NATIONAL CENTRE FOR SCIENTIFIC RESEARCH "DEMOKRITOS"

INSTITUTE OF BIOSCIENCES & APPLICATIONS

2018
ANNUAL REPORT

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DIRECTOR'S OFFICE
Director: D. KLETSAS

SCIENTIFIC ADVISORY BOARD
President: M. KONSTANTOPOULOU

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**
  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, E. Mavrogonatou
- **Nuclear Proteins and Chromatin Function**
  In charge: *Th. Sourlingas*
- **Cell and Matrix Biochemistry/ Pathobiology**
  In charge: *A. Chroni*
  P. Kitsiou, A. Tzinia, G. Drossopoulou
- **Molecular Carcinogenesis and Rare Disease Genetics**
  In charge: *M. Voutsinas*

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- **Molecular Genetics of Insects and Biotechnology**
  In charge: *L. Swevers, V. Labropoulou*
  Chemical Ecology and Natural Prodycts
  In charge: *M. Konstantopoulou*
- **Chronobiology**
  In charge: *A. Prombona*
- **Microbial Molecular Genetics**
  In charge: *V. Sophianopoulou*
  C. Gournas
- **Biophysics and Biotechnology of Membranes**
  In charge: *K. Stamatakis*

PROGRAMME C
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- **Theoretical Biology and Computational Genomics**
  In charge: *Y. Almirantis*
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  In charge: *M. Pelecanou*
  M. Saqnou, A. Panagiotopoulou
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  In charge: *M. Vlassi*
- **Designed Bioactive Molecules Laboratory**
  In charge: A. Papakyriakou

SERVICE UNITS

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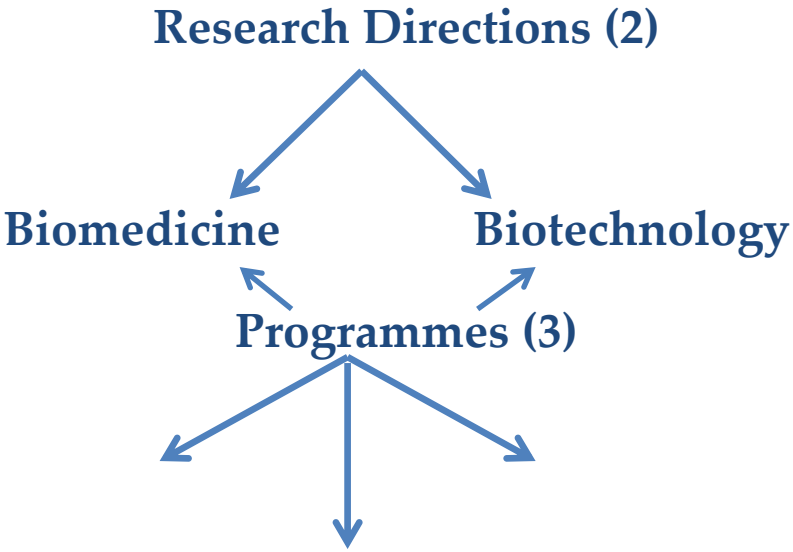
- **LABORATORY OF CELL & MATRIX PATHOBIOLGY**
  In charge: *P. Kitsiou*
- **LABORATORY OF MOLECULAR DIAGNOSIS OF GENETIC DISEASE**
  In charge: *G. Voutsinas*
- **LABORATORY OF CELL-BASED ASSAY SYSTEMS AND BIOACTIVE COMPOUNDS**
  In charge: *D. Kletsas – H. Pratsinis*

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
Papakyriakou Athanasios	Dr. Chemist
Pratsinis Haris	Dr. Chemist
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
Gournas Christos	Dr. Biologist
Mavrogonatou Eleni	Dr. Biologist
Sagnou Marina	Dr. Biologist/ Chemist

Functional Scientific Personnel

Angeliki Panagiotopoulou	Dr. Biochemist

Technical Specialists

Giannakas Nikolaos	Biologist
Stefanou Dimitra	Agronomist

RESEARCH TECHNICIANS

Avgeris Socratis *(MSc)*
Doulgeridis George
Kakkos Stilianos
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

EMERITUS & COLLABORATING SCIENTISTS

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

POSTDOCTORAL FELLOWS

Fellow	**Supervisor**
Bourtsala Angeliki	Chroni A.
Dafnis Ioannis	Chroni A
Giannogonas Panagiotis	Kletsas D.
Golfinopoulou Christina	Chroni A.
Halevas Eleftherios	Sagnou M.
Kolliopoulou Anna	Swevers L.
Kythraioti Georgia	Iatrou K.
Koutsoubeli Eleni	Konstantopoulou M.
Mamoucha Stavrtoula	Prombona A.
Matiadis Dimitris	Pelekanou M.
Mavroidi Barbara	Pelecanou M.
Mpakali Anastasia	Papakyriakou A.
Papadopoulou Adamantia	Kletsas D.
Trohatou Ourania	Drossopoulou G.

GRADUATE STUDENTS (PhD)

Student	**Supervisor**
Angelopoulou Maria	Kletsas D.
Biratsi Alda	Sophianopoulou V.
Broussos Panagiotis	Stamatakis K.
Galeou Aggeliki	Prombona A. *–PhD obtained*
Karoussiotis Christos	Georgoussi Z.
Kouroumalis Anastasios	Kletsas D.
Koutloglou Sofia	Georgoussi Z.
Liakou Eleni	Kletsas D.
Manikas Neoklis	Konstantopoulou M.
Mavridis Georgios	Papakyriakou A.
Megarioti Amalia	Gournas C.
Mountaki Christina	Chroni A.
Pallaki Paschalina	Georgoussi Z.

Papagiannis Achilleas	Chroni A.
Simeonof Alexandra	Georgoussi Z.
Vayenos Dimitris	Stamatakis K.

GRADUATE RESEARCH ASSOCIATES

Fellow	**Supervisor**
Athanasopoulou Foteini	Voutsinas G.
Chatzidaki Ismini	Voutsinas G.
Katopodi Annita	Chroni A.
Klamarias Lykourgos (Veterinarian)	Kletsas D.
Kosmidis Eleftherios	Vavouraki E.
Ninios Ioannis *(PhD)*	Vavouraki E.
Panagopoulou Lydia (MSc)	Vavouraki E.
Raptopoulos Dimitris *(PhD)*	Konstantopoulou M.
Sdralia Konstantia	Iatrou K.
Theophanidi Eleni	Drossopoulou G.
Valanti Effie	Chroni A.

GRADUATE STUDENTS (MSc)

Student (University)	**Supervisor**
Delimitsou Aggeliki (Univ. of Athens)	Voutsinas G.
Fotopoulou Asimina (Univ. Of Patras)	Kletsas D.
Giakoumidaki – Vogiatzi Aikaterini (Agricultural Univ. of Athens)	Stamatakis K.
Katarachia Stamatia (Univ. of Athens, *MSc*)	Voutsinas G.
Katrini Konstantina (Univ. of Athens, *MSc*)	Chroni A.
Kikidou Eleni (Univ. of Athens, *MSc*)	Kletsas D. - *MSc obtained*
Lesgidou Nastazia (Univ. of Athens, *MSc*)	Vlassi M. - *MSc obtained*
Pateraki Eva (Univ. of Athens, *MSc*)	Kletsas D.
Santorinaiou Anna (Univ. of Athens, *MSc*)	Kletsas D.
Sofokleous Valentinos (Univ. of Athens)	Sagnou M.
Tsimelis Efstathios (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**
Arfara Maria (Technical Univ. of Athens)	Sagnou M.
Charikleous Myrsini (Univ. of Athens)	Sophianopoulou V.
Chatoupi Merlin (Univ. of Portsmouth, UK))	Swevers L.
Daskalopoulou Maria Aikaterini (Univ. of Athens)	Panagiotopoulou A.
Dimozi Maria (Univ. of West Attica)	Kletsas D. - *dissertation completed*
Zakopoulou Tatiana (Spiros (Univ. of Athens)	Sophianopoulou V.
Gaitanos Spiros (Univ. of Athens)	Sophianopoulou V.
Giannioti Eleftheria (Univ. of Portsmouth, UK)	Gournas C.
Kafetzopoulos Grigoris (Univ. of Athens)	Georgoussi Z.
Koutrouli Isis (Univ. of Athens)	Georgoussi Z. – *dissertation completed*
Liatsis Douvitsas Orestis (Univ. of Patras)	Sagnou M.

Myridakis Antonis (Univ. of Athens)	Georgoussi Z.
Pantiora Panagiota (Agricultural Univ. of Athens)	Pelakanou M.
Papavranoussi – Daponte Danae (Univ. of Athens)	Georgoussi Z.
Skrempou Nikoleta (Agricultural Univ. of Athens)	Prombona A.
Spanoudakis Stefanos (Univ. of Athens)	Labropoulou V.
Taouxi Konstantina (Univ. of Athens)	Voutsinas G.
Tomaropoulos Vassileios (Agricultural Univ. of Athens)	Prombona A. .
Theodorou Iliana (Demokritus Univ. of Thrace)	Sophianopoulou V.

INTRODUCTION

The Institute of Biosciences and Applications (IBA) is one of the five Institutes 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 on age-related diseases, on biotechnology and the environment, as well as on structural and computational biology.

For the year 2018, I wish to congratulate the 25 faculty members of the IBA and the total 115 members (scientific, technical and administrative personnel) of the Institute, who contributed to the upgrading of the research and the developmental work produced. Of note, the scientific production during 2018 has been significantly increased in terms of number of publications, impact factors of the relevant journals and number of citations. I wish to thank the Vice Director Dr. G. Voutsinas and the members of the Scientific Committee of the IBA Dr. M. Konstantopoulou (President), Drs. Z. Georgoussi, H. Pratisins, L. Swevers and G. Voutsinas (Members) Drs. V. Sophianopoulou, A. Tzinia and H. Vavouraki (Alternate Members) and A. Kostakou (Representative of the administrative and technical personnel) for the orderly function of the Institute, as well as the Responsible of the Educational Committee Dr. A. Chroni and the Deputy Dr. M. Sagnou for the upgrading of the education within IBA.

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, Z. Georgoussi, and H. Pratsinis), 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, as well as of all the competitive grants the members of the IBA have increased significantly the number of young researchers, renewed the infrastructures and supported considerably the scientific and developmental effort of the Institute.

With great pleasure the IBA welcomes the newly elected researchers, Dr. C. Gournas and E. Mavrogonatou, and wishes every success in their new position. Congratulations to both!

During 2018 education within IBA has been greatly upgraded. Beyond the training of a significant number of post-doctorate fellows, post-graduate students, and diploma and pre-graduate students, as well as the participation of the majority of the faculty members in the pre- and post-graduate courses of a number of Universities in Greece and abroad, the Interinstitutional Post-Graduate Educational Program (IPEP) entitled "Applied Biochemistry: Clinical Chemistry, Biotecnology and Evaluation of Pharmaceutical Products" between IBA and the Department of Chemistry of the University of Patras has been established. Furthermore, the participation of the IBA in the IPEP "Athens International School for Neurosciences" has been renewed. In addition, IBA organized for the first time the "IBA Summer Camp for Lyceum Students", enabling 26 participating students to work for two weeks in the laboratories of the Institute and to perform small research projects. Finally, the researchers of the IBA have participated in the Summer School of NCSR "Demokritos", as well as in a number of activities for the dissemination of science to the general public, such as the "Researcher's Night", "Science on Board", "Mind the Lab" and for the support of sensitive social groups (Second chance school in Korydallos prison or refugee kids).

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

Dimirtis Kletsas, PhD
Institute Director
October 2019

PROGRAMME A:

REGULATION OF CELL FUNCTION

AGED-RELATED DISEASES

Research Group: Cellular Signalling and Molecular Pharmacology

Research Staff

Zafiroula-Iro Georgoussi, Research Director
Paschalina Pallaki, Graduate Student
Christos Karoussiotis, Graduate Student
Sofia Koutloglou, Graduate Student
Alexandra Simeonof, Graduate Student
Isis-Anzel Koutrouli, Undergraduate Student- *BSc obtained in 2018*
Danae Papavranousi-Daponte, Undergraduate Student
Antonis Myridakis, Undergraduate Student
Gregory Kafetzopoulos Undergraduate Student

Kostas Iatrou, Emeritus Scientist
Lydia Ignatiades, Collaborating Former Staff Scientist
Georgia Kythreoti, 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 signal transduction pathways mediated by G protein-coupled receptors (GPCRs) emphasizing on the protein players such as the RGS proteins, spinophilin, and transcription factors, which by interacting with them act as switches and modulate receptor signaling.

As a model we use the three opioid receptor subtypes (δ, μ and κ) due to their involvement in neurotransmission, neurogenesis and neuronal plasticity that result in various pathological conditions ranging from tolerance and dependence upon prolonged drug administration, to pain, inflammation and emotional behaviors such as anxiety and stress.

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

- Elucidation of novel signaling pathways mediated upon activation of the δ, κ and μ- opioid receptors that affect neurite outgrowth and neuronal plasticity in an attempt to define new pharmacological targets
- Identification of the roles of RGS family members and the neuronal protein spinophilin in opioid-mediated autophagy and neurotransmission
- Identification of transcription factors and genes which action is altered upon selective opioid administration, *bias signalling,* implicated in neuronal differentiation and finally in the,
- Characterization of new bioactive compounds for opioid or other GPCRs using cell based assays (throughput screens) in order to identify "*smart drugs*" to alleviate pain or other diseases of the central nervous system.

2018 Findings

Alternative signal transduction pathways mediated upon opioid receptor activation

Autophagy: an unexplored mechanism of opioid receptor function: 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) induces the autophagic machinery in neuronal cells and animal models**.** Our findings demonstrate also the signaling pathway via which activation of the κ-OR with selective agonists leads to alterations of specific autophagic genes. U50,488H administration in mice indicated that the region responsible for the κ-OR- mediated autophagy is the hippocampus.

The role of RGS4 protein*:* Previous observations from our lab have shown that RGS4 negatively regulates opioid receptor signaling that results in opioid dependent neuronal differentiation and neurite outgrowth via a "non-canonical" signaling pathway regulating STAT5B-inducible genes

(Georganta et al., 2010, 2013; Pallaki et al., 2017). Using primary neuronal cultures from RGS4$^{-/-}$ mice, we found that the levels of specific autophagic markers are dramatically reduced, suggesting a novel functional role of RGS4, that, of its possible involvement in the autophagic machinery.

Parallel studies and under the auspices of the COST-action-GLISTEN *(GPCR Ligand Interactions, Structures and Transmembrane Signaling)*, in collaboration with Prof. J. Selent, Pompeu Fabra University, Barcelona, we identified using molecular dynamics and site directed mutagenesis the structural determinants and the critical amino-acids responsible for the interaction of δ-opioid receptor (δ-OR) with RGS4 (Figure 1).

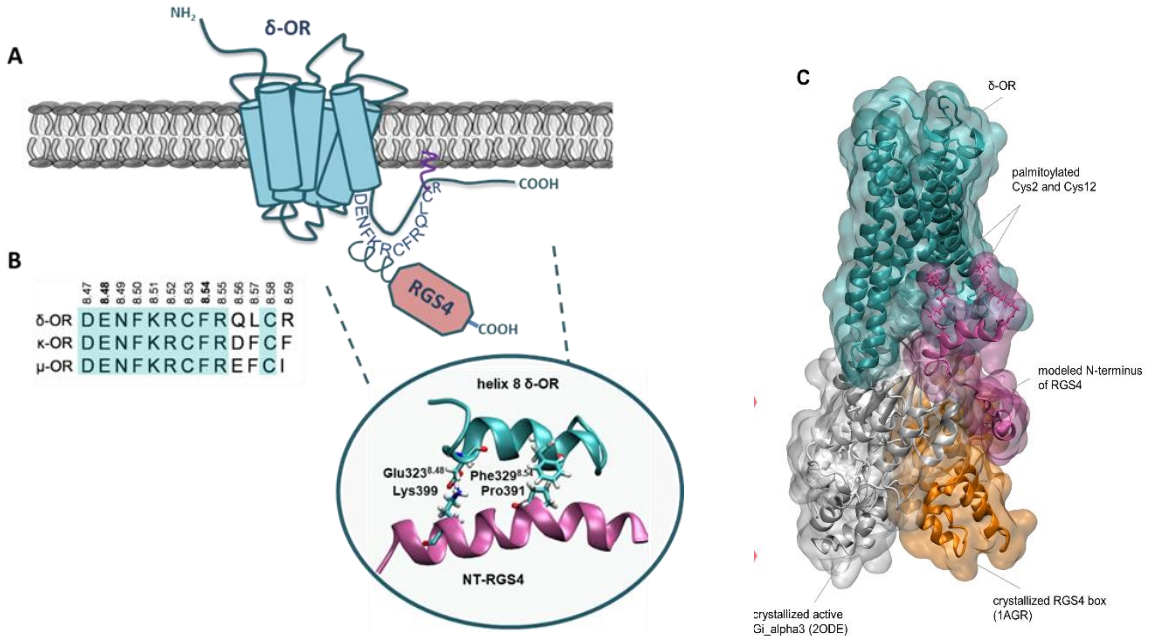


Figure 1: Molecular dynamics simulations combined with mutagenesis studies defined two critical regions responsible for the interaction of RGS4 with the δ-OR. One between Phe329 of helix 8 of δ-OR and Pro9 of the N-terminal region of RGS4 and a salt bridge between Glu323 of δ-OR and Lys17 of RGS4 (A). The high degree of conservation among opioid receptors (B), points to a conserved interaction mode between opioid receptors and RGS4 and allow drafting a structural model of a ternary complex including the δ-OR-Gi-RGS4 protein complex (C).

***The role of spinophilin*:** Spinophilin is a neuronal scaffold protein that directly interacts with the δ- and μ-opioid receptors to modulate their signalling (Fourla et al., 2012, Georgoussi et al., 2013). Our recent findings demonstrate that spinophilin is tyrosine phosphorylated by δ-OR agonists and that site-directed mutagenesis of tyrosines Y398A and Y483A alter spinophilin's function in opioid-receptor mediated signaling.

Parallel studies in animal models have shown that the levels of spinophilin are altered upon κ-opioid receptor administration with the selective agonist U50,488H via an autophagy mediated effect.

Pharmacological characterization of bioactive compounds in cell based throughput platforms:

Under our participation in the EU consortium «*NORMOLIFE NETWORK*» (collaboration with Drs L. Pasquinucci, G. Ronsisvalle & R. Turnaturi University of Catania) and using the facilities of the Research Infrastructure OPENSCREEN-GR 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.

Development of neuronal networks on Graphene microelectrode arrays and ZnO-nanostructures:

In collaboration with Drs P. Dimitrakis and H. Makarona of the INN Institute of NCSR"D" efforts are made to develop neuronal cells on graphene nanoribbon interconnects and to investigate the cellular (electrical) responses and their variations to stimulation (electrical and chemical).

Publications

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"*, M*olecules.* 16; 23(3). (IF: 2.861)

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

Articles in Press 2019

Karoussiotis C, Marti-Solano M, Stepniewski TM, Symeonof A, Selent J, Georgoussi Z. «*A highly conserved δ-opioid receptor region determines RGS4 interaction».* FEBS J. 2019 Aug 6. doi: 10.1111/febs.15033 (i.f.4.739)

Other Publications

P. Pallaki, I. Serafimidis, D. Thomaidou, M. Gaitanou, Z. Georgoussi (2018) "*A novel regulatory role of RGS4 in neuronal cell proliferation and sprouting mediated via STAT5B transcriptional responses*" FEBS OPEN BIO, 8, 380-380

P. Pallaki, I. Serafimidis, E. Papadimitriou, M. P. Papakonstantinou, D. Thomaidou, M. Gaitanou, Z. Georgoussi (2018) "*RGS4 Regulates Neurite Outgrowth and Cell Proliferation Mediated by STAT5B Transcriptional Responses*" The FASEB Journal 32 (1-supplement), 805.17-805.17

Z Georgoussi and C Karoussiotis (2019) *"κ-Opioid Receptor Activation Induces the Autophagic Machinery and Alters Dendritic Spine Density*" The FASEB Journal 33 (1-supplement), 663.13-663.13

Presentations at Scientific Conferences

Z. Georgoussi, P. Pallaki, I. Serafimidis, E. Papadimitriou, M.P Papakonstantinou, D. Thomaidou, M. Gaitanou (2018). *"RGS4 Regulates Neurite Outgrowth And Cell Proliferation Mediated by STAT5B Transcriptional Responses*". Experimental Biology Congress, April 6-9, San Diego, USA

P. Pallaki, I. Serafimidis, D. Thomaidou, M. Gaitanou and Z. Georgoussi (2018). *"A novel regulatory role of RGS4 in neuronal cell proliferation and sprouting mediated via STAT5B transcriptional responses*" 43rd FEBS Congress, July 7-12, Prague, Czech Republic

P. Karakolis, P. Pallaki, G. Sirakoulis, I.G. Karafyllidis, P. Normand, Z. Georgoussi and P. Dimitrakis (2018). *"Graphene material for neuromorphic and neurohybrid systems".* Volga Neuroscience Meeting, July 22-27, Nizhny Novgorod – Samara – Nizhny Novgorod, Russia

P. Pallaki, I. Serafimidis, A. Symeonof, D. Thomaidou, M. Gaitanou and Z. Georgoussi (2018). "*A novel regulatory role of RGS4 in neuronal cell proliferation and sprouting mediated by opioids through STAT5B transcriptional responses*". Cell Signaling Workshop, November 12-17, Jerusalem, Israel

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 Institutes Pasteur, Fleming, BRFA.

- Co-corganizer of the course «*Cellular and Molecular Neurosciences»* of Athens International Master's Programme in Neurosciences, 40 hours
- Supervisor of the PhD dissertations of the Graduate students: Paschalina Pallaki, Sofia Koutloglou, Christos Karoussiotis and Alexandra Symeonof.
- Supervisor of the BSc theses of the Undergraduate students: D. Papavranousi-Daponte, Antonis Myridakis, Gregory Kafetzopoulos and Isis Koutrouli, Department of Biology, Kapodistrian University of Athens.
- Member of the Advisory Committee in the Department of Biology of the Kapodistrian University in Athens for the PhD students P. Pallaki, S. Koutloglou and C. Karoussiotis, A. Symeonof.
- «*Signaling of Neurotransmitter Receptors*», teaching responsibilities in the Master Course program of the Division of Biochemistry and Molecular Biology, Department of Biology, Kapodistrian University of Athens, 16 hours, 25 students.
- Teaching in the Master Course program of the Medical School, Kapodistrian University of Athens. "*Molecular and Applied Physiology*", "*G-protein coupled Receptors in Health, Disease and in Drug Development"*, (4 hours, 40 students).
- Teaching in the Interdepartmental Master Course program of Kapodistrian University of Athens, Department of Biochemistry and Molecular Biology "*Molecular basis of Human Disease"* entitled "*G-Protein Coupled Receptors in Health and Disease",* (6 hours, 30 students).
- Teaching in the Athens "*International Master's Programme in Neurosciences*" National Kapodistrian University, Department of Biology, «*Signaling of Neurotransmitter Receptors*» (16 hrs, 18 students)
- Teaching in the Bilateral Masters Course of the IBA, NCSR"D" in collaboration with the faculty of Chemistry, University of Patras, on *"Applied Biochemistry, Medicinal Chemistry, Biotechnology, Pharmaceutical products",* entitled: *"Cellular Signaling of Transmembrane Receptors-Molecular Pharmacology"* (2 h, 7 students)
- IBA-Summer Scientific Laboratories for High School students on *"Protein Expression Methodologies in Different Cell Systems"* (hands on, group of 3 students).
- **Isis Erietta Anzel Koutrouli defended her Diploma Thesis in the faculty of Biology of the Kapodistrian University of Athens** entitled *"RGS4 protein effects on STAT5B transcriptional responses upon δ-opioid receptor activation and pharmacological characterization of new opioid compounds" (Scientific Advisor: Z. Georgoussi)*

Distinctions and Awards

"Akogionoglou Award": Paschalina Pallaki was awarded with the Akogionoglou Award-2018 of IBA for her excellent performance and scientific achievements during her PhD studies in the laboratory of Cellular Signaling and Molecular Pharmacology.

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

Other Scientific Activities

Z. Georgoussi:
Other Scientific and Administrative activities

- National Representative, Intergovernmental Framework for European Cooperation in Science and Technology, COST-action- CA18133 entitled "*European Research Network on Signal Transduction (ERNEST*)".
- National Representative, Intergovernmental Framework for European Cooperation in Science and Technology, COST action-CM1207: "GLISTEN": *GPCR-Ligand Interactions, Structures and Transmembrane Signalling*".

- Member of the Administrative and Educational board of the «Athens International Master's Programme in Neurosciences».
- Member of the evaluation committee for the Msc Students of the «Athens International Master's Programme in Neurosciences».
- Member of the Research Consortium «*Normolife Network*" responsible for the identification of novel opioid compounds to alleviate pain.
- Member of the evaluation Committee for the recruitment of the Associate Professorship position, Department of Biochemistry, University of Thessaly.

Reviewer in scientific Journals

Cellular Signaling, Cell Communication and Signaling, Molecular Pharmacology and Experimental Therapeutics, Neurophychopharmacology, Neuropharmacology Journal of Biotechnology, BιoMed Cell Biology, Journal of Biological Chemistry, Journal of Computational Systems Biology, Letters in Drug Design & Discovery, Current Drug Discovery Technologies, CNS Neuroscience & Therapeutics, Neurochemisty, International, Pharmaceutical Biology, Nature Neuroscience.

Reviewing of funding applications

- Research Foundation- Flanders (Fonds Wetenschappelijk Onderzoek - Vlaanderen, FWO), Belgium
- National Research Development and Innovation Office (NKFIH) of Hungary
- Cyprus Research Promotion Foundation (RPF)
- Operational Programme Competitiveness, Entrepreneurship and Innovation (EPAnEK)
- Hellenic General Secretary for Research and Technology (GSRT)
- State Scholarship Foundation (IKY).
- The Hellenic Foundation for Research and Innovation (H.F.R.I)

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

- Elected Member of the Scientific Council of IBA
- Elected alternate member of the Committee of Ethics of NCSR"D"
- Member of the working group 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 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 2 publications): 8,180

Citations for 2018 (without self-citations): 37

Citations for 2014-2018 (without self-citations): 175

h-factor: 18 (Scopus), 20 (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
For the 2018: Covered expenses for participation in GLISTEN symposium

The Hellenic Foundation for Research and Innovation (H.F.R.I) Scholarship for PhD candidates (funding S. Koutloglou) entitled "*Regulation of opioid receptors by protein interactions"*
Duration: 08/2017-08/2018
Total budget: 14.400 €

Kostas Iatrou: Insect Physiology and Ethology and Applications

Research Interests

- Control of olfactory functions in the malaria mosquito vector *Anopheles gambiae*.
- Oogenesis in lepidopteran insects as a model of terminal differentiation induced by ecdysteroids.
- Genetically modified nuclear polyhedrosis viruses as tools for genetic transformation of insect and mammalian cells.
- Production of recombinant proteins in insect cell cultures.
- Development of cell-based assays for fast screening of natural and synthetic collections of small molecule and discovery of novel regulators of cellular functions.
- Critical evaluation of statistical ecological models applied for the detection of climate change on biodiversity of marine phytoplanktonic ecosystems and based on data collected from the Eastern Aegean Sea. The original data have been submitted by Lydia Ignatiades for open access use in the MedOBIS database (L. Ignatiades).

2018 Findings

We have completed the pharmacological and functional characterization of three novel ORco antagonists of ORco, the common subunit of mosquito ORx/ORco odorant receptor heteromers (cation channels), whose discovery using a recently developed cell-based screening platform that exploits the expression of ORco and a relevant luminescence-producing reporter gene in lepidopteran insect cells, we reported last year. Specifically, for one of the identified antagonists that was shown, in collaboration with Dr. Antonios Michaelakis (Benaki Phytopathological Institute), to be a strong repellent of laboratory populations of the Asian tiger mosquito *Aedes albopictus* that can vector several pathogens including the yellow fever, dengue fever, Chikungunya fever, Saint Louis and Japanese encephalitis, West Nile, and Zika viruses. Our studies resulted in the determination of the minimal doses of compounds and mixtures thereof that offer the desired level of protection of humans against *A. albopictus* and, presumably, other mosquito species as well in laboratory tests.

We have also completed the screening of the available library of natural volatile organic compounds (VOCs) using the same screening platform with the aim of identifying additional agonists or antagonists of mosquito olfactory receptor function acting as attractants or repellents of the African malaria mosquito vector *Anopheles gambiae*. In addition to the 3 ORco antagonists discussed above, we have found and characterized pharmacologically 10 more ORco antagonists. Six of them showing the best pharmacological properties *in vitro* were tested for *in vivo* repellence activity against *A. albopictus* and found to be active. Further studies to determine minimal doses that offer the desired level of protection of humans against *A. albopictus* and other mosquito species are in progress.

Publications

Kröber T, Koussis K, Bourquin M, Tsitoura P, Konstantopoulou M, Awolola TS, Dani FR, Qiao H, Pelosi P, Iatrou K, Guerin PM. (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.

Thireou T, Kythreoti G, Tsitsanou KE, Koussis K, Drakou CE, 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. 98:48-61. doi: 10.1016/j.ibmb.2018.05.001.

Presentations at Scientific Conferences

Iatrou, K, P Tsitoura, N Sdralia, M Konstantopoulou (2018). Cell-Based Screening Platforms for Identification of Modifiers of Odor-Triggered Mosquito Behaviors Acting through Binding to the ORco Subunit of Odorant Receptor Heteromers. Annual Experimental Biology meeting (EB 2018), April 21-25, 2018, San Diego, CA, USA

Patents 2018

Iatrou, K., Guerin P.M., Kröber, T. and Konstantopoulou, M. (2015). Methods, compounds and compositions for repelling insects and/or arachnids. USPTO Non-Provisional **USA Patent No. US 9,615,585 B2, 2018** (from PCT/EP2014/055170). Priority date 14/03/2013.

Iatrou, K., Guerin P.M., Kröber, T. and Konstantopoulou, M. (2015). Methods, compounds and compositions for repelling insects and/or arachnids. EPO Non-Provisional European Patent application No. EP14712237.8 (UEINS1-0008EP) (from PCT/EP2014/055170) filed 23/10/2015. **Notice of Allowance dated 21/10/2018**. Priority date 14/03/2013.

Other Scientific Activities

Participation in editorial boards of scientific journals:
Subject editor, “The Journal of Insect Science".
Section editor, “Mediterranean Marine Science Journal” (L. Ignatiades)
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 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 “Environmental Toxicology”, “Insect Molecular Biology”, “Journal of Steroid Biochemistry and Molecular Biology”, “Frontiers in Physiology”, “International Journal of Tropical diseases”, “Applied Microbiology and Biotechnology”, “BMC Molecular Biology”, “Insect Biochemistry and Molecular Biology”, "Journal of Insect Physiology", “BioMed Research International", "Cellular and Molecular Life Sciences".
Reviewer of scientific manuscripts for “Environmental Monitoring and Assessment”, “The Science of the Total Environment”, “Marine Ecology-Progress series” (L. Ignatiades)

Total Impact Factor (for 2 publications): 7,512

Citations for 2018 (without self-citations)
Iatrou K: 170 (Scopus)
Ignatiades L: 106 (Scopus)

Citations for 2014-2018 (without self-citations)
Iatrou K: 908 (Scopus)
Ignatiades L: 499 (Scopus)

h-factor:
Iatrou K: 35 (Scopus – 08/2019), 43 (Google Scholar – 08/2019)
Ignatiades L: 21 (Scopus), 26 (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 group: 7.200€.
Funding of the group for 2018: 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: 2017-2019
Total program funding: 40.000€
Funding of the group for 2018: 10.000€.

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, Senior Researcher
Eleni Mavrogonatou, Researcher
Adamantia Papadopoulou, Postdoctoral Fellow
Panagiotis Giannogonas, Postdoctoral Fellow
Eleni Liakou, Graduate Student
Maria Angelopoulou, Graduate Student
Anastasios Kouroumalis, Graduate Student
Eleni Kikidou, Collaborating Graduate Student *(MSc) - MSc obtained in 2018*
Eva Pateraki, Collaborating Graduate Student *(MSc)*
Anna Santorinaiou, Collaborating Graduate Student *(MSc)*
Efstathios Tsimelis, Collaborating Graduate Student *(MSc) - MSc obtained in 2018*
Asimina Fotopoulou, Collaborating Graduate Student *(MSc)*
Maria Dimozi, Training Student - *BSc obtained in 2018*

Research Interests

The Laboratory is focusing on the investigation of the mechanisms of ageing and longevity. Cellular senescence - as a result of successive duplications *in vitro* - and premature senescence - as a response of the cells to exogenous stresses - are investigated. The structural and functional characteristics of the senescent cell in comparison to those of the young, as well as of the cancer cell are studied. 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.

In addition, tissue repair during development and ageing is studied, with an emphasis on the role of growth factors, and especially that of TGF-β. The mechanisms regulating cell proliferation and extracellular matrix production, as well as the responsible intracellular signaling pathways are investigated. In parallel, alternative regulatory mechanisms of cell proliferation and differentiation, such as autocrine regulation, cell-matrix interactions, cell responses to exogenous stresses (e.g. ionizing and UV radiation) or the effect of mechanical forces are studied.

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

2018 Findings

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 proteoglycan syndecan 1 (SDC1).

- We showed that senescent fibroblasts downregulate proteoglycan decorin, which plays an anti-cancer role by inhibiting paracrine interactions between stromal and cancer cells, which is reinforced by the action of cancer cells. These findings indicate a side effect of radiotherapy, which secondarily can promote carcinogenesis.

- We showed that senescent fibroblasts downregulate proteoglycan decorin, which plays an anti-cancer role by inhibiting paracrine interactions between stromal and cancer cells, further reinforced by the action of cancer cells. These findings indicate a side effect of radiotherapy, which secondarily can promote carcinogenesis.
- We also demonstrated that inflammatory cytokine TNF-α may lead dermal fibroblasts to premature senescence through the activation of p38 MAPK and through reactive oxygen species' accumulation.
- We also showed that the inflammatory/catabolic phenotype of senescent intervertebral disc cells remains generally unaltered under the harsh environmental conditions prevailing in the disc characterized by nutrient and growth factor deprivation, hyperosmolality and hypoxia.
- Additionally, we demonstrated that the anti-proliferative and inflammatory phenotype of senescent fibroblasts is preserved when cellular morphology is altered.
- It was also shown that cellular morphology and ability for adhesion, differentiation and proliferation are maintained when cells are cultured onto photolithographically micropatterned silicon substrates.
- In parallel, we continued our research on the study of cytoprotective mechanisms towards UV radiation (Figure 1).
- Finally, we continued our research on the investigation of natural products and novel synthetic compounds with anti-cancer, anti-oxidant and cosmetic applications.

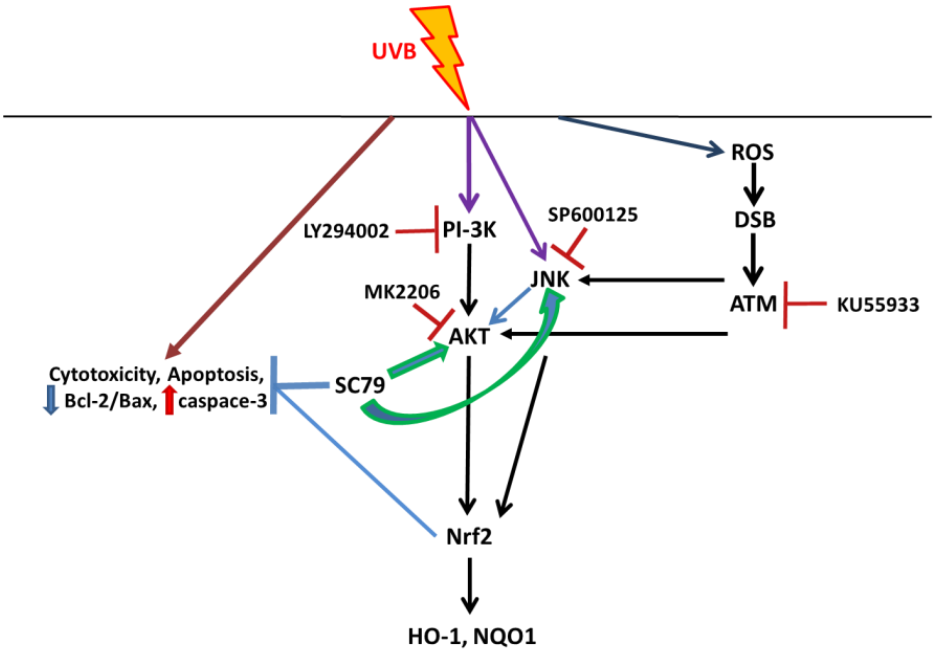


Figure 1. Proposed model presenting ultraviolet radiation-induced biochemical pathways in human skin fibroblasts. *High doses of ultraviolet radiation result in the production of reactive oxygen species that are genotoxic for the cells and lead them to apoptosis. Exposure of the cells to ultraviolet radiation activates PI3K / Akt and JNKs pathways and then induces the transcription factor Nrf2 and the cellular anti-oxidant response through the up-regulation of the genes encoding HO1 and NQO1 enzymes. SC79 protects the cells against the cytotoxic effect of UV radiation by activating the JNK-Akt-Nrf2 pathway (Angelopoulou et al., in preparation).*

Publications

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.

Al Naqbi, S.R., Pratsinis, H., Kletsas, D., Eliades, T., Athanasiou, A.E. (2018). *In vitro* assessment of cytotoxicity and estrogenicity of Vivera® retainers. J Contemp Dent Pract. 19, 1163-1168.

Bourkoula, A., Mavrogonatou, E., Pavli, P., Petrou, P.S., Douvas, A.M., Argitis, P., Kletsas, D., Kakabakos, S.E. (2018). Guided cell adhesion, orientation, morphology and differentiation on silicon substrates photolithographically micropatterned with a cell-repellent cross-linked poly(vinyl alcohol) film. Biomed Mater. 14, 014101.

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.

Crespo, I., Giménez-Dejoz, 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-oxopyrimido[4,5-c]quinoline-2-acetic acid derivatives as selective and potent inhibitors of human aldose reductase. Eur J Med Chem. 152, 160-174.

Pratsinis, H., Mavrogonatou, E., Kletsas, D. (2018). Scarless wound healing: From development to senescence. Adv Drug Deliv Rev. pii: S0169-409X, 30063-2.

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.

Mavrogonatou, E., Konstantinou, A., Kletsas, D. (2018) Long-term exposure to TNF-α leads human skin fibroblasts to a p38 MAPK- and ROS-mediated premature senescence. Biogerontology. 19, 237-249.

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.

Zoumpopoulou, G., Tzouvanou, A., Mavrogonatou, E., Alexandraki, V., Georgalaki, M., Anastasiou, R., Papadelli, M., Manolopoulou, E., Kazou, M., Kletsas, D., Papadimitriou, K., Tsakalidou, E. (2018). 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.

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 (Basel). 3, pii: E13.

Articles in Press

Mavrogonatou, E., Pratsinis, H., Kletsas, D. (2019). The role of senescence in cancer development. Semin Cancer Biol. pii: S1044-579X, 30127-0. (IF: 9,658)

Kouroumalis, A., Mavrogonatou, E., Savvidou, O.D., Papagelopoulos, P.J., Pratsinis, H., Kletsas, D. (2019). Major traits of the senescent phenotype of nucleus pulposus intervertebral disc cells persist under the specific microenvironmental conditions of the tissue. Mech Ageing Dev. 177, 118-127. (IF: 3,603)

Mavrogonatou, E., Pratsinis, H., Papadopoulou, A., Karamanos, N.K., Kletsas, D. (2019). Extracellular matrix alterations in senescent cells and their significance in tissue homeostasis. Matrix Biol. 75-76, 27-42. (IF: 6,986)

Papadopoulou A, Todaro A, Eliades T, Kletsas D. (2019) Effect of hyperglycaemic conditions on the response of human periodontal ligament fibroblasts to mechanical stretching. Eur J Orthod. pii: cjz051. doi: 10.1093/ejo/cjz051. (IF: 1,841)

Koumantou, D., Barnea, E., Martin-Esteban, A., Maben, Z., Papakyriakou, A., Mpakali, A., Kokkala, P., Pratsinis, H., Georgiadis, D., Stern, L.J., Admon, A., Stratikos, E. (2019). Editing the immunopeptidome of melanoma cells using a potent inhibitor of endoplasmic reticulum aminopeptidase 1 (ERAP1). Cancer Immunol Immunother. (in press). (IF: 4,900)

Fokialakis, N., Alexi, X., Aligiannis, N., Boulaka, A., Meligova, A.K., Lambrinidis, G., Kalpoutzakis, E., Pratsinis, H., Cheilari, A., Mitsiou, D.J., Mitakou, S., Alexis, M.N. (2019). Biological evaluation of isoflavonoids from *Genista halacsyi* using estrogen-target cells: Activities of glucosides compared to aglycones. PLoS One. 14, e0210247. (IF: 2,776)

Travasarou, A., Angelopoulou, M.T., Vougogiannopoulou, K., Papadopoulou, A., Aligiannis, N., Cantrell, C.L., Kletsas, D., Fokialakis, N., Pratsinis H. (2019). Bioactive metabolites of the stem bark of *Strychnos aff. darienensis* and evaluation of their antioxidant and UV protection activity in human skin cell cultures. Cosmetics 6, 7. (IF: -)

Articles in Books and Conference Proceedings

Angelopoulou, M., Mavrogonatou, E., Pratsinis, H., Rizou, S., Gorgoulis, V.G., Kletsas, D. (2018). Mechanisms of UVB-mediated cytotoxicity on skin fibroblasts. Wound Repair Regen. 26, A17.

Presentations at Scientific Conferences

M. Angelopoulou, E. Mavrogonatou, H. Pratsinis, S. Rizou, V.G. Gorgoulis, D. Kletsas (2018). Mechanisms of UVB-mediated cytotoxicity on skin fibroblasts. Scarcon ETRS Congress 2018, May 31-June 2, Amsterdam, The Netherlands

E. Mavrogonatou, A. Papadopoulou, H. Pratsinis, P. Panagiotou, V. Gorgoulis, N. Karamanos, S. Werner, D. Kletsas (2018). Senescent fibroblasts as modulators of tumor microenvironment. FEBS Advanced Lecture Course FEBS-ECM 2018 “Extracellular Matrix: Cell regulation, epigenetics and modeling”, September 27-October 2, Patras, Greece (invited)

H. Pratsinis, L. Kikidou, S. Grammatikaki, E. Livaniou, D. Kletsas (2018). Effects of thymosinic peptides on human skin fibroblasts: role in wound repair. FEBS Advanced Lecture Course FEBS - ECM 2018 “Extracellular Matrix: Cell Regulation, Epigenetics and Modeling”, September 27-October 2, Patras, Greece

D. Kletsas (2018). Cellular senescence in the intervertebral disc: Molecular mechanisms, role in tissue degeneration and putative pharmacological target. 12th Annual Congress of the Hellenic Spine Society, November 1-4, Volos (invited)

D. Kletsas (2018). Interplay between Cellular Senescence and Cancer. 4th Symposium of Advances in Cancer Immunology and Immunotherapy. November 29–December 1, Athens, Greece (invited)

A. Kouroumalis, E. Mavrogonatou, H. Pratsinis, O.D. Savvidou, P.J. Papagelopoulos, D. Kletsas (2018). Development of an assay system for the evaluation of senolytic and senomorphic compounds in intervertebral disc cells. 69th Congress of the Hellenic Society of Biochemistry and Molecular Biology, November 23-25, Larissa

M. Angelopoulou, E. Mavrogonatou, H. Pratsinis, S. Rizou, V.G. Gorgoulis, D. Kletsas (2018). The extended activation of the JNK-Akt-Nrf2 pathway by the ATM-p53 pathway protects fibroblasts from UVB-mediated cytotoxicity. 69th Congress of the Hellenic Society of Biochemistry and Molecular Biology, November 23-25, Larissa

A. Bourkoula, E. Mavrogonatou, P. Pavli, P.S. Petrou, A.M. Douvas, P. Argitis, D. Kletsas, S.E. Kakabakos (2018). Evaluation of photolithograpically micropatterned surfaces for guided cell adhesion, morphology and proliferation. 69th Congress of the Hellenic Society of Biochemistry and Molecular Biology, November 23-25, Larissa

E. Mavrogonatou, A. Papadopoulou, H. Pratsinis, E. Liakou, S. Rizou, K. Evangelou, P.N. Panagiotou, N.K. Karamanos, V.G. Gorgoulis, D. Kletsas (2018). Decreased expression of the proteoglycan decorin fills in the tumor-promoting phenotype of ionizing radiation-induced senescent human breast stromal fibroblasts. 69th Congress of the Hellenic Society of Biochemistry and Molecular Biology, November 23-25, Larissa

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 Eleni Kikidou, Efstathios Tsimelis, Eva Pateraki and Asimina Fotopoulou (D. Kletsas)

Supervision of the thesis for the acquisition of a Master's degree of Anna Santorinaiou (D. Kletsas / H. Pratsinis)

Supervision of the thesis for the acquisition of a Bachelor's degree of Maria Dimozi (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 senescence and tissue homeostasis", Post-graduate Master's Degree in Cosmetology, Department of Pharmacy of the University of Athens, 10 students (D. Kletsas)

"Cell senescence: Molecular mechanisms and role in tissue homeostasis", Harokopio University, 2 hours, 15 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 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)

In collaboration with the scientific staff of the Institute: 1. The Inter-Institutional Joint Post-Graduate Programme (JPGP) in "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" between the Institute of Biosciences and Applications and the University of Patras and 2. the 1st Summer Camp of the Institute of Biosciences and Applications for High School students, June 25 - July 6, 2018 were organized (D. Kletsas)

Participation in the Inter-Institutional Joint Post-Graduate Programme (JPGP) in "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" between the Institute of Biosciences and Applications and the University of Patras, 6 hours, 10 students (D. Kletsas, H. Pratsinis and E. Mavrogonatou)

Participation in the 1st Summer Camp of the Institute of Biosciences and Applications for High School students, June 25 - July 6, 2018, 27 students (D. Kletsas, H. Pratsinis and E. Mavrogonatou)

Member of examination committees for Ph.D. and MSc theses:

Eirini-Stavroula Komseli, Ph.D. thesis, "The differential role of cdc6 factor in normal and cancer cells" (Medical School, University of Athens) (D. Kletsas)

Sotirios P. Fortis, Ph.D. thesis, "Immunological identity inside the tumor and in the peripheral blood as prognostic biomarkers of breast cancer" (Medical School, University of Athens) (D. Kletsas)

Ioanna Sougleri, Ph.D. thesis, "Contribution of *Helicobacter pylori* infectious agents to the activation of factors regulating extracellular matrix structure" (Department of Chemistry, University of Athens) (D. Kletsas and H. Pratsinis)

Saira Munir, Ph.D. thesis, "The adaptive response of mesenchymal stem cells to danger signals regulates neutrophil activation in cutaneous trauma and tissue repair" (Department of Dermatology and Allergic Diseases, Ulm University, Germany) (D. Kletsas)

Efstathios Tsimelis concluded his M.Sc. thesis entitled "Study of proteoglycans' expression in senescent stromal cells" in the framework of the Master's Degree Programme 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)

Eleni Kikidou concluded her M.Sc. thesis entitled "Thymosine peptides with a putative healing action" in the framework of the Master's Degree Programme 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:

Member of the Sectoral Scientific Council for Bio-Medical Sciences of the National Council for Research and Innovation (D. Kletsas)

Substitute Member of the National Committee on the welfare of animals used for scientific purposes (D. Kletsas)

Member of the Federation of the European Biochemical Societies Fellowships Committee (D. Kletsas)

Member of the Regional Research and Innovation Council (D. Kletsas)

Vice President of the Administrative Board of the Hellenic Society for Biochemistry and Molecular Biology (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)

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

Section Editor of the section "Ageing Phenotypes" of Encyclopedia of Biomedical Gerontology (Elsevier) (D. Kletsas)

Participation in editorial boards of scientific journals:

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

Guest Editors of the Special Issue "Anti-aging Properties of Natural Compounds" of the scientific journal "Cosmetics" (H. Pratsinis, D. Kletsas)

FEBS Advanced Lecture Course "Extracellular Matrix: Cell Regulation, Epigenetics and Modeling", September 27-October 2, Patras, Greece. Member of the Scientific Committee (D. Kletsas)

Participation in committees for the reviewing of research proposals:

Hellenic Foundation for Research and Innovation (H.F.R.I), Research Grants Council of Hong-Kong (D. Kletsas)

Reviewing of manuscripts in scientific journals:

Ageing Research Reviews, Matrix Biology, PLoS ONE, Wound Repair and Regeneration, Mechanisms of Ageing and Development (2), European Spine Journal (5), Biogerontology, Connective Tissue Research, Free Radicals in Biology and Medicine, Journal of Bone and Mineral Research, Cosmetics, Journal of Orthopedic Research (2), Journal of Orthopedic Research Spine, Journal of Medicinal Food, European Cells and Materials (2), Journal of International Medical Research, Journal of Investigative Dermatology, BBB-Molecular Basis of Disease (D. Kletsas)

Biotechnology Progress, International Journal of Molecular Sciences, Journal of Photochemistry and Photobiology, Marine Drugs, Mechanisms of Ageing and Development, Molecules (4), PLoS ONE (H. Pratsinis)

PLoS ONE, International Journal of Environmental Research and Public Health (2), International Journal of Molecular Sciences (3), Biomedicine & Pharmacotherapy (2), American Journal of Orthodontics & Dentofacial Orthopedics (13), iMedPub (2), Toxics (3), Nanomaterials (2), European Spine Journal, Symmetry, BAOJ Pathology (2), Journal of Photochemistry & Photobiology, B: Biology, Dental Materials (E. Mavrogonatou)

Other lectures or presentations of scientific content:

D. Kletsas "Intervertebral disc ageing and degeneration" Seminar on Mechanical Diagnosis and Therapy, May 12, 2018, Athens (invited speaker)

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

D. Kletsas:
Director of IBA & Member of the Administrative Board of NCSR "Demokritos"
Head of the Ethics Committee of NCSR "Demokritos" (until 7/2018)
Scientific Supervisor of the Experimental Animal Colony
Supervisor of the Fluorescence Activated Cell Sorting Facility

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

Impact Factors:
D. Kletsas (for 10 publications): 49,105
H. Pratsinis (for 4 publications): 20,352
E. Mavrogonatou (for 7 publications): 40,370

Citations 2018 (without self-citations):
D. Kletsas: 696
H. Pratsinis: 171
E. Mavrogonatou: 107

Total Citations 2014-2018 (without self-citations):
D. Kletsas: 3037
H. Pratsinis: 831
E. Mavrogonatou: 275

h-factor:

D. Kletsas: 44 (Scopus), 49 (Google Scholar)
H. Pratsinis: 28 (Scopus), 30 (Google Scholar)
E. Mavrogonatou: 12 (Scopus), 12 (Google Scholar)

Current External Funding

Project entitled *Matrix glycans as multifunctional pathogenesis factors and therapeutic targets in cancer (GLYCANC),* EU-funded (*MSCA-RISE-2014),* Scientific Supervisor Dr. D. Kletsas.
Duration: 2015-2019
Total programme funding: 567.000 €
Funding of the lab for 2018: 18.585,00 €.

Project entitled *Effect of TNF-α and glucose on the response of human PDL fibroblasts to mechanical stretching,* funded by the University of Zurich, Scientific Supervisor Dr. D. Kletsas.
Duration: 2016-2018
Total programme funding: 14.928,34 €
Funding of the lab for 2018: 6.968,64 €.

Funding from the Department of Dermatology and Allergic Diseases, Ulm University, Germany, in the framework of a common research programme on the study of stromal cellular senescence in carcinogenesis with Scientific Supervisor Dr. D. Kletsas.
Funding of the lab for 2018: 20.000 €.

Project entitled *New bioactive compounds with anticancer/antioxidant potential from sponge-associated cyanobacteria,* funded by the Operational Programme "Human Resources Development, Education and Lifelong Learning 2014-2020" (PA), M.I.S. 5004698 and Academic Supervisor Assist. Prof. Spyros Gkelis.
Duration: 2018-2019
Total programme funding: 19.550 €
Funding of the lab for 2018: 5.650 €.

Scholarship for doctoral candidate A. Kouroumalis supporting the Ph.D. project entitled *Effect of external environment on the gene expression and function of intervertebral disc cells* provided by the Hellenic Foundation for Research and Innovation and the General Secretariat for Research and Technology (code 2200).
Duration: 2018-2019
Total programme funding: 19.800 €
Funding of A. Kouroumalis for 2018: 10.800 €.

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,* Scientific Supervisor Dr. D. Kletsas.
Duration: 2017-2020
Total programme funding: 740.000 €
Funding for 2018: 296.000,00 €.

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,* Scientific Supervisor Dr. D. Kletsas (since September 2017).
Duration: 2017-2020

Total programme funding: 899.600 €
Funding for 2018: 147.100,00 €.

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,* Scientific Supervisor Dr. D. Kletsas.
Duration: 2017-2020
Total programme funding: 211.250 €
Funding for 2018: 43.000,00 €.

Research Group: Nuclear Proteins and Chromatin Function

Research Staff
Thomae Sourlingas, Senior Researcher
Kalliope Sekeri, Collaborating Former Staff Scientist

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 histones and their post translational epigenetic modifications in the regulation of the mammalian biological clock in cell cultures (in collaboration with Dr. Prombona, head of the Chronobiology Lab).

2018 Findings

Chromatin conformational changes are prerequisites for gene transcription, replication, etc. They are brought about by changes in the histone subtype constitution of chromatin and histone epigenetic modifications. Deregulation of these histone epigenetic factors may be involved in aberrant gene expression in cancer. Histone deacetylase inhibitors (HDACIs) are used as tools for the investigation of epigenetic regulation of chromatin and they can be used alone, or in combination with other anticancer agents, in therapeutic regimens. For these reasons, we studied histone H3 acetylation, trimethylation and dimethylation in the absence and presence of the HDACI, sodium butyrate, in three leukemic cell lines (K562, NB4, Molt4) as compared to normal lymphocytes. Acetylation and trimethylation of histone H3 are modifications that activate gene expression, while dimethylation of H3 inhibits gene expression. The endogenous acetylation levels were slightly lower in lymphocytes as compared to leukemic cells, while trimethylation levels were similar. Dimethylation was higher in lymphocytes. These results are consistent with the fact that peripheral blood lymphocytes are usually in the Go phase. In the presence of butyrate there is a statistically significant increase in acetylation levels in all cell types, with the NB4 cells showing the highest statistically significant difference amongst non treated and treated cells. No differences were found in the trimethylation levels of K562 and Molt4 cells with butyrate treatment. On the other hand, in the presence of butyrate, NB4 cells showed increased H3 trimethylation levels and a smaller, but statistically significant increase, was also found in normal lymphocytes. No differences were found in the dimethylation levels of lymphocytes and Molt4 cells with butyrate. However, the H3 dimethylation

levels of NB4 and K562 cells showed a statistically significant increase and a statistically significant decrease, respectively in the presence of butyrate. These results will be combined with mortality levels so as to ascertain whether these histone factors can be used as biomarkers of the efficacy of HDACIs.

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).

Other Activities for the Institute of Biosciences & Applications

Responsible for the organization of bibliographic seminars of the graduate students of IB-A.

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, *Reviewer 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 2018 (without self-citations): 28

Total Citations 2014-2018 (without self-citations): 133

h-factor: 11 (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
Angeliki Bourtsala, Postdoctoral Fellow
Ourania Trohatou, Postdoctoral Fellow
Christina Gkolfinopoulou, Graduate Student
Christina Mountaki, Graduate Student
Achilleas Papagiannis, Graduate Student
Konstantina Katrini, Graduate Student (MSc)
Christianna Moutzouvi, Undergraduate Student
Effie Valanti, Graduate Research Associate
Eleni Theofanidi, Graduate Research Associate
Annita Katopodi, Graduate Research Associate
Nikolaos Giannakas, Technical Specialist

Research Interests

1. Neurodegenerative Disorders:

A) 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.

B) Study of cell survival mechanisms in age-related diseases like Alzheimer Disease and type II Diabetes; The role of MMP-9 and the potential for enzyme administration to be a viable option for therapeutic purposes is being studied.

2. Molecular mechanisms of dyslipidemias and atherosclerosis

A) Elucidation of disorders of high density lipoprotein (HDL) metabolism that affect 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.

3. Diabetes Mellitus and Diabetic Nephropathy

A) Cross talk between nephrin and survival signaling pathways in pancreatic insulin producing beta cells.

B) Effect of liraglutide (a human GLP-1 analogue) 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.

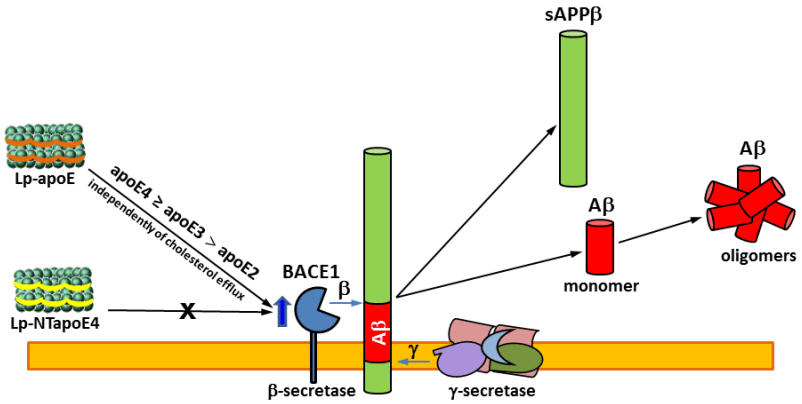
i) Mode of liraglutide action in prevention of podocyte and β-cell apoptosis and on the process of regeneration of β-cells from mesenchymal stem cells (MSCs). Renoprotective role of VitaminD3 on glomerular kidney function, using animal models of Type2 Diabetes.

ii) 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. Interactions with signaling pathways that regulate podocyte survival.

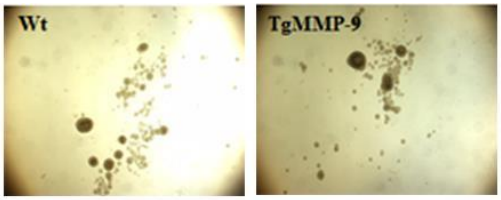
2018 Findings

1. <u>Neurodegenerative Disorders:</u>

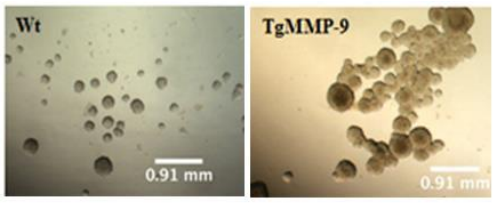
A) ApoE-containing lipoprotein particles can have a direct effect on Aβ production and oligomerization in neuronal cells and therefore contribute to Alzheimer's disease pathogenetic processes, independently of their capacity to promote cholesterol efflux. (Dafnis et al, Biochem. J. 2018)



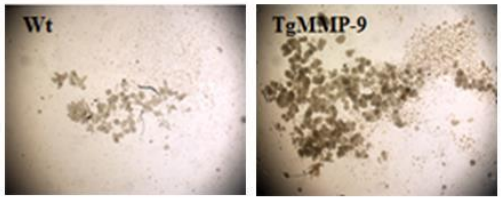
B) Given the protective effect of mild overexpression of MMP-9 on amelioration of AD and T2DM pathology, the possibility of releasing MMP-9 to the brain via neural stem cells (NCSs) overexpressing the enzyme is being studied. To this end, NSC cultures were developed to study the molecular mechanisms that determine NSC proliferation and differentiation.



2nd passage:
- 13% increased number of neurospheres
- 88% increased single cell number*

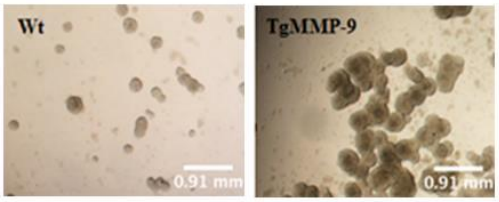


2nd passage:
- 18% increased neurosphere size*



3rd passage:
71% increased number of neurospheres
- 169% increased single cell number*

*Counted using a hemocytometer



3rd passage:
- 44% increased neurosphere size*

*Image J arbitrary units: sphere diameter length >0.20mm

2. <u>Dyslipidemia and atherosclerosis</u>

Missfolding and enhanced aggregation of hereditary apoE3 mutants may constitute the mechanism behind the association of these mutants and lipoprotein glomerulopathy, a rare renal disease characterized by lipoprotein thrombi in glomerular capillaries. (Katsarou et al, J. Lipid Res. 2018)

3. <u>Diabetes Mellitus and Diabetic Nephropathy</u>

A-B) In mouse pancreatic β-cells, nephrin signaling promotes cell survival by inhibiting apoptosis. Liraglutide, a long lasting human GLP-1 analogue, is used for the treatment of type 2 diabetes, since it

improves glucose metabolism. Treatment of diabetic animals with liraglutide resulted in a) re-establishment of both nephrin expression and islet size and b) inhibition of islet β-cell apoptosis. The mechanism of action of liraglutide involves activation of PI3K/AKT/BAD-FoxO pathway which in turn promotes β-cell survival by inhibiting apoptosis.

C) Diabetic nephropathy (DN) is a major chronic complication in diabetic subjects. The number of DN patients progressing to end-stage renal disease, requiring renal replacement therapy continues to increase. Therefore, there is an urgent need for a regenerative strategy. Treatment of isolated rat glomeruli with secreted condition media (CM) from human Amniotic Fluid Mesenchymal Stem/Stromal Cells (CM-AF-MSC) significantly decreased the high-glucose-mediated apoptosis and promoted glomerular survival, suggesting that this approach may provide a valuable tool for cell therapy applications regarding DN.

Publications

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

Bourtsala A., Dafnis I. Chroni A., Farmaki T. and Galanopoulou D. Study of the involvement of phosphatidic acid formation in the expression of wound-responsive genes in cotton. Lipids 53, 589-599 (2018).

Dafnis I., Argyri L., and Chroni A. Amyloid-peptide β 42 enhances the oligomerization and neurotoxicity of apoE4: the C-terminal residues Leu279, Lys282 and Gln284 modulate the structural and functional properties of apoE4. Neuroscience 394, 144-155 (2018). (Figure selected for the front cover).

Nissilä E., Hakala P., Leskinen K., Roig A., Syed S., van Kessel K. P. M., Metso J., de Haas C. J. C., Saavalainen P., Meri S., Chroni A., van Strijp J. A. G., Öörni K., Jauhiainen M., Jokiranta T. S., Haapasalo K. Complement Factor H and Apolipoprotein E Participate in Regulation of Inflammation in THP-1 Macrophages. Front. Immunol. 9:2701/ doi: 10.3389/fimmu.2018.02701 (2018).

Katsarou M., Stratikos E. and Chroni A. Thermodynamic destabilization and aggregation propensity as the underlying mechanism behind the genetic association of apoE3 mutants and Lipoprotein Glomerulopathy. J. Lipid Res., 59, 2339-2348 (2018).

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. 64 (1) pp 1-16.

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. Pp 9294-9306.

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.

Hatziioanou, D., Barkas, G., Critselis, E., Zoidakis, J., Gakiopoulou, H., Androutsou, M., Drossopoulou, G., Charonis, A., Vlahakos, D.V. Chloride Intracellular Channel 4 Overexpression in the Proximal Tubules of Kidneys from the Spontaneously Hypertensive Rat: Insight from Proteomic Analysis. Nephron 138, 60-70, (2018).

Articles in Books and Conference Proceedings

Nissilä E., Roig A., Öörni K., Syed S., Chroni A., de Haas C., van Kessel K., Leskinen K., van Strijp J., Saavalainen P., Jauhiainen M., Jokiranta T. S., Haapasalo K. Complement Factor H down regulates complement mediated inflammation on THP-1 macrophages and monocytes. Mol. Immunol., 102: 195 (2018).

Presentations at Scientific Conferences

Chroni A., Apolipoprotein E structural properties: insights into function and pathogenesis of human diseases. 9th International Conference of the Hellenic Crystallographic Association, 5-7 October 2018, Patras (invited speaker)

Dafnis I., Mountaki C., Raftopoulou C., Megalou E. and Chroni A. Effect of lipoprotein-associated apoE isoforms and carboxyl-terminal truncated forms on amyloid-beta peptide pathology and transporter-mediated cholesterol efflux in neuronal cells. BIOACTIVE LIPIDS: From Chemistry to Biology and Medicine, 29-31 March 2018, Athens

Tziomalos K., Katrini K., Gkolfinopoulou C., Papagianni M., Christou K., Angelopoulou S.-M., Sofogianni A., Savopoulos C., Hatzitolios A. I. and Chroni A. Association between HDL antioxidant activity and acute ischemic stroke severity and outcome. 1st Olympiad in Cardiovascular Medicine, International Symposium on Experimental & Clinical Cardiovascular Medicine, 17-19 May 2018, Athens

Kavetsou E., Katopodi A., Argyri L., Pontiki E., Hadjipavlou-Litina D., Chroni A. and Detsi A. NOVEL MULTI-SUBSTITUTED COUMARIN ANALOGUES: SYNTHESIS AND BIOACTIVITY PROFILE. 4th International Conference "Current Trends of Cancer Theranostics", 1-5 July 2018, Trakai, Lithuania

Katopodi A., Kavetsou E., Kalospyros A., Pontiki E., Hadjipavlou-Litina D., Chroni A. and Detsi A. NEW BIOACTIVE COMPOUNDS SHARING THE COUMARIN FRAMEWORK AS A COMMON STRUCTURAL FEATURE. 8th International Conference On Oxidative Stress in Skin Medicine and Biology, 6-9 September 2018, Andros, Greece

Nissilä E., Roig A., Öörni K., Syed S., Chroni A., de Haas C., van Kessel K., Leskinen K., van Strijp J., Saavalainen P., Jauhiainen M., Jokiranta T. S., Haapasalo K. Complement Factor H down regulates complement mediated inflammation on THP-1 macrophages and monocytes. XXVVII International Complement Workshop, 16-20 September 2018, Santa Fe, New Mexico, USA

Katsarou M., Stratikos E. and Chroni A. Thermodynamic destabilization and aggregation propensity as the underlying mechanism behind the genetic association of apoE3 mutants and lipoprotein glomerulopathy. Athenian Days of Lipidology, Atherosclerosis and Vascular Disease, 1-3 November 2018, Athens

Dafnis I., Raftopoulou C., Mountaki C., Megalou E., Zannis V. I. and Chroni A. Apolipoprotein E (apoE) isoforms and carboxyl-terminal truncated apoE4 forms influence neuronal amyloid-beta peptide (Aβ) production. 69^{o} Congress of the Hellenic Society of Biochemistry and Molecular Biology, 23-25 November 2018, Larissa

Tziomalos K., Katrini K., Kontana A., Gkolfinopoulou C., Didaggelos T., Savopoulos C., Hatzitolios A.I., Chroni A. Diabetes mellitus is associated with reduced activity of paraoxonase-1 in patients with acute ischemic stroke. 32^{o} Congress of the Hellenic Association for the Study and Education of Diabetes Mellitus, 14-18 November 2018, Thessaloniki

Tziomalos K., Katrini K., Papagianni M., Christou K., Gkolfinopoulou C., Angelopoulou S., Sofogianni A., Savopoulos C., Hatzitolios A.I., Chroni A. Impaired antioxidative activity of HDL is associated with more severe acute ischemic stroke. 8^{o} Congress of the Hellenic Atherosclerosis Society, 29 November-1 December 2018, Athens

Tziomalos K., Katrini K., Papagianni M., Christou K., Gkolfinopoulou C., Angelopoulou S., Mantziou C., Savopoulos C., Hatzitolios A.I., Chroni A. Paradoxical correlation of paraoxonase-1 activity and in-hospital mortality in patients with acute ischemic stroke. 8^{o} Congress of the Hellenic Atherosclerosis Society, 29 November-1 December 2018, Athens

Tziomalos K., Katrini K., Papagianni M., Christou K., Gkolfinopoulou C., Angelopoulou S., Ztriva E., Savopoulos C., Hatzitolios A.I., Chroni A. The reduced antioxidative activity of HDL is associated with

increased incidence of death during the first year following acute ischemic stroke. 8^{o} Congress of the Hellenic Atherosclerosis Society, 29 November-1 December 2018, Athens

Tziomalos K., Katrini K., Papagianni M., Christou K., Gkolfinopoulou C., Angelopoulou S., Kontana A., Savopoulos C., Hatzitolios A.I., Chroni A. Paraxoxonase-1 activity is not associated with long-term outcome of patients that suffered acute ischemic stroke. 8^{o} Congress of the Hellenic Atherosclerosis Society, 29 November-1 December 2018, Athens

Valanti E., Vafiadaki E., Theofilatos D., Kardassis D., Chroni A., Zannis V. Sanoudou D. Functional characterization of the signaling pathway PI3K/AKT during human endothelial cell migration following treatment with reconstituted HDL-apoE3. 8^{o} Congress of the Hellenic Atherosclerosis Society, 29 November-1 December 2018, Athens

Trohatou O., Drossopoulou G., Tsilibary E., Charonis A. And Iatrou C. Activation of nephrin signaling prevents glucose-induced podocyte dysregulation. 20th Meeting of the Hellenic Society of Nephrology, May 2018, Athens.

Other Scientific Activities

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

Participation in research panels of research proposals:
A. Chroni: 1) Evaluator of proposals submitted under the Call “New hypotheses in basic research to support the emergence of innovative and high risk /high pay off basic research projects in the field of Alzheimer’s disease and related disorders” of the Fondation Alzheimer, Paris, France.
2) Evaluator of scholarship applications for PhD Thesis implementation that are funded by IKY

Scientific publications reviewer:
A. Chroni: Neurobiology of Disease, BBA - Molecular Basis of Disease; BBA - Molecular and Cell Biology; Current Bioinformatics, Atherosclerosis; PLOS ONE
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

1. Best poster presentation award
   Katsarou M., Stratikos E. and Chroni A. Thermodynamic destabilization and aggregation propensity as the underlying mechanism behind the genetic association of apoE3 mutants and lipoprotein glomerulopathy. Athenian Days of Lipidology, Atherosclerosis and Vascular Disease, 1-3 November 2018, Athens

2. Best oral presentation award
   Valanti E., Vafiadaki E., Theofilatos D., Kardassis D., Chroni A., Zannis V. Sanoudou D. Functional characterization of the signaling pathway PI3K/AKT during human endothelial cell migration following treatment with reconstituted HDL-apoE3. 8o Congress of theHellenic Atherosclerosis Society, 29 November-1 December 2018, Athens

Educational Activities

Christianna Moutzouvi presented her diploma thesis entitled “Production of apoE4 bioengineered mutant apoE4[R189A] and analysis of the effect of mutation on apoE4 structure and function” at the Department of Chemistry, University of Athens.

A. Chroni:

1. Member of the Inter-Departmental Committee and faculty in the joined MSc Programme “Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products” of the Department of Chemistry of the University of Patras and of the Institute of Biosciences and Applications of NCSR "Demokritos" Title of lecture: «Methods for analysis and characterization of proteins, lipids and hydrocarbons» (2 hrs - 7 students, Course: «Biochemical Analysis- Clinical Biochemistry».
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 for C. Gkolfinopoulou and C. Mountaki, MSc supervisor for K. Katrini and diploma thesis supervisor for C. Moutzouvi
4. Member of PhD Advisory Committee of C. Gkolfinopoulou at the Department of Chemistry, University of Athens, E. Valanti at the School of Medicine, University of Athens and A. Papagianni at the School of Medicine, Aristotle University of Thessaloniki
5. Chair of PhD Advisory Committee of C. Mountaki at the Department of Chemistry, University of Athens
6. Lecture entitled «Cardiovascular disease: causes and therapeutic approaches», 53rd Summer School of NCSR “Demokritos”, 2-13 July 2018, (1 h lecture, 250 students)
7. Presentation of "IBA Research Activities and Educational Opportunities", 53rd Summer School of NCSR “Demokritos”, 2-13 July 2018, (30 min, 250 students)

A. Tzinia:
Participation in the Scientific Summer Camp, Institute of Biosciences and Applications (June 2018)

P. Kitsiou:
Lecture entitled «Beta-cell survival signaling pathways: Study of the mechanisms of beta-cell apoptosis for the treatment of type 2 diabetes mellitus», 53rd Summer School of NCSR “Demokritos”, 2-13 July 2018.

G. Drossopoulou:
1. Guest Lecturer in the postgraduate specialisation programme (MSc) “Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products”, Department of Chemistry, University of Patras and Institute of Biosciences and Applications (IBA), NCSR Demokritos. (4 hours – 7 students). Lectures on “Biochemical Analysis – Clinical Biochemistry).
2. Scientific Summer Camp, Institute of Biosciences and Applications (June 2018)
3. Guest lecturer in MSc postgraduate program “Molecular and Applied Physiology”, Medical School, University of Athens «Regulation of Apoptosis in disease progression: Is it desirable or must be avoided?» October 2018 (3 hours lecture - 32 students)
4. Guest lecturer in MSc postgraduate course Clinical Biochemistry – Molecular Diagnostics, Unit: Physiology Chapters, Department of Biology, National and Kapodistrian University of Athens, “Metabolic Syndromes – Diabetes Mellitus and its complications”. (3 hours – 28 students)

Other Activities for the Institute of Biosciences & Applications

A. Chroni**:** 1) Member of the Scientific Board of IBA (until 5/2018). 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 9 publications)**:** 36,75

Citations 2018 (without self-citations): A. Chroni: 131, A. Tzinia: 72, P. Kitsiou: 20, G. Drossopoulou: 63. Total: 286 (Scopus)

Total citations 2014-2018 (without self-citations): A. Chroni: 740, A. Tzinia: 318, P. Kitsiou: 123, G. Drossopoulou: 335. Total: 1570 (Scopus)

h-factor: A. Chroni: 22(Scopus), 25(Google Scholar); A. Tzinia: 17(Scopus); P. Kitsiou: 10(Scopus); G. Drossopoulou: 13(Scopus)

Current External Funding

Project entitled *Complementary neuroprotective action of currant as a natural dietary supplement. Highlighting the mechanisms of action of currant using animal models of neurodegenerative diseases*, funded under the call "RESEARCH-CREATE-INNOVATE" of the Ministry of Economy and Development of Greece/ NSRF 2014-2020 with Principal Investigator for NCSR Demokritos Dr. A. Chroni.
Duration: 2018-2021
Total funding (lab): 188.000€
Funding of the lab for 2018: 33.600€

Project entitled *High Density Lipoprotein (HDL) Structure, Function and Dysfunction: Prospects for New Diagnostic and Therapeutic Approaches for Cardiovascular Disease,* funded under the call "Supporting researchers with an emphasis on young researchers" of the Ministry of Education and Religious Affairs of Greece/ NSRF 2014-2020, with Principal Investigator Dr. A. Chroni.
Duration: 2018-2020
Total funding (lab): 40.600€
Funding of the lab for 2018: 16.240

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 2018: 3.000€

Program 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
Principal Investigator: G. Drossopoulou
Duration: 2017-2020
Funding of the lab for 2018: 27.650€

Program entitled "Nephroprotective role of VitaminD3", funded by AENORASIS SA
Principal Investigator: G. Drossopoulou
Duration: 2017-2021
Funding of the lab for 2018: 13.825€

Research Group: Molecular Carcinogenesis and Rare Disease Genetics

Research Staff

Gerassimos Voutsinas, Research Director
Angeliki Delimitsou, Collaborating Graduate Student
Stamatia Katarachia, Collaborating Graduate Student
Ismini Chatzidaki, Graduate Research Associate
Foteini Athanasopoulou, Graduate Student
Konstantina Taouksi, Undergraduate 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

2018 Findings

Malignant cells exhibit significant resistance to FAS-mediated cell death, through different processes, including FAS mutations, soluble FAS expression, or FAS transcriptional dysregulation by P53, eventually escaping from immune surveillance. Since thyroid carcinomas were shown to be resistant to FAS-mediated apoptosis, we investigated the above mechanisms in thyroid carcinoma samples. Thirty-seven thyroid carcinoma samples were analyzed for mutations in FAS exon 9 and TP53 exons 5–8 and protein expression by means of immunohistochemistry. Moreover, thyroid carcinoma mRNA samples were subjected to reverse transcription – PCR, to evaluate the relative expression of transmembrane FAS versus its soluble form. Analysis revealed indications for TP53 mutations in the anaplastic carcinomas, but not in the other thyroid specimens examined for TP53 or FAS exon 9 mutations. FAS receptor expression was observed in almost all thyroid specimens (97%) with significant up-regulation in papillary carcinomas. P53 nuclear staining was observed only in anaplastic carcinomas. Full-length FAS mRNA was detected in all specimens examined, with soluble FAS mRNA being either absent or present in very low amounts. Our results denote that FAS death domain or TP53 DNA-binding domain mutations, down-regulation of FAS receptor expression, or expression of FAS soluble isoform are not responsible for the seeming inhibition of FAS-mediated apoptosis in papillary thyroid carcinoma cells.

Publications

Fanourakis, G., A.A. Saetta, A.C. Lazaris, M. Miaouli, G.E. Voutsinas, E. Patsouris, S. Tseleni-Balafouta (2018) Resistance to Fas-Mediated Apoptosis Does Not Correlate to Structural Alterations or Expression Changes of the Death Receptor in Papillary Thyroid Carcinomas, Pathobiology 85(5-6):304-310.

Articles in Press

Giannopoulou A.F., E.G. Konstantakou, A.D. Velentzas, S.N. Avgeris, M. Avgeris, N. C. Papandreou, I. Zoi, V. Filippa, S. Katarachia, A.D. Lampidonis, A. Prombona, P. Syntichaki, C. Piperi, E.K. Basdra, V. Iconomidou, E. Papadavid, E. Anastasiadou, I.S. Papassideri, A.G. Papavassiliou, G.E. Voutsinas, A. Scorilas, D.J. Stravopodis (2019) Gene-Specific Intron Retention Serves as Molecular Signature that Distinguishes Melanoma from Non-Melanoma Cancer Cells in Greek Patients, International Journal of Molecular Sciences 20(4): 937-970. (IF: 3.687)

Delimitsou A., F. Fostira, D. Kalfakakou, P. Apostolou, I. Konstantopoulou, C. Kroupis, A.G. Papavassiliou, Z. Kleibl, E. Stratikos, G.E. Voutsinas+, D. Yannoukakos+ (2019) Functional characterization of CHEK2 variants in a Saccharomyces cerevisiae system, Human Mutation 40(5):631-648, +equal authorship. (IF: 5.359)

Giannopoulou A.F., A.D. Velentzas, E.G. Konstantakou, M. Avgeris, S.A. Katarachia, N.C. Papandreou, N.I. Kalavros, V.E. Mpakou, V. Iconomidou, E. Anastasiadou, I.K. Kostakis, I.S. Papassideri, G.E. Voutsinas, A. Scorilas, D.J. Stravopodis (2019) Revisiting Histone Deacetylases in Human Tumorigenesis: The Paradigm of Urothelial Bladder Cancer, International Journal of Molecular Sciences 20(6). pii: E1291. (IF: 3.687)

Kachrilas S., A. Dellis, A. Papatsoris, S. Avgeris, D. Anastasiou, A. Gavriil, M. Horti, S. Tseleni Balafouta, K. Livadas, D.J. Stravopodis, G. Alivizatos, G.E. Voutsinas+, C. Deliveliotis+ (2019) PI3K/AKT pathway genetic alterations and dysregulation of expression in bladder cancer, J BUON 24(1):329-337, +equal authorship. (IF: 1.379)

Presentations at Scientific Conferences

Delimitsou A., F. Fostira, P. Apostolou, I. Konstantopoulou, C. Kroupis, Z. Kleibl, E. Stratikos, G.E. Voutsinas*, D. Yannoukakos* (2018) Functional characterization of CHEK2 missense variants, 8th ESO-CNIO Conference on Familial Cancer, May 17-18, 2018, Madrid, Spain (*These authors jointly supervised this work).

Delimitsou A., F. Fostira, D. Kalfakakou, P. Apostolou, I. Konstantopoulou, C. Kroupis, G. Papavassiliou, Z. Kleibl, E. Stratikos, G.E. Voutsinas*, D. Yannoukakos* (2018) Functional evaluation of CHEK2 variants in Saccharomyces cerevisiae, 3nd Conference of the Hellenic Association of Medical Geneticists, November 2-4, 2018, National Research Foundation, Athens, Greece. (*These authors jointly supervised this work).

Educational Activities

Lectures for and lab training of high-school students at the IBA 2018 Summer Camp, July 2018.

Lecture entitled "Rare Diseases" at the 53rd NCSR Demokritos Summer School, July 5, 2018 (number of attendants: approx. 40 individuals, teaching hour: 30 minutes).

Poster entitled "Genetic Analysis of Tuberous Sclerosis in Greek Patients" for the Researcher's Night 2018, September 28, 2018.

Lecture for high-school students from Athens College during their visit at the IBA, November 14, 2018.

Teaching of 4 undergraduate courses: “Introduction to Molecular Biology” (3 semesters) and “Environmental Health” (1 semester) at the American College of Greece (Deree College), Agia Paraskevi Attikis, January - December 2018 (number of attendants: approx. 80 people, teaching hours: 184).

Lecture entitled "Contemporary Biology: Certainties and Concerns", 3rd High School of Heraklion Attikis, Wednesday 7 March 2018 (number of attendants: approx. 50 individuals, teaching hours: 2).

Lecture entitled "Research on Rare Diseases" in the course "Molecular Biology - Systemic and in silico approaches" of the Master's Degree in "Applications of Biology in Medicine" of the Departments of Biology and Medicine of the National and Kapodistrian University of Athens, 2 May 2018, Athens (number of attendants: approx. 20 individuals, teaching hours: 3).

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: European Spine Journal, Scientific Reports (2 articles), Journal of Genetics, IGI Global (2 articles), OncoTargets and Therapy (3 articles), Journal of Cellular and Molecular Medicine, and Cancer Management and Research.
2. Reviewer for the Union for International Cancer Control (1 proposal).
3. Association of Medical Geneticists of Greece (SIGE).
4. Greek Alliance for Rare Diseases (Member of the Scientific Committee).
5. 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, 2018).
3. Member of the Research Council of the Institute (ESI) (June 21, 2017 – December 31, 2018).
4. Member of the Objections Committee of NCSR “Demokritos” (June 8, 2017 – December 31, 2018).
5. Member of 2 Reviewer Committees for hiring new research personnel at the IBA (12-01-18 και 28-03-18)
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) (05-06-18).

Impact factors (for 3 publications): 1,592

Number of citations for 2018 (without self-citations): 59

Number of citations 2014-2018 (without self-citations): 368

h-factor: 18

Current External Funding

Project entitled *Genetic Analysis of Tuberous Sclerosis,* funded by Novartis Hellas, with Dr. G. Voutsinas as Head of Research for NCSR “Demokritos”.
Duration: 2017-2018
Total Funding: 16.000€
Funding of the laboratory for 2018: 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
Stefanos Spanoudakis, 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) 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.

4) 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.

5) Reverse genetics system for Flock House virus (FHV). Generation of recombinant FHV that cause silencing of essential genes by RNAi in the insect *Spodoptera frugiperda*.

6) Transcriptional response of immune-related genes after exposure to viral capsid proteins: a new approach for the identification of pathogen-associated molecular patterns.

7) Bioinformatics tools for the analysis of small RNAs in sequencing databases.

2018 Findings

Resistance mechanisms against insecticides - Functional expression of proteins that are involved in chemical insecticide resistance.
Previous genetic analysis of strains of mites (*Tetranychus urticae*) that are resistant to insecticides identified two different alleles of the CCE04 esterase that showed high expression. Insect cells and the expression system of *Pichia* were used for functional expression of the proteins and allowed their testing in inhibition and competition experiments. Enzyme kinetics showed that the two enzymes bind to spiroclofen and that the active metabolite spiroclofen-enol does not inhibit enzyme activity (collaboration with Dr. J. Vontas, Agricultural University of Athens).

Antiviral immune response in insects.
Development and optimization of methods for the identification of molecules, mainly antimicrobial peptides (AMPs), that block the entrance of the recombinant virus (AcMNPV-YFP) in insect cells. In parallel was studied the role of AMPs during infection with CPV virus and the transcriptional response of the immune system in larvae of *Bombyx mori*.

Transcriptional response of immune-related genes following exposure to viral capsid protein in lepidopteran cells.
Different approaches were used to investigate whether the major capsid protein of cytoplasmic polyhedrosis virus could act as "pathogen-associated molecular pattern" in lepidopteran cell lines. Although in general no robust transcriptional response was observed, two exceptions were noted, i.e. the induction of *dicer-2* and *attacin* in Sf21 and Bm5 cells, respectively. The study represents a new strategy for the identification of PAMPs in insect viruses (work by Yongchao Zhao, South China Agricultural University, Guangzhou, China).

Metabolomics study of infection of silkworm cells by Cricket Paralysis virus (CrPV, *Dicistroviridae*). Non-targeted and targeted approaches were used to identify changes in the metabolome of Bm5 cells during infection of CrPV. Interesting patterns were noted, such as the increase in amino-acids and carbohydrates during the persistent state of infection and the depletion of glucose and glutamine during pathogenicity. The data indicate that metabolites accumulate during viral persistence before their consumption for large scale viral replication and virion production (collaboration with Luoluo Wang and Dr. Smagghe, Ghent University, Belgium).

Pubications

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.

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.

Swevers, L., Liu, J., and Smagghe, G. (2018). Defense mechanisms against viral infection in *Drosophila*: RNAi and non-RNAi. Viruses 10, 230.

Taning, C.N.T., Christiaens, O., Li, X., Swevers, L., Casteels, H., Maes, M., and Smagghe, G. (2018). Engineered Flock House Virus for Targeted Gene Suppression Through RNAi in Fruit Flies (*Drosophila melanogaster*) in Vitro and in Vivo. Front. Physiol. 9, 805.

Zhao, Y., Sun, J., Labropoulou, V., and Swevers, L. (2018). Beyond baculoviruses: additional biotechnological platforms based on insect RNA viruses. Adv. Insect Physiol. 55, 123-162.

Denecke, S., Swevers, L., Douris, V., and Vontas, J. (2018). How do oral insecticidal compounds cross the insect midgut epithelium? Insect Biochem. Mol. Biol. 103, 22-35.

Articles in press

Swevers, L. (2019). An update on ecdysone signalling during insect oogenesis. Curr. Opin. Insect Sci. 31, 8-13. (IF = 3.784)

Wang, L., Cappelle, K., Santos, D., Vanden Broeck, J., Smagghe, G., and Swevers, L. (2019). Short-term persistence precedes pathogenic infection: Infection kinetics of cricket paralysis virus in silkworm-derived Bm5 cells. J, Insect Physiol. 115, 1-11.(IF = 2.862)

Zhao, Y., Kolliopoulou, A., Ren, F., Lu, Q., Labropoulou, V., Swevers, L., and Sun, J. (2019). Transcriptional response of immune-related genes after endogenous expression of VP1 and exogenous exposure to VP1-based VLPs and CPV virions in lepidopteran cell lines. Mol. Genet. Genomics doi: 10.1007/s00438-019-01551-1 (In Press). (IF = 2.879)

Feng, M., Ren, F., Zhou, Y., Zhang, N., Lu, Q., Swevers, L., and Sun, J. (2019). Correlation in Expression between LTR Retrotransposons and Potential Host *Cis*-Targets during Infection of Antherea pernyi with ApNPV Baculovirus. Viruses 11, 421. (IF = 3.811)

Kolliopoulou, A., Santos, D., Taning, C.N.T., Wynant, N., Vanden Broeck, J., Smagghe, G., and Swevers, L. (2019). PIWI pathway against viruses in insects. WIREs RNA. 2019, e1555. (IF = 4.928)

Liu, J., Swevers, L., Kolliopoulou, A., and Smagghe, G. (2019). Arboviruses and the Challenge to Establish Systemic and Persistent Infections in Competent Mosquito Vectors: The Interaction With the RNAi Mechanism. Front. Physiol. 10, 890. (IF = 3.201)

Wei, P., Demaeght, P., De Schutter, K., Grigoraki, L., Labropoulou, V., Vontas, J., Nauen, R., Dermauw, W., Van Leeuwen, Th. (2019). Overexpression of an alternative allele of carboxyl/choline esterase 4 (CCE04) of Tetranychus urticae is associated with high levels of resistance to the keto-enol acaricide spirodiclofen . Pest Management Science (pending revision) (IF: 3.255)

Presentations at Scientific Conferences

Zhao, Y., Sun, J., and Swevers, L. (2018). Viral-like particles based on cytoplasmic polyhedrosis virus for delivery of dsRNA in insects. 2nd iPlanta Conference "RNAi: the future of crosstalk", 14-16 February, Poznań, Poland.

Swevers, L. (2018). RNAi for insect pest control: prospects and challenges. European Biotechnology Congress, 26-28 April, Athens, Greece.

Swevers, L., Zhao, Y., Sun, J., Kolliopoulou, A., Taning, C.N.T., Christiaens, O., and Smagghe, G. (2018). Examination of the potential of virus-induced gene silencing and viral-like particles for environmentally safe insect pest control. XI European Congress of Entomology, 2-6 July, Naples, Italy.

Liu, J., Smagghe, G., and Swevers, L. (2018). Sensitive response of RNA interference in lepidopteran and dipteran cell lines. XI European Congress of Entomology, 2-6 July, Naples, Italy.

Taning, C.N.T., Christiaens, O., Swevers, L., and Smagghe, G. (2018). The potential of virus-based RNAi products: from lab to field. 2nd COST iPlanta Training School CA15223 "RNAi applications; from lab to field", 27-28 September, Rothamsted Research, Harpenden, UK.

Liu, J., Smagghe, G., and Swevers, L. (2018). Sensitivity analysis of RNA interference response in lepidopteran and dipteran cell lines. 2018 ESA, ESC and ESBC Joint Annual Meeting "Crossing Borders: Entomology in a Changing World", 11-14 November, Vancouver, BC, Canada.

Swevers, L., Zhao, Y., Sun, J., Kolliopoulou, A., Taning, C.N.T., Christiaens, O., and Smagghe, G. (2018). RNA Virus-Induced Gene Silencing and Viral-like Particles from dsRNA Viruses for Delivery of RNAi in Insects. 2018 ESA, ESC and ESBC Joint Annual Meeting "Crossing Borders: Entomology in a Changing World", 11-14 November, Vancouver, BC, Canada.

Other Scientific Activities

Participation in editorial boards of scientific journals:
Member of the editorial board of the scientific journals: «Archives of Insect Biochemistry and Molecular Biology» 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 for the funding agency «Agence Nationale de la Recherche (ANR)» (one proposal) (France) (L. Swevers).

Reviewer of research articles:
Reviewer for the journals «Comparative Biochemistry and Physiology B» (2x), «Frontiers in Physiology» (2x), «G3:Genes/Genomes/Genetics», «Insect Biochemistry and Molecular Biology» (8x), «International Journal of Biological Sciences», « International Journal of Molecular Sciences» (2x), «Insect Molecular Biology», «Journal of Insect Physiology» (2x), «Journal of Invertebrate Pathology», «Journal of Insect Science» (3x), «Molecular Genetics and Genomics», «Molecules», «Pest Management Science» (5x), «PLoS ONE» (2x), «Scientific Reports» (2x), «Toxins» (3x) (L. Swevers).
Reviewer for the journal «Genome Biology and Evolution» (1x) (V. Labropoulou)
"Publons" Award: Top 1% in Field (Plant & Animal Science, Multidisciplinary). For the most pre-publication peer-reviews (L. Swevers).

Educational activities

Member of PhD evaluation committee (external examiner): «RNAi-based antiviral immunity in lepidopteran and orthopteran insects», Dulce Santos, Animal Physiology and Neurobiology Division, Department of Biology, K.U. Leuven, Belgium (L. Swevers).

Other activities for the Institute of Biosciences & Applications

Member of the Scientific Board of the institute (L. Swevers).

Member of the Confocal Microscopy Unit of IB-A (V. Labropoulou).

Member of the management committee for the projects of IB-A BIOIMAGING-GR and SANITURA and member of the research team of OPENSCREEN-GR (Responsible Scientist: Dr. D. Kletsas) (V. Labropoulou).

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 6 publications): 19,154

Citations for 2018 (without self-citations)
Swevers L: 230
Labropoulou V: 43

Total Citations 2014-2018 (without self-citations): 1131
Swevers L: 1045
Labropoulou V: 225

h-factor:
L. Swevers: 29 (Scopus), 32 (Google Scholar)
V. Labropoulou: 12 (Scopus), 13 (Google Scholar)

Current External Funding

Project FWO–Vlaanderen (Belgium) with title *Optimizing RNA interference for insect pest control* and coordinator for the Greek participation Dr. L. Swevers.
Duration: 1/2016-12/2019.
Coordinator: G. Smagghe (Belgium)
Total funding of the project: 800.000€
Total funding of the laboratory: 0€
Funding of the laboratory for 2018: 0€.

COST Action CA15223 with title *Modifying plants to produce interfering RNA (iPlanta)* with national delegate Dr. Luc Swevers, funded by the EU.
Duration: 10/2016-4/2020
Total funding (period from 05/2018 until 05/2019): 167.911,50 €
Funding of the laboratory for 2018: 0 €.

Project with title *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 2018: 3.500€

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 (PhD)

Eleni Koutsoumpeli, Postdoctoral Fellow

Neoklis Manikas, PhD candidate

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.

2018 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. The biological production of pheromones will be a breakthrough technology that will allow pheromones to be an efficient and cost effective alternative to chemical insecticides (Figure 1).

For the determination of the homologation of biologically produced pheromones to those chemically produced, electrophysiological studies for the response of male moth antennae to the biopheromones by means of EAG and GC-EAD were performed. Through In the framework of OLEFINE funding the Laboratory acquired a GC-SSR, a specialized apparatus coupling Gas Chromatograph to a Single Sensillum Recorder. GC-EAD/GC-SSR is an important tool for electrophysiological studies and to our knowledge unique in Greece.

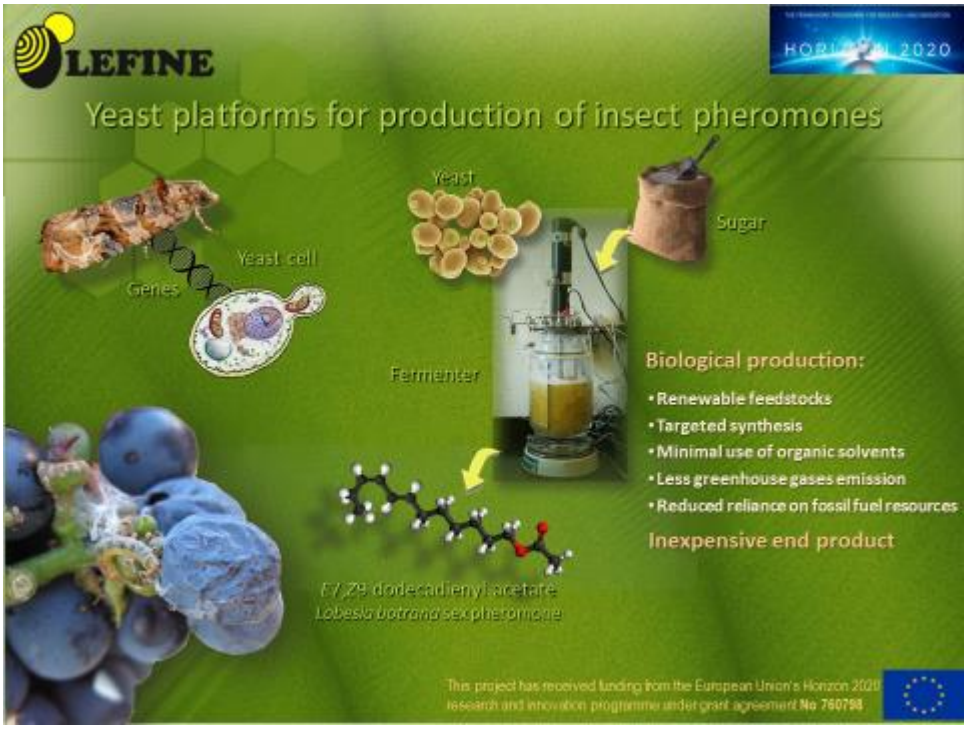
In addition, new insect colonies were established, the cotton bollworm (*Helicoverpa armigera*) and the tomato leafminer (*Tuta absoluta*), which will be used in electrophysiology and behavior assays.

Identification of semiochemicals (infochemicals) and other bioactive metabolites of natural origin (Biological Control Agents, BCAs) as "smart insecticides" to be incorporated in integrated pest management programs against insects of agricultural and medicinal interest.

Initial determination of bioactive metabolites of natural origin (plant or microbial) affecting the mortality and the physiology of insect pest was performed and the characterization of their chemical structure is currently under progress by means of GC/MS. In collaboration with the laboratory of Cellular Proliferation and Ageing of IBE the cytostatic/cytotoxic and antioxidant action of these extracts and their fraction is being assessed.

The development of controlled release systems for semiochemicals through their enclosure in non-toxic, biodegradable, UV-proof and environmentally friendly polymeric matrices was continued.

In collaboration with the Medical School and the Agricultural University of Athens the psycho-physiological approach of olfactory stimuli of therapeutic gardens is being studied.



Publications

Kröber Th., Koussis K., Bourquin M., Tsitoura P., Konstantopoulou M., Awolola T., Dani F., Qiao H., Pelosi P., Iatrou K., and. Guerin P. (2018). Odorant-binding protein-based identification of natural spatial repellents for the Africa malaria mosquito *Anopheles gambiae*. Insect Biochemistry and Molecular Biology 96: 36-50.

Articles in press

Michaelakis A., Anastasaki E., Milonas P., Papachristos D., Kontodimas D., Pontikakos C., Raptopoulos D., Babilis N. and Konstantopoulou M. (2019) Efficacy of communication disruption of *Thaumetopoea pityocampa* (Lepidoptera: Thaumetopoeidae) with low pheromone load formulation. Hellenic Plant Protection Journal (accepted for publication). (if: 0,565)

Presentations at Scientific Conferences

Iatrou K., Tsitoura P., Sdralia N. and Konstantopoulou M. (2018). Cell-Based Screening Platforms for Identification of Modifiers of Odor-Triggered Mosquito Behaviors Acting through Binding to the ORco Subunit of Odorant Receptor Heteromers. Experimental Biology 2018 meeting, San Diego, USA. The FASEB Journal vol. 32 no. 1 Supplement 656.6.

Patents

Iatrou, K., Guerin P.M., Kröber, T. and Konstantopoulou, M. (2018). Methods, compounds and compositions for repelling insects and/or arachnids. European Patent Publication No. 20160029643

(from PCT/EP2014/055170) filed 27/02/2017.EP Patent Application Serial No. 14712237.8 (UEINS1-0008EP).

Other Distinctions and Awards

Award from the Athens Chamber of Commerce and Industry (ACCI) and the Region of Attica for innovative activity at the level of scientific research and at business level, (2nd Athens Business Forum, ACCI, Zappeion, Athens, 13/11/2018).

Other Scientific Activities

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

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

Member of the international claim committee for the XII European Entomological Congress 2022 held in Crete.

Reviewer of research proposals for Ministry of Education, Research and Religion and State Scholarships Foundation (IKY).

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.

President of the evaluation committee of the "D" Competition on "Customs clearance and intra-Community receipt procedures, and transfer to NCSR" D "of all types of materials, instruments and other objects of foreign origin for a period of one (1) year with the right to extend one (1) year ».

Educational Activities

Participation in the Interinstitutional Program of Postgraduate Studies: «Applied Biochemistry Clinical Chemistry and Biotechnology, evaluation of pharmaceutical plants» between of IBE and Department of Chemistry of University of Patras.

Participation as a rapporteur in the Educational meeting of the A΄ Psychiatric Clinic of the Medical School of EKPA (Aiginio Hospital, 5-11 / 2018) on the topic: "The Psychiatric Clinical and Research Meeting with Critical Aesthetic and Olfaction environmental causes".

Invited speaker to the Cyprus University of Technology workshop entitled: «Medicinal and Aromatic Plants in Cyprus-Prospectives» with oral presentation: «Aromatic plants: source of new pest-control compounds for curtailing infectious diseases».

Lecture entitled: «Chemical Ecology and Natural Products» at 53o summer school of NCSR “D”.

Participation in Summer Scientific Laboratories (25/6-6/7/2018) organized by IBE for Lyceum students. Title of the laboratory proposal: «Determinations of natural products with bioactive activity as “smart” insecticides with agriculture and medical interest.”

Participation in information of Lyceum students of Deutsche Schule Athene (DSA) (April 2018) and American College (Psychico) during their visit at the laboratory.

Other activities for the Institute of Biosciences & Applications

President of the Scientific Advisory Board (ESI) of the Institute (06/2018), Member of ESI (01/2018).

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".

Participation as full member in the project of project team project: SANITURA (Determination of objectives and development of innovative approaches for applications in health and the environment), funded by GSRT (Strategy Development Action Research and Technology Organizations, Operational Program "Competitiveness, Entrepreneurship and Innovation ", NSRF 2014- 2020.

Acquisition of permission of a protocol for the treatment of animals (rats) entitled: "Repellents that reduce the chewing of cables by rats"

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

Impact Factors (for 1 publication): 3,618

Citations 2018 (without self-citations): 48

Total Citations 2014- 2018 (without self-citations): 254

h-factor: 13 (Scopus), 15 (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 €
Laboratory Funding for 2018: 213.300,32€

Research Group: Chronobiology

Research Staff
Anastasia Prombona, Senior Researcher
Stavroula Mamoucha, Postdoctoral fellow
Angeliki Galeou, Post-Graduate Student - *PhD obtained in 2018*
Vassileios Tomaropoulos, Training Student
Nikoleta Skrempou, 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 *in vitro* systems.

The circadian clock of plants

This project considers rhythmically expressed genes in *P. vulgaris* primary leaves during the synchronization of the circadian clock by different photoperiods and the application of light at night. In addition, we investigate the regulation of clock gene expression and the molecular mechanisms of the oscillator function by implementation of an *in vitro* protoplast system from *P. vulgaris* leaves.

The circadian clock of mammals-implication in pathological conditions

In this project we investigate the role of the biological circadian clock in carcinogenesis, as to the regulation by the circadian clock of the expression of the oncogene *c-MYC* as well as the interaction of the oncoprotein with components of the circadian clock. We are also interested in the regulation of gene expression related to chromatin remodeling at the promoters of clock genes under physiological and pathological conditions. The effect of bioactive and pharmaceutical compounds on the clock function is also investigated.

2018 Findings

Our laboratory aims at understanding the regulation of expression and the role of central clock components in the plant *Phaseolus vulgaris* and in animal cell culture systems. The objective of our recent investigations, in regard to the *P. vulgaris* clock, is to decipher the involvement of circadian oscillator genes in the rhythmic leaf movements, by examining the process of entrainment. Although rhythmic leaf movements are known since historical times, the genes involved in this physiological process are elusive. We studied the effect of light applied at different times of the photoperiod on the synchronization of rhythmic leaf movements and on the expression of two central clock genes, concomitantly. We showed that the morning-specific clock gene *PvLHY* and the evening-specific *PvTOC1* are phase-shifted following the same pattern. However, the leaves' rhythmic movements are synchronized according to a different pattern, but in a circadian manner. By these results, we, for the first time, document that rhythmic transcription is not the only prerequisite for rhythmic leaf movements (submitted for publication). This constitutes a new finding and opens the way for alternative research directions, that is, control by the clock on posttranscriptional level. In additional experiments, we investigate the regulatory role of clock proteins utilizing the bean protoplast transformation system.

Regarding the study of the interaction of the oncoprotein c-MYC and the mammalian circadian clock, our experiments aim at understanding the interaction of c-MYC with the positive transcriptional complex BMAL1/CLOCK. Preliminary results show that specific motifs are necessary for this interaction (unpublished results).

A. B.

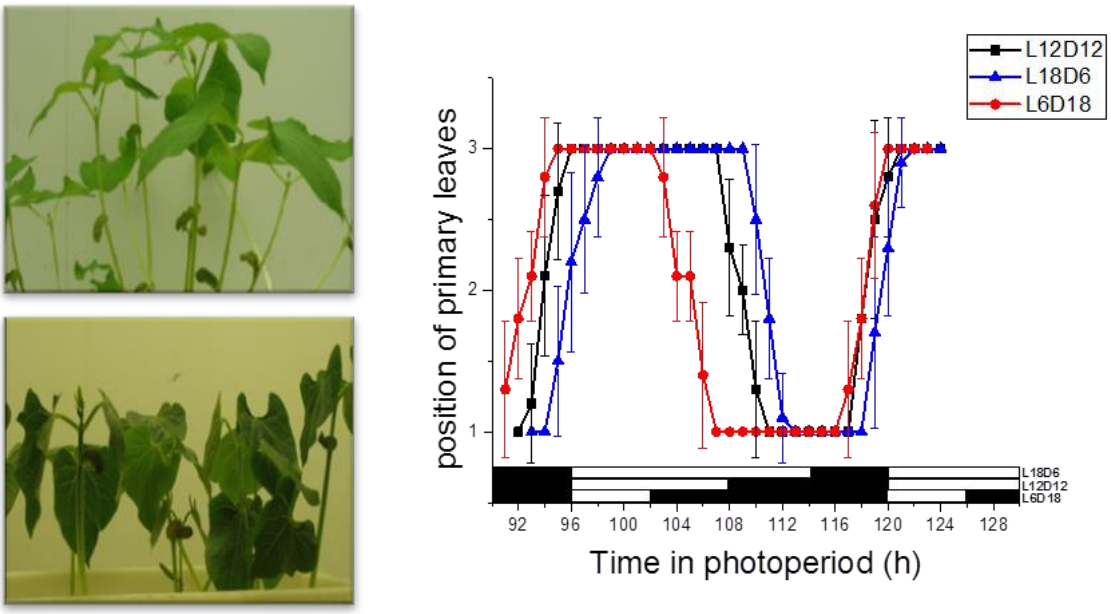


Figure. 1. *Nyctinastic leaf movements of the common bean are rhythmic with a period of 24-hours. A. During the day the green leaves are placed perpendicular to the stem (upper picture) and during the night in parallel position (nyctinasty) (lower picture). B. The phase of the rhythm changes in response to the imposed photoperiod. The value 1 corresponds to the nyctinastic position of the leaves, the value 3 to the opened position and value 2 corresponds to all intermediate positions. On the x-axis white bars depict the day and black bars the night of each photoperiod. Error bars are calculated from 20 individually recorded plants at each time point.*

Publications

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.

Perdikaki, A., Galeou, A., Pilatos, G., Prombona, A., Karanikolos, G.N. (2018) Ion-Based Metal/Graphene Antibacterial Agents Comprising Mono-Ionic and Bi-Ionic Silver and Copper Species. Langmuir 34(37), pp. 11156-11166.

Articles in Press

Giannopoulou, A.F., Konstantakou, E.G., Velentzas, A.D., Avgeris, S.N., Avgeris, M., Papandreou, N.C., Zoi, I., Filippa, V., Katarachia, S., Lampidonis, A.D., Prombona, A., Syntichaki, P., Piperi, C., Basdra, E.K., Iconomidou, V., Papadavid, E., Anastasiadou, E., Papassideri, I.S., Papavassiliou, A.G., Voutsinas, G.E., Scorilas, A., Stravopodis, D.J. (2019) Gene-specific intron retention serves as molecular signature that distinguishes melanoma from non-melanoma cancer cells in Greek patients. International Journal of Molecular Sciences 20(4), 937 (if: 4.183)

Presentations at Scientific Conferences

Mamoucha S., Prombona A. **(2018) In vitro antibacterial activity of essential oil from Mediterranean *Laurus nobilis*** 9th Congress of Hellenic Ecological Society, Herakleion, Crete, 4-7 October, Abstract book p. 200

Mamoucha S., Prombona A. **(2018) Antibacterial activity tests of selected plant essential oils**, 5th Panhellenic Interdisciplinary Med Congress, 21-24 June, Kalamata, e-poster P5.

Educational Activities

Angeliki Galeou defended her PhD thesis, entitled: *Study of circadian clock function and resynchronization in bean (Phaseolus vulgaris),* in the Department of Botany, School of Science, National and Kapodistrian University of Athens, on the 7th of June, 2018.

Other Activities for the Institute of Biosciences & Applications

President of the Scientific Council of IB-E (until 5/2018)

Member in charge for the presentation of IB-E activities to schools.

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

Impact Factors (for 2 publications): 6,91

Citations 2018 (without self-citations): 17

Total Citations 2014-2018 (without self-citations): 60

h-factor: 8

Research Group: Microbial Molecular Genetics

Research Staff
Vickyi Sophianopoulou, Research Director
Christos Gournas, Researcher
Alda Biratsi, Postgraduate Graduate Student
Amalia Megarioti, Postgraduate Graduate Student
Myrsini Charicleous, Undergraduate Student
Ilianna Theodorou, Undergraduate Student
Tatiana Zakopoulou, Undergraduate Student
Spiros Gaitanos, Training Student
Elefteria Giannioti, Training Student (Erasmus Student)

Research Interests

Our group is primarily interested in the function, regulation and organization 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 understand 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 homeostasis of lipids, and how these phenomena are related to fungal pathogenicity. (*I. Vangelatos et al., 2010; C. Scazzocchio et al., 2011; A. Athanasopoulos et al., 2013, 2015; Athanasopoulos et al., 2019*).

Our models of choice are two of the most genetically tractable organisms: The non-pathogenic ascomycetes *Aspergillus nidulans* and the budding yeast *Saccharomyces cerevisiae*, fungi that have been extensively exploited for the discovery of a plethora of mechanisms underlying biological processes and for which state of the art genetic tools are available.
Our group has contributed 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.

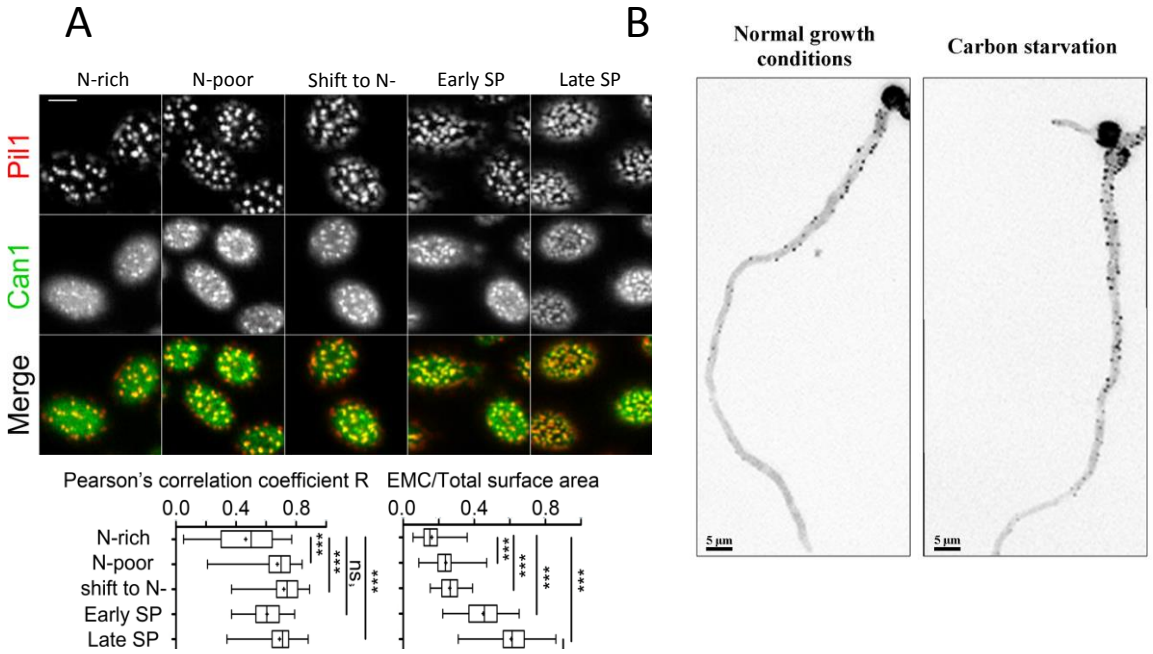
In addition, our group is interested in elucidating the molecular mechanism(s) underlying detoxification of toxic amino acid analogues. L-Azetidine-2-Carboxylic Acid (AZC) is a toxic analogue of proline, produced by the flowering plant *Convallaria majalis* (valley lilly), certain species of the genus *Polygonatum* and beets (*Beta vulgaris*). In nature, AZC has a protective role for the plants that produce it, while 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.

2018 Findings

Study of the mechanisms of detoxification of toxic amino acid analogues:

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. Our results showed that, the hydrolase AzhA is responsible for the detoxification of AZC. AzhA is highly conserved in plant-pathogen fungi of great ecological and economic importance. Additional evidence from phylogenetic analyses supports the view that the *azhA* gene has been transferred horizontally from fungi to bacteria.



A. Confocal microscopy images of a strain of Aspergillus nidulans expressing the eisosomal protein PilA tagged with mRFP in normal growth conditions and upon carbon starvation, at 25 ^{0}C. Scale bar: 5 μm B. Confocal microscopy images of a yeast strain expressing Pil1-mCherry and Can1-GFP, in different conditions of nitrogen availability. Eisosomes are induced in nitrogen poor conditions (N-poor) conditions or nitrogen starvation (Shift to N-) but mainly as the cultures reach the early (early) and late (late) stationary phase of growth (SP).

Study of the lateral compartmentalization of the plasma membrane:

In *A. nidulans,* the number of PilA eisosomal foci increases 3-fold in the hyphae of the fungus upon shift on carbon or nitrogen starvation (3h at 25 ^{0}C). The number and intensity of PilA foci is higher in carbon starvation, while it decreases with increased starvation-time. In addition, PilA foci were found to localize in regions of apical growth during carbon or nitrogen starvation, and not only to the PM of non-growing quiescent spores or germlings under normal growth conditions.

In *S. cerevisiae*, Can1 the Arg transporter, accumulates in MCCs in the absence of substrate and there it is protected from ubiquitin-dependent endocytosis and degradation. This accumulation is because of sphingolipid-dependent slower diffusion and requires intact biosynthesis of complex sphingolipids. In the presence of Arg, because of a change in conformation, Can1 moves out of MCCs and becomes accessible to the ubiquitylation machinery promoting its endocytic degradation.

In *S. cerevisiae* eisosomes expand in number and size at the stationary phase of growth, providing protection in nutrient transporters against a massive endocytosis occurring in parallel with autophagy. This way cells are able to start more efficiently growing once nutrients become available again.

Publications

Gournas, C., Athanasopoulos, A., and Sophianopoulou, V. (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. *19*, 1398.

Gournas, C., Gkionis, S., Carquin, M., Twyffels, L., Tyteca, D., and André, B. (2018). Conformation-dependent partitioning of yeast nutrient transporters into starvation-protective membrane domains. Proc. Natl. Acad. Sci. *115*, E3145–E3154.

Saliba, E., Evangelinos, M., Gournas, C., Corrillon, F., Georis, I., and André, B. (2018). The yeast H+-ATPase Pma1 promotes Rag/Gtr-dependent TORC1 activation in response to H+-coupled nutrient uptake. Elife *7*, e31981.

Articles in Press

Athanasopoulos, A., André, B., Sophianopoulou, V. and Gournas, C. (2019). Fungal Plasma membrane domains. FEMS Microbiology Reviews (IF 11,524)

Articles in Books and Conference Proceedings

Biratsi, A., Gournas, C., Athanasopoulos, A., and Sophianopoulou V. (2018). Efficient enzymatic degradation and assimilation by soil fungi of a plant-protectant natural amino acid analogue. European Biotechnology Congress 2018, April 26-28, Athens, Greece. *Journal of Biotechnology*, Volume 280, Supplement, 30 August 2018, Pages s49-s50.

Biratsi, A., Gournas, C., Athanasopoulos, A., and Sophianopoulou V. (2018). Characterization of two distinct pathways for the detoxification and utilization of L-Azetidine-2-carboxylic acid in *Aspergillus nidulans.* Abstract of the 43rd FEBS Congress "Biochemistry forever" P.07-075, July 7-12, Prague, Czech Republic.

Presentations at Scientific Conferences

Biratsi, A., Gournas, C., Athanasopoulos, A., and Sophianopoulou V. (2018). "Efficient enzymatic degradation and assimilation by soil fungi of a plant-protectant natural amino acid analogue". European Biotechnology Congress, April 26-28, Athens Greece.

C. Gournas, S. Gkionis, M. Carquin, L.Twyffels, D. Tyteca, B. André (2018). Sphingolipid- and Conformation-dependent Partitioning of Yeast Transporters into Starvation-protective Membrane Domains. Proteostatic Mechanisms in Health and Disease, The Final COST Action BM1307 Meeting. February 22-24, Athens, Greece.

C. Gournas, S. Gkionis, M. Carquin, L. Twyffels, D. Tyteca, B. André (2018). Conformation-dependent partitioning of nutrient transporters into endocytosis-protective membrane domains. Lysosomes and Endocytosis Gordon's Conference. June 17-22, Boston, USA.

G. Kapetanakis, C. Gournas, M. Prevost, B André, I. Georis. Structural and functional analysis of yeast Aqr1 involved in amino acid excretion. 2018. Yeast Genetics Meeting, August 22-26, California, USA.

Educational activities

As member of the IBA team I have visited the Second Opportunity Secondary School in Korydallos Prison and I presented a lecture entitled: Cell: the unit of life - What is DNA and chromosomes, in the framework of an educational course entitled "Natural Sciences", 14 May 2018 (V. Sophianopoulou). (Other team members from IB-A: D. Kletsas, L. Drosopoulou, M. Sagnou, A. Panagiotopoulou).

Presentation entitled "Biological roles of the fungal-specific Plasma Membrane Eisosome Compartment (EMC)". 53rd Summer School of NCSR "Demokritos" 2-13 July 2018 (A. Athanasopoulos, V. Sophianopoulou).

Summer Camp IB-A 2018: "Genetic Engineering-Cloning" (A. Athanasopoulos, A. Biratsi, I. Theodorou, V. Sophianopoulou).

Invited presentation entitled «The conformation of yeast nutrient transporters controls both their substrate-induced ubiquitylation and their partitioning into starvation-protective plasma membrane domains», Institut de Biologie et de Médecine Moléculaire, Université Libre de Bruxelles (ULB) (C. Gournas).

Invited presentation entitled «The conformation of yeast nutrient transporters controls both their substrate-induced ubiquitylation and their partitioning into starvation-protective plasma membrane domains Department of Pharmacy, Université Libre de Bruxelles (ULB) (C. Gournas).

Invited presentation entitled «Conformation-dependent control of yeast nutrient transporters: substrate-induced ubiquitylation and partitioning into starvation-protective plasma membrane domains», “Prague Membrane discussions”, Institute of Experimental Medicine, Czech Academy of Sciences (C. Gournas).

Participation in the Inter-Institutional Joint Post-Graduate Programme (JPGP) of IBA NCSR “D” & Department of Chemistry, University of Patras in “Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products” and lecture entitled “Lateral compartmentalization and function of plasma membrane: eisosomes and transmembrane transporters” (7 students, V. Sophianopoulou 4 hours, C. Gournas 1 hour).

“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).

Teaching assistant, as postdoctoral researcher, at the practicals of the course «Genetics», Département de Biologie Moléculaire, Faculté des Sciences, ULB, Belgium. 40 hours, 40 students (C. Gournas).

Member of the Advisory Committee for the PhD thesis of A. Biratsi, Department of Biology, National and Kapodistrian University of Athens (V. Sophianopoulou).

Member of the Advisory Committee for the diploma thesis of M. Charicleous, University of Crete (V. Sophianopoulou).

Member of the Advisory Committee for the diploma thesis of I. Theodorou University of Thrace (V. Sophianopoulou).

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 (V. Sophianopoulou).

Other Distinctions and Awards

- FEBS Scholarship for participation and presentation of work at the 43rd Febs Congress "Biochemistry forever" Prague, Czech Republic 2018 (A. Biratsi).
- Award of the best Poster of the European Biotechnology Congress 2018, April 26-28, Athens, Greece (A. Biratsi).

Other Activities for the Institute of Biosciences & Applications

Member of the Evaluation Committee for the recruitment of Post-graduate students within the Inter-Institutional Joint Post-Graduate Programme (JPGP) of IBA NCSR “D” & Department of Chemistry, University of Patras in “Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products” (2018-2019) (V. Sophianopoulou).

Other administrative activities

- Vice Director of IBA (07/2017-07/2018) (V. Sophianopoulou).
- Head of the Microbial Molecular Genetics lab of IB-A (2004-today) (V. Sophianopoulou).
- Member of the Protocols Evaluation Committee of the Experimental Animal Colony of IBA (V. Sophianopoulou).
- Member of the Advisory Committee on Scientific Issues of NCSR “D” (03/2017 - 03/2018) (V. Sophianopoulou).
- Substitute member of the Executive Body for the recruitment of an Associate Professor in the field of "Microbial Biotechnology", Department of Biochemistry and Biotechnology, University of Thessaly (V. Sophianopoulou).

- Substitute member of the Executive Body for the recruitment of an Assistant Professor in the field of Genetics, Department of Biotechnology, Agricultural University of Athens (V. Sophianopoulou).

Scientific activities

- Member of the editorial board of *Scientific Reports* (Published by Springer Nature) (V. Sophianopoulou)
- Referee of peer-review articles published in International Journals
  Biomolecules (V. Sophianopoulou).
  Scientific Reports (C. Gournas).
- Member of the organization and scientific committee of the European Biotechnology Congress 2018, April 26-28, Athens Greece (V. Sophianopoulou).
- Referre of Abstracts of the European Biotechnology Congress 2018(V. Sophianopoulou).
- Referee of Abstracts of the 4th International Conference on Agricultural and Biological Sciences (ABS 2018) (V. Sophianopoulou).
- Reviewer of IKY PhD student scholarships (V. Sophianopoulou).
- Reviewer of Cyprus Research Promotion Foundation, Program "Excellence Hubs" (C. Gournas).

Impact Factor (for 3 publications): 21,314

Citations 2018 (without self-citations):
V. Sophianopoulou: 82
C. Gournas: 77

Total Citations 2014-2018 (without self-citations)
V. Sophianopoulou: 273
C. Gournas: 204

h-factor:
V. Sophianopoulou: 17
C. Gournas: 10

Current external funding

Project entitled *Plasma membrane organization in quiescence,* by the Fondation Santé - Biomedical Research Grants and scientific coordinator Dr. C. Gournas.
Duration: 02/2019 - 02/2020
Total funding for the laboratory: 25.0000 € (+ 25.000€)
Funding of the laboratory during 2018: 0€

Project entitled *Study of the role of eisosomal proteins in the quiescent state of fungi,* funded by the ministry of finance and development (Support in researchers, emphasizing on new Researchers, 2nd cycle. Scientific coordinator, Dr. C. Gournas, Academic advisor Dr. V. Sophianopoulou.
Duration: 15 months (expected to start within 2019)
Total funding for the laboratory: 45.000 €
Funding of the laboratory during 2018: 0€

Research Group: Biophysics and Biotechnology of Membranes

Research Staff
Kostas Stamatakis, Senior Researcher
George Papageorgiou, Collaborating Former Staff Scientist
Meropi Tsimilli – Michael, Collaborating Scientist
Dimitris Vayenos, Graduate Student
Panagiotis Broussos, Graduate Student
Aikaterini Giakoumidaki – Vogiatzi, Graduate 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.

2018 Findings

Light state transitions (STs) is a reversible physiological process that oxygenic photosynthetic organisms use in order to minimize imbalances in the electronic excitation delivery to the reaction centers of Photosystems I and II, and thus to optimize photosynthesis. STs have been studied extensively in plants, green algae, red algae and cyanobacteria, but sparsely in algae with secondary red algal plastids, such as diatoms and haptophytes, despite their immense ecological significance. In the present work, we examine whether the haptophyte alga *Phaeocystis antarctica*, and dinoflagellate cells that host kleptoplasts derived from *P. antarctica*, both endemic in the Ross Sea, Antarctica, are capable of light adaptive STs. In these organisms, Chl *a* fluorescence can be excited either by direct light absorption, or indirectly by electronic excitation (EE) transfer from ultraviolet light absorbing mycosporine-like amino acids (MAAs) to Chl *a* (Stamatakis et al., Biochim. Biophys. Acta 1858 [2017] 189-195). Here we show that on adaptation to PS II-selective light, dark-adapted *P. Antarctica* cells shift from light state 1 (ST1; more EE ending up in PS II) to light state 2 (ST2; more EE

ending up in PS I), as revealed by the spectral distribution of directly-excited Chl *a* fluorescence and by changes in the macro-organization of pigment-protein complexes evidenced by circular dichroism (CD) spectroscopy. In contrast, no STs are clearly detected in the case of the kleptoplast-hosting dinoflagellate cells, and in the case of indirectly excited Chls *a*, via MAAs, in *P. antarctica* cells.

Articles in Press

Stamatakis, K., Broussos, P-I, Panagiotopoulou, A., Gast, R.J., Pelecanou, M., Papageorgiou G.C. (2019). Light-adaptive state transitions in the Ross Sea haptophyte Phaeocystis antarctica and in dinoflagellate cells hosting kleptoplasts derived from it. Biochim Biophys Acta (Bioenergetics) in press. IF 4.41

Impact Factor (for 1 publication): 4,41

Citations 2018 (without self-citations): 72

Total citations 2014-2018 (without self-citations): 321

h-factor: 14(Web of Science), 17 (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 scale

- Deviations from randomness at the level of nucleotide n-tuplets and at the "middle" length scale: 'word' use, clustering of similar nucleotides etc. Patterns related to the functionality of genomic regions and to the global genome structure. 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 elements.
- 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.

Foundations of Science – Epistemology of the limits

- Modern science and traditional knowledge – Convergence and interactions.
- Convergence and interactions between the sciences and humanities.
- Causality and extended causality. From Aristotle to C.G.Jung – Meaningfulness and non-causal correlation.
- Epistemic consequences of alternative medicine – Foundations of homeopathy.

2018 Findings

Earlier (Almirantis, *Homeopathy* (2013) 102, 114-122), and during this year, we undertook an attempt for a better understanding of the foundations of the action of high dilutions in homeopathic healing. We also considered questions related to the 'Benveniste Affair', its consequences and broader issues in an attempt to understand homeopathy.

The healing potential of homeopathic remedies, as determined in homeopathic pathogenic trials (HPTs) and verified by medical experience, are often found to be meaningfully connected with the symbolic content attributed to the original materials (tinctures, metals etc) through tradition or modern semantics. Such a connection is incompatible with a biomolecular mechanistic explanation of the healing action of remedies. The physiological effects of crude substances are often similar to the symptoms of illnesses cured by the corresponding homeopathic remedy. This is considered a manifestation of the *similia* principle. Evidence is brought in our published work that in several cases the inverse situation occurs, with the healing properties of the crude substance and those of its homeopathic preparation partially coinciding, the remedy usually having broader healing properties. The existence of these two possibilities in the relationship of medicinal actions of remedy and the crude substance offers evidence in favor of a direct involvement of the level of significances in the mechanism underlying the homeopathic phenomenon. Finally, an experimental methodology is proposed, which may bring the result of double-blind randomized studies for homeopathic remedies

closer to the reported performance of homeopathy in real life medical practice. If successful, this method would be a further indication of a non-local, significance-related interpretation of homeopathy.

Publications

Almirantis Y., Tsitinidis K. (2018). Ultra-high dilutions and homeopathy: can they be explained without non-local theory? *Homeopathy* 107, 189-195.

Almirantis Y., Charalampopoulos P., Gao J., Iliopoulos CS., Mohamed M., Pissis SP. & Polychronopoulos D. (2018). On overabundant words and their application to biological sequence analysis. Theoretical Computer Science. TCS-D-17-00866R1.

Articles in Press

K. Apostolou-Karampelis, D.Polychronopoulos & Y.Almirantis. Introduction of 'Generalized Genomic Signatures' for the quantification of neighbour preferences leads to taxonomy- and functionality-based distinction among sequences. *Scientific Reports* (2019). DOI:10.1038/s41598-018-38157-3. [I.F. 4.53]

Other Scientific Activities

Reviewer of scientific papers for: Journal of Oral Health and Dentistry, BMC Bioinformatics, Current Bioinformatics, Gene, Homeopathy, Scientific Reports, Mathematical Problems in Engineering, Brain & Neuroscience Research, και για το ECCB 2018 meeting.

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, University of Athens.
- 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, University of Athens.

Impact Factor (for 2 publications): 1,95

Citations 2018 (without self- citations): 36

Total Citations 2014-2018 (without self- citations): 182

h-factor: 14 (Scopus)

Research Group: Designed Bioactive Molecules Laboratory

Research Staff

Athanasios Papakyriakou, Senior Researcher

Anastasia Mpakali, Postdoctoral Fellow

Georgios Mavridis, Graduate Student

Research Interests

Study of the structure and dynamics of HLA complexes with extended antigenic peptides with respect to their stability against aminopeptidase activity of ERAP1, ERAP2 and LAP.

Study of the allosteric effect of a tetrapeptide at the dynamical coupling between the C-terminus binding region and the active site of ERAP1, with the aim to investigate the mechanism of antigenic peptide C-terminus recognition by ERAP1.

Structure-based discovery of allosteric inhibitors of the aminopeptidase IRAP, using the recent, high-resolution co-crystal structure of ERAP1 with pseudopeptide inhibitors.

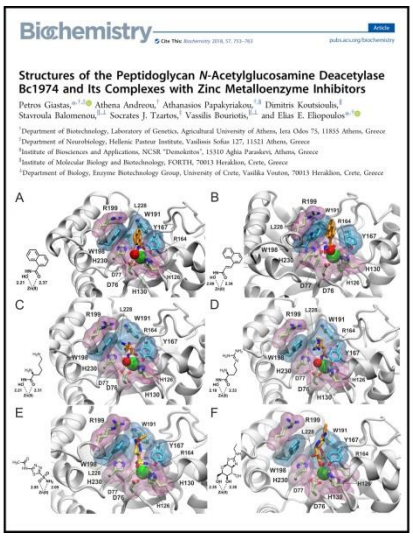
Biophysical study of LMTK3 kinase activity using small molecule inhibitors and computational study of their interaction (Collaboration with Prof. G. Giamas, University of Sussex, UK)

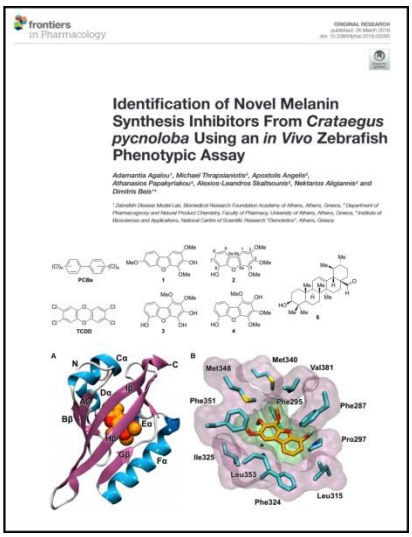
2018 Findings

The disruption of the N-terminus binding region of antigenic peptides loaded onto the MHC-I, in particular by mutations of residues that stabilize the terminal amino group via hydrogen bonds into alanine, do not mediate significant structural changes to the MHC-I/peptide complex, as shown by their crystallographic structures. Instead, these mutations alter the dynamics of the antigenic peptide, and specifically, the N-terminal moiety of the peptide can partially dissociate from the antigen binding groove more freely, which results in higher rates of their hydrolysis by the ER-resident aminopeptidase ERAP1. (J. Biol. Chem. 2018, 293(20), 7538-7548).

The crystal structure of the catalytic region NodB of the peptidoglycan N-acetylglucosamine deacetylase from Bacillus cereus, Bc1974, has been resolved in the ligand-free form, in addition to 4 co-crystal structures with known metalloenzyme inhibitors and 2 hydroxamate aminoacids, all of which target the catalytic zinc. Using a model of the natural substrate in conjunction with docking calculations, we proposed a catalytic mechanism for the deacetylation of peptidoglycan substrates (Biochemistry. 2018, 57(5), 753-763).

We identified 3 compounds that display reversible inhibition of melanin synthesis and do not act via inhibition of Tyrosinase. We identified that the compounds can bind to the Aryl Hydrocarbon Receptor (AHR) using molecular docking calculations and verified activation of the AHR signaling pathway showing the induction of the expression of target genes. (Front Pharmacol. 2018, 9, 265)





Publications

Papakyriakou, A., Reeves, E., Beton, M., Mikolajek, H., Douglas, L., Cooper, G., Elliott, T., Werner, J.M., James, E. (2018). The partial dissociation of MHC class I-bound peptides exposes their N terminus to trimming by endoplasmic reticulum aminopeptidase 1. J. Biol. Chem. 293(20), 7538-7548.

Giastas, P., Andreou, A., Papakyriakou, A., Koutsioulis, D., Balomenou, S., Tzartos, S.J., Bouriotis, V., Eliopoulos, E.E. (2018). Structures of the Peptidoglycan N-Acetylglucosamine Deacetylase Bc1974 and Its Complexes with Zinc Metalloenzyme Inhibitors. Biochemistry. 57(5), 753-763.

Agalou, A., Thrapsianiotis, M., Angelis, A., Papakyriakou, A., Skaltsounis, A.L., Aligiannis, N., Beis, D. (2018). Identification of Novel Melanin Synthesis Inhibitors From Crataegus pycnoloba Using an in Vivo Zebrafish Phenotypic Assay. Front Pharmacol. 9, 265.

Mettou, A., Papaneophytou, C., Melagraki, G., Maranti, A., Liepouri, F., Alexiou, P., Papakyriakou, A., Couladouros, E., Eliopoulos, E., Afantitis, A., Kontopidis, G. (2018). Aqueous Solubility Enhancement for Bioassays of Insoluble Inhibitors and QSPR Analysis: A TNF-α Study. SLAS Discovery, 23, 84-93.

Presentations at Scientific Conferences

A. Papakyriakou, E. Scherer, A. Bailey, L. Bolton, T. Elliott and J. M. Werner (2018) NMR and MD study of the structure and dynamics of peptide-loaded MHC-I provide novel insight into the plasticity of the antigen-binding domain. British Biophysical Society biennial meeting, July 11-13, 2018, Southampton, UK

A. Papakyriakou, E. Scherer, A. Bailey, L. Bolton, T. Elliott and J. M. Werner (2018) Escaping the Groove: Structural Plasticity of MHC I. 28th International Conference on Magnetic Resonance in Biological System, August 18-24, 2018, Dublin, UK.

A. Andreou, P. Giastas, A. Papakyriakou and E. E. Eliopoulos. (2018) Target Filtering for Structure Based Drug Design. Crystal Structures of Bacillus cereus group PDAs Complexed with Inhibitors Reveal Pharmacophore Requirements for Optimizing Inhibitor Potency. 19th International Conference of the Hellenic Crystallographic Association. October 5-7, 2018, Patras, Greece

Other Scientific Activities

Journal referee at: Molecules, International Journal of Molecular Sciences, Pharmaceuticals (MDPI)

Other Activities at the NSCR "Demokritos"

Member of the Scientific Advisory Committee of "Lefkippos" Technology Park in NCSRD.

Impact Factors (for 4 publications): 12,8

Citations 2018 (without self- citations): 101

Total Citations 2014-2018 (without self- citations): 404

h-factor: 16

Current External Funding

Research grant *ARIA "Atomic Resolution Insight into the Antigen processing machinery"*, funded by from the Hellenic Foundation for Research & Innovation and GSRT with Dr A. Papakyriakou as scientific coordinator.
Duration: 11/10/2018-10/10/2021
Total Program Funding: 180.000€
Funding of the lab for 2018: 90.000€

Research Group: Structural Studies of Biomolecules and Pharmaceuticals with NMR

Research Staff
Maria Pelecanou, Research Director
Marina Sagnou, Researcher
Angeliki Panagiotopoulou, **Functional Scientist B**
Barbara Mavroidi, Postdoctoral Fellow
Dimitris Matiadis, Postdoctoral Fellow
Eleftherios Halevas, Postdoctoral Fellow
Valentinos Sofokleous, Postgraduate Student
Maria-Aikaterini Daskalopoulou, Undergraduate Student
Maria Arfara, Undergraduate Student
Orestis Liatsis Douvitsas, Training Student
Panayota Pantiora, Training Student
Merlin Chatoupi, Training Student (Erasmus Programme)

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, encapsulation,** and **biological evaluation** of the new compounds/agents in appropriate systems. Biological evaluation includes interaction studies - mainly with CD –with biomolecules, biochemical, microscopic and cellular assays in cancer and primary cell lines, as well as *in vivo* biodistribution in experimental animals in collaboration with INRASTES.
Recently, our research activity focuses on:

- pharmacophore molecules/bioactive natural products (with typical examples 2- (4'-aminophenyl)benzothiazole, curcumin, isatin, crocine, acteoside, quercetin, etc.), as well as their complexes (with copper, palladium, platinum, gallium, zinc, silver, etc) with dual action from the pharmacophore and the metal. The compounds of interest are studied either free or encapsulated in nanostructures (nanoparticles, liposomes) for increased bioavailability and targeted transport/action.
- 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.
- inhibitors of the aggregation of *β*-amyloid peptide (Aβ) of Alzheimer's disease 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).

2018 Findings

In 2018, the presence in the Lab of two new post-doctoral fellows, namely D. Matiadis (organic synthesis) and E. Halevas (complexation, encapsulation in nanostructures) in combination with our long-term post-doctoral fellow B. Mavroidi (biological evaluation) greatly enhanced the activity of the team in the utilization of natural products in the production of novel bioactive compounds. Characteristic examples include • synthesis of pyrazolo derivatives of monoketo curcuminoids and of their corresponding metal complexes with significant antifungal activity (< 1 μg/mL) • synthesis and crystallographic analysis of complexes of vanadium-curcumin and gallium-chrysin and their

encapsulation in cationic liposomic nanocarriers and magnetic nanoparticles as anticancer agents • synthesis and biological evaluation of novel hyper-branched dendrimeric nanocarriers with encapsulated artemisinin.

In 2018 our work on the complexes of benzothiazole and benzimidazole with radioactive ^{99m}Tc and stable Re which present very significant penetration of the blood-brain- barrier was published. The complexes present ideal properties for diagnosis (^{99m}Tc) and therapy (Re) of Alzheimer's disease (AD). A patent application on the findings was filed with the Hellenic Industrial Property Organisation (22-3-18). In the same field of AD, the biological evaluation of derivatives of the natural indole isatin with CD, cellular assays, and electronic microscopy, as well as analogous studies with the natural products curcumin, quercetin and derivatives are in the process of manuscript preparation. In the field of anticancer agents, the synthesis and evaluation of curcuminoids as photosensitizres in the photodynamic treatment of cancer in collaboration with the National Technical University of Athens, was completed. Furthermore, new complexes of Re with compounds capable of intercalating into DNA were synthesized and evaluated as anticancer agents with multivalent potential.

Our activity is also expanding to new areas and collaborations taking advantage of the IB-A infrastructure with characteristic examples: • the CD study of live photosynthetic cells (Dr. K. Stamatakis, IB-A) • the 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) • the application of metabonomics in the study of the effectiveness of pesticides (Dr. K. Aliferis, Lecturer, Agricultural University, Athens).

Publications

Tsoukala, M., Ioannou, P. C., Panagiotopoulou, A., Pelecanou, M., Raptopoulou, C. P., Psycharis, V., Kyritsis, P. (2018). Self-assembled tetrameric H_2O clusters in the crystal lattice of $[Cu(\mu_2OH)\{Ph_2P(O)NP(O)Ph_2\text{-}\kappa1O,O'\}(1,10\text{-phen-}\kappa_2N,N')]_2 \bullet 2H_2O$. J. Coord. Chem. 71, 4047–4057.

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. 34, 1089-1101.

Triantis, C., Shegani, A., Kiritsis, C., Ischyropoulou, M., Roupa, I., Psycharis, V., Raptopoulou, C., Kyprianidou, P., Pelecanou, M., Pirmettis, I., Papadopoulos, M. (2018). Dicarbonyl cis-$[M(CO)_2(N,O)(C)(P)]$ (M = Re, ^{99m}Tc) Complexes with a New [2 + 1 + 1] Donor Atom Combination. Inorg. Chem. 57, 8354-8363.

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 1H NMR metabolomics. Pestic. Biochem. Physiol. 148, 50-61.

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.

Bonomi, C., Alexandri, A., Vind, J., Panagiotopoulou, A., Tsakiridis, P., Panias, D. (2018). Scandium and Titanium Recovery from Bauxite Residue by Direct Leaching with a Brønsted Acidic Ionic Liquid. Metals 8(10), 834.

Sevastos, A., Kalampokis, I.F., Panagiotopoulou, A., Pelecanou. M., Aliferis, K.A. (2018). Fusarium graminearum ^{1}H NMR metabolomics. Data in Brief 19, 1162-1165

Articles in Press

Liargkova, T., Eleftheriadis, N., Dekker, F., Voulgari, E., Avgoustakis, C., Sagnou, M., Mavroidi, B., Pelecanou, M., Hadjipavlou-Litina, D. (2019). Small multitarget molecules incorporating the enone moiety. Molecules 24, 1–31 (IF 3.060)

Sagnou, M., Mavroidi, B., Shegani, A., Paravatou-Petsotas, M., Raptopoulou, C., Psycharis, V., Pirmettis, I., Papadopoulos, M., Maria Pelecanou. (2019). Remarkable brain penetration of cyclopentadienyl $M(CO)_3^+$ (M = ^{99m}Tc, Re) derivatives of benzothiazole and benzimidazole paves the way for their application as diagnostic, with Single Photon Emission Computed Tomography (SPECT), and therapeutic agents for Alzheimer's disease. J. Med. Chem. 62, 2638-2650 (IF: 6.259)

Halevas, E., Mavroidi, B., Swanson, C., Smith, G., Moschona, A., Hadjispyrou, S., Salifoglou, A., Pantazaki, A., Pelecanou, M., Litsardakis, G. (2019). Magnetic cationic liposomal nanocarriers for the efficient drug delivery of a curcumin-based vanadium complex with anticancer potential. J. Inorg. Biochem. 199, 1-17 (IF: 3.224)

Stamatakis, K., Broussos, P. I., Panagiotopoulou, A., Gast, R. J., Pelecanou, M., Papageorgiou, G. C. Light-adaptive state transitions in the Ross Sea haptophyte Phaeocystis antarctica and in dinoflagellate cells hosting kleptoplasts derived from it. Biochim. Biophys. Acta Bioenerg. 1860, 102-110 (IF: 4.441)

Roupa, I., Kaplanis, M., Raptopoulou, C., Pelecanou, M., Pirmettis, I., Papadopoulos, M., Psycharis, V. (2019). Crystal structure of *fac*-aqua[(E)-4-(benzo[d]thiazol-2-yl)-N-(pyridin-2-ylmethylidene)anilinej 2N,N0]tricarbonylrhenium(I) hexafluoridophosphate methanol monosolvate. Acta Cryst. E, 75, 580–584 (IF: 0.347)

Matiadis, D., Tsironis, D., Stefanou, V., Elliott, A.G., Kordatos, K., Zahariou, G., Ioannidis, N., McKee, V., Panagiotopoulou, A., Igglessi-Markopoulou, O., Markopoulos, J. (2019). Synthesis, characterization and antimicrobial activity of N-acetyl-3-acetyl-5-benzylidene tetramic acid-metal complexes. X-ray analysis and identification of the Cd(II) complex as a potent antifungal agent. J. Inorg. Biochem. 194, 65-73 (I.F. 3.224)

Presentations at Scientific Conferences

B. Mavroidi, M. Sagnou, I. Roupa, C. Methenitis, M. Paravatou-Petsotas, I. Pirmettis, M. Papadopoulos, M. Pelecanou (2018). Synthesis and evaluation of a *fac*-$[Re(CO)_3]^+$ complex bearing 2-(4′-aminophenyl)benzothiazole as anticancer agent. 3rd International edition of the symposium on Technetium and Other Radiometals in Chemistry and Medicine (TERACHEM 2018), September 26-29, 2018, Bressanone, Italy

M. Kaplanis, I. Roupa, B. Mavroidi, M. Paravatou – Petsotas, M. Pelecanou, I. Pirmettis, M. Papadopoulos (2018). Rhenium(I) DNA-intercalating complexes as anticancer agents. 3rd International edition of the symposium on Technetium and Other Radiometals in Chemistry and Medicine (TERACHEM 2018), 26-29 September, 2018, Bressanone, Italy

A. Shegani, M. Kaplanis, C. Kiritsis, M. Ischyropoulou, M. Vlastara, C. Tsoukalas, P. Bouziotis, M. Pelecanou, I. Pirmettis, M. Papadopoulos (2018). Synthesis and labelling of a phenylboranate derivative with ^{68}Ga for molecular recognition of overexpressed sialic acid on tumor cells. 3rd International Symposium on TECHNETIUM and other RADIOMETALS in CHEMISTRY and MEDICINE. September 26-29, 2018, Bressanone (Bolzano), Italy

M. Ischyropoulou, M. Kaplanis, A. Shegani, I. Roupa, C. Kiritsis, C. Raptopoulou, V. Psycharis, M. Pelecanou, I. Pirmettis, M. Papadopoulos (2018). New neutral and cationic "2+1" Re/^{99m}Tc$(CO)_3$ complexes with 1,3,5-triaza-7-phosphaadamantane and its N-benzyl derivative. 3rd International Symposium on TECHNETIUM and other RADIOMETALS in CHEMISTRY and MEDICINE. September 26-29, 2018, Bressanone (Bolzano), Italy

K. Makrypidi, M. Ischyropoulou, A. Shegani, A. Papasavva, E. Papadopoulou, C. Raptopoulou, V. Psycharis, M. Pelecanou, M. Papadopoulos, I. Pirmettis (2018). Synthesis and characterization of $Re(CO)_3^+$ and $^{99m}Tc(CO)_3^+$ dithiocarbamate-isocyanide "2 + 1" mixed ligand complexes using $[Cu(MIBI)_4]BF_4$. 3rd International Symposium on TECHNETIUM and other RADIOMETALS in CHEMISTRY and MEDICINE. September 26-29, 2018, Bressanone (Bolzano), Italy

A. Papasavva, A. Shegani, I. Roupa, M. Ischyropoulou, C. Kiritsis, C. Triantis, M. Pelecanou, M. Papadopoulos, I. Pirmettis (2018). A series of radiolabeled mannosylated dextran derivatives for sentinel lymph node detection. 3rd International Symposium on TECHNETIUM and other RADIOMETALS in CHEMISTRY and MEDICINE. September 26-29, 2018, Bressanone (Bolzano), Italy

I. Roupa, M. Kaplanis, A. Shegani, B. Mavroidi, C. Raptopoulou, V. Psycharis, M. Paravatou – Petsotas, M. Pelecanou, I. Pirmettis, M. Papadopoulos (2018). Synthesis, characterization and in vitro biological assessment of novel mixed "2 + 1" rhenium (I) complexes with a benzothiazole derivative. 3rd International Symposium on TECHNETIUM and other RADIOMETALS in CHEMISTRY and MEDICINE. September 26-29, 2018, Bressanone (Bolzano), Italy

E. Halevas, B. Mavroidi, M. Pelecanou, A. Hatzidimitriou, A. Pantazaki, G. Litsardakis (2018). Multiscale study of hybrid magnetic dendrimeric nanocarriers of novel anticancer Ga(III)-flavonoid complexes for targeted drug delivery. 15th International Conference on Nanosciences & Nanotechnologies (NN18), July 3-6, 2018, Thessaloniki, Greece

B. Mavroidi, M. Sagnou, I. Roupa, C. Methenitis, M. Paravatou-Petsotas, I. Pirmettis, M. Papadopoulos, M. Pelecanou (2018). Biological evaluation of a *fac*-$[Re(CO)_3]^+$ complex bearing 2-(4′-aminophenyl)benzothiazole for tumor therapy. 69th Panhellenic Conference of the Hellenic Society of Biochemistry and Molecular Biology (EEBMB2018), November 23 – 25, 2018, Larissa, Greece

E. Halevas E, M. Pelecanou, M. Sagnou, B. Mavroidi, A. Pantazaki, A. Hatzidimitriou, G. Katsipis, T. Lialiaris, D. Chronopoulos, A. Salifoglou, G. Litsardakis (2018). Magnetic nano-formulations for drug delivery applications of natural polyphenol-metal complexes against cancer. 30th International Symposium on the Chemistry of Natural Products and the 10th International Congress on Biodiversity (ISCNP30 & ICOB10), November 25 – 29, 2018, Athens, Greece

A. Stergios, A. Panagiotopoulou, I. F. Kalampokis, K. A. Aliferis. Study of the potential of olive mill waste from a two-phase system in olive tree plant protection and monitoring of the quality of olive oil through the use of GC/EI/MS-^{1}H NMR metabolomics. 19^o Panhellenic Phytopathological Congress, October 30 –November 1, 2018, Athens, Greece.

Patent 2018

"Tricarbonyl complexes of transition metals with benzo-heterocyclic derivatives of the cyclopentadienyl anion with high penetration of the blood-brain barrier for application in diagnosis and therapy of diseases of the CNS" Application filed with the Hellenic Industrial Property Organisation (No 20180100128, 22/03/18) with depositors the NCSR "Demokritos" and the researchers M. Pelecanou (IB-A), M. Sagnou (IB-A), M. Papadopoulos (INRASTES) and I. C. Pirmettis (INRASTES), while the post-doctoral fellows B. Mavroidi (IB-A) and A. Shegani (INRASTERS) are included in the inventors.

Educational Activities

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)

Leactures in the framework of the Interdisciplinary Postgraduate Program of the Faculty of Chemistry, University of Patras and the IB-A, NCSR "Demokritos" titled "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceuticals ". 10 students (M. Sagnou)

Participation in the "Researchers' Night" 2018: Presentation of interactive activities, hands-on experiments and games for children and teenagers (M. Sagnou, B. Mavroidi, D. Matiadis, M. Zachariadis, O. Liatsis-Douvitsas)

Participation in the "Summer School 2018", NCSR "Demokritos" with the presentation "NMR Spectroscopy Laboratory for Liquid Samples; Principles and Applications of NMR Spectroscopy" (A. Panagiotopoulou)

Participation in "Summer Camp 2018" IB-A, NCSR "Demokritos": Scientic activities and hands-on experiments in the actual research Labs of IB-A (M. Sagnou, A. Panagiotopoulou, B. Mavroidi, D. Matiadis, E. Halevas)

Participation in the educational activity "Science on Board - Blue Star Ferries - Demokritos" which was held at the island of Rhodes and included actions concerning chemistry, biology, computing to understand the importance of technological breakthroughs, observation, experimentation and the value of the research process for society (M. Sagnou)

Participation in the educational activity "Mind the Lab" which was held at the Doukissis Plakentias Metro Station and included actions describing the secrets of life and cells (M. Sagnou)

Participation in the educational activity " Demokritos Visits Prisons" which was held at the Second Opportunity School of Korydallos Prisons and included actions such as: "Cell: the unit of life" and "What is DNA and chromosomes" (M. Sagnou, A. Panagiotopoulou)

Other Scientific Activities

Review of scientific publications:
Inorganic Chemistry (M. Pelecanou)
Molecules, Nutrients (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

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 6 publications): 13,441

Citations 2018 (without self-citations):

M. Pelecanou: 64
M. Sagnou: 51
A. Panagiotopoulou: 4

Total Citations 2014-2018 (without self-citations):
M. Pelecanou: 388
M. Sagnou: 231

A. Panagiotopoulou: 19

h-factor:
M. Pelecanou: 20 (Scopus)
M. Sagnou: 13 (Scopus)
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 M. Pelecanou as scientific coordinator.
Duration: 2017-2020
Total Program Funding: 65.459,88 €
Funding of the lab for 2018: 21.819,968 €.

Project entitled *Nature-loaded Targeted Nanoparticles for Prostate Cancer Therapy*, funded by Stavros Niarchos Foundation and Biohellenika S.A with M. Sagnou as scientific coordinator.
Duration: 2018-2021
Total Program Funding: 65.459,88 €
Funding of the lab for 2018: 21.819,968 €.

Program entitled *Evaluation of compounds as diagnostic agents for cancer*, funded by Hygeia Foundation with M. Pelecanou as scientific coordinator.
Duration: 2017-2020
Total Program Funding: 10.000 €
Funding of the lab for 2018: 5.000 €.

Project entitled *Innovative Radiopharmaceuticals with Fluoride-18: Research, Development and Introduction to the Greek Market for Diagnosis / Progression of Major Diseases with PET*, funded by EREVNO-DIMIOURGO-KENOTOMO with I. Pirmettis (INRASTES, NCSR "D") as scientific coordinator. Responsible for IB-A: M. Pelecanou
Duration: 2017-2020
Total Program Funding: 998.075 €
Funding of the programme for 2018: 153.000 €.

Proposals submitted in 2018 and approved

- Project entitled *Synthesis and characterization of magnetic dendrimeric nanocarriers with encapsulated flavonoid metal complexes for targeted anticancer activity* in the framework of "Supporting Researchers with Emphasis on Young Researchers - Round B" of the Operational Program "Human Resource Development, Education and Lifelong Learning" (ESPA 2014-2020).
  Young Researchers: Dr E. Halevas, Dr. B. Mavroidi
  Scientific Coordinator: M. Pelecanou
- Project entitled *Monocarbonyl analogs of Curcumin (MAC) as larvae against the mosquito Culex pipiens "* in the framework of "Supporting Researchers with Emphasis on Young Researchers - Round B" of the Operational Program "Human Resource Development, Education and Lifelong Learning" (ESPA 2014-2020).
  Young Researchers: Dr. D. Matiadis
  Scientific Coordinator: Dr A. Michaelakis, Benaki Phytopathological Institute

Research Group: Protein Structure and Molecular Modeling

Research Staff

Metaxia Vlassi, Research Director

Nastazia Lesgidou, Collaborating Graduate Sudent *(MSc) – MSc obtained in 2018*

Research Interests

- Protein folding
- Sequence/structure relationships of amino-acid repeats / Role in protein-protein interactions
- Molecular dynamics of proteins & Molecular dynamics simulations
- Kinases
- Protein interactions
- Intrinsically disordered proteins
- Structure & dynamics of enzymes as potential therapeutic targets

The approach we follow includes *in silico* techniques such as homology/comparative 3D-modeling and molecular dynamics simulations.

Findings 2018

With the aim to elucidate sequence/structure/function relationships of proteins linked to diseases (kinases in particular) in 2018,

- We continued our *in silico* structural studies -through molecular dynamics (MD) simulations- of the tyrosine kinase Tyk2 and of its variant P1104A, which is related to protection against autoimmune diseases. Analysis of our MD results so far (see Figure), suggests that the structural consequences of this particular amino-acid change include stabilization of non-functional conformations of the resulting protein, adding to the idea that reduced Tyk2 kinase activity may be the mechanism for protection against autoimmune diseases. This work contributes to establishing Tyk2 as a potential therapeutic target against this type of diseases and was presented (oral presentation by M. Vlassi) at the **17th European Congress on Computational Biology** (see section *Congresses*, below) and **published in** the **Bioinformatics** journal (see *Publication*: ***Lesgidou et al. Bioinformatics 2018***). Part of this work was included in the Master's thesis (UoA) of N. Lesgidou.

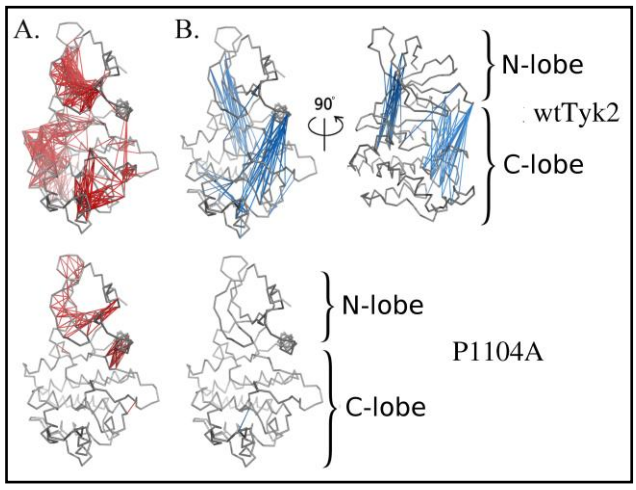


Figure: Cross-correlation analysis of the MD simulations of Tyk2 kinase and its P1104A variant *suggests that the communication of various domains, necessary for Tyk2 function, is largely interrupted in the case of the variant that in turn, is expected to affect the allosteric regulation of its activity. Blue and red lines represent positive and negative correlations, respectively (see also Lesgidou et al Bioinfomatics 2018)*

Furthermore, to build on the above study, a proposal to obtain access to the supercomputer facility ARIS @GRNET was submitted in 2018 (project ID: KIN_IMMUN_MD) and was approved in 29-11-2018 (obtained resources: 900.000,0 core hours for 1 year).

- In addition, in the framework of our studies towards the elucidation of structure/function relationships of kinases linked to diseases, using *in silico* mutagenesis we predicted the consequences

of two novel large deletions of the *CHEK2* gene, identified (by our collaborator D. Giannoukakos) in Greek breast cancer patients. Our predictions elucidated at the atomic level the structural consequences of these mutations on the resulting CHEK2 kinase and contributed to a deep understanding of their role in carcinogenesis. Our *in silico* data were included in a work **published in** the **Journal of Human Genetics** (see *Publication*: ***Apostolou et al JHG* 2018**).

Finally, in 2018, potential users have registered to obtain access to updated versions of the **GROMITA-GUI** we have previously developed in the lab (***http://gromita.bio.demokritos.gr***).

Publications

Lesgidou,N., Eliopoulos,E., Goulielmos, G.N., Vlassi, M* (2018) Insights on the alteration of functionality of a tyrosine kinase 2 variant: a molecular dynamics study. ***Bioinformatics***, 34 (17), i781–i786 (doi: 10.1093/bioinformatics/bty556).

Apostolou, P,Fostira, F, Mollaki, V, Delimitsou, A, Vlassi, M, Pentheroudakis, G, Faliakou, E, Kollia, P, Fountzilas, G, Yannoukakos, D, Konstantopoulou, I (2018) Characterization and prevalence of two novel CHEK2 large deletions in Greek breast cancer patients. ***Journal of Human Genetics*** 63(8), 877-886.

Presentations at Scientific Conferences

N. Lesgidou, E. Eliopoulos, G. N Goulielmos and M. Vlassi* (2018). Insights on the alteration of functionality of a tyrosine kinase 2 variant: a molecular dynamics study. 17th European Conference on Computational Biology –ECCB 2018, 8-12 Sept 2018, Athens, Greece *(*Oral presentation by M.V.*)

N. Lesgidou and M. Vlassi (2018) Investigating the Structural Consequences of a Protective TYK2 Gene Polymorphism Linked to Autoimmune Diseases Using Molecular Dynamics Simulations, Hellenic Bioinformatics 11, 2018 November 15-18, 2018 Thessaloniki, Macedonia, Greece

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 was approved for funding in June 2018 (see *funding* section).

Educational Activities

- **N. Lesgidou conluded her MSc Thesis** entitled: "*Prediction of structural and functional consequences of gene mutations on proteins linked to autoimmune diseases using molecular dynamics simulations*" in the framework of the Master's degree programme "Bioinformatics" of the University of Athens (Completed: December 2018)
- Lecture entitled "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).
- Lecture entitled: "Protein Structure – Experimental & Theoretic approaches" in the framework of the post-graduate program (towards a Masters degree) entitled: Applied Biochemistry: Clinical

Chemistry, Biotechnology, Pharmaceutical Products evaluation" co-organized by the University of Patras and IBA of NCSR "Demokritos"

Other Activities for the Institute of Biosciences & Applications

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

Member of one evaluation committee for researcher promotion (INRASTES, NCSR "D")

Member of various committees of NCSR "D"

Responsible for the operation of various common equipment of the IBA

Impact Factors (for 2 publications): 7,473

Citations 2018 (without self- citations): 19

Total Citations 2014-2018 (without self- citations): 98

h-factor: 14

Current External Funding

Project entitled *"INSPIRED: The National Research Infrastructures on Integrated Structural Biology, Drug Screening Efforts and Drug Target Functional Characterization",* implemented under the Action "Reinforcement of the Research and Innovation Infrastructure", funded by the Operational Programme "Competitiveness, Entrepreneurship and Innovation" (NSRF 2014-2020) and co-financed by Greece and the European Union (European Regional Development Fund) (Role of M. Vlassi: member of the group of Scientists of NCSR "Demokritos" node and responsible for the Computational activities of the node) (Coordination: NHRF).
Duration: Sept 2018 – Sept 2021
Funding for the computational activities of the NCSR "D" node: 36.000€.

Project entitled "*MD simulations of variants of a kinase linked to autoimmune diseases*" (project ID:KIN_IMMUN_MD) in the framework of the 6th Call for Production Projects Accessing the supercomputer system ARIS @ GRNET (P.I.: M. Vlassi.).
Duration Dec 2018-Dec 2019
Total resources: 900.000 core hours
Total resources for 2018: ~70.000 core hours

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

- ***HUMAN TISSUE BANK***
- ***ANIMAL HOUSE***
- ***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)
Lydia Panagopoulou, Graduate Research Associate (MSc)
Eleutherios Kosmidis, Graduate Research Associate (MSc)
Stylianos Kakkos, Research Technician

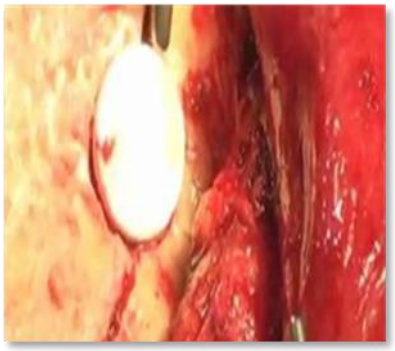
Laboratory Description – Research Interests

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 operation, it has delivered more than 50.000 tissue grafts without any reported quality-related problems. All procedures taking place in the Bank are fully computerized and accredited according to ISO 9001/2015. It is a great concern for us to constantly be updated in quality control topics and to ensure our compliance with the Greek and European Standards.

The produced grafts are delivered to various 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 process of new types of tissues, the development of new techniques and new graft products.

Its research activities are therefore based on collaborations with universities and healthcare institutions, 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 resulted in and funded 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.

2018 Findings

In 2018, 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 355 bone grafts to be used in Dentistry and Orthopedic Surgery. Moreover, we have delivered 11 cranium graft preparations to Neurosurgery Depts.

Scientific collaboration with hospitals, University labs, etc., has resulted in the processing of new types of tissues, the application of new optimized techniques and the production of improved and customized products e.g. for child facial surgery.

Presentations at Scientific Conferences

H. Vavouraki, El.Kosmidis, Y. Ninios, G. Arealis. Design of a new instrument set up for the development of a special shape bone graft. 29th Annual Meeting of the European Society for Biomaterials, September 9–13, 2018, Maastricht, the Netherlands.

H. Vavouraki: Tissue Bank – New Horizons, Session: "Novel Concepts in Biomaterials", 11th Hellenic congress of the Hellenic Society for Biomaterials, 23-25/11/2018 NCSR "DEMOKRITOS", Athens.

S.A. Lazarou, Y.P. Ninios, E.N. Vavouraki, Development of a new corticocancellous allograft for use in children schistoprosopia surgery – Early results. 11th Hellenic congress of the Hellenic Society for Biomaterials, Athens 23-25/11/2018, NCSR "DEMOKRITOS", Athens.

Educational Activities

IBA: 2018 Summer camp, 2 hours

NCSR "DEMOKRITOS": 53rd Summer School, 1 hour

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

Scientific Responsible of Human Tissue Bank.

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

Alternate member of the Scientific Council of IBA (Institute of Biosciences & Applications)

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

Member of Ethics Committee of NCSR "DEMOKRITOS" (Until 7/2018)

Other Scientific Activities

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

Member of Scientific Committee and Reviewer of the Journal ACTA ORTHOPAEDICA ET TRAUMATOLOGICA HELLENICA (peer-review Journal in English)

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

Organization of the 11th Annual Conference of the Hellenic Society of Biomaterials, NCSR "DEMOKRITOS", 23-25/12/2018, Athens

Research Proposals Assessor

Citations 2018 (without self-citations): 5

Total Citations 2014-2018 (without self-citations): 56

h-factor: 14

Current External Funding

Project for specialized scientific services entitled *Research, Development and Delivery of Tissue grafts - products of Tissue Repair*, funded by the public and private sector, with Dr H. Vavouraki as scientific coordinator.
Duration: 2012-2020
Income of the lab for 2018: 25.200 €

Project entitled TALOS-BIO - Development of a new, specially designed bone graft to accompany the EPO patented TALOS, used in Neurosurgery, funded by GSRT with Dr H. Vavouraki as scientific coordinator.
Duration: 6/2018-12/2020
Total Program Funding: 188.800 €
Funding of the lab for 2018: 75.520 €

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ANIMAL HOUSE

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 House has three facilities accredited according to the ΠΔ 56/2013 (2069/15-04-2014)

- Facility for Animal Reproduction EL25BIO019
- Facility for Animal Disposal EL25BIO020
- Facility for Animal Experimentation EL25BIO039

The Animal House during 2018 maintained and reproduced inbred strains of experimental animals. The following strains are currently available:

- Mice, strain CFW SWISS ALBINO
- Mice FOX SCID ALBINO and NSC SCID (immunocompromised)
- Mice SKH1 (hairless)
- Mice C57Bl/6 (wild type and transgenic AD 5xFAD and TgMMP-9)
- Rats, WISTAR ALBINO
- Rats, FISCHER (CDF)
- Rabbits, NZW ALBINO

During 2018 the Animal House 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	46	10	0	41	0	0	7	**104**
Institute of Nuclear & Radiological Sciences and Technology, Energy & Safety	48	0	298	72	3	0	212	**633**
Institute of Nanosciences and Nanotechnology	0	0	90	0	0	0	0	**90**
Institute of Informatics and Telecommunications	0	0	0	0	0	0	18	**18**
External Users	116	0	0	0	0	41	30	**187**
Total	**210**	**10**	**388**	**113**	**3**	**41**	**267**	**1032**

The function of the Animal House, according to the Law, is supported by the following Committees:

Committee for the Evaluation of the Research Protocols

Members: D. Kletsas (President), L. Klamarias, E. Livaniou, a representative from the the Veterinary Division of the Attica Prefecture - Substitutes: V. Sophianopoulou, D. Mastellos

and

Committee for the Wellbeing of Laboratory animals

Members: D. Kletsas (President), L. Klamarias, E. Livaniou, J. Zafiropoulos, G. Doulgeridis

During 2018:

The Animal House has upgraded the accreditation of the Quality Management System to ELOT EN ISO 9001:2015 and all the planned inspections have been performed.

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 (NSG SCID mice) have been developed.

A Colony with Aged Laboratory Animals has been created.

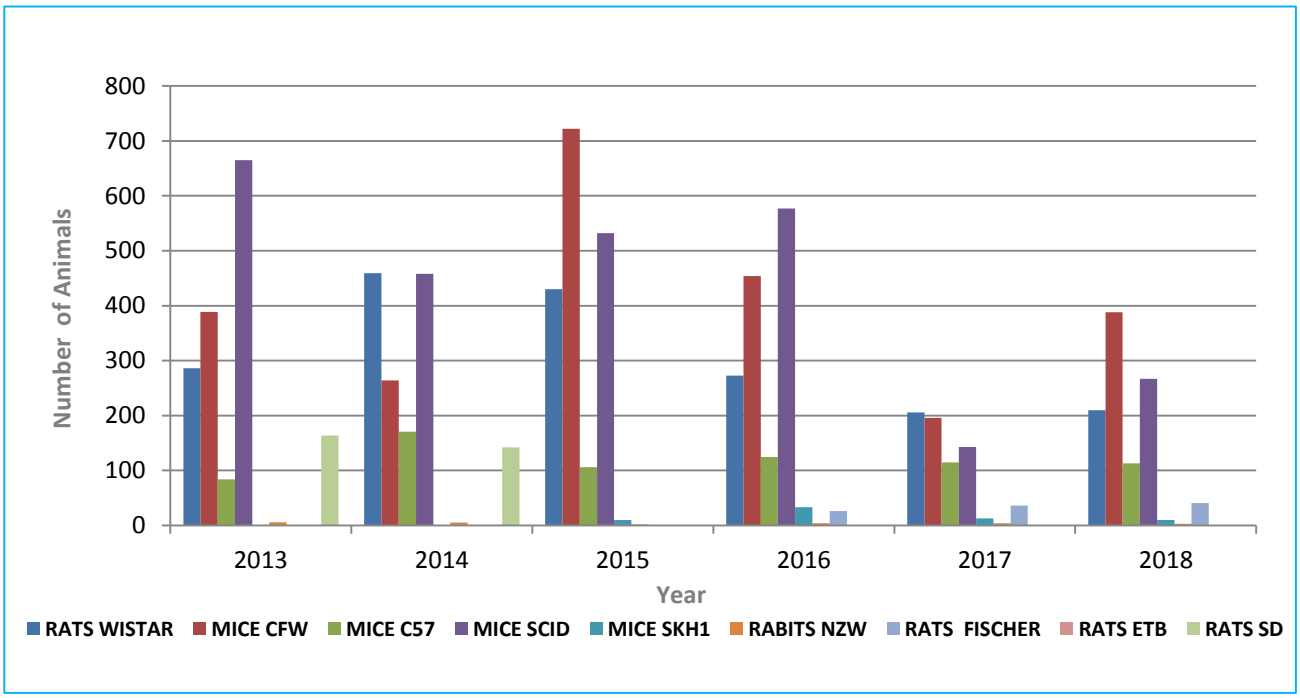
The Committee for the Wellbeing of Laboratory Animals and the Committee for the Approval of Research Protocols of the Facility met regularly throughout 2018 and approved or renewed nine (9) research protocols.

The Safety Regulation and the Regulation of Medical Inspection have been renewed.

The Director of the Animal House has been appointed as Member of the National Committee for the Wellbeing of the Laboratory Animals.

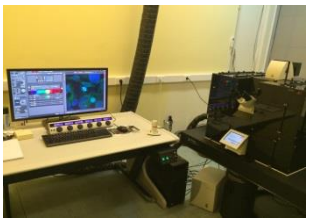
The 2nd one-day Seminar for the users of the Facility has been organized.

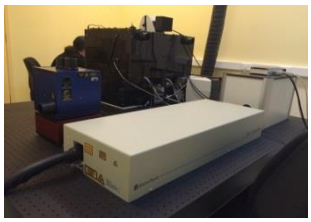
DISPOSAL OF LABORATORY ANIMALS 2013-2018



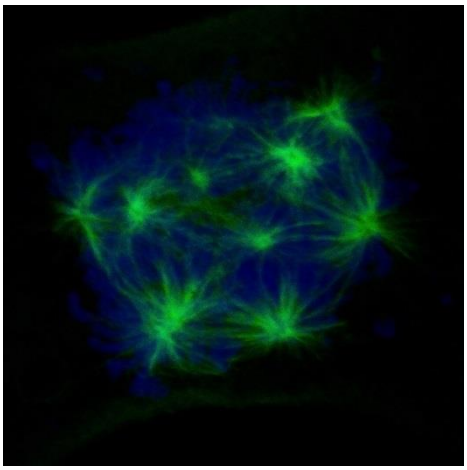
LASER CONFOCAL MICROSCOPY LABORATORY

Research Staff
Dimitris Kletsas, **Research Director**, **Scientific and Administrative Responsible**
Vassiliki Labropoulou, Senior Researcher
Haris Pratsinis, Researcher
Marina Sagnou, Researcher
Michalis Zachariadis, Technician *(PhD)*





Laboratory Description – Progress



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 Nikon E600 Confocal Microscope and a state-of-the-art Leica TCS SP8 multiphoton microscope, with capabilities that cover a wide range of application 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 (with specialized software programss uch as ImageJ / Fiji and Imaris (Bitplane)

The Confocal/Multiphoton Microscopy Unit in the year 2018 recorded more than 400 operating hours, many of which have been collaborations with external research centers and universities. The unit collaborated with 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
- Study 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

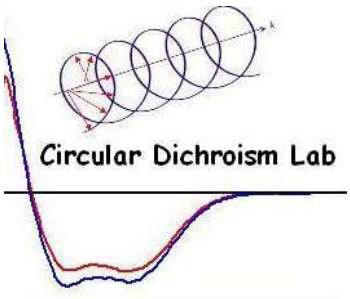
- Functional characterization of opioid receptor
- Imaging and cellular identification of new dendrimers, liposomal preparations and nanostructures for the transport of bioactive substances
- Imaging of biofilm in the nasal mucosa of patients with chronic rhinosinusitis and correlation with their clinical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

IBA 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 in which participate, besides the Institute and other 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 Peltier system for temperature control. This CD infrastructure was acquired in 1998 within the framework of the "Center for Crystallographic Studies of Macromolecules (CCM)", which was financed through a grant (EPET) from the General Secretariat for Research and Technology as a network of three Institutes of the NCSR "Demokritos" (the former Biology, Physical Chemistry, Radioisotopes & Radiodiagnostics Products) and other Greek academic institutions. It is located at room Y-35 of the Institute of Biosciences & Applications and is operating under the supervision of IB-A scientists. In 2013 (13/06/2013), the CD Lab was included in the category of Specialized Services of NCSR "D", whereas in 2018, after re-categorization, the service was classified in the category of Specialized Services with Research Activity (decision of the Board of Directors 28-03-2018, Protocol # 010/2018-299 4/4/2018).

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 interaction/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.

2018 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. The Scientists involved also contributed to the training of new users (students, researchers) as well as to addressing technical and scientific problems related to CD applications.

In 2018, as in previous years, the CD Lab has supported research projects of at least 12 groups of the 3 participating NCSR "D" Institutes and other Greek academic institutions such as the National and Kapodistrian University of Athens (Pharmaceutical Dept, Chemistry Dept), the Aristotle University of Thessaloniki (Chemistry Dept), the University of Thessaly (Biochemistry & Biotechnology Dept) and the NHRF (Institute of Biology, Pharmaceutical Chemistry and Biotechnology). In addition, CD experiments,

analysis of the results and writing of a report were also performed in 2018 in the framework of service providing to two Greek companies. Income from the provision of services is solely used to cover the operation and repair needs of the spectrophotometer.

The CD Laboratory participates in the Project: "INSPIRED: The National Research Infrastructures on Integrated Structural Biology, Drug Screening Efforts and Drug Target Functional Characterization" (coordinator: NHRF)*",* implemented under the Action "Reinforcement of the Research and Innovation Infrastructure", funded by the Operational Programme "Competitiveness, Entrepreneurship and Innovation" (NSRF 2014-2020) and co-financed by Greece and the European Union (European Regional Development Fund), which was approved for funding for 3 years in June 2018.

LABORATORY OF CELL & MATRIX PATHOBIOLOGY

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

Laboratory Description - Objective

The laboratory of Cell & Matrix Pathobiology focus on isolation, culture and characterization of stem cells from different tissues of various organisms aiming at their use in therapeutic applications in the frame of Regenerative Medicine.

The laboratory successfully isolates and characterizes human umbilical cord, human umbilical cord blood (UCB) stem cells and stem cells from other sources (skin and fat tissue). The mesenchymal stem cells isolated from fat tissue are used by orthopedists for the confrontation of damage of articulations (such as knee and hip).

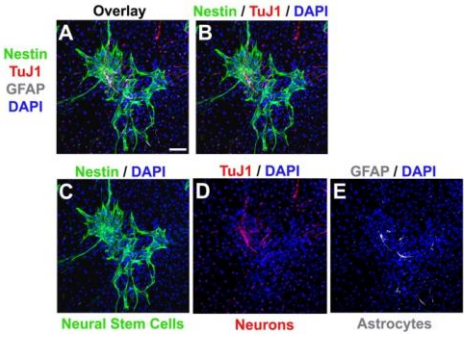


Figure: Culture of OECs results to enriched population of neural stem cells (NSC), as it appears from the use of appropriate indicators. These cells maintain the ability of proliferation and renewal.

During 2014 and 2015 the laboratory fulfilled the isolation and proliferation of mesenchymal stem cells from abdominal fat tissue of patients (14 incidents) for homologous transplantation in chronic arthropathies (collaboration with Dr N. Kralli).

In addition, 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).

2018 Findings

During 2018, the laboratory focused on the isolation and culture of mesenchymal stem cells isolated from mouse fat tissue. Characterization of the above mentioned cells was achieved by the use of flow cytometry.

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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.

2018 Findings

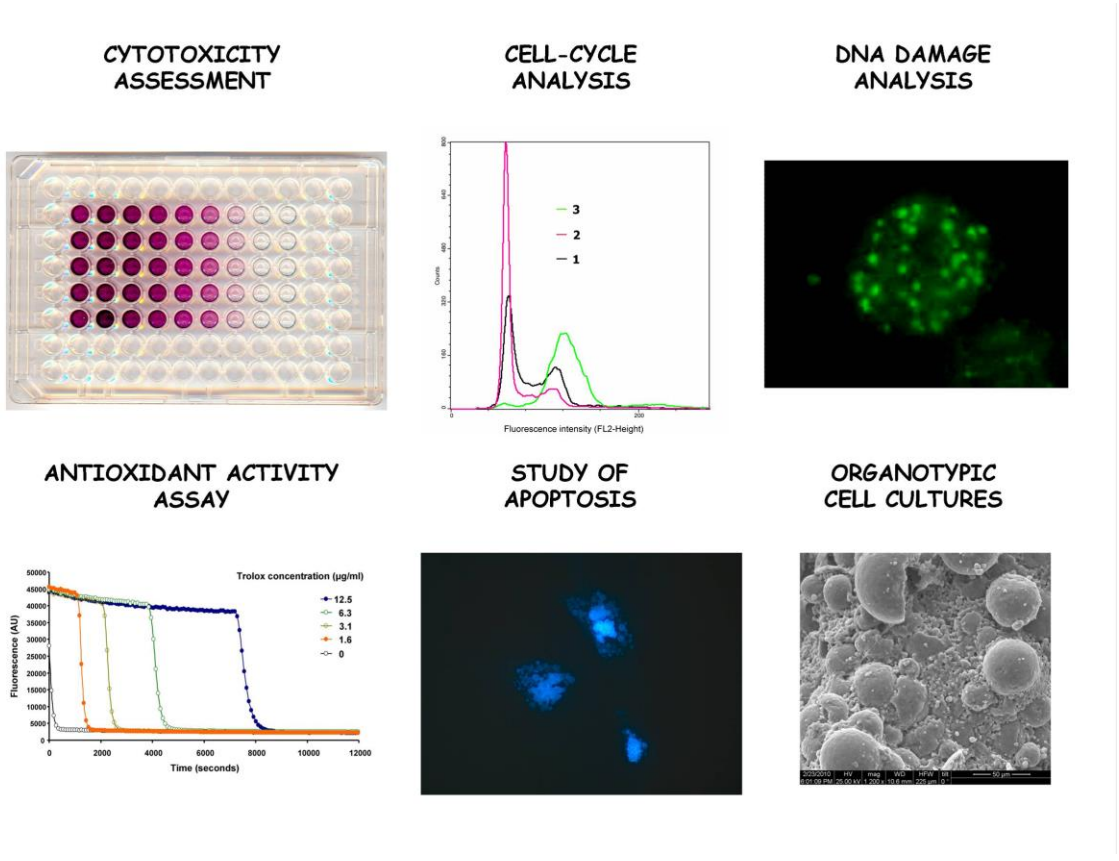
In each family, together with the patient(s), the parents are regularly tested. Initially, the patient(s) is screened for mutations, whereas after the mutation has been identified, screening of the parents takes place. In a second step, if desired, other family members may be tested. All tests are performed after an informed consent has been filled. During 2018, our laboratory tested nine (9) families for TSC. Patients from five (5) families had a definitive clinical diagnosis of Tuberous Sclerosis, while four (4) had a diagnosis of possible Tuberous Sclerosis. Pathogenic mutations were identified in four (4) out of the nine (9) families. Two (2) relatives coming from two (2) independent families have been also examined. In both cases the results were negative. Finally, it should be noted that due to bureaucratic reasons, function of the laboratory was temporarily suspended (July 6, 2018).

LABORATORY OF CELL-BASED ASSAY SYSTEMS AND BIOACTIVE COMPOUNDS

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

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.

2018 Findings
During 2018, an already established collaborative project with the Prof. Dr. med. Karin Scharffetter-Kochanek, Head Universitätsklinikum Ulm, Dermatologie und Allergologie, for studying the role of senescent stromal cells in carcinogenesis in cell –based systems and animal models was continued.



EDUCATIONAL ACTIVITIES

EDUCATION

The Institute of Biosciences and Applications' educational programme, that has been successfully implemented for the last forty years, continued also in 2018. This programme includes:

a) training of postdoctoral researchers
b) supervision of postgraduate students performing their PhD, MSc and diploma thesis' projects, as well as training of undergraduate students
c) organization of courses and seminars at postgraduate level
d) participation in courses at the Annual Summer School of NCSR "Demokritos" for undergraduate and graduate students
e) organization of a Summer Camp for Lyceum students
f) participation in activities that aim to promote science, inform the public on research activities in IBA and promote research careers to young people.

During 2018, **14** postdoctoral researchers were trained at IBA, while **20** PhD students and **6** MSc students performed their projects at the Institute under the supervision of IBA researchers.

During 2018, **1** of our graduate students completed her PhD thesis and **3** students completed their Master's theses.

Moreover, during 2018, **10** undergraduate students from Greek Universities performed their diploma thesis' projects at IBA. Additionally, **6** undergraduate students performed research practice in IBA laboratories.

In addition to the above, scientists of IBA participated in courses and gave lectures within the framework of Postgraduate Programmes of several Greek Universities:

- *Lecture entitled "Research on Rare 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 entitled "Signaling of Neurotransmitter Receptors" in the "Athens International Master's Programme in Neurosciences"* (**Dr. Z. Georgoussi**, Department of Biology, 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)
- *Lecture entitled "Cell senescence and tissue homeostasis" in the framework of the postgraduate course "Cosmetology" (***Dr. D. Kletsas**, Department of Pharmacology, University of Athens)
- *Lecture entitled "Cell senescence: Molecular mechanisms and role in tissue homeostasis" (***Dr. D. Kletsas***,*Harokopio University)
- *Teaching in the Post-graduate Master's Degree "Applications of Biology in Medicine" with lectures entitled "Cell proliferation and tissue homeostasis. Growth factors: Structure, receptors and signal transduction. Cell senescence and tissue homeostasis. Methodologies for the study of*

cell proliferation" and laboratorty visits (**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)
- *Participation in the Inter-Institutional Joint Post-Graduate Programme (JPGP) in "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" between the Institute of Biosciences and Applications and the University of Patras"* (**Dr. D. Kletsas, Dr. H. Pratsinis and Dr. E. Mavrogonatou**, IBA NCSR "D" & Department of Chemistry, University of Patras)
- *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).
- *Participation in the Inter-Institutional Joint Post-Graduate Programme (JPGP) in "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" between the Institute of Biosciences and Applications and the University of Patras" and lecture entitled "Methods for the study of proteins, lipids and carbohydrates"* (**Dr. A. Chroni**, IBA NCSR "D" & Department of Chemistry, University of Patras)
- *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)
- *Participation in the Inter-Institutional Joint Post-Graduate Programme (JPGP) in "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" between the Institute of Biosciences and Applications and the University of Patras" and lecture entitled "Biochemical Analysis – Clinical Biochemistry"* (**Dr. G. Drossopoulou**, IBA NCSR "D" & Department of Chemistry, University of Patras)
- *Lecture entitled "Regulation of Apoptosis in disease progression: Is it desirable or must be avoided?" in the framework of the graduate course* "Molecular and Applied Physiology" (**Dr. G. Drossopoulou**, Medical School, University of Athens)
- *Lecture entitled "Metabolic Syndromes – Diabetes Mellitus and its complications" in the framework of the graduate course* "Clinical Biochemistry – Molecular Diagnostics" (**Dr. G. Drossopoulou**, Department of Biology, University of Athens)
- *Lecture entitled "Compartmentalization and function of plasma membrane, eisosomes and transmembrane transporters" in the framework of the postgraduate course "Applications of Biology in Medicine"* **(Dr. V. Sophianopoulou**, Department of Biology & Medical School, University of Athens)
- *Participation in the Inter-Institutional Joint Post-Graduate Programme (JPGP) in "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" between the Institute of Biosciences and Applications and the University of Patras" and lecture entitled "*Lateral compartmentalization and function of plasma membrane: eisosomes and transmembrane transporters*"* (**Dr. V. Sophianopoulou & Dr. C. Gournas**, IBA NCSR "D" & Department of Chemistry, University of Patras)
- *Participation in the Inter-Institutional Joint Post-Graduate Programme (JPGP) in "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" between the Institute of Biosciences and Applications and the University of Patras" and lecture entitled "*DNA translation in pro- and eukaryotic cell*"* (**Dr. V. Sophianopoulou**, IBA NCSR "D" & Department of Chemistry, University of Patras)

- Laboratory exercises for the undergraduate course "Genetics" (**Dr. C. Gournas**, Département de Biologie Moléculaire, Faculté des Sciences, ULB, Belgium)
- *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)
- *Participation in the Inter-Institutional Joint Post-Graduate Programme (JPGP) in "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" between the Institute of Biosciences and Applications and the University of Patras" and lecture entitled "Protein Structure – Experimental & Theoretic approaches"* (**Dr. M. Vlassi**, IBA NCSR "D" & Department of Chemistry, University of Patras)
- *Participation in the Inter-Institutional Joint Post-Graduate Programme (JPGP) in "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" between the Institute of Biosciences and Applications and the University of Patras" and lecture entitled "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceuticals"* (**Dr. M. Sagnou**, IBA NCSR "D" & Department of Chemistry, University of Patras)

In 2018 the **joined MSc Programme "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products"** organized by the Department of Chemistry of the University of Patras and the Institute of Biosciences and Applications of NCSR "Demokritos" **was established (ΦΕΚ 3923/2018)**. During 2018, **9** postgraduate students were enrolled in this programme. These students attended courses in University of Patras and IBA. Currently, they perform their MSc thesis' projects. IBA researchers taught in all four courses of the MSc programme:

- Biochemical Analysis – Clinical Biochemistry (**Drs G. Drossopoulou, A. Chroni, M. Konstantopoulou)**
- Advanced Biochemistry (**Drs G. Drossopoulou, Z. Georgoussi, C. Gournas, D. Kletsas, E. Mavrogonatou, H. Pratsinis, V Sophianopoulou, M. Vlassi**)
- Molecular Pharmacology – Immunology (**Drs Z. Georgoussi, B. Labropoulou, A. Papakyriakou, M. Sagnou, L. Swevers)**
- Molecular and Cellular Biology – Molecular Biotechnology (**Drs A. Chroni, G. Drossopoulou, C. Gournas, D. Kletsas, B. Labropoulou, E. Mavrogonatou, H. Pratsinis, V Sophianopoulou, T. Sourlingas, L. Swevers, E. Vavouraki, G. Voutsinas**)

In addition, IBA participates **in the joined MSc Programme "Athens International Master's Programme in Neurosciences" (ΦΕΚ 3802/2018). Dr. Z. Georgoussi** participates in this programme.

During 2018, the Institutes' graduate students participated in journal clubs and presented Research in Progress seminars (see list in last page). In addition a series of seminars by invited speakers was held in IBA (see list in last page).

In July 2018, during the **Annual Summer School of NCSR "Demokritos"** several IBA researchers (see list in last page) gave talks for undergraduate and graduate students on current topics in Biosciences and on the research activities of the institute.

In 2018, IBA organized the **1st Summer Camp for Lyceum students**. Twenty six (**26**) students, from several schools in and outside of the Attica region, attended this two-week school (25/6/2018 - 6/7/2018). School's programme included a series of visits to the Institute's laboratories, presentation on the Institute's research activities and hands-on expertise and theoretical know-how on laboratory techniques used for biochemical, molecular biology and cellular biology studies. The students were divided into groups and participated in two research projects (one per week) in laboratories of the Institute. At the end of the two-week school, the students presented their results to IBA members, as well as to their teachers and parents. IBA's researchers that acted as instructors in this Summer Camp were: **Drs G. Drossopoulou, Z. Georgoussi, P. Kitsiou, D. Kletsas, M. Konstantopoulou, B. Lambropoulou, E. Mavrogonatou, A. Papakyriakou, M. Pelekanou, H. Pratsinis, A. Prombona, M. Sagnou, V. Sofianopoulou, L. Swevers , A. Tzinia, E. Vavouraki, G. Voutsinas.**

In 2018, the "G. Akogyounoglou" prize which is being awarded annually to IBA graduate students with the most outstanding research performance, was awarded to the PhD candidates Paschalina Pallaki and Christina Golfinopoulou.

Furthermore, IBA's researchers participated in the following information-educational activities:

«Researcher's Night», 5/10/2018 (**Dr. M. Sagnou**)

«Science on Board» - Blue Star Ferries and NCSR "Demokritos" collaboration 13-14/10/2018 (**Dr. M. Sagnou**)

«Mind the Lab» - A Day full of Science at Athens Metro stations, 21/10/2018 (**Dr. M. Sagnou**)

IBA responded to the invitation of **the Second Chance School of Korydallos "George Zouganelis"** and organized a series of lectures on "Cell: the unit of life - What is DNA and chromosomes" as well as microscopic observations. (**Drs D. Kletsas, V. Sofianopoulou, G. Drossopoulou, M. Sagnou and A. Panagiotopoulou**)

Finally, during 2018 **Drs. H. Pratsinis** and **A. Prombona** carried out presentations on the institute's research activities and guided tours to the Institute's laboratories for High School and University students.

COMPLETION/AWARD OF DOCTORAL THESES IN 2018

GRADUATE STUDENT	TITLE OF DOCTORAL THESIS	SUPERVISOR (in IBA)	UNIVERSITY
Angeliki Galeou	*Study of the circadian clock function and resynchronization of the bean plant (Phaseolus vulgaris)*	A. Prombona	Department of Biology University of Athens

COMPLETION OF MASTER THESES IN 2018

GRADUATE STUDENT	TITLE OF MSc THESIS	SUPERVISOR (in IBA)	UNIVERSITY
Efstathios Tsimelis	*Study of proteoglycans' expression in senescent stromal cells*	D. Kletsas	Department of Biology University of Athens
Eleni Kikidou	*Thymosine peptides with a putative healing action*	D. Kletsas	Pharmacy Department University of Athens
Nastazia Lemonia Lesgidou	*Prediction of structural and functional consequences of gene mutations on proteins linked to autoimmune diseases using molecular dynamics simulations*	M. Vlassi	Department of Biology University of Athens

LECTURE CONTRIBUTIONS OF THE INSTITUTE OF BIOSCIENCES & APPLICATIONS TO THE 2018 SUMMER SCHOOL OF THE NCSR "DEMOKRITOS"

(July 2018)

DATE	SPEAKER	TITLE
1/7/2018	**Dr. D. Kletsas** IBA, NCSR "Demokritos"	Cell senescence and tissue homeostasis
1/7/2018	**Dr. L. Swevers** IBA, NCSR "Demokritos	CRISPR/Cas and gene editing
1/7/2018	**Dr. A. Chroni** IBA, NCSR "Demokritos	Cardiovascular disease: causes and therapeutic approaches
1/7/2018	**Dr. G. Drossopoulou** IBA, NCSR "Demokritos"	Renal diseases: Could regenerative medicine contribute to therapeutic approaches?
1/7/2018	**Dr. C. Gournas** IBA, NCSR "Demokritos"	Exploring plasma membrane compartmentalization to develop a new generation of antifungal drugs
1/7/2018	**Dr. P. Kitsiou** IBA, NCSR "Demokritos	Beta-cell survival signaling pathways: Study of the mechanisms of beta-cell apoptosis for the treatment of type 2 diabetes mellitus
1/7/2018	**Dr. H. Pratsinis** IBA, NCSR "Demokritos"	*In vitro* studies of natural and synthetic bioactive products
6/7/2018	**Dr. M. Konstantopoulou** IBA, NCSR "Demokritos	Chemical Ecology and Natural Products

SEMINAR PROGRAMME 2018 OF THE GRADUATE STUDENTS
INSTITUTE OF BIOSCIENCES & APPLICATIONS

DATE	SPEAKER	TITLE
18/4/2018	**A. Kouroumalis** IBA, NCSR "Demokritos"	Study of the effect of the environment on gene expression and function of intervertebral disc cells
2/5/2018	**M. Angelopoulou** IBA, NCSR "Demokritos"	Protective mechanisms of human dermal fibroblasts against UVB radiation
9/5/2018	**A. Galeou** IBA, NCSR "Demokritos"	Study of the function and the synchronization of the bean (*Phaseolus vulgaris*) circadian clock
16/5/2018	**C. Mountaki** IBA, NCSR "Demokritos"	The role of apolipoprotein E isoforms on cellular cholesterol efflux and amyloid peptide β production in neuronal cells
23/5/2018	**C. Karoussiotis** IBA, NCSR "Demokritos"	Autophagy: The role of κ-opioid receptor
30/5/2018	**C. Golfinopoulou** IBA, NCSR "Demokritos"	Structural and functional characterization of natural occurring apolipoprotein A-I mutants
13/6/2018	**S. Koutloglou** IBA, NCSR "Demokritos"	Opioid receptors: Regulation via interactions with cytoplasmic proteins
15/6/2018	**D. Vagenos** IBA, NCSR "Demokritos	Study of the photosynthesis of cyanobacteria: an environmentally friendly energy source
20/6/2018	**P. Pallaki** IBA, NCSR "Demokritos	Alternative pathways of cellular signaling by opioid receptors during neurogenesis
11/7/2018	**A. Delimitsou** IBA, NCSR "Demokritos	Functional evaluation of known variants of unknown clinical significance and characterization of new mutations in genes involved in hereditary breast-

		ovaries cancer
23/7/2018	**A.Biratsi** IBA, NCSR "Demokritos	Study of the genes responsible for the detoxification and catabolism of L-(-) azetidine-2-carboxylic in *Aspergillus nidulans*

SEMINAR PROGRAMME 2018 OF INVITED SPEAKERS
INSTITUTE OF BIOSCIENCES & APPLICATIONS

DATE	SPEAKER	TITLE
17/4/2018	**Prof. Anastasios Melis** Department of Plant and Microbial Biology, University of California, Berkeley, USA	On fuels and chemicals: cyanobacterial heterologous terpene hydrocarbons production
17/12/2018	**Prof. Georgios Giamas** School of Life Sciences, University of Sussex, UK	LMTK3 kinase: a novel target for cancer therapy

COLLECTIVE DATA

COLLECTIVE DATA ON PRODUCTIVITY OF SCIENTIFIC PROGRAMMES

	PROGRAMME			
	A	B	C	INSTITUTE
Researchers & ELE	11	7	6	25*
Technical Specialist	1	1	-	2
Collaborating & Emeritus Scientists	3	3	1	7
Postdoctoral Fellows	7	3	4	14
Graduate Students (PhD)	10	5	1	16
Graduate Students (MSc)	7	3	2	12
Graduate Research Associates	6	1	-	11[!!!]
Undergraduate Students	6	9	4	19
Research Technicians	1	-	-	5[@]
Administrative Staff and Technical Support Personnel	-	-	-	4
Total Personnel	**52**	**32**	**18**	**115**
Publications in Peer-Reviewed Journals	**25**	**12**	**15**	**52**
Cumulative Impact Factor in Peer-Reviewed Journals	**103.142**	**51.061**	**35.441**	**189.644**
Proceedings in Conferences	**2**	**2**	**-**	**4**
Total Publications	**27**	**14**	**15**	**56**
Citations	**1660**	**541**	**275**	**2481[#]**
International Patents	**-**	**1**	**-**	**1**
Greek Patents	**-**	**-**	**1**	**1**
Presentations to International Conferences	**15**	**12**	**13**	**40[$]**
Presentations to Greek Conferences	**16**	**-**	**4**	**22[$]**
Total Presentations to Conferences	**31**	**12**	**17**	**63**

** 1 Scientist of Human Tissue Bank is included*

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

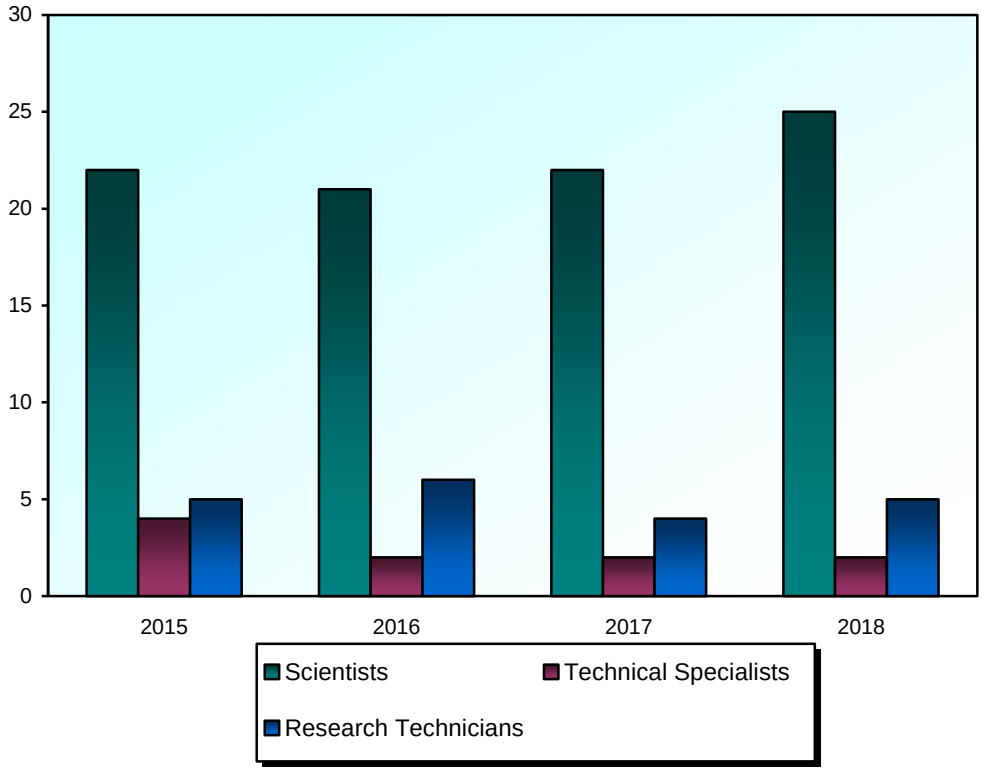
@ 2 Research Technicians who are occupied in Experimental Animal Colony and 1 Research Technician who is occupied in Confocal Laser Microscopy are included

The citations of Human Tissue Bank are included

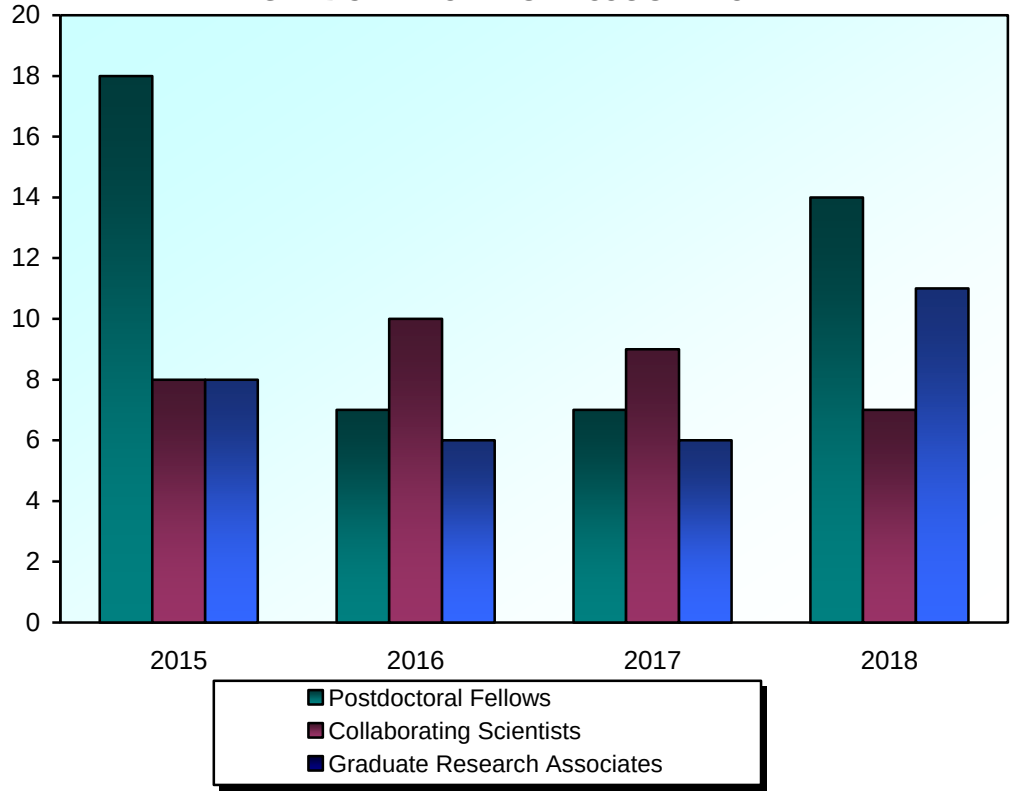
$ *The presentations of* Human Tissue Bank and 1 common presenation in A and B programme are included

CHANGES OF IBA STAFF
DURING 2015-2018

TENURED EMPLOYEES

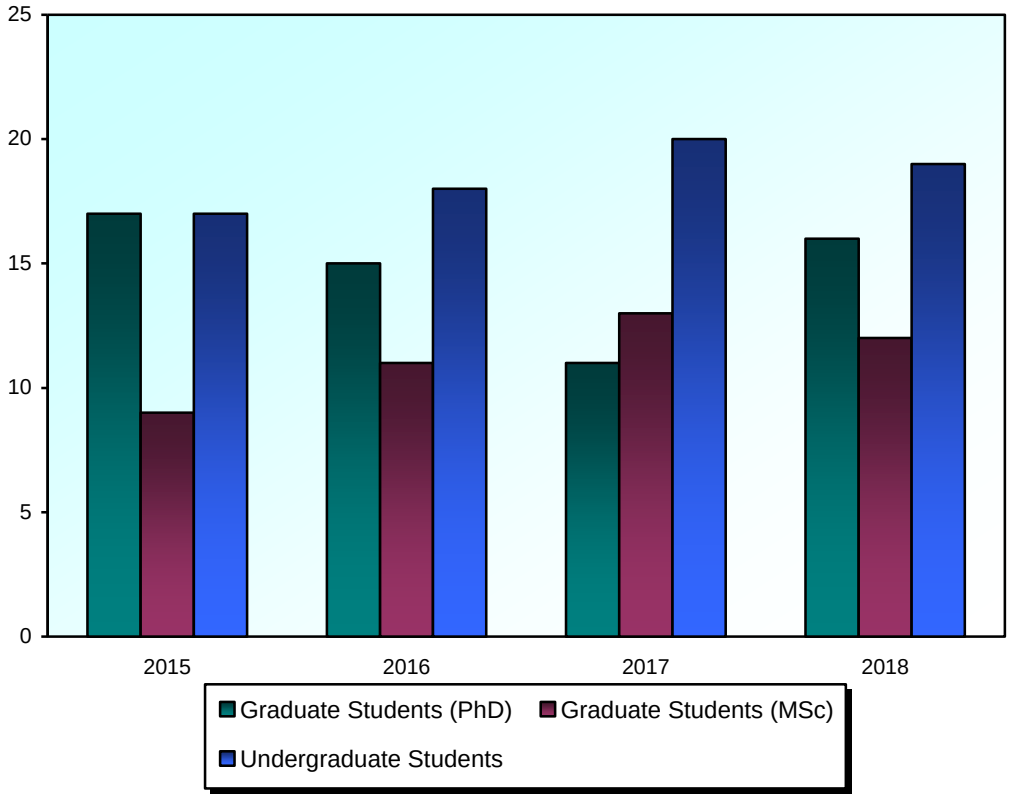


POSTDOCTORAL FELLOWS, COLLABORATING SCIENTISTS & GRADUTE RESEARCH ASSOCIATES

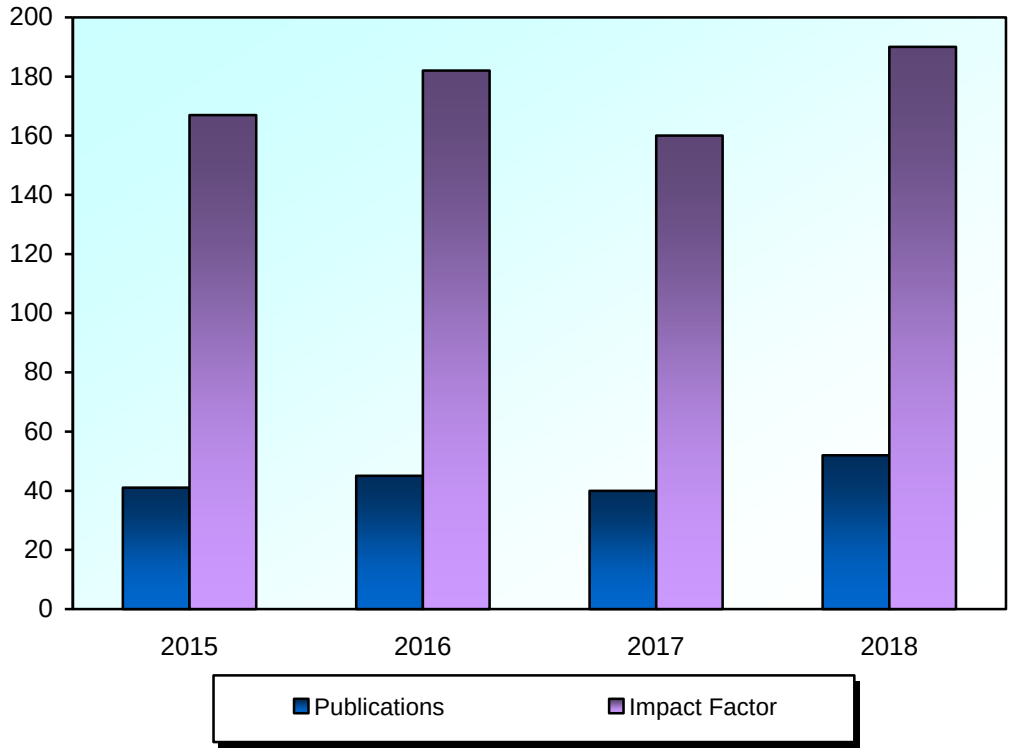


CHANGES OF IBA STAFF
DURING 2015-2018

GRADUATE STUDENTS



PUBLICATIONS IN PEER-REVIEWED JOURNALS AND CUMULATIVE IMPACT FACTOR DURING 2015-2018



CITATIONS OF THE INSTITUTE 2015-2018