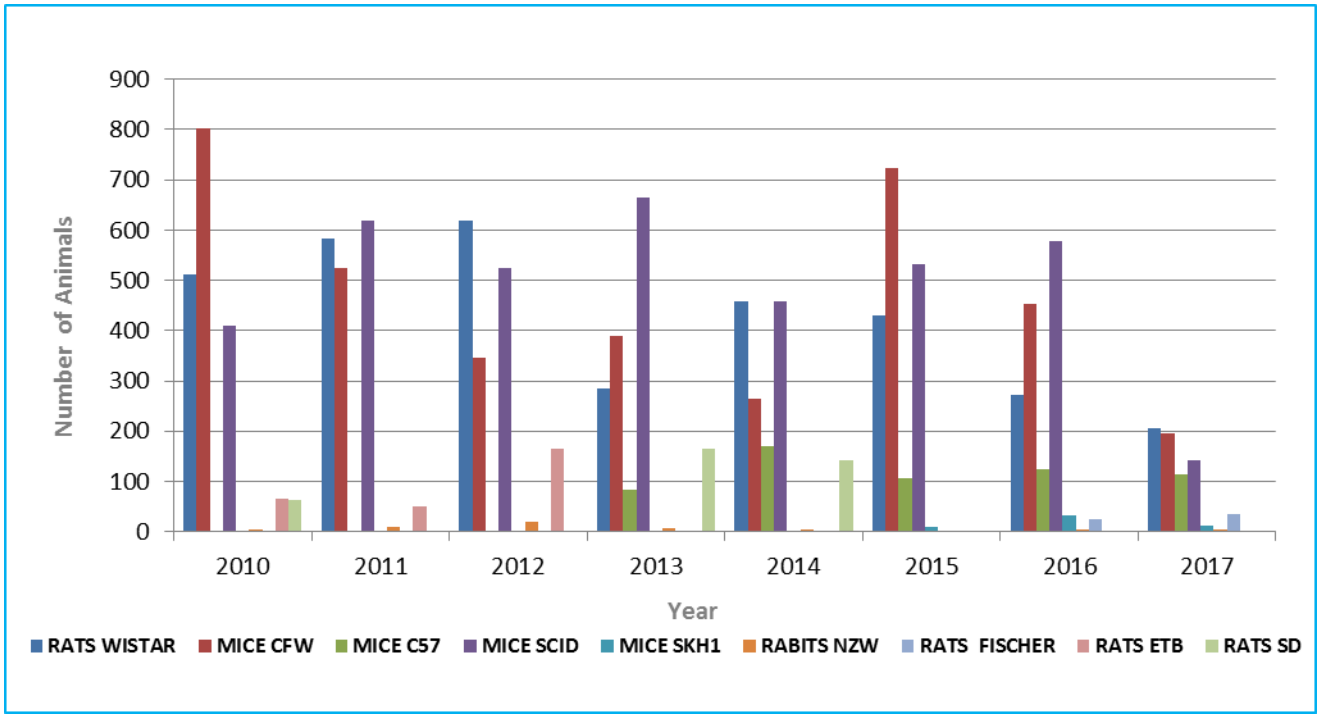
The Facility has been inspected by the Veterinary Division of the Attika Prefecture.

The animal colonies of the Facility have been renewed and new colonies (mice C57Bl/6) have been developed.

The Committee for the Wellbeing of Laboratory Animals and the Committee for the Approval of Research Protocols of the Facility met regularly throughout 2017 and approved or renewed five (5) research protocols.

A one-day Seminar for the users of the Facility has been organized.

DISPOSAL OF LABORATORY ANIMALS 2010-2017

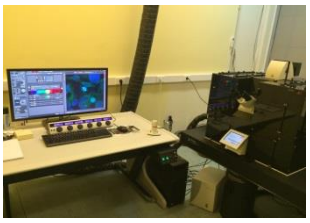


LASER CONFOCAL MICROSCOPY LABORATORY

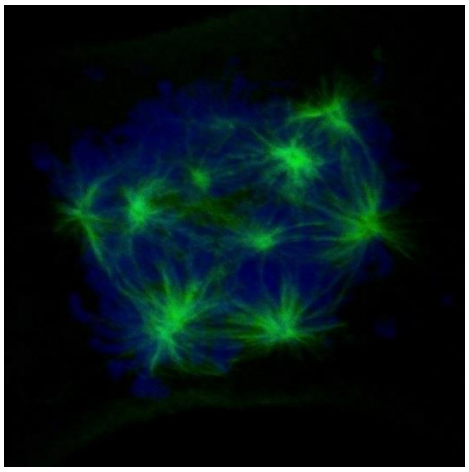
Research Staff

Dimitris Kletsas, Research Director, Scientific and Administrative Responsible

Vassiliki Labropoulou, Senior Researcher
Haris Pratsinis, Researcher
Marina Sagnou, Researcher
Michalis Zachariadis, Technician



Laboratory Description



The Confocal/Multiphoton Microscopy Unit of the Institute of Biosciences and Applications of NCSR "Demokritos" has been operating since July 2016 with a new generation, modern equipment, serving the imaging needs of both the research laboratories of the Institute and other Institutes of NCSR "D", as well as external Research centers and Universities such as the NKUA, the NTUA, the Agricultural University of Athens as well as some Hospital Units. The unit is equipped with a Leica TCS SP8 MP multiphoton microscope, with capabilities that cover a wide range of applications of optical microscopy:

- Multi-Channel Fluorescence Microscopy, covering UV, Visible and Infrared Spectrum
- Multi-color 3D Imaging
- Live Cell Imaging
- 2-Photon Microscopy
- Second Harmonic imaging
- Förster Resonance Energy Transfer (FRET) to monitor molecular interactions in live or fixed specimens
- Fluorescence Recovery After Photobleaching (FRAP)
- Spectral unmixing of fluorescent dyes
- Cell/tissue Colocalization analysis
- Calcium Imaging
- Differential Interference Contrast (DIC) microscopy (known as Nomarski microscopy)
- Image processing and analysis

The Confocal/Multiphoton Microscopy Unit in the year 2017 recorded more than 300 operating hours, ¼ of which involved collaborations with external Research centers and Universities. The unit collaborated with at least 9 research teams from the IB-A and INN as well as with various third-party academic institutions in protocols dealing with:

- The study of new chemical compounds aiming at the discovery of new active or imaging agents
- The study of the induction of genotoxic lesions and cell senescence
- The expression of specific proteins associated with mechanisms involved in age-associated diseases such as dyslipidemia, diabetes mellitus and Alzheimer's disease
- Functional characterization of opioid receptors

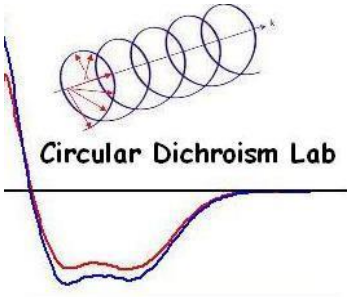
- Imaging and cellular identification of new dendrimers, liposomal preparations and nanostructures for the transport of bioactive substances
- Imaging of biofilm in the nasal mucosa of patients with chronic rhinosinusitis and correlation with their clinical characteristics

The activities of the Confocal/Multiphoton Microscopy Unit support the scientific work of the various research teams, contributing to scientific publications, doctoral theses and the development of collaborations among the users of the Unit. Moreover, the Unit actively supports the various NCSR "D" educational programs participating in presentations, demonstrations and workshops.

At the same time, IB-A participates in the "Greek Research Infrastructure for the Visualization and Monitoring of Fundamental Processes in Biology and Medicine (BIOIMAGING-GR)", which is funded by GSRT and in which participate, besides the Institute, 10 additional Research centers and Universities.

CIRCULAR DICHROISM (CD) LABORATORY

Research Staff
Metaxia Vlassi, Research Director
Maria Pelecanou, Research Director
Aggeliki Panagiotopoulou, Functional Scientific Personnel B



Users' Committee:
Metaxia Vlassi
Maria Pelecanou
Angeliki Chroni
Georgios Nounesis (INRASTES)
Stratos Stratikos (INRASTES)

Laboratory Description - Objective

The equipment of the Circular Cichroism (CD) Laboratory includes a JASCO-715 spectropolarimeter equipped with a Peltier system for temperature control. This CD infrastructure was acquired in 1998 within the framework of the "Center for Crystallographic Studies of Macromolecules (CCM)", a network of three Institutes of the NCSR "Demokritos" (the former Biology, Physical Chemistry, Radioisotopes & Radiodiagnostics Products) and other Greek academic institutions, financed through a grant (EPET) from the General Secretariat for Research and Technology. It is located at room Y-35 of the Institute of Biosciences & Applications and is operating under the supervision of IB-A scientists. Since 2013 (13/06/2013), the CD Lab is one of the official Laboratories for the Provision of Specialized Services of NCSR "D".

Circular Dichroism (CD) is a well-established spectroscopic technique based on the differential absorption of circularly polarized light from optically active molecules and it is widely used for

- Conformational analysis of biological macromolecules (e.g. proteins)
- Investigation of protein-protein interactions as well as interactions/complexation of proteins with various ligands, metals, stabilizers, inhibitors, drugs, etc. and interactions/complexation of nucleic acids
- Investigation of the influence of denaturants, solvents and ligands on the conformation and stability of macromolecules
- Monitoring conformational changes under different conditions/thermal stability studies
- Comparative structure and stability studies of proteins and their mutants

The CD method is highly accurate, sensitive, non-destructive to the sample and gives reliable and reproducible results.

2017 Findings

The CD unit has been widely used since 1998 by research teams of NCSR "D" and of other academic/research institutions from all over Greece, for structural analysis and studies of interactions of biological macromolecules. It should be noted that the CD spectropolarimeter is one of the few in Greece and the only one in Athens that provides specialized scientific services to external users. The CD unit has contributed so far to scientific publications and doctoral dissertations as well as to the development of collaborations both within NCSR "D" and with other research institutes. It has also

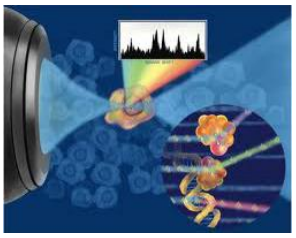
contributed to the training of new users (students, researchers) as well as to solving scientific problems related to CD applications.

In 2017, as in previous years, the CD Lab has supported research projects of at least 12 groups from the 3 participating NCSR "D" Institutes and other Greek academic institutions such as the National and Kapodistrian University of Athens (Dept. of Chemistry, Dept. of Pharmacy), the National Technical University of Athens (Dept of Chemical Engineering), the University of Patras, the University of Thessaloniki and the NHRF (Institute of Biology, Pharmaceutical Chemistry and Biotechnology). Income from the provision of services is solely used to cover the operation and repair needs of the infrastructure.

The CD Laboratory participates in the Project: "Instruct-EL /INSPIRED: The National Research Infrastructures on Integrated Structural Biology, Drug Screening Efforts and Drug Target Functional Characterization", which after a successful evaluation (27-4-16) is included in the Roadmap of National Infrastructures. A related grant application submitted to “GSRT” is currently under re-evaluation (curation).

LABORATORY OF CELL & MATRIX PATHOBIOLOGY

Research Staff
Paraskevi Kitsiou, Senior Researcher (Administrative Responsible)
Athina Tzinia, Senior Researcher
Garyfallia Drossopoulou, Researcher



Laboratory Description - Objective

The specialized services and products provided by the laboratory of Cell & Matrix Pathobiology focus on isolation, characterization and culture of stem cells and other cell types, in order to be used in applications of regenerative medicine. In addition specialized assays for cell survival and apoptosis /cell toxicity were performed.

Services, Products and Activities

The research protocols used in the laboratory were resulted from inquiring studies, developed in the frame of programs that were funded by the General Secretariat of Research and Technology (GGET) and Biophylaxis, S.A.

The potential clinical applications of stem cells are currently expanded in various fields of intensive scientific research such as regenerative medicine and repair of tissue mainly bones, contacts, cartilages and neuron, cardiovascular diseases, transplantations of stem blood cells and autoimmune diseases.

The laboratory provides expertise and services related to regenerative medicine and clinical analyses including:

- Isolation and characterization of human umbilical cord and human umbilical cord blood (UCB) stem cells, stem cells from other sources (skin, fat tissue, etc).
- Isolation and subculture of human and mouse olfactory neuroblasts
- Isolation of other cells types (endothelial cells, neuronal cells, etc).

More specifically:

- The laboratory successfully isolates and characterizes human umbilical cord and human umbilical cord blood (UCB) stem cells and stem cells from other sources (skin and fat tissue). Therefore, the laboratory provides its expertise in the field, to Biophylaxis, S.A, a company focusing on isolation and cryoprotection of stem cells for use in regenerative medicine.
- The laboratory also isolates mesegchymal stem cells from fat tissue which are used by orthopedists for the confrontation of damage of articulations (such as knee and hip). During 2014 and 2015 the laboratory fulfilled the isolation and proliferation of mesegchymal stem cells from abdominal fat tissue of patients (14 incidents) for homologous transplantation in chronic arthropathies (collaboration with Dr N. Kralli).
- Also the laboratory has been expanded in isolation and culture of stem cells emanating from olfactory mucous, in collaboration with Dr A. Charonis and Dr P. Politis {Research, Biomedical Research Foundation Academy of Athens (BRFAA), as well as: Dr Pedro Escada, Dr José Pratas-Vital (Hospital de Egas Moniz, Centro Hospitalar de Lisboa Ocidental, Lisbon, Portugal), Dr Ch. Gogo (EKPA, Attikon Hospital, B' Neurosurgical Clinic). The olfactory mucous is of great importance because it contains nervous tissue which regenerates very rapidly due to its high content of stem cells (OECs). The isolated stem cells can be placed in wounded regions of vertebral column of paraplegic or tetraplegic patients aiming at the regeneration of nervous tissue. This pioneering process provides the possibility of using neural stem cells in targeted therapeutic approaches. The results from inquiring studies on OECs were presented in 8th Hellenic Spine Congress, 24-26 October 2014, Larissa, Greece (Trohatou O., Politis P., Drossopoulou G., Tsilibary E.P. and Gogos C. (2014). Isolation and culture of OECs: Applications in neurodegenerative diseases. 8th Hellenic Spine Congress, 24-26 October 2014, Larissa, Greece).

Infrastructure

The laboratory is equipped to support cellular, biological and biochemical research activities. The following list indicates major pieces of equipment:

- Tissue culture room with laminar flow hood, CO2 incubators, light microscope, stereoscope, etc.
- Table-top refrigerated centrifuge and microfuges
- Vibratome, horizontal and vertical gel & blotting apparatus, power supplies etc.
- Refrigerators, freezer, water-baths, balances, PH meters, sonicator, PCR and Real time-PCR apparatuses.
- Liquid nitrogen container for cell cryopreservation

Funding

Research activities of LABORATORY OF CELL & MATRIX PATHOBIOLOGY are founded by by the General Secretariat of Research and Technology (GGET) and Biophylaxis, S.A.

LABORATORY OF MOLECULAR DIAGNOSIS OF GENETIC DISEASES

Research Staff
Gerassimos Voutsinas, Research Director
Socratis Avgeris, Research Technician

Laboratory Description - Objective

The Laboratory of Molecular Diagnosis of Genetic Diseases was founded in 2011 and specializes in genetic testing of Tuberous Sclerosis Complex (TSC) and Neurofibromatosis types 1 and 2 (NF1 and NF2). The protocols used in the lab derive from previous research and have been developed in the frame of programs funded by the General Secretariat for Research and Technology (GSRT) and the American College of Greece (Deree).

Establishment of genetic testing for TSC by mutation detection in *TSC1* and *TSC2* genes, and for NF1 and NF2, in *NF1* and *NF2* genes, allows confirmation of clinical diagnosis in patients whether these fulfill or not the agreed criteria. At the same time, it may contribute decisively to differential diagnosis, clearly distinguishing TSC or NF from diseases with a similar phenotype. It is also possible to confirm or exclude the presence of disease in patient relatives, who do not exhibit a relevant phenotype, as well as to separate hereditary from *de novo* cases. Genetic counseling sessions are mandatory before and after testing.

It is important to note that these genetic tests are complicated and time-consuming, as each family usually has a different mutation, since there are no hot spots for mutations in the above genes. Finally, to emphasize the importance of family testing and subsequent genetic counseling, it is stressed that while both neurocutaneous syndromes are autosomal dominant (100% penetrance), their expressivity varies significantly so that within the same family the symptoms of a patient may be even difficult to detect, whereas another may exhibit a particularly severe phenotype.

2017 Findings

During 2017, twenty seven (27) TSC families have been tested in our laboratory. In each family, mutation detection analysis was performed in the patient's sample. After identification of the mutation, both parents were tested. In a third step, other family members were tested, when desirable. All testing took place after informed consent. Patients from twenty (20) families had a definite clinical diagnosis for TSC, whereas seven (7) had a possible TSC diagnosis. Pathogenic mutations have been identified in sixteen (16) out of the twenty-seven (27) families.

LABORATORY OF CELL-BASED ASSAY SYSTEMS AND BIOACTIVE COMPOUNDS

Personnel

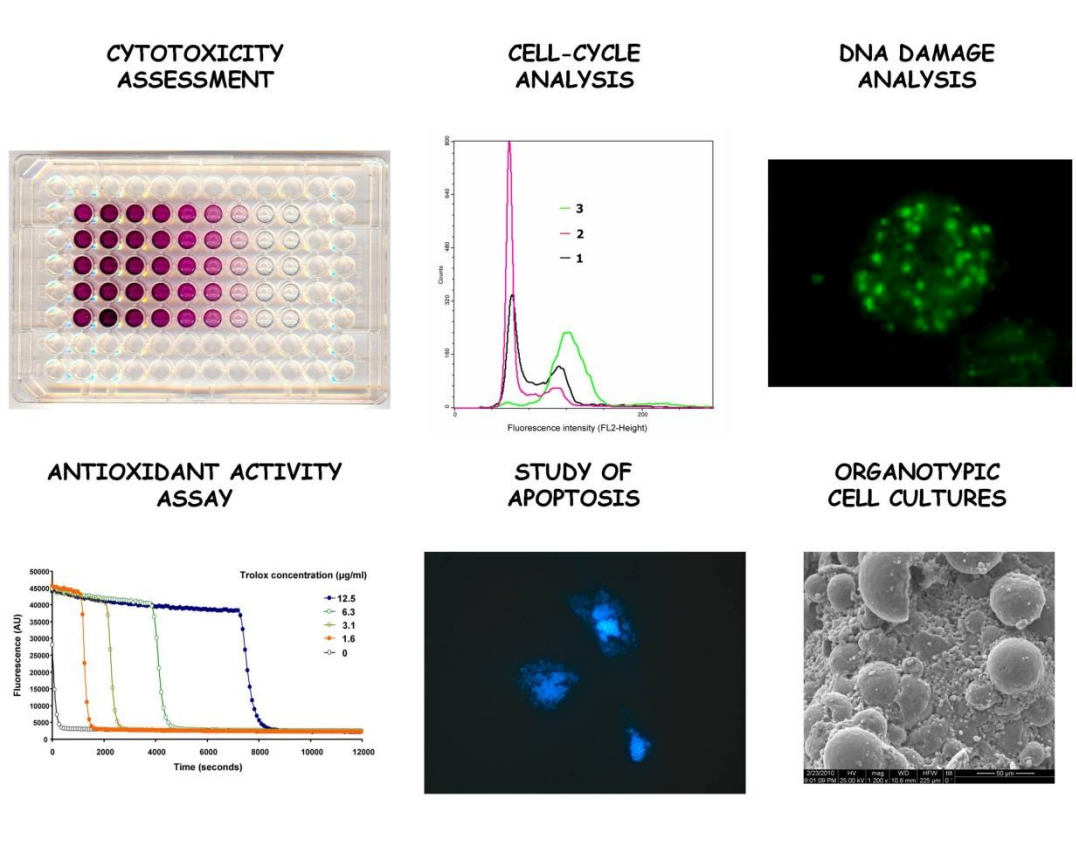
Dimitris Kletsas, Research Director
Harris Pratsinis, Senior Researcher
Eleni Mavrogonatou, Postdoctoral Fellow
Adamantia Papadopoulou, Postdoctoral Fellow
Maria Angelopoulou, Graduate Research Associate (*MSc*)
Anastasios Kouroumalis, Graduate Research Associate (*MSc*)

Laboratory Description

The activities of the Laboratory comprise the isolation of primary somatic or mesenchymal stem cells, and the development of the appropriate cell assay systems for the evaluation of synthetic or natural bioactive products regarding their wound healing, anti-ageing, and anti-cancer properties.

2017 Findings

During 2017, a collaborative project was established with the Universitätsklinikum Ulm, Dermatologie und Allergologie, Head Prof. Dr. med. Karin Scharffetter-Kochanek for studying the role of senescent stromal cells in carcinogenesis.



EDUCATIONAL ACTIVITIES

EDUCATION

The Institute of Biosciences & Applications continues its Graduate Course Programmme, which has been successfully carried out for the past 40 years. This Programme includes:

a. Training of young scientists at the postdoctoral level
b. Pre-graduate and graduate thesis work
c. Courses at the graduate level
d. Lecture Contributions to the Summer School of the NCSR "Demokritos"

During the year 2017, 7 scientists were trained at the postdoctoral level at our Institute. Furthermore, 10 graduate students worked toward the completion of their doctoral thesis research work under the supervision of scientists of the Institute and on projects which were given to them by their respective supervisors.

During the year 2017, 1 of our graduate students finished her PhD thesis and 6 students completed their Master's theses.

Moreover, 10 students from Greek Universities are carrying out their pre-graduate project thesis work at the Institute. Additionally, during 2017, 6 students did practical job training in laboratories at the Institute.

In addition to the above, scientists of IBA carried out the following series of courses and seminars within the framework of the Graduate School Programme of the Greek Universities:

- *Lectures entitled "Molecular diagnosis of genetic diseases" included in the course for "Molecular Biology – Systemic and in silico approaches", in the framework of the Post-Graduate Specialization Diploma "Biological Applications in Medicine"* (**Dr. G. Voutsinas**, Department of Biology and Medical School, University of Athens)
- *Lecture entitled "G protein- coupled receptors in health and disease" in the framework of the postgraduate course "Biochemistry"* (**Dr. Z. Georgoussi**, Department of Biology, University of Athens)
- *Teaching in the framework of the postgraduate course "Molecular Base of Human Diseases"* (**Dr. Z. Georgoussi,** Department of Biology, University of Athens)
- *Teaching in the framework of the postgraduate programme* "Molecular and Applied Physiology" (**Dr. Z. Georgoussi,** Medical School, University of Athens)
- *Teaching in the "Athens International Master's Programme in Neurosciences"* (**Dr. Z. Georgoussi**, Department of Biology, University of Athens)
- *Lecture entitled "Cell senescence: the Janus' s faces of tissue homeostasis" in the framework of Open Educational Program "Molecular Medicine"* (**Dr. D. Kletsas,** Medical School, University of Athens)
- *Lecture entitled* "Cell senescence and carcinogenesis" *in the framework of the class entitled "Thoracic oncology"*, (**Dr. D. Kletsas**, Medical School, University of Athens)
- *Lecture entitled "Cell senescence and tissue homeostasis" in the framework of the postgraduate course "Physiology***"** (**Dr. D. Kletsas,** Medical School, University of Athens)
- *Teaching in the Post-graduate Master's Degree "Applications of Biology in Medicine" in the framework of the course "Cell proliferation and tissue homeostasis. Growth factors: Structure, receptors and signal transduction. Cell senescence and tissue homeostasis. Methodologies for the study of cell proliferation"* (**Dr. D. Kletsas, Dr. H. Pratsinis and Dr. E. Mavrogonatou**, Department of Biology, University of Athens)
- *Lecture entitled "Cell systems in the research of carcinogenesis" in the framework the Post-graduate Master's Degree "Neoplastic Disease in Humans: Diagnosis, Modern Treatment and Research* (**Dr. H. Pratsinis,** Medical School, University of Athens)
- *Lecture entitled "Cell senescence" in the framework the Post-graduate Master's Degree "Clinical Chemistry"* **(Dr. H. Pratsinis,** Department of Chemistry, University of Athens)

- *Lecture entitled Cell Cycle: Checkpoints and Consequences for Normal Cellular Function when Cell Cycle Progress Dysfunctions in the framework of the course"Cell cultures – Tissue cultures" within the postgraduate programme "Application of Biology in Medicine* (**Dr. Th. Sourlingas**, Department of Biology & Medical School, University of Athens).
- *Teaching the undergraduate course "Biochemistry" (6th semester),* (**Dr. A. Chroni**, Department of Chemistry, University of Athens)
- *Lecture entitled "Lipids and apolipoproteins: from atherosclerosis to Alzheimer's disease" in the framework of the graduate course "Clinical Chemistry II"* (**Dr. A. Chroni**, Department of Chemistry, University of Athens)
- *Lecture entitled "RNA-mediated gene silencing: pathways and applications in medicine and agriculture" in the framework of the postgraduate course "Molecular Biology: Systemic and in silico approaches" of the postgraduate diploma of specialization of the Department of Biology and Medical School of UoA* (**Dr. L. Swevers**, Department of Biology & Medical School, University of Athens).
- *Lectures entitled "Molecular Biology: Systemic and in silico Approaches" in the framework of the postgraduate course "Applications of Biology in Medicine"* **(Dr. V. Sophianopoulou**, Department of Biology & Medical School, University of Athens)
- *Teaching in the framework of the postgraduate program "Bioinformatics", the course "Introduction to Computational Biology"* **(Dr. I. Almyrantis,** Department of Biology, University of Athens)
- *Teaching in the framework of the postgraduate program "Clinical Biochemistry and Molecular Diagnostics", the course "Introduction to Computational Biology"* **(Dr. I. Almyrantis,** Department of Biology, University of Athens)
- *Lectures on "Principles of X-Ray Crystallography: Applications in Structural Biology" in the framework of the postgraduate program (towards a Masters degree) entitled "Clinical Biochemistry – Molecular Diagnosis"* (**Dr. M. Vlassi**, Department of Biology, Chemistry & Nursing, University of Athens)
- *Lectures on "Principles of X-Ray Crystallography: Applications in Structural Biology" in the framework of the postgraduate program (towards a Masters degree) entitled "Clinical Chemistry"* (**Dr. M. Vlassi**, Department of Chemistry, University of Athens)

During July 2017, the Summer School of NCSR "Demokritos" was held and had included talks from the researchers of the Institute of Biosciences & Applications and of invited speakers coming from other Greek Institutions and abroad. The seminars of IBA related to the Summer School are presented analytically in the following pages.

In parallel, the 5th Hellenic Forum for Science, Technology and Innovation was held (5-7 July 2017), whereby IBA organized a workshop entitled "Ageing and Age-related Diseases" coordinated by Dr. D. Kletsas with the following invited speakers: Dr. K. Baxevanis ("Agios Savvas" General Hospital), Prof. G. Nomikos (Harokopio University), Prof. E. Douni (Agricultural Univ. of Athens) and Prof. L. Stefanis (BRFAA).

Within the framework of the Graduate School Programme, are also organized, on a regular basis, bibliographical seminars and seminars presenting progress in current research work. These seminars are presented by all the graduate students of the Institute and supplemented by scientific seminars presented by other researchers of the Institute as well as invited guest speakers from other Greek or foreign Educational and/or Scientific Research Institutes. The seminars accomplished the past year (2017) are presented analytically in the following pages.

Finally, the educational endeavours of IBA also include those accomplished by **Dr. H. Pratsinis and Dr. A. Prombona**, who give informative seminars to High School and University students.

COMPLETION/AWARD OF DOCTORAL THESES IN 2017

GRADUATE STUDENT	TITLE OF DOCTORAL THESIS	ADVISOR (in IBA)	UNIVERSITY
Archontia Kaminari	Study of the effect of metalloproteinase-9 (MMP-9) on the insulin-dependent survival pathway in Alzheimer's disease	A.Tzinia/ E. Tsilibary	Department of Biology University of Athens

COMPLETION OF MASTER THESES IN 2017

GRADUATE STUDENT	TITLE OF MSc THESIS	ADVISOR (in IBA)	UNIVERSITY
Christina Mountaki	Role of apolipoprotein E isoforms in regulation of neuronal cholesterol efflux and amyloid-beta peptide generation	A.Chroni	Department of Biology University of Athens
Angeliki Konstantinou	Comparative study of the regulation of fibroblast cells' proliferation and senescence after exposure to oxidative stress and cytokines	D. Kletsas	Department of Biology University of Athens
Olga Tsourou	Study of the effect of bacterial toxins on the physiology of human dermal fibroblasts	D. Kletsas	Medical School University of Athens
Georgia Chaldaiopoulou	The role of cytokines in the aging of intervertebral disc	D. Kletsas	Department of Biology University of Athens
Despoina Nikopoulou	Study of the putative healing effect of extracts of the marine arthropod *Ceratothoaoestroides*	D. Kletsas	Pharmacy Department University of Athens
Stefania-Diana Grammatikaki	Peptides with possible healing action	D. Kletsas	Pharmacy Department University of Athens

LECTURE CONTRIBUTIONS OF THE INSTITUTE OF BIOSCIENCES & APPLICATIONS TO THE 2017 SUMMER SCHOOL OF THE NCSR "DEMOKRITOS"

(July 2017)

DATE	SPEAKER	TITLE
4/7/2017	**Dr. D. Kletsas** IBA, NCSR "Demokritos"	Cell senescence and tissue homeostasis
10/7/2017	**Dr. L. Swevers** IBA, NCSR "Demokritos	The democratization of genome editing: from zinc fingers to CRISPR/Cas
10/7/2017	**Dr. G. Drossopoulou** IBA, NCSR "Demokritos"	Age-Related Diseases: Can regenerative medicine contribute in therapeutic approaches
11/7/2017	**Dr. H. Pratsinis** IBA, NCSR "Demokritos	*In vitro* studies of natural and synthetic bioactive products
12/7/2017	**Dr. A. Chroni** IBA, NCSR "Demokritos"	"Good" cholesterol HDL: understanding its biological role and evaluation of its clinical use for diagnosis and treatment of human diseases
13/7/2017	**Dr. M. Konstantopoulou** IBA, NCSR "Demokritos"	Chemical Ecology and Natural Products

SEMINAR PROGRAMME 2017 OF THE GRADUATE STUDENTS INSTITUTE OF BIOSCIENCES & APPLICATIONS

DATE	SPEAKER	TITLE
18/1/2017	**M. Angelopoulou** IBA, NCSR "Demokritos"	Protective mechanisms of human dermal fibroblasts against UVB radiation
1/2/2017	**S. Koutloglou** IBA, NCSR "Demokritos"	Opioid receptors: Interactions with cytoplasmic proteins"
8/2/2017	**C. Karoussiotis** IBA, NCSR "Demokritos"	Autophagy: The role of κ-opioid receptor
5/4/2017	**A. Delimitsou** IBA, NCSR "Demokritos"	Functional evaluation of known variants of unknown clinical significance and characterization of new mutations in genes involved in cell cycle regulation and DNA repair mechanisms

SEMINAR PROGRAMME 2017 OF INVITED SPEAKERS INSTITUTE OF BIOSCIENCES & APPLICATIONS

DATE	SPEAKER	TITLE
13/11/2017	**Prof. A. Moustakas** Department of Medical Biochemistry and Microbiology, Uppsala University, Sweden"	Plasticity in tumor cell differentiation

COLLECTIVE DATA

COLLECTIVE DATA ON PRODUCTIVITY OF SCIENTIFIC PROGRAMMES

	PROGRAMME			
	A	**B**	**C**	**INSTITUTE**
Researchers	10	6	5	22*
Technical Specialist	1	1	-	2
Collaborating Scientists	2	5	1	8
Postdoctoral Fellows	4	2	1	7
Graduate Students	8	3	-	11
Collaborating Graduate Students	10	2	1	13
Graduate Research Associates	3	1	-	6!!!
Undergraduate Students	9	8	3	20
Research Technicians	1	-	-	20
Administrative Staff and Technical Support Personnel	-	-	-	4
Total Personnel	**48**	**27**	**11**	**97**
Publications in Peer-Reviewed Journals	**25**	**8**	**8**	**40#**
Cumulative Impact Factor in Peer-Reviewed Journals (number of publications)	**104.472 (23)**	**36.14 (8)**	**19.247 (8)**	**159.573# (40)**
Proceedings to Conferences	**3**	**1**	**1**	**5**
Total Publications	**28**	**9**	**9**	**45#**
Citations	**1400**	**506**	**184**	**2090***
International Patents	-	1	-	1
Greek Patents	-	1	-	1
Presentations to International Conferences	**15**	**5**	**11**	**31**
Presentations to Greek Conferences	**25**	**6**	**11**	**42**
Total Presentations to Conferences	**39**	**11**	**22**	**72**

** 1 Scientist of Human Tissue Bank is included*

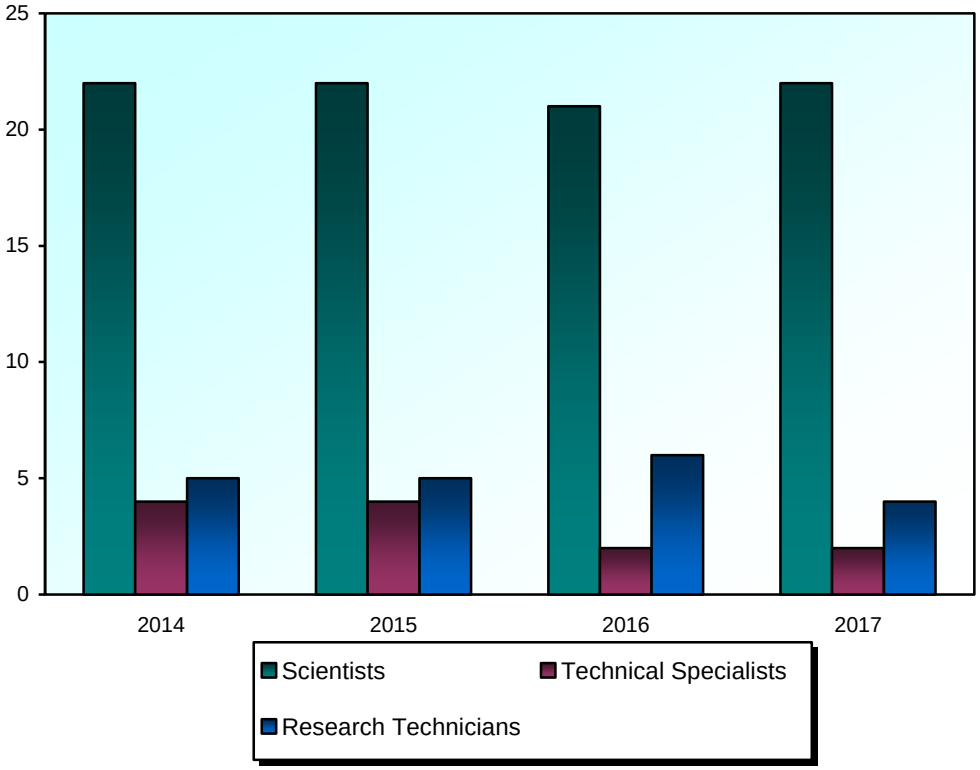
!!! 1 Collaborating Graduate Associates of Human Tissue Bank and 1 of Experimental Animal Colony are included

@ 2 Research Technicians who are occupied in Experimental Animal Colony and 1 Research Technician who is occupied in Confocal Laser Microscopy are included

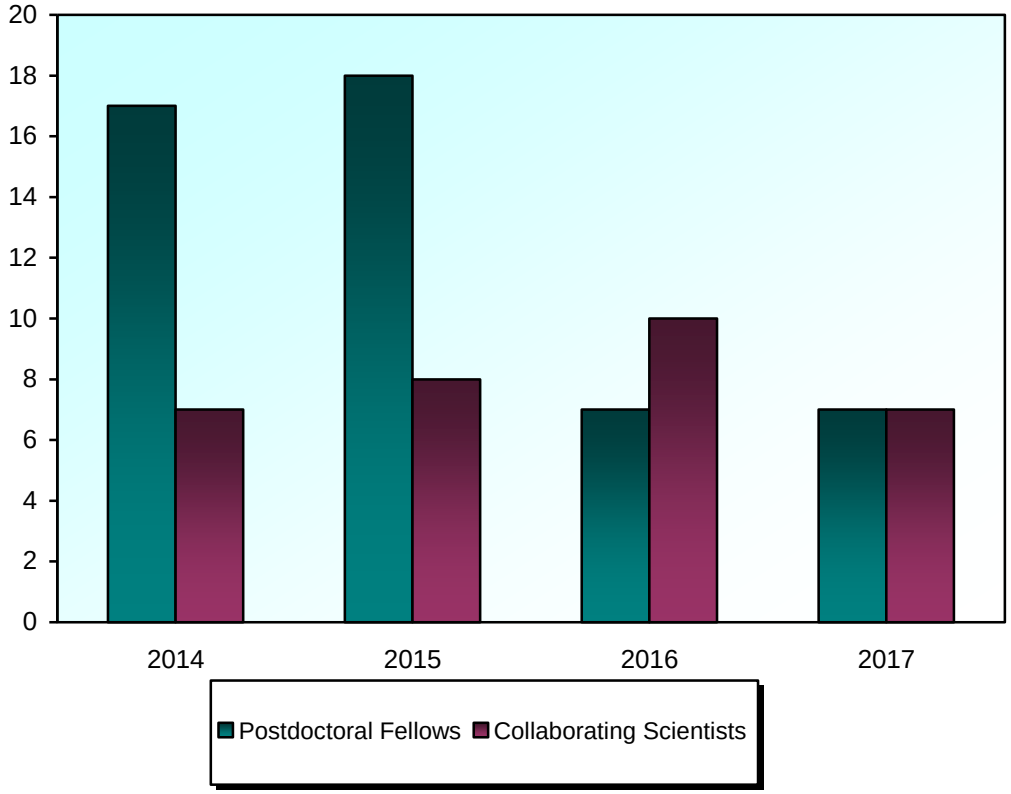
 # 1 common publication in A and B Programme is included

CHANGES OF IBA STAFF
DURING 2014-2017

TENURED EMPLOYEES

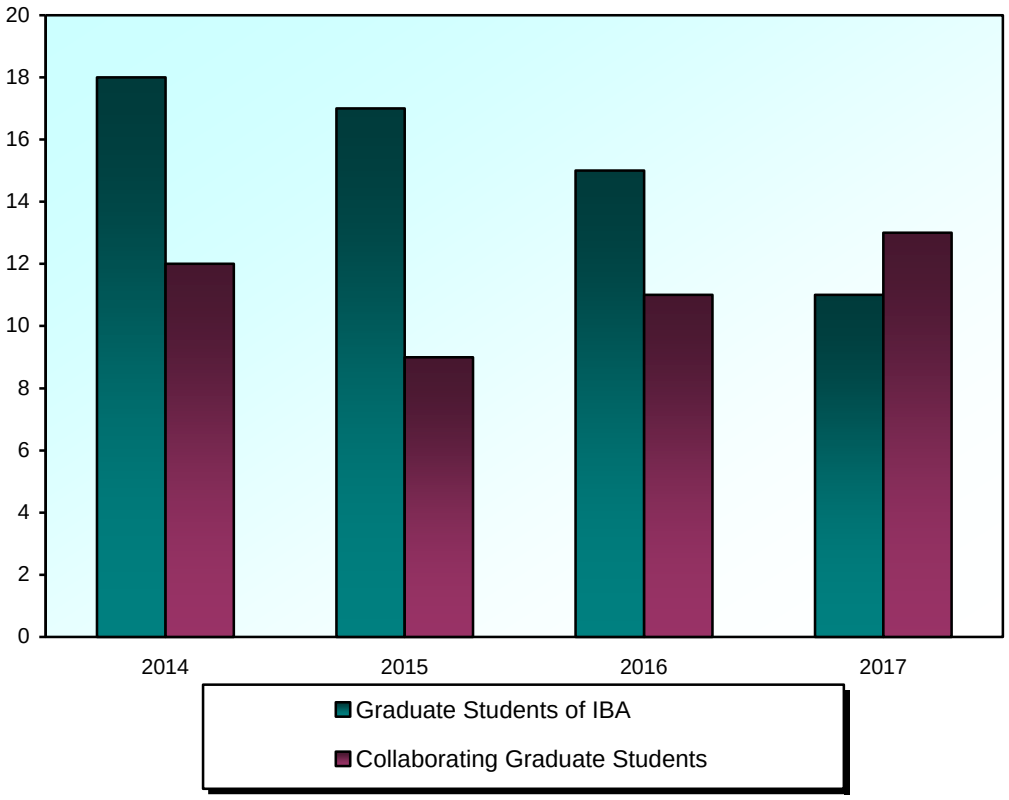


POSTDOCTORAL FELLOWS & COLLABORATING SCIENTISTS

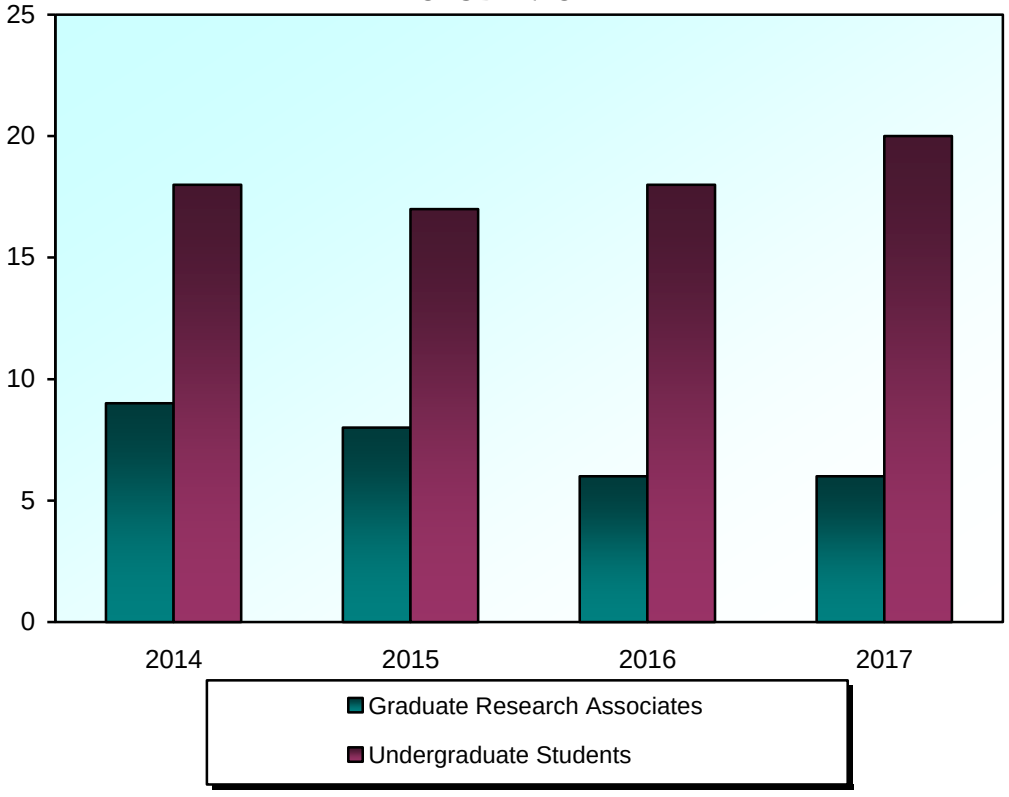


CHANGES OF IBA STAFF
DURING 2014-2017

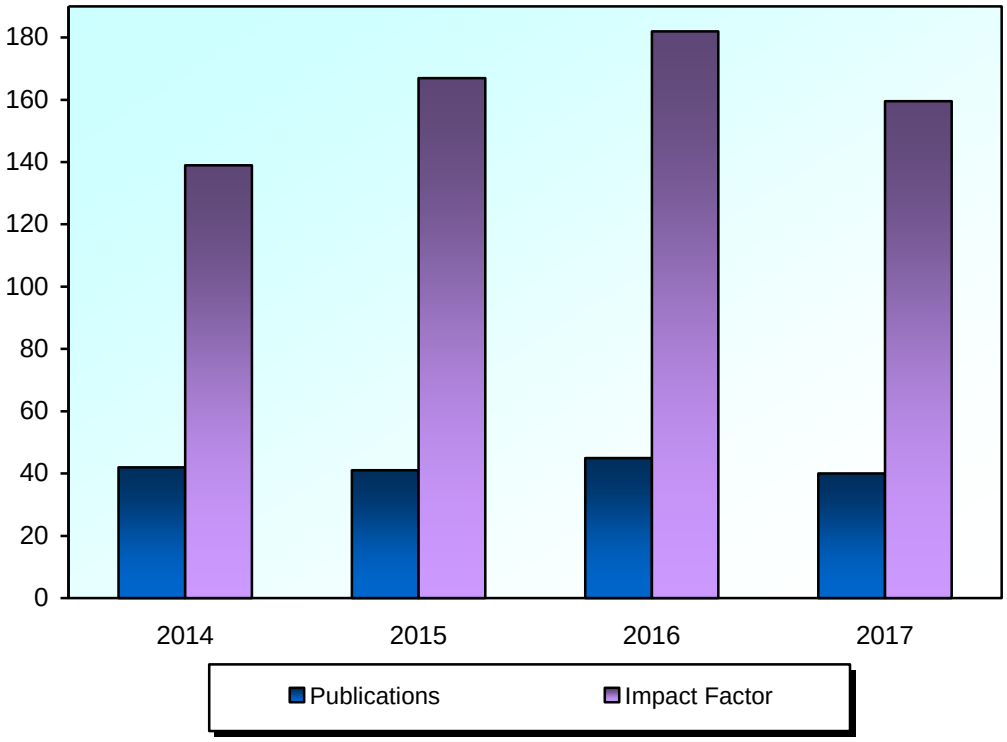
GRADUATE STUDENTS



GRADUATE RESEARCH ASSOCIATES AND UNDERGRADUATE STUDENTS



PUBLICATIONS IN PEER-REVIEWED JOURNALS AND CUMULATIVE IMPACT FACTOR DURING 2014-2017



CITATIONS OF THE INSTITUTE 2014-2017