

ΔΗΜΟΚΡΙΤΟΣ



DEMOKRITOS

NATIONAL CENTRE FOR SCIENTIFIC RESEARCH



**INSTITUTE
OF BIOSCIENCES
& APPLICATIONS**

**ANNUAL REPORT
2019**





**NATIONAL CENTRE FOR SCIENTIFIC RESEARCH
"DEMOKRITOS"**

INSTITUTE OF BIOSCIENCES & APPLICATIONS

ANNUAL REPORT 2019

AGIA PARASKEVI

OCTOBER 2020

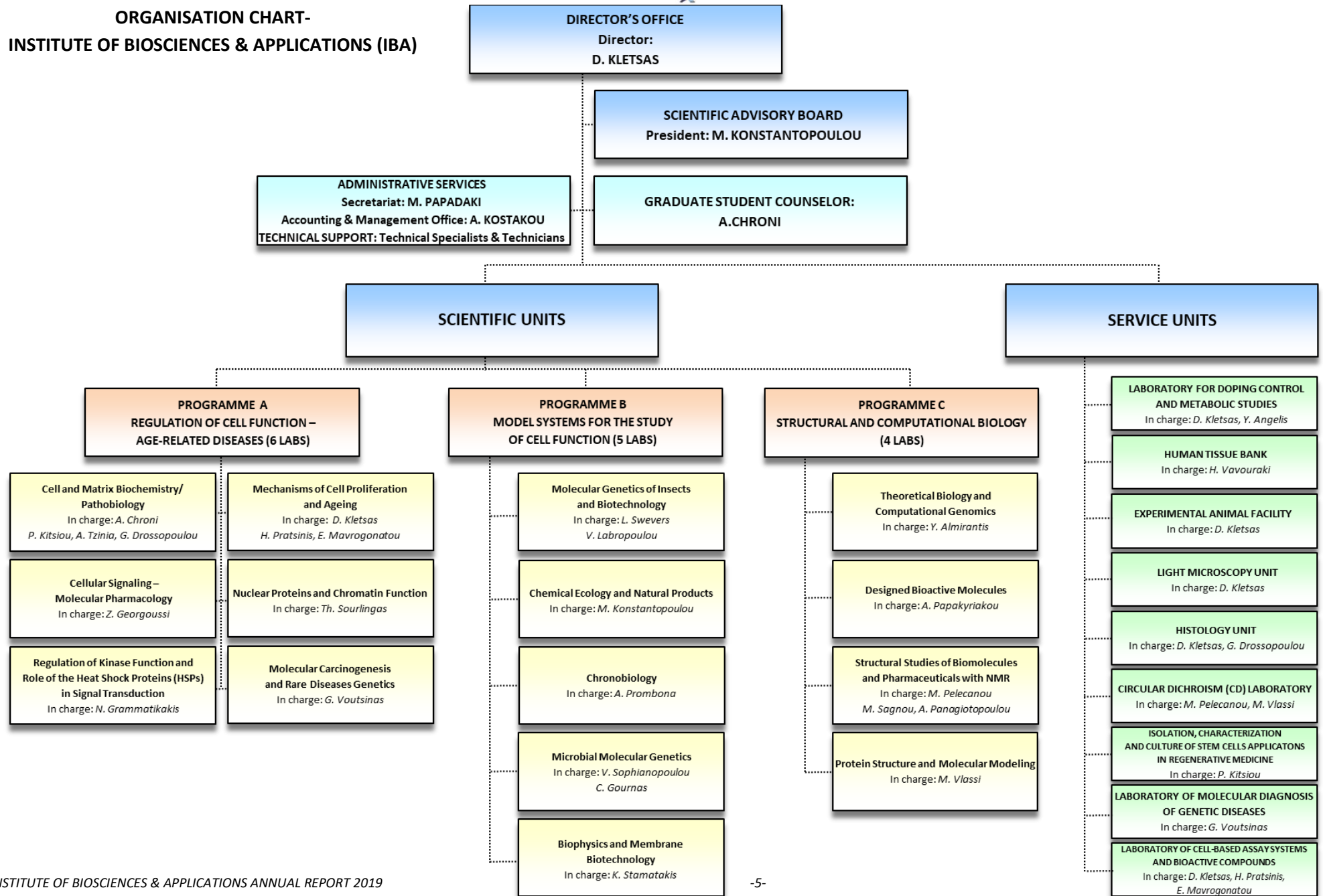
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**ORGANISATION CHART-
INSTITUTE OF BIOSCIENCES & APPLICATIONS (IBA)**



IBA PERSONNEL

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Dr. Biologist

SCIENTIFIC STAFF

Research Directors

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Dr. Theoretical Biologist

Chroni Angeliki

Dr. Chemist

Georgoussi Zafiroula-Iro

Dr. Biochemist

Kletsas Dimitris

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Sophianopoulou Vassiliki

Dr. Molecular Biologist, Microbiologist

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Dr. Biologist

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Dr. Physicist-Chrystallographer

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Senior Researchers

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Stamatakis Konstantinos

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Researchers

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Dr. Biologist

Mavrogonatou Eleni

Dr. Biologist

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Dr. Biologist/ Chemist

Functional Scientific Personnel

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TECHNICAL SPECIALISTS

Angelis Yannis

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Dr. Biologist

Avgeris Socratis

Technologist (MSc)

Fragkaki Argyro

Dr. Chemist

Kioukia Nassia
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 Stefanou Dimitra

Dr. Pharmacist
 Dr. Chemist
 Agronomist

ADMINISTRATIVE & TECHNICAL SUPPORT

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 Pavlaki Maria
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 Vlahos Panayiotis (*MSc*)
 Vlahou Maria
 Zafeiropoulos Giannis

Accountant
 Research Technician
 Laboratory Animal Caretaker
 Administrative Officer
 Technician (Retired)
 Electronics Engineer
 Technologist
 Administrative Officer
 Supporting Personnel
 Administrative Officer
 Network Administrator
 Administrative Officer
 Laboratory Animal Technician

EMERITUS & COLLABORATING SCIENTISTS

Scientists

Iatrou Kostas (Dr. Biochemist & Molecular Biologist) – *Emeritus*
 Ignatiades Lydia (Dr. Hydrobiologist) – *Collaborating*
 Papageorgiou George (Dr. Biophysicist) – *Collaborating*
 Papageorgiou Spyros (Dr. Physicist) – *Collaborating*
 Sekeri Kalliope (Dr. Biochemist) – *Collaborating*
 Tsimilli-Michael Merope – *Collaborating*

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 Almirantis Y.
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 Stamatakis K.

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 Galeou Angeliki
 Giannogonas Panagiotis
 Halevas Eleftherios
 Kaminari Archontia
 Kolliopoulou Anna
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IBA Researcher

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 Konstantopoulou M.
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 Sagnou M.
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 Konstantopoulou M.
 Iatrou K.
 Prombona A.

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 Mpakali Anastasia
 Papadopoulou Adamantia
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Pelecanou M.
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 Kletsas D.
 Drossopoulou G.

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 Dedemadi Anastasia-Georgia (*MSc*)
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 Klamarias Lykourgos (Veterinarian)
 Kosmidis Eleutherios
 Lesgidou Nastazia-Lemonia
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 Raptopoulos Dimitris (*PhD*)
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 Voutsinas G.
 Iatrou K.
 Drossopoulou G.
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PhD CANDIDATES AND MSc STUDENTS

PhD candidate (University)

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 Kouroumalis Anastasios (NKUA)
 Koutloglou Sofia (NKUA)
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 Papagiannis Achilleas (AUTH)

Supervisor in IBA

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 Papakyriakou A.
 Voutsinas G.
 Chroni A.
 Georgoussi Z.
 Kletsas D.
 Georgoussi Z.
 Kletsas D.
 Sagnou M.
 Konstantopoulou M.
 Papakyriakou A.
 Gournas C.
 Chroni A.
 Georgoussi Z.
 Chroni A.

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 Sofokleous Valentinos (NKUA)
 Vayenos Dimitris (NTUA)
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 Katrini Konstantina (NKUA) – *MSc obtained*
 Kelemen Marina – Gemma (Univ. of Patras)
 Nigianni Georgia (Univ. of Patras)
 Ntogka Christina (NKUA)
 Pateraki Eva (NKUA) – *MSc obtained*
 Santorinaiou Anna (NKUA) – *MSc obtained*
 Valianatos Alexandros (NKUA)

Swevers L.
 Georgoussi Z.
 Sagnou M.
 Stamatakis K.
 Swevers L.

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Pratsinis H.
 Kletsas D.
 Kletsas D.
 Chroni A.
 Kletsas D.
 Sagnou M.
 Kletsas D.
 Kletsas D.
 Kletsas D. / H. Pratsinis
 Sophianopoulou V.

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Student (University)

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 Argyrou Minas (AUA)
 Baxevani Chrysanthi (AUA)
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 Daskalopoulou Maria-Aikaterini (NKUA)
 Gaitanos Spiros (NKUA)
 Giakoumidaki-Vogiatzi Aikaterini (AUA)
 Giannioti Eleftheria (Univ. of Portsmouth, UK)
 Kafetzopoulos Gregory (NKUA) – *Dissertation completed*
 Kalampaliki Agoritsa (AUA)
 Kokkinas Evangelos (AUA)
 Mllioris Zisis (AUA)
 Myridakis Antonis (NKUA)
 Pantiora Panayota (AUA)
 Papavranoussi-Daponte Danae (NKUA) – *Dissertation completed*
 Pariou Stavroula-Ioanna (NKUA)
 Pouloupoulou Marisofi (UTH)
 Smyrniotis Stefanos – *Dissertation completed*
 Taouksi Konstantina (NKUA) – *Dissertation completed*
 Tomaropoulos Vasileios (AUA)
 Voulgaris Panayiotis (NKUA)
 Zakopoulou Tatiana (NKUA)

Supervisor in IBA

Panagiotopoulou A.
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 Stamatakis K.
 Mavrogonatou E.
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 Sophianopoulou V.
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 Sophianopoulou V.
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 Papakyriakou A.
 Prombona A.
 Vavouraki H.
 Georgoussi Z.
 Pelecanou M.
 Georgoussi Z.
 Swevers L.
 Prombona A.
 Voutsinas G.
 Voutsinas G.
 Prombona A.
 Stamatakis K.
 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 multidisciplinary 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 in various areas of life sciences and especially 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. In addition, the Institute houses a considerable number of laboratories, some of them unique in Greece, providing advanced technological research services to the Public and the Private Sector.

For the year 2019, I wish to congratulate the 25 faculty members of the IBA and the total 137 members of the Institute, who contributed to the upgrading of the research and the developmental work produced. 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. A. Chroni, Z. Georgoussi, H. Pratsinis and L. Swevers (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.

During 2019, the implementation of important programs for the function and upgrading of the infrastructure of the IBA continued. A special reference is needed to those colleagues who worked, in collaboration with all the members of the Institute (researchers, technical and administrative staff), for the implementation of these projects, namely SANITURA (Drs. V. Labropoulou and H. Pratsinis), OPENSREEN-GR (Drs. K. Iatrou, A. Chroni, Z. Georgoussi, and H. Pratsinis), BIOIMAGING-GR (Drs. V. Labropoulou, H. Pratsinis, and M. Sagnou) and INSTRUCT (Drs. A. Chroni, A. Panagiotopoulou, M. Pelecanou and M. Vlasi). The successful implementation of these projects, as well as of all the competitive grants of 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. In addition, a significant replenishment of the infrastructure of the Institute was achieved. In this context, the creation of the IBA Histology Unit constitutes a substantial upgrading of the Institute. Finally, IBA succeeded in participating in the emblematic action “The Routes of Bee” funded by GSRT aiming to highlight the potential biological actions of selected categories of Greek honey.

In 2019 Dr. K. Stamatakis was promoted to the position of Research Director (Grade A’) as merited. Furthermore, the procedure leading to the election of the new member of IBA Dr. I. Sotiropoulos in the position of Researcher Grade C’ have started within 2019 and finalized within 2020. We would like to wish him every success in his new position! Congratulations to both colleagues!

A very important development for our Institute was the integration of the Laboratory for Doping Control and Metabolic Studies, which belonged to the Hellenic Sports Research Institute. This Laboratory, which is one of the few international equivalent laboratories, possesses an excellent infrastructure and a highly experienced personnel. In addition, a significant funding has been already secured for its further upgrading in terms of new instruments and personnel. At the same time, the 10 members of this Laboratory joined our Institute, and we wish to welcome them with great pleasure! We are certain that this development will lead to the successful fulfillment of the very important mission of the Laboratory to secure a doping-free sporting environment and to protect the athletes’ health. Finally, in collaboration with the other laboratories of IBA, it will play a key role in the upgrading of the research and the developmental work produced.

Our Institute has a long tradition in postgraduate education since the 1960s. During 2019 education within IBA has been greatly upgraded. The training of a significant number of post-doctorate fellows, post-graduate students, and diploma and pre-graduate students continued, while the majority of the faculty members participated in post-graduate courses of a number of Universities in Greece. The second cycle of lessons and MSc theses in the framework of the Interinstitutional Post-Graduate Educational Program (IPEP) entitled “Applied Biochemistry: Clinical Chemistry, Biotechnology and Evaluation of Pharmaceutical Products” between IBA and the Department of Chemistry of the University of Patras was carried on. Furthermore, the participation of the IBA in the IPEP “Athens International School for Neurosciences” has been renewed. In addition, the “IBA Summer Camp for Lyceum Students”, enabling participating students to work for two weeks in the laboratories of the Institute and to perform small research projects, was organized for the second successive year. In collaboration with the European Learning Laboratory for the Life Sciences (ELLS) of the European Molecular Biology Laboratory (EMBL), a training course for secondary school biology teachers was planned within 2019 and was organized with great success in 2020. Finally, the researchers of the IBA 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. Congratulations to all colleagues participating in these activities.

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.

Dimitris Kletsas, PhD
IBA Director
October 2020

PROGRAMME A

"REGULATION OF CELL FUNCTION – AGE-RELATED DISEASES"

Research Group: Cellular Signaling–Molecular Pharmacology

Research Staff

Zafiroula-Iro Georgoussi, Research Director

Paschalina Pallaki, Graduate Student

Christos Karoussiotis, Graduate Student

Alexandra Symeonof, Graduate Student

Sofia Koutloglou, Graduate Student (absent for maternity reasons)

Danae Papavranousi-Daponte, Undergraduate Student-*BSc obtained in 2019*

Gregory Kafetzopoulos Undergraduate Student-*BSc obtained in 2019*

Antonis Myridakis, Undergraduate Student

Minas Argyrou, Undergraduate Student

Kostas Iatrou, Research Director (Emeritus)

Lydia Ignatiades, Research Director (Retired)

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 G protein-coupled receptors (GPCRs) signal transduction pathways. We give special emphasis on mechanisms acting beyond the G protein paradigm that are implicated in various physiological and pathological conditions.

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

More specifically our objectives are focused on four interconnected thematic areas, which include:

- The elucidation of novel signaling pathways - proteins, transcription factors and genes - whose function is altered upon selective opioid administration and are implicated in neuronal differentiation and outgrowth.
- The understanding of the mechanism of functional selectivity - *biased signalling*- of the δ and κ -opioid receptors.
- The identification of the role of opioid-induced autophagy in neuronal plasticity under stress conditions in animal models.
- The pharmacological characterization of new bioactive compounds for opioid or other GPCRs using high throughput cell-based screening assays in order to identify “*smart drugs*” to alleviate pain or other diseases of the central nervous system.

2019 Findings

Alternative signal transduction pathways induced upon opioid receptor activation

Autophagy: an unexplored mechanism of the κ -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 upon agonist administration. The brain region responsible for the κ -OR-mediated autophagic flux is the hippocampus. Moreover, we identified the responsible players involved and defined a putative signaling pathway through which activation of the κ -OR with selective agonists leads to alterations of specific autophagic gene expression (Figure 1).

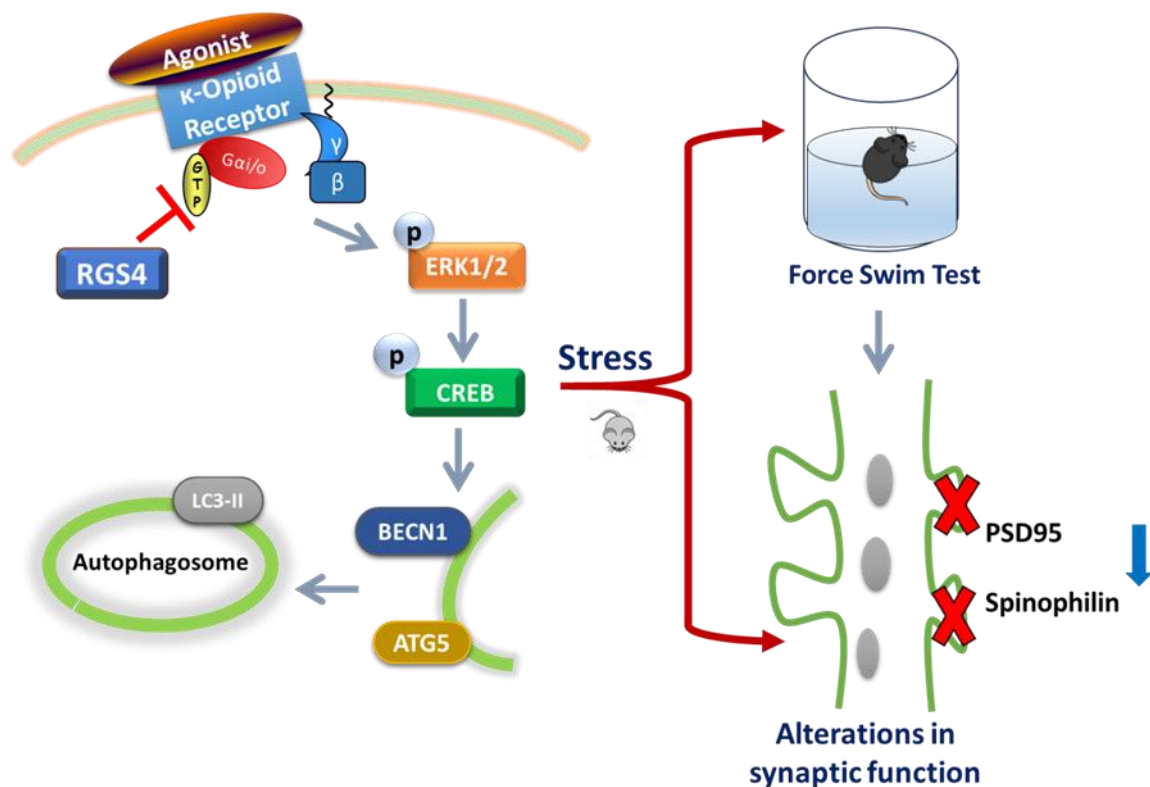


FIGURE 1: Schematic representation of a putative signaling pathway through which activation of the κ -opioid receptor with selective agonists induces the autophagic machinery and leads to synaptic alterations and morphology in hippocampal neurons under stress conditions.

The role of spinophilin: We have found that spinophilin, a neuronal dendritic spine scaffold protein, directly interacts with the κ -opioid receptor and alters opioid receptor signaling. Further studies have shown that administration of the selective κ -OR agonist U50,488H in mice results in alterations of the synaptosomal proteins spinophilin and PSD95 in hippocampal lysates with concomitant decrease of various autophagic markers. Similar results were also obtained from mice subjected to a force swim stressor test. These results suggest that κ -OR activation induces the autophagic machinery via a novel signaling pathway that leads to synaptosomal alterations in the hippocampus under stress conditions (Figure 1).

The role of RGS4 protein: Previous observations from our lab have shown that RGS4 negatively regulates the opioid receptor signaling pathway that results in opioid-dependent neuronal differentiation and neurite outgrowth. This negative regulatory mechanism is exerted by a “non-canonical” signaling pathway regulating STAT5B-inducible gene expression (Georganta et al., 2010, 2013; Pallaki et al., 2017). Using primary neuronal cultures from RGS4^{-/-} mice, we have found that the levels of specific autophagic markers are dramatically reduced, a result suggesting a novel functional role for RGS4, that of its possible involvement in the autophagic machinery. Parallel studies in collaboration with Prof. J. Selent, Pompeu Fabra University, Barcelona, under the auspices of the COST-action-GLISTEN (*GPCR Ligand Interactions, Structures and Transmembrane Signaling*) using molecular dynamics and site directed mutagenesis have identified the structural determinants and the critical amino-acids responsible for the interaction of δ -opioid receptor with RGS4.

Pharmacological characterization of bioactive compounds in cell-based throughput platforms:

In the context of our participation in the EU consortium «*NORMOLIFE NETWORK*» (collaboration with Drs L. Pasquinucci, G. Ronsisvalle & R. Turnaturi, University of Catania), our group characterized the pharmacological profile of new bioactive compounds that exert functional selectivity towards a specific opioid receptor pathway (*biased agonism*), thus providing new perspectives for the use of opioid analogs for pain management.

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

In collaboration with Drs P. Dimitrakis and E. Makarona of the INN Institute of NCSR “D” efforts are made to develop neuronal cells on ZnO or graphene nanoribbon interconnects in an attempt to investigate the cellular (electrical) responses and their plausible variations upon electrical or chemical stimulation.

Publications

Karoussiotis C., Marti-Solano M., Maciej Stepniewski, T., Symeonof, A., Selent J. and Georgoussi, Z. (2019) «*Delimiting a δ -opioid receptor region essential for RGS4 recruitment*» *FEBS J* 287(4):736-748 doi.org/10.1111 /febs.15033 (IF: 4.739)

Articles in Press 2020

Pasquinucci L., Parenti C., Ruiz-Cantero M. C., Georgoussi Z., Pallaki P., Cobos E.J., Amata E., Marrazzo A., Prezzavento O., Arena E., Dichiara M., Salerno L., Turnaturi R. (2020) Novel N-Substituted Benzomorphan-Based Compounds: From MOR-Agonist/DOR-Antagonist to Biased/Unbiased MOR Agonists. *ACS Med. Chem. Lett* doi: 10.1021/acsmchemlett. 9b00549 (IF: 3.737)

Other Publications

Georgoussi Z. and Karoussiotis C. (2019). “ κ -Opioid Receptor Activation Induces the Autophagic Machinery and Alters Dendritic Spine Density”. *FASEB Journal* 201, (supplement issue) Vol. 33, 663.13

Karoussiotis C., Sotiriou A., Polissidis A., Papavranoussi-Daponte D., Nikolettou V. and Georgoussi Z. (2020). “The role of κ -opioid receptor-induced autophagy in synaptic alterations”. *FASEB Journal*, Vol. 34, S1, <https://doi.org/10.1096/fasebj.2020.34.s1.02897>

Presentations at Scientific Conferences

Z. Georgoussi and C. Karoussiotis (2019) “ *κ -Opioid Receptor Activation Induces the Autophagic Machinery*” Experimental Biology 2019, Orlando, FL, USA 4-7 April 2019.

P. Pallaki, C. Karoussiotis, A. Polissidis, I. Serafimidis, Z. Georgoussi (2019). “*RGS4 exerts a regulatory role in neuronal homeostasis through autophagy*”. ERNEST meeting GPCR Pharmacology-Activation, Signaling and Drug Design, October 28-30, 2019, Belfast, UK.

Z. Georgoussi, C. Karoussiotis, M. Marti-Solano, T. Maciej Stepniewski, A. Symeonof, A., and J. Selent (2019). “*A highly conserved δ -opioid receptor region determines RGS4 interaction*”. ERNEST meeting GPCR Pharmacology-Activation, Signaling and Drug Design, October 28-30, 2019. Belfast, UK.

P. Pallaki, C. Karoussiotis, A. Polissidis, I. Serafimidis, Z. Georgoussi (2019). “*The role of Regulator of G protein signaling 4 in neuronal cell death and differentiation*”. 7th Panhellenic Forum of Young Scientists of the Hellenic Society of Biochemistry and Molecular Biology, 28 November 2019, Athens (oral presentation).

P. Pallaki, C. Karoussiotis, A. Polissidis, I. Serafimidis, Z. Georgoussi (2019). *“The role of Regulator of G protein signalling 4 in neuronal cell death and differentiation”*. 70th Hellenic Society of Biochemistry and Molecular Biology, 29-31 November 2019, Athens.

C. Karoussiotis, A. Sotiriou, D. Papavranoussi-Daponte, A-V. Polissidis, V. Nikolettou and Z. Georgoussi (2019). *“The role of κ -opioid receptor-induced autophagy in synaptic alterations”*., 7th Panhellenic Forum of Young Scientists of the Hellenic Society of Biochemistry and Molecular Biology, 28 November 2019, Athens.

C. Karoussiotis, A. Sotiriou, D. Papavranoussi-Daponte, A-V. Polissidis, V. Nikolettou and Z. Georgoussi (2019). *“The role of κ -opioid receptor-induced autophagy in synaptic alterations”* 70th Hellenic Society of Biochemistry and Molecular Biology, 29-31 November 2019, Athens (oral presentation).

Educational Activities

- Member of the organizing committee for the establishment of the International Masters course in Neurosciences entitled *“Athens International Master’s Programme for Neurosciences”* together with the Kapodistrian University of Athens, the NHRF, BRFAA, the Institute Pasteur and the Fleming Institute.
- Co-organizer of the course *“Cellular and Molecular Neurosciences”* of Athens International Master’s Programme in Neurosciences, 20 hours.
- Supervisor of the PhD dissertations of the Graduate students: Paschalina Pallaki, Christos Karoussiotis, Sofia Koutloglou and Alexandra Symeonof.
- Supervisor of the BSc theses of the Undergraduate students: D. Papavranoussi-Daponte, Antonis Myridakis, Gregory Kafetzopoulos, Department of Biology, Kapodistrian University of Athens and Minas Argyrou, Agricultural University of Athens.
- Member of the Advisory Committee in the Department of Biology of the Kapodistrian University of Athens for the PhD students P. Pallaki, S. Koutloglou, C. Karoussiotis and A. Symeonof.
- 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”*, (3 hours, 35 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 on *“Signaling of Neurotransmitter Receptors”* and *“Neuropeptides”* (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”* (4hrs, 7 students).
- IBA-Summer Scientific Laboratories for High School students on *“Protein Expression Methodologies in Different Cell Systems”* (hands on, group of 3 students).
- **Gregory Kafetzopoulos defended his Diploma Thesis in the faculty of Biology of the Kapodistrian University of Athens** entitled *“The role of κ -OR induced autophagy in synaptic alterations”* (Scientific Advisor: Z. Georgoussi).
- **Danae Papavranoussi-Daponte defended her Diploma Thesis in the faculty of Biology of the Kapodistrian University of Athens** entitled *“Identification of the signaling pathway implicated in κ -OR induced autophagy”* (Scientific Advisor: Z. Georgoussi).

Distinctions and Awards

Paschalina Pallaki was awarded with a COST- scholarship (registration and lodging) to attend the Inaugural meeting of the “*European Research Network on Signal Transduction*” on “*GPCR Pharmacology: Activation, Signaling and Drug Design*”, October 27-31, 2019, Belfast, UK.

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, Neuropharmacology, Journal of Biotechnology, BioMed Cell Biology, Journal of Biological Chemistry, Journal of Computational Systems Biology, Letters in Drug Design & Discovery, Current Drug Discovery Technologies, CNS Neuroscience & Therapeutics, Neurochemistry, International, Pharmaceutical Biology, Nature Neuroscience.

Reviewing of funding and evaluation 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
- Member of the working group of the National Roadmap Research Infrastructure “OPENSREEN-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
- Responsible scientist for the ultracentrifuges Beckman Coulter OPTIMA-MAX και L8-80M and the Speed Vac, Savant of the IBA, NCSR “D”

Impact factor (for 1 publication): 4.739

Citations for 2019 (without self-citations): 33

Citations for 2015-2019 (without self-citations): 184

h-factor: 18 (Scopus), 20 (Google Scholar)

Current external funding

Programme EU–COST Action CA18133 entitled *European Research Network on Signal Transduction (ERNEST)* funded by the EU–COST Action with Dr. Z. Georgoussi as Member and National Representative of the Management Committee

Duration: 04/2019- 03/2023

For the 2018: Covered expenses for participation in the Conference “*GPCR Pharmacology: Activation, Signalling and Drug Design*”, Belfast, UK.

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.
- Assessment of statistical ecological models for the impact of the climatic change on the biodiversity of sea phytoplanktonic systems based on analysis of data of the MedOBIS database generated by L. Ignatiades concerning the Eastern Aegean Sea (L. Ignatiades).

2019 Findings

Insect odorant receptors (ORs) are heterotetrameric ion channels consisting of a common subunit, ORco, and one of multiple variable subunits, ORx, to which odorants acting as specific receptor agonists or antagonists bind, in as yet unknown molar ratios. In cells expressing only ORco, functional homomeric channels are formed that are activated by specific ORco agonists. We have previously shown that mosquito repellents that block odor-specific responses of multiple *Anopheles gambiae* ORs, act as ORco-specific antagonists, thus allosteric antagonists for the heteromeric receptors. Additionally, the responses of heteromeric receptors induced by ORx-agonists are enhanced in the presence of an ORco agonist, a finding suggesting that its binding causes structural rearrangements in liganded ORx heteromers.

In 2019, we have completed the examination of a collection of 100 volatile organic compounds (VOCs) of natural origin for the presence of regulators of mosquito olfaction-controlled behaviours using an insect cell-based ORco expression platform that allows a functional detection of *A. gambiae* ORco agonists and antagonists. The screening for relevant bioactive ligands resulted in the identification of 15 hits acting as ORco antagonists. In collaboration with the Benaki Phytopathological Institute (Dr. Antonios Michaelakis), we have established the functional relevance of the identified hits using *in vivo* repellence assays against the tiger mosquito *Aedes albopictus*, which is capable of vectoring a number of infectious agents. The identified ORco antagonists displayed significant mosquito repellent activities, with some of them causing anosmia-like effects to mosquitoes similar to equivalent doses of the widely used insect repellent DEET. Binary mixtures of the most active compounds caused stronger repellence effects than single

compounds, a finding suggestive of functional synergies caused by combinatorial structural changes within the ORco subunit that affect the function of the heteromeric ORs. Antagonist competition assays against a known ORco agonist demonstrated the presence of different, orthosteric and allosteric binding sites for the antagonists on ORco and provided a mechanistic rationale for consequent structural changes in the heteromeric ORs manifested by the enhanced repellent activities of the blends. These results demonstrate that natural ORco antagonists may modify olfaction-based mosquito behaviors in a predicted fashion. Moreover, the screening platform employed in this study may yield enhanced possibilities for personal protection against mosquito-borne infectious diseases.

Original articles In Press for 2020

Kythreoti, G, Sdralia, N, Tsitoura, P, Papachristos, P, Michaelakis, AP, Karras, V, Ruel, DM, Yakir, E, Bohbot, JD, Schulz, S and Iatrou, K (2020). Volatile allosteric antagonists of mosquito odorant receptors inhibit normal odor-dependent behaviors. *bioRxiv* doi: <https://doi.org/10.1101/2020.04.26.062919> (preprint depository for submitted publication - no impact factor)

L. Ignatiades (2020). Taxonomic diversity, size-functional diversity, and species dominance interrelations in phytoplankton communities: a critical analysis of data interpretation. *Marine Biodiversity* 50:58 (IF: 1.240)

Conference presentations

K Iatrou, S Schulz, G Kythreoti, N Sdralia, P Tsitoura, A Michaelakis, DP Papachristos (2019). Identification of modifiers of odor-triggered mosquito behaviors acting through binding to the ORco subunit of odorant receptor heteromers. Annual Experimental Biology meeting (EB 2019), April 6-9, 2019, Orlando, FL, USA

K. Iatrou (2019). Odors, odorant binding proteins, odorant receptors and olfactory function in Anopheline mosquitoes - From the search for new olfaction regulators to molecular pharmacology. The 4th International Conference of Insect Genomics & the 7th International Symposium on Insect Physiology, Biochemistry and Molecular Biology, 2-6 July 2019, Chongqing, China (*Plenary talk*)

Other scientific activities

Participation in editorial boards of scientific journals

- Member, Editorial Boards for "Sericologia", "Insect Biochemistry and Molecular Biology", "Archives of Insect Biochemistry and Physiology" και "BioMed Research International".
- Section editor, "Mediterranean Marine Science Journal" (L. Ignatiades)

Reviews of scientific journal articles

- Article reviewer for "Insect Science", "BMC Molecular Biology", "Insect Biochemistry and Molecular Biology", "Journal of Insect Physiology", "BioMed Research International", "Current Research in Biotechnology", "Acta Tropica", "Journal of Agricultural and Food Chemistry", "Development", "Heliyon", "Scientific Reports".
- Article reviewer for "Environmental Monitoring and Assessment", "The Science of the Total Environment", "Marine Ecology-Progress series" (L. Ignatiades)

Additional activities

National Representative and Management Committee Member for EU-COST Action CA18133 "European Research Network on Signal Transduction (ERNEST)"

Citations for 2019 (without self-citations)

Iatrou K: 176 (Scopus)

Ignatiades L: 112 (Scopus); 177 (Google Scholar)

Citations for 2015-2019 (without self-citations)

Iatrou K: 920 (Scopus)

Ignatiades L: 611 (Scopus); 984 (Google Scholar)

h-factor:

Iatrou K: 35 (Scopus); 44 (Google Scholar)

Ignatiades L: 21 (Scopus); 27 (Google Scholar)

Current external funding

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: 2017-2021

Total program funding for Greek group: 40.000€

Funding of the group for 2019: 0€.

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

Anastasios Kouroumalis, Graduate Student

Eleni Liakou, Graduate Student

Maria Angelopoulou, Graduate Student

Maria Adamopoulou, Graduate Student

Eva Pateraki, Collaborating Graduate Student (*MSc*) - *MSc obtained in 2019*

Anna Santorinaiou, Collaborating Graduate Student (*MSc*) - *MSc obtained in 2019*

Asimina Fotopoulou, Collaborating Graduate Student (*MSc*) - *MSc obtained in 2019*

Christina Ntogka, Collaborating Graduate Student (*MSc*)

Marina-Gemma Kelemen, Collaborating Graduate Student (*MSc*)

Charalambia Almpani, Collaborating Graduate Student (*MSc*)

Eleni Kaplani, Collaborating Graduate Student (*MSc*)

Vania-Nicole Byrne, Collaborating Undergraduate Student (*BSc*)

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 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.

2019 Findings

Main goal of the Laboratory is the study of the mechanisms implicated in cellular senescence, of the senescent phenotype and of the role of senescent cells in tissue homeostasis and in the manifestation of age-related diseases. Low back pain constitutes one of the major chronic age-related diseases, mainly attributed to intervertebral disc degeneration. In our Laboratory we have shown the presence of senescent cells in degenerated intervertebral discs that own a catabolic and inflammatory phenotype and we have shed light in the mechanisms leading to intervertebral disc cells' senescence. Most recent studies have established the key role of senescent cells in the

degeneration of the tissue. Most studies assessing intervertebral disc cells' physiology have been performed under classic cell culture conditions. However, intervertebral disc cells reside in a very harsh environment characterized by nutrients'/growth factors' deprivation, hyperosmolality and hypoxia. In this direction, we have shown that under these conditions, senescent intervertebral disc cells retain their molecular profile and their specific catabolic and inflammatory phenotype, making thus clear that studies performed under classic cell culture conditions can lead to safe conclusions about the tissue's physiology.

In vitro cultures of senescent cells are characterized by significant morphological alterations, including their bigger size and enlargement. Given that these changes are not observed *in vivo*, we investigated the traits of senescent fibroblasts after restoration of their typical fibroblastic morphology by culturing them on special photolithographically micropatterned substrates. Our findings showed that fibroblasts can normally grow and multiply on these substrates, while senescent cells retain their specific catabolic and inflammatory phenotype, which proves that cell morphology alterations are senescence-driven rather than inducers of senescence [Figure 1].

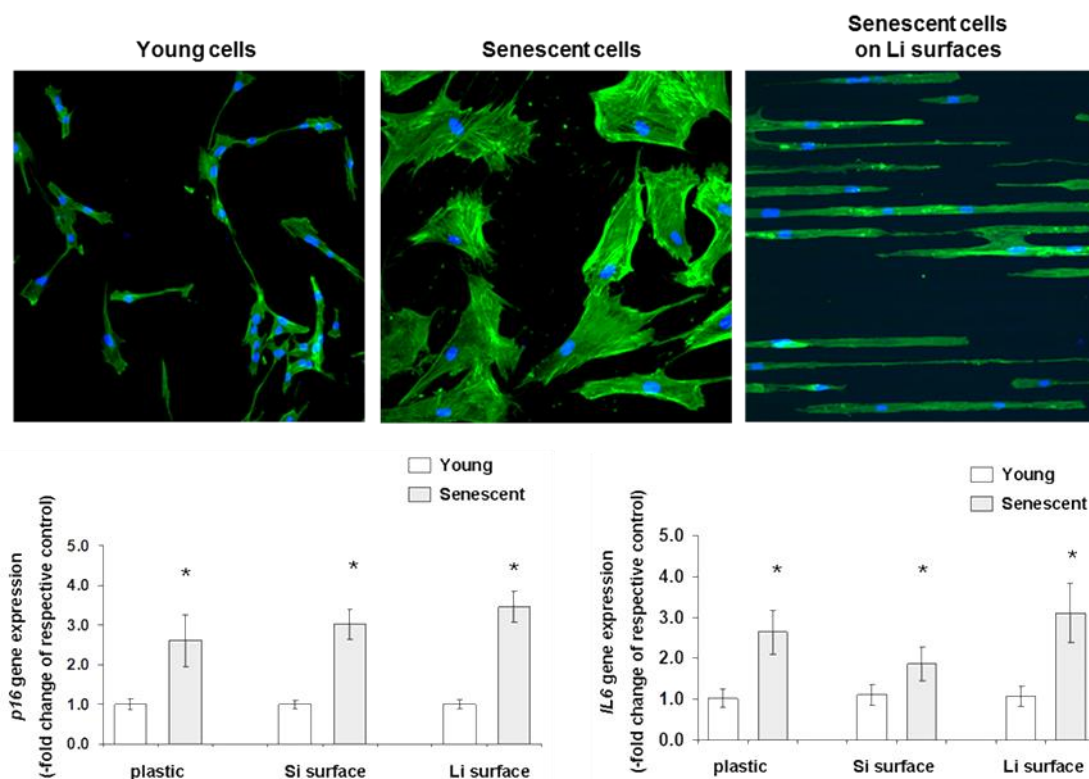


Figure 1: Morphology of early-passage and senescent human skin fibroblasts cultured on two-dimensional surfaces and of senescent fibroblasts cultured on photolithographically micropatterned substrates. Gene expression of classic markers of cellular senescence, such as the cyclin-dependent kinase inhibitor $p16^{INK4a}$ and IL-6 is retained when the morphology of senescent cells is restored to that of early-passage cells [Si: silicon substrate, Li: photolithographically micropatterned substrate] [Papadopoulou et al. *Biogerontology* (in press)].

In previous works of our Laboratory, we have shown that mechanical forces lead fibroblasts of the periodontal ligament to osteoblastic differentiation. We showed that hyperglycemia prevailing under diabetic conditions down-regulates this cellular response as a result of the provoked hyperosmotic stress.

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

substances extracted from the plant *Strychnos aff. darinensis* with anti-oxidant and protective against UV radiation action and bioactive compounds with anti-cancer properties extracted from sponge-associated marine cyanobacteria from the Greek Seas were discovered.

Publications

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.

Pratsinis, H., Mavrogonatou, E., Kletsas, D. (2019). Scarless wound healing: From development to senescence. *Adv Drug Deliv Rev.* 146, 325-343.

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.

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.* 41, 583-590.

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.* 68, 1245-1261.

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.

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

Articles in Press

Kanioura, A., Petrou, P., Kletsas, D., Tserepi, A., Chatzichristidi, M., Gogolides, E., Kakabakos, S. (2020). Three-dimensional (3D) Hierarchical Oxygen Plasma Micro/Nanostructured Polymeric Substrates for Selective Enrichment of Cancer Cells from Mixtures with Normal Ones. *Colloids Surf B Biointerfaces*, 187, 110675. (IF: 3.973)

Panagiotaki, K.N., Spyrou, K., Zachariadis, M., Pratsinis, H., Kouloumpis, A., Boutsika, L.G., Enotiadis, A., Gournis, D., Giannelis, E.P., Sideratou, Z. (2020). Non-porous phosphonated ionic silica nanospheres as nanocarriers for efficient intracellular delivery of doxorubicin. *Mater. Today Commun.* In press. (IF: 1.895)

Konstantinou, D., Mavrogonatou, E., Zervou, S.K., Giannogonas, P., Gkelis, S. (2020). Bioprospecting sponge-associated marine cyanobacteria to produce bioactive compounds. *Toxins (Basel)* 12, 73. (IF: 3.895)

Feretis, T., Katselis, C., Papanikolaou, I.G., Apostolou, K., Tsikalakis, S., Toutouzas, K.G., Theodoropoulos, G., Trigka, E.A., Saetta, A.A., Alexakis, N., Konstandoulakis, M., Tsarea, K., Karamperi, M., Kletsas, D., Patsouris, E., Manouras, A., Zografos, G.C., Papalois, A. (2020). ATSC transplantation contributes to liver regeneration following paracetamol-induced acute liver injury through differentiation into hepatic-like cells. *American Journal of Stem Cells* (accepted). (IF: 4.000)

Kanioura, A., Constantoudis, V., Petrou, P., Kletsas, D., Tserepi, A., Gogolides, E., Chatzichristidi, M., Kakabakos, S. (2020). Oxygen plasma micro-nanostructured PMMA plates and microfluidics for increased adhesion and proliferation of cancer versus normal cells: The role of surface roughness and disorder. *Micro and Nano Engineering*. In press. (IF: -)

Zoumpopoulou, G., Papadimitriou, K., Alexandraki, V., Mavrogonatou, E., Alexopoulou, K., Anastasiou, R., Georgalaki, M., Kletsas, D., Tsakalidou, E., Giaouris, E. (2020). The microbiota of Kalathaki and Melichloro Greek artisanal cheeses comprises functional lactic acid bacteria. *LWT Food Science and Technology*. In press. (IF: 3.714)

Zilelidou, E.A., Milina, V., Paramithiotis, S., Zoumpopoulou, G., Poimenidou, S.V., Mavrogonatou, E., Kletsas, D., Papadimitriou, K., Tsakalidou, E., Skandamis, P.N. (2020). Differential modulation of *Listeria monocytogenes* fitness, *in vitro* virulence and transcription of virulence-associated genes in response to the presence of different microorganisms. *Appl Environ Microbiol*. In press. (IF: 4.077)

Papadopoulou, A., Cantele, A., Koletsj, D., Eliades, T., Kletsas, D. (2020) Short- and long-term treatment with TNF- α inhibits the induction of osteoblastic differentiation in cyclic tensile-stretched periodontal ligament fibroblasts. *Eur. J. Orthod.* (accepted). (IF: 2.202)

Papadopoulou, A., Kanioura, A., Petrou, P.S., Argitis, P., Kakabakos, S.E., Kletsas, D. (2020) Reacquisition of a spindle cell shape does not lead to the restoration of a youthful state in senescent human skin fibroblasts. *Biogerontology*. In press. (IF: 3.805)

Presentations at Scientific Conferences

E. Mavrogonatou, A. Papadopoulou, H. Pratsinis, D. Kletsas (2019). Extracellular matrix alterations in senescent stromal fibroblasts and implications for tumor growth. 7th FEBS Advanced Lecture Course FEBS - MPST 2019, May 2-7, 2019, Porto-Heli, Greece. (invited)

H. Pratsinis, A. Santorinaiou, L. Kikidou, E. Livaniou, D. Kletsas (2019). Effects of thymosinic peptides on human skin fibroblasts related to wound repair. 7th FEBS Advanced Lecture Course FEBS - MPST 2019, May 2-7, 2019, Porto-Heli, Greece.

H. Pratsinis (2019). Biological activities of the carob tree products. 1st Mediterranean Conference "Carob Tree: The Coming Back", April 20, 2019, Panormo, Greece.

D. Kletsas (2019) Interplay between cellular senescence and cancer" 19th International Conference on Progress in Vaccination Against Cancer. September 7-9, Athens, Greece. (invited)

E. Mavrogonatou, A. Papadopoulou, H. Pratsinis, D. Kletsas (2019). Senescent cells as modulators of the tumor microenvironment. Annual Meeting of the International Cell Senescence Association (ICSA) Cellular Senescence: the bright & dark side, September 9-12, 2019, Athens, Greece. (invited)

A. Kouroumalis, E. Mavrogonatou, O. D. Savvidou, P. J. Papagelopoulos, H. Pratsinis, D. Kletsas (2019). Major traits of the senescent phenotype of nucleus pulposus intervertebral disc cells persist under the specific microenvironmental conditions of the tissue. Annual Meeting of the International Cell Senescence Association (ICSA) Cellular Senescence: the bright & dark side, September 9-12, 2019, Athens, Greece.

D. Veroutis, Ch. Chamilos, K. Evangelou, V. Gorgoulis, D. Kletsas (2019). Identification of senescent cells in the intervertebral discs by using lipofuscin detection. Annual Meeting of the International Cell Senescence Association (ICSA) Cellular Senescence: the bright & dark side, September 9-12, 2019, Athens, Greece.

D. Kletsas (2019). Senescent fibroblasts as modulators of tumor microenvironment. EMBO Workshop "Mesenchymal cells in inflammation, immunity and cancer" May 19-23, Athens, Greece. (invited)

D. Konstantinou, S.K. Zervou, E. Mavrogonatou, P. Giannogonas and S. Gkelis (2019). A preliminary assessment on the potential of sponge-associated cyanobacteria to produce bioactive compounds. The 11th International Conference on Toxic Cyanobacteria (ICTC), May 5-10, 2019, Kraków, Poland.

D. Kletsas (2019) "Cellular senescence: Basic parameter for carcinogenesis". 32nd Meeting of Stomatology. April 13, Athens. (Special Speaker)

D. Kletsas (2019) "The role of cellular senescence in tissue healing". 8th Congress of Wound and Ulcer Healing, September 12-13, Athens. (invited)

A. Kouroumalis, E. Mavrogonatou, H. Pratsinis, O. D. Savvidou, P. J. Papagelopoulos, D. Kletsas. The senolytic effect of sulforaphane on nucleus pulposus intervertebral disc cells depends on the specific conditions prevailing in the tissue. 70th Congress of the Hellenic Society of Biochemistry and Molecular Biology, November 29-December 1, Athens.

E. Mavrogonatou, A. Fotopoulou, A. Papadopoulou, H. Pratsinis, D. Kletsas (2019). The effect of ionizing radiation on human breast cancer-stroma interactions. 70th Congress of the Hellenic Society of Biochemistry and Molecular Biology, November 29-December 1, Athens.

A. Papadopoulou, A. Cantele, A. Todaro, D. Koletsi, T. Eliades, D. Kletsas (2019). Hyperglycaemic and inflammatory conditions inhibit mechanical loading elicited osteoblastic differentiation potential of human periodontal ligament fibroblasts. 70th Congress of the Hellenic Society of Biochemistry and Molecular Biology, November 29-December 1, Athens.

H. Pratsinis, A. Papastathopoulos, N. Lougiakis, P. Marakos, N. Pouli, D. Kletsas (2019). Discovery of novel 5-arylcarboximidamidopyrazolo[3,4-c]pyridines as potential anticancer agents: Synthesis, cytotoxicity and kinase inhibitory activity. 70th Congress of the Hellenic Society of Biochemistry and Molecular Biology, November 29-December 1, Athens.

R.A.A. Beta, A. Kanoura, D. Dalkidis, Z.V. Arsenopoulou, D. Kletsas, N.A.A. Balatsos (2019). Deciphering the role of PARN in circadian gene expression. 70th Congress of the Hellenic Society of Biochemistry and Molecular Biology, November 29-December 1, Athens.

D. Manou, M.A. Golfinopoulou, P. Bouris, D. Kletsas, M. Goette, B. Greve, N.K. Karamanos, A.D. Theocharis (2019). Serglycin modulates the aggressive behavior and differentiation of glioblastoma cells. 70th Congress of the Hellenic Society of Biochemistry and Molecular Biology, November 29-December 1, Athens.

D. Kletsas (2019) "Cellular senescence and cancer". 3rd Annual Meeting on Cancer Biology and New Molecules in Cancer Therapeutics". November 28-30, Athens. (invited)

D. Kletsas (2019) "Cellular senescence in the intervertebral disc: Molecular mechanisms, role in tissue degeneration and α putative pharmacological target" 13th Annual Congress of the Hellenic Spine Society, October 31-November 3, Ioannina. (invited)

Other Scientific Activities

Participation in Greek and international scientific bodies and organizations:

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)

Member of the FEBS Fellowships Committee (D. Kletsas)

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

National Representative in the Committee “Health, demographic change and wellbeing” of Horizon 2020 (D. Kletsas)

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

Member of the Regional Research and Innovation Council of Attica Region (ΠΣΕΚ-A) (D. Kletsas)

Member of the Ethics Committee of BSRC “Alexander Fleming” (D. Kletsas)

Co-organizer (along with V. Gorgoulis and V. Krizhanovsky) of the Annual Meeting of the International Cell Senescence Association (ICSA) Cellular Senescence: the bright & dark side, September 9-12, 2019, Athens, Greece (D. Kletsas)

Member of the Organizing Committee of the 7th FEBS Advanced Lecture Course FEBS-MPST 2019: Matrix Pathobiology, Signaling and Molecular Targets. May 2-7, 2019, Porto-Heli, Greece (D. Kletsas)

Participation in editorial boards of scientific journals:

Editorial board member of the Journals “Ageing Research Reviews”, “Biogerontology”, “Mechanisms of Ageing and Development”, “Experimental Gerontology”, “European Spine Journal”, “PLOS ONE” and “Journal of Orthopaedic Research Spine”, “Antioxidants” (D. Kletsas)

Editorial board member of the Journal “Cosmetics” (H. Pratsinis)

Participation in committees for the reviewing of research proposals:

Swiss National Science Foundation, Research Grants Council of Hong-Kong (D. Kletsas)

Editing of scientific book publications (e.g. conference proceedings, monographs, textbooks or manuals, etc.):

Section Editor in Encyclopedia of Biomedical Gerontology (Elsevier Inc. ISBN 978-0-12-816076-3) (D. Kletsas)

Reviewing of manuscripts in scientific journals:

FASEB J, Molecules, Matrix Biology (2), Matrix Biology Plus (2), Ageing Research Reviews, Mechanisms of Ageing and Development, Biogerontology (2), Experimental Gerontology, Oxidative Medicine and Cellular Longevity, PLOS One, Cell Division, Dose Response, European Spine Journal (4), Wound Repair and Regeneration, American Journal of Orthodontics & Dentofacial Orthopedics (D. Kletsas)

American Journal of Plant Sciences, Cancers, Cells, Chemistry and Biodiversity, Cosmetics, Marine Drugs, Matrix Biology, Molecules (5), Nutrients, PLoS ONE, Rejuvenation Research (H. Pratsinis)

PLoS ONE (4), International Journal of Environmental Research and Public Health (3), International Journal of Molecular Sciences (2), Biomedicine & Pharmacotherapy (4), American Journal of Orthodontics & Dentofacial Orthopedics (11), Nanomaterials (2), European Spine Journal, Marine Drugs (2), Chronic Diseases and Translational Medicine, Cells (4), Molecules (2), Cancers, Sensors & Actuators: B. Chemical, Oxidative Medicine and Cellular Longevity (E. Mavrogonatou)

Other lectures or presentations of scientific content:

D. Kletsas (2019) “Cellular senescence in the intervertebral disc: a novel target for therapeutic approaches”. Regular Educational Program of the College of Greek Orthopedic Surgeons “Bio-Technological Developments in Orthopaedics”, May 11, Athens (invited).

D. Kletsas (2019) "Senescent cells as modulators of tumor microenvironment". Institute of Biomedical Sciences of the Academy of Athens, October 17, Athens (invited).

Educational Activities

Member of the special inter-institutional committee and lecturer in the Joint Post-Graduate Programme (JPGP) in "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" (D. Kletsas)

Responsible for the Organization of the IBA Summer Camp for Lyceum Students (24/6-5/7/2019) (D. Kletsas)

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

Supervision of the theses for the acquisition of a Master's degree of Eva Pateraki, Asimina Fotopoulou, Christina Ntogka, Marina-Gemma Kelemini and Eleni Kaplani (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 Master's degree of Charalampia Almpani (H. Pratsinis)

Supervision of the thesis for the acquisition of a Bachelor's degree of Vania-Nicole Byrne (E. Mavrogonatou)

"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)

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, 9 students (D. Kletsas, H. Pratsinis and E. Mavrogonatou)

Participation in the 2nd Summer Camp of the Institute of Biosciences and Applications for High School students, June 24 - July 5, 2019, 20 students (D. Kletsas, H. Pratsinis and E. Mavrogonatou)

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

Anastasia-Gerassimoula Tavianatou, PhD thesis, "The effect of hyaluronate, at the molecular and cellular level, on breast cancer cells with differentiated expression of estrogen receptors" (Department of Chemistry, University of Patras) (D. Kletsas, H. Pratsinis)

Aikaterini Gioti, PhD thesis, "Investigation of the mechanism of action of natural and edible product in the pathophysiology of prostate cancer. Study of single administration and co-administration with a chemotherapeutic drug" (Harokopio University) (D. Kletsas)

Niki-Vaia Kolovou, PhD thesis, "Investigation of the factors associated with longevity syndrome (over 90 years)" (Harokopio University) (D. Kletsas)

Eva Pateraki concluded her M.Sc. thesis entitled "Effect of pharmaceutical interventions in intervertebral disc cells' homeostasis" 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)

Anna Santorinaiou concluded her M.Sc. thesis entitled "Effect of thymosine peptides on human skin fibroblasts" 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/ H. Pratsinis)

Asimina Fotopoulou concluded her M.Sc. thesis entitled "The effect of cellular senescence on the expression of extracellular matrix components in stromal fibroblasts" in the framework of the Master's Degree Programme of the Department of Chemistry of the University of Patras "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products". The thesis was unanimously accepted and awarded the degree "Excellent" (Scientific Supervisor D. Kletsas)

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"
Scientific and Administrative Responsible of the Experimental Animal Facility
Scientific and Administrative Responsible of the Light Microscopy Unit
Responsible for the function 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 4 publications): 27.949

H. Pratsinis (for 5 publications): 33.784

E. Mavrogonatou (for 3 publications): 26.108

Citations 2019 (without self-citations):

D. Kletsas: 670

H. Pratsinis: 178

E. Mavrogonatou: 96

Total Citations 2015-2019 (without self-citations):

D. Kletsas: 3717

H. Pratsinis: 1017

E. Mavrogonatou: 371

h-factor:

D. Kletsas: 45 (Scopus), 49 (Google Scholar)

H. Pratsinis: 28 (Scopus), 32 (Google Scholar)

E. Mavrogonatou: 13 (Scopus), 15 (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 2019: 18.585 €.

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" (NSRF), MIS 5004698, Academic Supervisor Assist. Prof. Spyros Gkelis.

Duration: 2018-2019

Total programme funding: 19.550 €

Funding of the lab for 2019: 13.900 €.

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 2019: 9.000 €.

Current External Funding IBA

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

Duration: 2017-2020

Total programme funding: 740.000 €

Funding for 2019: 140.000 €.

Project entitled *OPENSREEN-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 2019: -

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: 57.000 €.

Project entitled *Ensuring long-term sustainability of excellence in chemical biology within Europe and beyond (EU-OPENSREEN-DRIVE)*, funded by the European Union (Action “Reinforcement of the Research and Innovation Infrastructure”, Operational Programme “Competitiveness, Entrepreneurship and Innovation”, NSRF 2014-2020), Scientific Supervisor in IBA Dr. D. Kletsas.

Duration: 2019-2023

Total programme funding: 16.875 €

Funding for 2019: 8.156,25 €.

Project entitled “*The Routes of Bee*”, funded by GSRT (*Flagship national initiative for creating research networks in the value chains of "Olive", "Vineyard", "Honey" and "Livestock", NSRF 2014-2020*), Scientific Supervisor in IBA Dr. D. Kletsas.

Duration: 2017-2020

Total programme funding: 39.200 €

Funding for 2019: 15.680 €.

Research Group: Nuclear Proteins and Chromatin Function

Research Staff

Thomae Sourlingas, Senior Researcher B' Grade

Kalliope Sekeri, Research Collaborator, Retired A' Grade

Anastasia-Georgia Dedemadi, Collaborating Graduate Student (MSc)

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 activate or inactivate 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 deacetylase 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).

2019 Findings

Cancer and Histones

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 three histone H3 epigenetic modifications (acetylation, trimethylation and dimethylation) and three histone H1 subtypes (H1.0, H1.3 and H1.5) in the absence and presence of the HDACI, sodium butyrate, in three leukemic cell lines (K562, NB4, Molt4) as compared to normal lymphocytes. Of importance are our findings showing that in the presence of sodium butyrate histone H3 acetylation and trimethylation and the histone H1 subtype, H1.0 increase significantly. Interestingly, we also found that while the levels of H1.3 subtype do not change, those of H1.5, a subtype associated with condensed heterochromatin, change with statistically significant differences in two of the three leukemic cell lines (Molt4 and NB4). The H1.5 levels in the K562 cell line remain unchanged. These results

indicate that these histone factors may possibly be used as biomarkers of the efficiency of HDACIs (A.-G. Dedemadi).

Psychotic Disorders and H1 Subtypes

Given that the histone H1 class plays a significant role in chromatin reorganization, we chose to study the protein levels of specific H1 subtypes. We found that there is a significant decrease in the H1.0, a subtype that is associated with heterochromatin (condensed, inactive chromatin) in leucocytes of hospitalized relapsed patients with schizophrenia. A relapse means that the patient had a schizophrenic episode due to drug abstinence or to the ineffectiveness of treatment. We repeated these experiments chronic patients on medication and we again found a statistically significant decrease in H1.0. These findings are of major importance because they show that the decrease in H1.0 is not a symptom of the illness, nor a result of the drug treatment, but may be a basic fundamental element in the etiology of this pathological condition (within the framework of collaborations and graduate work, M. Xydous, A. Prombona, C. Panagiotopoulou, A.-G. Dedemadi).

Book Chapters

Sourlingas, T., Chrysanthou-Piterou, M., Panayotacopoulou, M., Sekeri, K. Epigenetic modifications in psychotic disorders: The plasticity of chromatin and the role of chromatin. In: "Biopathology and Psychic Health" (C. Nikolaou, S. Hatzipanagiotou and G. N. Papadimitriou, eds.). Section 9, 5th Issue, Medical Publications B, Athens, in press.

Other scientific activities

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 Professor I. Angelopoulos, University of Athens, Medical School, 1st Department of Psychiatry, Eginition Hospital. We are studying changes in the expression levels of histone genes in leucocytes of patients with bipolar disorder and schizophrenia.

Educational Activities

Seminar: "Cell Cycle: Checkpoints and Consequences for Normal Cellular Function when Cell Cycle Progression 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).

Seminar: "DNA organization, histones and chromatin function" within the framework of the course "Molecular and Cell Biology – Molecular Biotechnology" of the Graduate Masters' Program, "Applied Biochemistry, Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products", Institute of Biosciences and Applications and University of Patras (2 hours, 10 students).

Took part in the 2nd Summer School of the Institute of Biosciences and Applications for High School Students, June 24th-July 5th, 27 students (T. Sourlingas, A.-G. Dedemadi)

Other activities in the Institute of Biosciences and Applications

Responsible for the organization of research 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.

Citations for 2019 (without self-citations): 17

Total citations for 2015-2019 (without self-citations): 194

h-factor:

Scopus: 11

Google Scholar: 13

Research Group: Cell and Matrix Biochemistry/ Pathobiology

Research Staff

Angeliki Chroni, Research Director

Athina Tzinia, Senior Researcher

Paraskevi Kitsiou, Senior Researcher

Garyfalia Drossopoulou, Senior Researcher

Archontia Kaminari, Postdoctoral Researcher

Ioannis Dafnis, Postdoctoral Researcher

Angeliki Bourtsala, Postdoctoral Researcher

Ourania Trohatou, Postdoctoral Fellow

Christina Gkolfinopoulou, PhD student – *Defended*

Christina Mountaki, PhD student

Achilleas Papagiannis, PhD student

Konstantina Katrini, MSc student – *Defended*

Effie Valanti, collaborating scientist

Eleni Theofanidi, Collaborating scientist

Research Interests

1. Study of molecular mechanisms of neurodegenerative conditions and diseases of the Central Nervous System

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's Disease and type II Diabetes.

2. Molecular mechanisms of dyslipidemias and atherosclerosis

A) Elucidation of the mechanisms underlying disorders of high density lipoprotein (HDL) metabolism that result in changes of 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) Study of pancreatic β -cell survival mechanisms under diabetic conditions: i) Cross talk between nephrin and survival signaling pathways in pancreatic insulin producing beta cells ii) Effect of liraglutide (a human GLP-1 analogue) on nephrin signaling and islet β -cell survival in db/db lepr $^{-/-}$ type 2 diabetic mice.

B) 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 models of Type2 Diabetes. Role in prevention and/ or treatment of diabetic nephropathy. Interactions with signaling pathways that regulate podocyte survival.

2019 Findings

1. Study of molecular mechanisms of neurodegenerative conditions and diseases of the Central Nervous System

Alzheimer's disease (AD) is the most common neurodegenerative disease affecting more than 40 million people worldwide. AD is also called "type III diabetes" because of its similarities to peripheral type II diabetes, where insulin resistance is observed. That leads to neurodegeneration due to the interference of A β oligomers in insulin signaling, regulated by GSK-3 and AKT phosphorylation. Therefore, our research interests focused on the study of molecules, in particular isatinthiomycarbazones (ITSCs), which have previously been shown to inhibit the toxicity caused by A β oligomers. Our precedents suggest that the ability of ITSCs to inhibit A β aggregation and toxicity may therefore inhibit phosphorylation of GSK-3 and AKT, rescuing insulin signaling. Hence, promising molecules for further exploration as preventers of AD-related neurodegeneration might arise.

It has been suggested that polyphenolic compounds from grapes and raisins have beneficial effects against AD. Their effect though against the AD-related pathogenic functions of apoE4 is unknown. We showed that the polyphenolic extract of raisins and individual polyphenolic compounds resveratrol, quercetin, kaempferol and epigallocatechin gallate reduce the oxidative stress caused by pathogenic forms of apoE4 in neuronal cells (Figure 1).

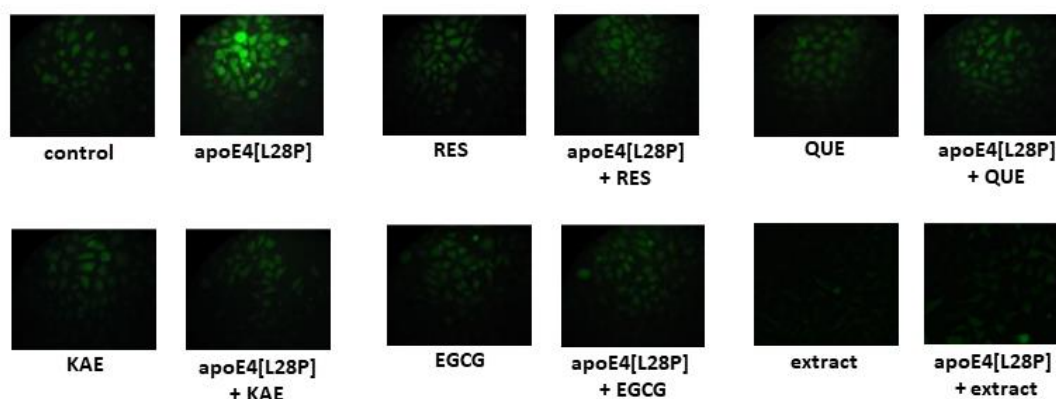


Figure 1. Effect of raisin compounds resveratrol (RES), quercetin (QUE), kaempferol (KAE) and epigallocatechin gallate (EGCG) and of polyphenolic extract from raisins on the ability of apoE4[L18P]-containing lipoproteins to induce oxidative stress in human SK-N-SH neuroblastoma cells.

2. Study of the molecular mechanisms of dyslipidemia and atherosclerosis

HDL has important anti-atherogenic functions, including antioxidant effects. We prospectively studied 199 consecutive patients admitted with acute ischemic stroke and followed them up until discharge. We measured HDL antioxidant capacity, HDL-associated paraoxonase-1 (PON1) activity and HDL-associated myeloperoxidase (MPO) levels. We showed that the impaired antioxidative activity of HDL is associated with more severe acute ischemic stroke and might also predict a worse functional outcome in these patients.

3. Diabetes Mellitus and Diabetic Nephropathy

A) In mouse pancreatic β -cells (β TC-6), nephrin signaling promotes cell survival by inhibiting apoptosis. It was observed that expression of nephrin was decreased and β -cell apoptosis was increased in islets of diabetic mice. In addition, nephrin expression was decreased in isolated islets exposed to increased glucose concentrations whereas the expression of several nephrin-associated proteins, such as CD2AP, was not affected by glucose. Therefore, it is likely that reduction of nephrin expression constitutes a premature and specific indicator of glucotoxicity in β -cells.

B) 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.

Peer-reviewed publications

- 1) Chroni A, Kardassis D. (2019). HDL dysfunction caused by mutations in apoA-I and other genes that are critical for HDL biogenesis and remodelling. *Curr. Med. Chem.* 26, 1544-1575.
- 2) Valanti E. K., Chroni A., Sanoudou D. (2019). The future of apolipoprotein E mimetic peptides in the prevention of cardiovascular disease. *Curr. Opin. Lipidol.* 30, 326-341.
- 3) Tziomalos K., Katrini K., Papagianni M., Christou K., Gkolfinopoulou C., Angelopoulou S. M., Sofogianni A., Savopoulos C., Hatzitolios A. I., Chroni A. (2019). Impaired antioxidative activity of high-density lipoprotein is associated with more severe acute ischemic stroke. *Metabolism* 98, 49-52.
- 4) Divolis G., Stavropoulos A., Manioudaki M., Apostolidou A., Doulou A., Gavriil A., Dafnis I., Chroni A., Mummery C., Xilouri M., Sideras P. (2019). Activation of both TGF β and BMP signaling pathways upon traumatic brain injury restrains pro-inflammatory and boosts tissue reparatory responses of reactive astrocytes and microglia. *Brain Commun.* 1, fcz028.

Peer-reviewed publications accepted to be published in 2020

Gkolfinopoulou C., Bourtsala A., Chroni A. (2020). Structural and functional basis for increased HDL-cholesterol levels due to the naturally occurring V19L mutation in human apolipoprotein A-I. *Biochim. Biophys. Acta Mol. Cell. Biol. Lipids In Press* (IF: 4.402)

Book chapters or proceedings

- 1) Mountaki C., Dafnis I. and Chroni A. Protective effect of currant polyphenolic compounds against pathogenic functions of apolipoprotein E4 associated with Alzheimer's disease. *FEBS Open Bio*, 9 (Suppl. 1): 230 (2019).
- 2) Gkolfinopoulou C., Bourtsala A. and Chroni A. The natural human apoA-I mutation V19L, that has been associated with increased HDL-cholesterol levels, alters apoA-I and HDL structure and functionality. *Atherosclerosis*, 287: e106 (2019).

Meeting presentations

- 1) C. Gkolfinopoulou, A. Bourtsala, A. Chroni (2019) The natural human apoA-I mutation V19L, that has been associated with increased HDL-cholesterol levels, alters apoA-I and HDL structure and functionality. 87th European Atherosclerosis Society Congress, May 26-29, 2019, Maastricht, the Netherlands
- 2) C. Mountaki, I. Dafnis, A. Chroni (2019). Protective effect of currant polyphenolic compounds against pathogenic functions of apolipoprotein E4 associated with Alzheimer's disease. 44th FEBS Congress, July 6-11, 2019, Krakow, Poland
- 3) O. Trohatou, A. Mantsiou, M. Makridakis, A. Vlahou, A. Charonis, M. Roubelakis and Drossopoulou G. (2019). Secreted conditioned media from human amniotic fluid mesenchymal stem/stromal cells ameliorate podocyte injury in isolated diabetic rat glomeruli. 31st European Renal Cell Study Group Meeting, March 28-31, 2019, Korinthos, Greece

4) Tziomalos K., Katrini K., Papagianni M., Christou K., Gkolfinopoulou C., Angelopoulou S. M., Ztriva E., Savopoulos C., Hatzitolios A. I., Chroni A. (2019). Decreased antioxidant capacity of HDL is associated with an increased risk of death during the first year after ischemic stroke. Panhellenic Conference of the Hellenic Stroke Organization, 7-9 March 2019, Athens

5) Papagiannis A., Tziomalos K., Gkolfinopoulou C., Sofogianni A., Savopoulos C., Hatzitolios A. I., Chroni A. (2019) Association between HDL-mediated cholesterol efflux capacity and severity or outcome of acute ischaemic stroke. 8th Meeting of the working groups of the Hellenic Atherosclerosis Society, 29-30 November 2019, Athens

6) C. Mountaki, I. Dafnis, A. Chroni (2019). Currant polyphenolic compounds can prevent pathogenic functions of apolipoprotein E4 associated with Alzheimer's disease. 70th Congress of the Hellenic Society of Biochemistry and Molecular Biology, 29 November-1 December 2019, Athens

7) A. Kaminari, B. Mavroidi, A. Tzinia, M. Pelecanou, M. Sagnou. Biological evaluation of new isatin derivatives as inhibitors of neurodegeneration by modulating insulin signaling 70th HSBMB Conference 29 Nov-1 Dec 2019 Athens Greece

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

Organizing scientific conferences or participating in conference organizing committees:

A. Chroni: Member of the Organizing Committee of the "Insulin-Regulated Aminopeptidase IRAP 2019 international meeting", 27-30 August 2019, Nafplio

Participation in research panels of research proposals:

A. Chroni: 1) Evaluator of scholarship applications for supporting postdoctoral researchers funded by IKY – 2nd call, 2) Evaluator of proposals submitted under the Call "Support of Researchers with Emphasis to Young Researchers - 2nd Call" of the Operational Program "Human Resources Development, Education and Lifelong Learning" (NSRF 2014-2020)

G. Drossopoulou: Evaluator of proposals submitted under the 2nd Call of the Operational Program "Research-Create-Innovate" (NSRF 2014-2020).

Review of Scientific publications:

A. Chroni: Frontiers Neurology, Journal of Lipid Research, Neurochemistry International, Angiology, Bioscience Reports, Kidney International, Pharmaceutical Medicine, Lipids, Neuronal Signaling, Reviews in the Neurosciences, ACS Chemical Neuroscience

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 scientific activities not covered by the previous questions:

A. Chroni: Invited Speaker, Round Table "Genetics", Athenian Days of Lipidology, Atherosclerosis and Vascular Disease, Hellenic Society of Lipidology, Atherosclerosis and Vascular Disease, 3-5 October 2019, Athens

Title: "Relation between apolipoprotein A-I/HDL functionality and cardiovascular risk"

Scientific distinctions and awards

PhD candidate Christina Gkolfinopoulou received the “Akogiounoglou Award” for excellence in PhD studies of the Institute of Biosciences and Applications of NCSR “Demokritos”

Educational Activities

A. Chroni:

1. Member of the Inter-Departmental Committee 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”.
2. 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: “Cardiovascular disease and current therapeutic approaches”

(1hr – 7 students, Course: “Molecular and Cellular Biology – Molecular biotechnology”)

Title of lecture: «Methods for analysis and characterization of proteins, lipids and hydrocarbons» (2 hrs - 9 students, Course: «Biochemical Analysis- Clinical Biochemistry»).

3. Guest lecturer in graduate course “Clinical Chemistry”, “Clinical Chemistry-Molecular Diagnostics” Graduate Program, Faculties of Biology, Chemistry and Nursing, University of Athens.

Title of lecture: “Alzheimer’s disease: a) diagnosis (clinical, laboratory, imaging), b) risk factors (genetic factors, age, sex, cardiovascular factors, traumatic injuries, depression, medications, etc.), c) latest data on the mechanisms of occurrence and progression of the disease and on treatment ”(2 hours – 15 students)

4. PhD supervisor for C. Gkolfinopoulou and C. Mountaki, MSc supervisor for K. Katrini.

Christina Gkolfinopoulou defended her PhD Thesis at the Department of Chemistry of the University of Athens (February 2019) entitled: "Structural and functional characterization of natural apolipoprotein A-I mutants. Study of the atheroprotective properties of high density lipoprotein (HDL) ".

Konstantina Katrini defended her MSc thesis at the Department of Chemistry of the University of Athens (February 2019) entitled: "Study of the functionality of HDL in patients with acute ischemic stroke".

5. 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.
6. Chair of PhD Advisory Committee of C. Mountaki at the Department of Chemistry, University of Athens.
7. Lecture entitled “Cardiovascular disease: causes and therapeutics”. 54th Summer School of NCSR “Demokritos”, July 2019, (1 h lecture, 250 students)
8. Member of the seven-member Examination Committee for the evaluation of thesis of M. Psykarakaki for obtaining a Doctoral Degree from the Chemistry Department of the University of Athens.
9. Member of the three-member Examination Committee for the evaluation of thesis of K. Katrini for obtaining a MSc from the Chemistry Department of the University of Athens.

10. Member of the three-member Examination Committee for the evaluation of thesis of K. Bento for obtaining a MSc from the Chemistry Department of the University of Athens.

A. Tzinia

Scientific Summer Camp, Institute of Biosciences and Applications (June-July 2019: 27 students)

P. Kitsiou:

Lecture entitled “Diabetes mellitus and pancreatic β -cell: Study of the cellular mechanisms and therapeutic approaches”, 54th Summer School of NCSR “Demokritos”, 2019 (1 hour).

G. Drossopoulou:

1) 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?” November 2019 (3 hours lecture - 33 students)

2) 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 – 22 students).

3) 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”.

4) Scientific Summer Camp, Institute of Biosciences and Applications (June-July 2019: 27 students)

Other Activities at the Institute of Biosciences and Applications

A. Chroni: Person in charge for education issues in the Institute of Biosciences and Applications (IBA). Representative of IBA in the Education Committee of NCSR “Demokritos”.

G. Drossopoulou: Person in charge for the Histology Unit of the Institute of Biosciences and Applications (IBA).

Impact factor (for 4 publications): 19,653

Citations 2019 (without self-citations): A. Chroni: 134, A. Tzinia: 86, P. Kitsiou: 20, G. Drossopoulou: 63. Total: 286 (Scopus)

Total Citations 2015-2019 (without self-citations): A. Chroni: 885, A. Tzinia: 426, P. Kitsiou 159, G. Drossopoulou: 409

h-factor: A. Chroni: 22 (Scopus), 26 (Google Scholar); A. Tzinia: 17 (Scopus); 19 (Google Scholar), P. Kitsiou: 10 (Scopus & Google Scholar); G. Drossopoulou: 14 (Scopus), 15 (Google Scholar)

Current External Funding

1) 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 Dr. A. Chroni as Principal Investigator for NCSR Demokritos.

Duration: 2018-2021

Total funding (lab): 188.000 €

Funding of the lab for 2019: 55.000€

2) 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 Dr. A. Chroni as Principal Investigator.

Duration: 2018-2020

Total funding (lab): 40.600€

Funding of the lab for 2019: 20.000

3) 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€

4) 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 Diseases Genetics

Research Staff

Gerassimos Voutsinas, Research Director (Researcher A')

Angeliki Delimitsou, Collaborating Graduate Student – *PhD completed*

Stamatia Katarachia, Collaborating Graduate Student

Ismini Chatzidaki, Post-graduate research collaborator

Foteini Athanasopoulou, Graduate student

Konstantina Taouksi, Undergraduate student – *Undergraduate dissertation completed*

Stefanos Smyrniotis, 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

2019 Findings

Gene-Specific Intron Retention Serves as Molecular Signature that Distinguishes Melanoma from Non-Melanoma Cancer Cells in Greek Patients: *c-MYC* and *Sestrin-1* genes proved to undergo intron retention specifically in melanoma. Interaction maps of proteins encoded by genes being potentially targeted by retained intron-accommodated miRNAs were generated and *SRPX2* was additionally delivered to our melanoma-specific signature. Novel ORFs were identified in *MCT4* and *Sestrin-1* introns, with potentially critical roles in melanoma development. In conclusion, the property of *c-MYC*, *Sestrin-1*, and *SRPX2* genes to retain specific introns could be clinically used to molecularly differentiate non-melanoma from melanoma tumors.

Functional characterization of CHEK2 variants in a *Saccharomyces cerevisiae* system: An *in vivo* yeast-based assay was used to functionally characterize 120 germline *CHEK2* missense variants, distributed along the protein sequence, as well as two large in-frame deletions, originating from genetic test results in breast cancer families, or selected from the ClinVar database. Of these, 32 missense and two in-frame deletions behaved as non-functional, 73 as functional, and 15 as semi-functional, after comparing growth rates of each strain with positive and negative controls. The results of this, largest to date, yeast-based assay, evaluating *CHEK2* variants, can complement and assist in the classification of rare *CHEK2* variants with unclear clinical significance.

Revisiting Histone Deacetylases in Human Tumorigenesis: The Paradigm of Urothelial Bladder Cancer: The HDAC/SIRT (super-)family contains 18 members, which are divided in five classes, with each family member being differentially expressed in normal urinary bladder tissues. Since a strong association between irregular HDAC expression/activity and tumorigenesis has been previously demonstrated, we herein attempt to review the accumulated published evidence that implicate HDACs/SIRTs as critical regulators in urothelial bladder cancer. Moreover, the most extensively investigated HDAC inhibitors (HDACis) are also analyzed, and the respective clinical trials are also described.

PI3K/AKT pathway genetic alterations and dysregulation of expression in bladder cancer: Three pathogenic mutations (two missense and one frameshift) were identified in exon 20 of *PIK3CA* {c.3140A>G (p.His1047Arg), c.[3172A>T(;):3174C>T] (p.Ile1058Phe), c.3203dupA (p.Asn1068Lysfs*5)} after laser capture microdissection, whereas *PTEN* mRNA expression was found to be downregulated in bladder cancer tissues compared to normal bladder urothelium.

Upregulation of cytoplasmic and nuclear p-AKT expression was detected in low grade tumors, whereas in infiltrating carcinomas p-AKT was shown to be downregulated and confined to the cytoplasm. PTEN expression was weak and mainly cytoplasmic in superficial tumors, but stronger and nuclear in the infiltrating tumors. In conclusion, PI3K/AKT pathway activation is crucial for bladder cancer initiation and progression. In this context, *PIK3CA*, p-AKT and nuclear PTEN could be used along with other biomarkers for prognosis and selection of appropriate therapy in the clinical management of bladder cancer.

Publications

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)

Articles accepted for publication in 2020

Iliou A., A. Panagiotakis, A.F. Giannopoulou, D. Benaki, M. Kosmopoulou, A.D. Velentzas, O.E. Tsitsilonis, I.S. Papassideri, G.E. Voutsinas, E.G. Konstantakou, E. Gikas, E. Mikros and D.J. Stravopodis (2020). Malignancy Grade-Dependent Mapping of Metabolic Landscapes in Human Urothelial Bladder Cancer: Identification of Novel, Diagnostic, and Druggable Biomarkers, *International Journal of Molecular Sciences* 21: 1892. (IF: 4.556)

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.

Reviewer of research articles for: *Scientific Reports* (3 articles), *OncoTargets and Therapy*, *Cancers* (5 articles).

Educational Activities

Angeliki Delimitsou has presented her **Doctoral Thesis** entitled "Functional evaluation of variants of unknown clinical significance and characterization of new mutations in genes involved in hereditary breast-ovarian cancer" (June 2019), at the Department of Medicine of the National and Kapodistrian University of Athens (NKUA).

Konstantina Taouksi has presented her **Dissertation** entitled "Mitochondrial unfolded protein response (UPR^{mt}) in cancer" (September 2019), at the Department of Biology of the School of Sciences of the National and Kapodistrian University of Athens (NKUA).

Lecture entitled "Introduction to the human genome", Common Post-Graduate Program "Applied Biochemistry" of the Dept of Chemistry, University of Patras, and the Institute of BioSciences and Applications, NCSR "Demokritos", Tuesday 14 May 2019 (number of attendants: 10 students, teaching hours: 2).

Lectures and lab training of high-school students at the IBA 2019 Summer Camp, June-July 2019 (number of attendants: 3 pupils, teaching hours: 30).

Teaching of the undergraduate course: "Introduction to Molecular Biology" (4 semesters), American College of Greece (Deree College), Agia Paraskevi Attikis, January - December 2019 (number of attendants: 80 students, teaching hours: 184).

Lecture entitled "Pharmaceutical targeting of molecular chaperone Hsp90 in bladder cancer therapy", Athens Metropolitan College, Wednesday, February 6, 2019 (number of attendants: 30 students, teaching hours: 2).

Lecture entitled "Molecular mechanisms of carcinogenesis and pharmaceutical inhibition of selected cellular targets for therapy", Post-Graduate Program "Development of New Drugs: Research, Circulation, and Access", Department of Medicine, National and Kapodistrian University of Athens, February 22, 2019, Athens (number of attendants: 20 students, teaching hours: 3).

Lecture entitled "Molecular mechanisms of carcinogenesis and pharmaceutical inhibition of selected cellular targets for therapy", Post-Graduate Program "Applications of Biology in Medicine", Departments of Biology and Medicine, National and Kapodistrian University of Athens, April 16, 2019, Athens (number of attendants: approx. 20 individuals, teaching hours: 3).

Other Activities at the Institute of Biosciences and Applications and NCSR "Demokritos"

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".

Deputy Director of IBA (1-1-19 until 15-11-19 and 16-11-19 until 31-12-19).

Member of the Research Council of the Institute (ESI) (June 6, 2017 – the present day).

Member of the Research Committee of NCSR "Demokritos" (May 8, 2017 – the present day).

Member of 1 Reviewer Committee for research personnel promotion at the IBA (October 9, 2019).

Member of 11 Reviewer Committees for hiring scientific collaborators at IBA (January 25, March 5, March 19, April 1, April 9, April 10, May 8, July 10, July 30, September 5, October 2, October 17, 2019), and 1 Committee for the Evaluation of Offers in a relevant Competition (April 10, 2019).

Alternate member of the Supervisory Committee for the election of a Research Representative on the Board (May 14, 2019).

Alternate member of the Acceptance Committee for a Biological Macromolecule Crystallization robot system (November 26, 2019).

Impact factors (for 4 publications): 14.615

Number of citations for 2019 (without self-citations): 83

Number of citations 2015-2019 (without self-citations): 351

h-factor: 19

PROGRAMME B

"MODEL SYSTEMS FOR THE STUDY OF CELL FUNCTION"

Research Group: Molecular Genetics of Insects and Biotechnology

Research Staff

Luc Swevers, Research Director

Vasiliki Labropoulou, Senior Researcher

Anna Kolliopoulou, Postdoctoral Fellow

Min Feng, Postdoctoral Fellow

Yongchao Zhao, Collaborating Graduate Student

Feifei Ren, Collaborating Graduate Student

Stavroula-Ioanna Pariou, Diploma Student

Dimitra Stefanou, Technical Specialist

Dimitris Kopanelis, 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) 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, production of recombinant RNA viruses and “viral-like particles” (VLPs), 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 and moulting-accelerating compounds, functional expression of metabolic enzymes that are involved in insecticide resistance.
- (5) Antiviral immune response in insects. Development and improvement of methods for screening of molecules, mainly antimicrobial peptides (AMPs) that prevent viral entry in insect cells.

2019 Findings

Metabolomics studies of infection of insect cells by cricket paralysis virus (CrPV). The study revealed the importance of central carbon metabolism in the two types of infection (pathogenic and persistent) that were investigated although opposite changes in the levels of amino-acids and carbohydrates were observed. Characteristic changes were also detected in the abundance of the poly-amines spermine and spermidine.

The response of endogenous retroviral elements (ERVs) and PIWI-associated RNAs (piRNAs) during baculovirus infection of lepidopteran insects. Bioinformatics methods were employed to identify ERVs in the genome of the wild silkworm *Antheraea* and to study the changes in expression following baculovirus infection.

Production of viral-like particles based on lepidopteran cytovirus. Viral-like particles (VLPs) based on the major capsid protein were produced successfully by the baculovirus expression system and purified to high concentration by ultracentrifugation. Current efforts focus on the production of dsRNA by the baculovirus expression system and the development of methods for their recruitment to VLPs.

Antiviral immune response in insects. The expression and purification of antimicrobial peptides was continued and their ability to prevent bacterial growth was investigated. In parallel, studies were continued to investigate the action of antimicrobial peptides to prevent the entry of baculoviruses in insect cell lines. Other studies comprise the transcriptional response of immune

genes after viral infection and after “vaccination” with antimicrobial peptides and “cytokines”. The consequences of expression of “cytokines” were also investigated with functional experiments in Sf21 insect cells. The results did not show a strong transcriptional response following expression of SVC1, SVC2 and SVC3 (homologs of Vago) but present strong induction following expression of B2 of FHV virus.

Original publications

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

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.

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* 294, 887-899.

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 *Antheraea pernyi* with ApNPV Baculovirus. *Viruses* 2019, 11, 421.

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. *Wiley Interdiscip. Rev. RNA*. 2019, e1555.

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.

Feng, M., Zhang, N., Xie, T., Ren, F., Cao, Z., Zeng, X., Swevers, L., Zhang, X., and Sun, J. (2019). Chichen type III interferon produced by silkworm bioreactor induces ISG expression and restricts ALV-J infection in vitro. *Appl. Microbiol. Biotechnol.* 103, 8473–8483 (2019).

Santos, D., Mingels, L., Vogel, E., Wang, L., Christiaens, O., Cappelle, K., Wynant, N., Gansemans, Y., Van Nieuwerburgh, F., Smagghe, G., Swevers, L., and Vanden Broeck, J. (2019). Generation of Virus- and dsRNA-Derived siRNAs with Species-Dependent Length in Insects. *Viruses* 2019, 11, 738.

Wang, L.-L., Swevers, L., Rombouts, C., Meeus, I., Van Meulebroeck, L., Vanhaecke, L., and Smagghe, G. (2019). A Metabolomics Approach to Unravel Cricket Paralysis Virus Infection in Silkworm Bm5 Cells. *Viruses* 2019, 11, 861.

Original publications that are accepted for 2020

Swevers, L., Feng, M., Ren, F., and Sun, J. (2020). Antiviral defense against Cypovirus 1 (*Reoviridae*) infection in the silkworm, *Bombyx mori*. *Arch. Insect Biochem. Physiol.* 103, e21616. (IF: 1.198)

Wei P, Demaeght P, De Schutter K, Grigoraki L, Labropoulou V, Riga M, Vontas J, Nauen R, Dermauw W, Van Leeuwen T. (2020). 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 spiroticlofen. *Pest Manag Sci.* 276, 1142-1153. (IF: 3.255)

Presentations in Conferences

Y. Zhao, F. Ren, Q. Lu, J. Sun, L. Swevers (2019). Biotechnological solutions for delivery of dsRNA to crop pests that do not involve transgenic organisms. 3rd iPlanta Conference “What future for RNAi-

based products: RNAi modified plants or spray products”, February 27 – March 1, 2019, Oeiras, Portugal.

C.N.T. Taning, O. Christiaens, L. Swevers, L., G. Smagghe (2019). Exploiting an engineered insect virus as a delivery vehicle to improve RNAi effects in fruitflies. 3rd iPlanta Conference “What future for RNAi-based products: RNAi modified plants or spray products”, February 27 – March 1, 2019, Oeiras, Portugal.

O. Christiaens, C.N.T. Taning, L. Swevers, L., G. Smagghe (2019). Viral-based dsRNA delivery systems for use in pest and disease control. 15th ISRB (International Society for Biosafety Research) Symposium, April 1-4, 2019, Tarragona, Spain.

A. Kolliopoulou, Y. Zhao, C.N.T. Taning, O. Christiaens, F. Ren, Q. Lu, J. Sun, G. Smagghe, L. Swevers (2019). Virus-induced gene silencing in insects. 1st International Molecular Plant Protection Congress, April 10-13, 2019, Adana, Turkey.

C.N.T. Taning, O. Christiaens, X.X. Li, L. Swevers, H. Casteels, M. Maes, G. Smagghe (2019). A novel and efficient virus-based RNAi delivery system for fruitflies. IUPAC International Congress, May 19-24, 2019, Gent, Belgium.

C.N.T. Taning, O. Christiaens, L. Swevers, L., G. Smagghe, G. (2019). Improved RNAi effects in fruit flies by exploiting an engineered insect virus as a delivery vehicle. 8th International Symposium on Molecular Insect Science, July 7-10, 2019, Sitges, nr Barcelona, Spain.

S. Vlogiannitis, K. Mavridis, W. Dermauw, S. Snoeck, E. Katsavou, E. Morou, P. Harizanis, L. Swevers, T. Van Leeuwen, T., J. Vontas (2019). The 46th Apimondia International Apicultural Congress, September 8-12, 2019, Montreal, Canada.

O. Christiaens, Z.M. Reyna, M.G. Tardajos, M. Dash, K. Prentice, R. Sharma, N.L. Castellanos, K. De Schutter, L. Swevers, E. Van Damme, P. Dubruel, P., G. Smagghe, (2019). Factors on dsRNA stability and cellular uptake important for RNAi efficacy in pest insects. ESA (Entomological Society of America) 2019 Annual Meeting, November 17-20, 2019, St. Louis, MO, USA.

A. Kolliopoulou, D. Kontogiannatos, Y. Zhao, F. Ren, Q. Lu, J. Sun, J., L. Swevers (2019). Gene silencing goes viral: The use of baculovirus-encoded viral-like particles (VLPs) as a potential environmentally safe biotechnological RNAi application in insect pests. 70th National Conference Hellenic Society of Biochemistry & Molecular Biology, November 29- December 1, 2019, Athens, Greece.

Other scientific activities

Participation in editorial boards of scientific journals:

Member of the editorial board of the scientific journals: «Archives of Insect Biochemistry and 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).

Reviews for research journals:

Reviewer of scientific articles for the journals «Archives of Insect Biochemistry and Physiology» (5x), «Chemosphere», «Frontiers in Microbiology», «Heliyon», «Journal of Insect Physiology» (2x), «Journal of Invertebrate Pathology» (2x), «Journal of Pest Science» (2x), «Pest Management Science» (3x), «PLoS ONE» (2x), «Scientific Reports» (2x), «Science of the Total Environment », «Turkish Journal of Entomology», «WIREs RNA» (L. Swevers).

Educational activities

- Participation in the Bi-Institutional Program of Graduate Studies of «Applied Biochemistry: Clinical Chemistry, Biotechnology, Validation of Pharmaceutical Drugs» (collaboration with the Chemistry Department of the University of Patras)
 - Molecular Pharmacology – Immunology: hourly lecture with title: «RNAi as an antiviral defense system in insects» (L. Swevers)
 - Molecular Pharmacology – Immunology: hourly lecture with title: «Innate Immunity» (V. Labropoulou)
 - Molecular and Cellular Biology – Molecular Biotechnology: hourly lecture with title «The Baculovirus Expression System» (L. Swevers)
- Participation in «Summer Scientific Laboratories for High-School Students» (July 2019) (L. Swevers and V. Labropoulou).
- Completion of PhD thesis of Luoluo Wang: «A Metabolomics Study of Virus-Insect Interactions and its Potential for Bee Disease Monitoring». Faculty of Bioscience Engineering, Ghent University, Βέλγιο (October 2019). Member of the three member evaluation committee and co-supervisor (L. Swevers).
- Half-hourly lecture with title «CRISPR/Cas and the rise of genome editing techniques» at the Summer School of NCSR «Demokritos» (L. Swevers).

Other activities at IB-A and NCSR “D”

- Member of the scientific board of the institute (L. Swevers).
- Responsible for the following instruments: Fluostar Microplate Fluorometer, HPLC Hewlett Packard, microplate reader for luminescence and fluorescence TECAN InfiniTE M-200 (L. Swevers).
- Member of the committee of evaluation of the President of the Centre for the first half of his office (V. Labropoulou).
- Member of the committee of evaluation of the Director of the Institute for the first half of his office (V. Labropoulou).
- Member of the management committee for the project of BIOIMAGING-GR (V. Labropoulou).

Impact factors (for 9 publications): 29.878

Total citations for 2019 (without self-citations):

Swevers L: 262

Labropoulou V: 44

Total citations for 2015-2019 (without self-citations): 1272

Swevers L: 1194

Labropoulou V: 177

h-factor:

L. Swevers: 30 (Scopus), 34 (Google Scholar)

V. Labropoulou: 12 (Scopus), 14 (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 2019: 0€.

Project FWO–Vlaanderen (Belgium) with title *Characterization of extracellular RNA-signals and their role in antiviral immunity in insects* and coordinator for the Greek participation Dr. L. Swevers.
Duration: 1/2019-12/2022.

Coordinator: J. Vanden Broeck (Belgium)

Total funding of the project: 700.800€
Total funding of the laboratory: 0€
Funding of the laboratory for 2019: 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 11/18-4/20): 106.230€
Funding of the laboratory for 2019: 0 €.

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: 9/2017-2/2019.

Research Group: Chemical Ecology and Natural Products

Research Staff

Maria Konstantopoulou, Senior Researcher

Dimitris Raptopoulos, Graduate Research Associate (PhD)

Eleni Koutsoumpeli, Postdoctoral Fellow

Anastasia Fytrou, 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.

2019 Findings

In the framework of OLEFINE (OLEaginous yeast platforms for FINE chemicals) HORIZON 2020 biotechnological methods using yeasts were developed in order to produce insect sex pheromones.

To certify that yeast-produced pheromones are homologous to the chemically produced ones we tested the response of male insects' antennae to yeast-produced pheromones using electrophysiological methods ie EAG and EAD-GC (Figure1). In addition, we conducted behavioural tests with male insects in wind tunnel with movement tracking by means of a camera (behavioural tracking). For the verification of activity of yeast-produced pheromones under field conditions we conducted field tests in two regions of Greece (Northern and Central). In these experiments, homologation was affirmed.

We maintain artificial colonies of insects that are major pests of crops of significant economic importance to be used in electrophysiological and behavioural tests. We established a new colony of *Plodia interpunctella*, an important pest of stored products in our efforts to isolate enzymes involved in the biosynthesis of the insect's pheromone, in the framework of OLEFINE.

An important development for progress of the break-through technology of in-yeast pheromone production is the approval and funding of a new European Program called PHERA "Pheromones for

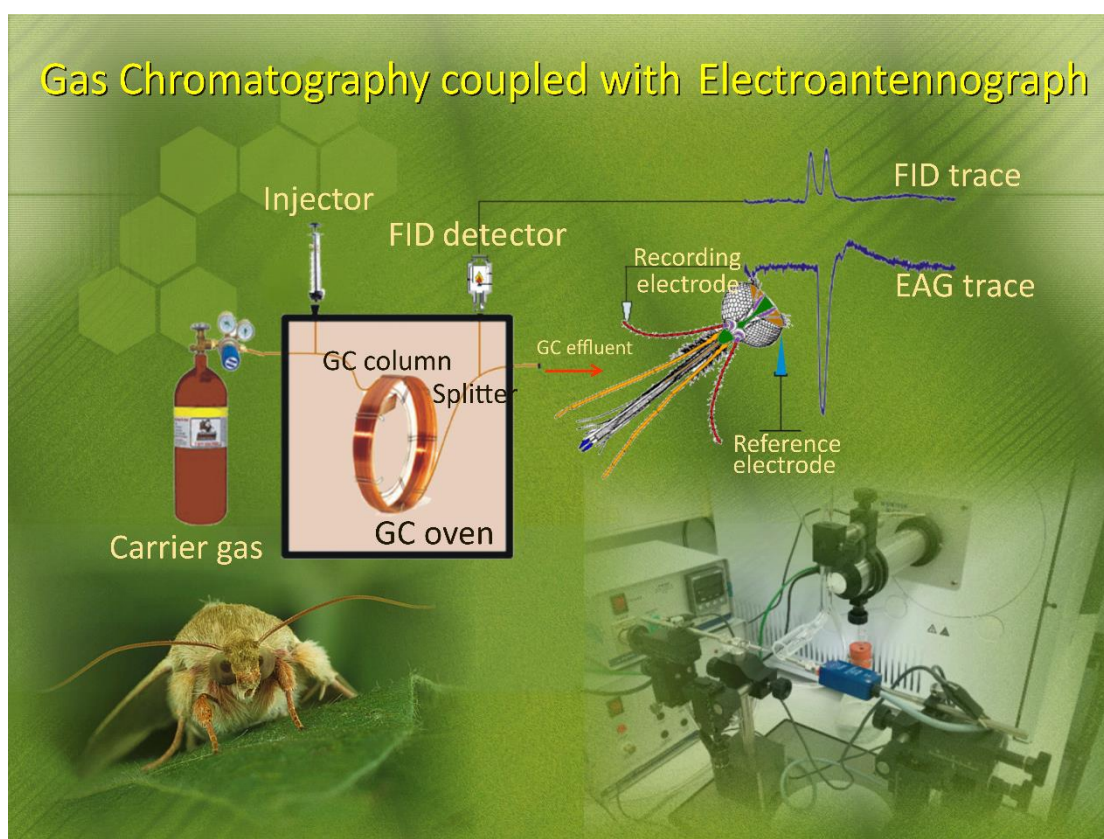
Row crop Applications" (2020-2023) (H2020-BBI-JTI-2019 GA 886662) in which the laboratory participates as a subcontractor.

In the context of the identification of infochemicals and other bioactive metabolites of plant/natural origin (Biological Control Agents, BCAs) to be used as "smart" insecticides we studied: i) the effect of secondary metabolites of *Pistacia lentiscus* and one strain of the fungus (SMU-21) on the viability of of adult of *Lobesia botrana* and ii) the effect/potency of essential oils of aromatic plants as well as the determination of their active chemical compounds on insect larvae as well as their electro-physiological response in adult insects. We proceeded to the chemical analysis of plant fractions by gas chromatography-mass spectrometry (GC-MS) to determine the bioactive substances that confer to the observed activity. Work in progress.

In collaboration with the Laboratory of Cell Proliferation and Aging of IBA we examined the the cytostatic / cytotoxic action as well as the antioxidant action of plant extracts and their fractions from a collection of extracts which was created and maintained in the laboratory.

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

We continued studying the psychophysiological effect of therapeutic gardens to olfactory stimuli in collaboration with the Medical School and the Agricultural University of Athens.



Publications

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 13: 1-12.

Presentations at Scientific Conferences

Fytrou A., Koutsoumpeli E. and Konstantopoulou M.A Effect of secondary metabolites of *Pistacia lentiscus* and *Mucor hiemalis* strain (SMU-21) on the viability of *Lobesia botrana* adults. 18^o Panhellenic Meeting of Hellenic Entomological Society, 15-18 October, Komotini, Abstract:112-113

Koutsoumpeli E. Raptopoulos Dimitris and Konstantopoulou M.A. Biologically produced pheromones: Electrophysiological responses of *Helicoverpa armigera* 18^o Panhellenic Meeting of Hellenic Entomological Society 15-18 October, Komotini. Abstract:108-109

Other Scientific Activities

Union of Greek Researcher representative in National Council for Research and Innovation (NCRI)

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

Researcher and Specialist Functional Scientist representative in NCSR “Demokritos” Board of Directors

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

Member of organizing committee of XII European Entomological Congress 2022 held in Crete

Reviewer of research proposals for General Secretary Research and Technology

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, Insects.

Educational Activities

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

Other activities for the Institute of Biosciences & Applications

President of the Scientific Advisory Board (ESI) of the Institute (06/2019-06/2020).

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 “OPENSREEN-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.

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

Impact Factors (for 1 publication): 0.565

Citations 2019 (without self-citations): 57

Total Citations 2015- 2019 (without self-citations): 273

h-factor: 13 (Scopus), 16 (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 2019: 337.533,52 €

Research Group: Chronobiology

Research Staff

Anastasia Prombona, Senior Researcher

Angeliki Galeou, Postdoctoral Fellow (until March)

Stavroula Mamoucha, Postdoctoral Collaborator

Vasileios Tomaropoulos, Agricultural University of Athens, Biotechnology Department, Diploma student

Marisofi Pouloupoulou, University of Thessaly, Department of Biochemistry and Biotechnology, Summer practice student

Evangelos Kokkinas, Agricultural University of Athens, Biotechnology Department, Summer practice student

Research Interests

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

The circadian clock of plants

This project focuses on the study of rhythmically expressed genes in *P. vulgaris* primary leaves and their synchronization under 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-correlation with pathological conditions

This project concentrates on the study of the role of the biological circadian clock in carcinogenesis, more specifically in the regulation by the circadian clock of the expression of the oncogene *c-MYC* and the interaction of the oncoprotein with components of the circadian clock. In addition, we investigate the effect of bioactive and pharmaceutical compounds on the clock function and the oncogenesis. The regulation of gene expression related to chromatin remodeling at the promoters of clock genes under physiological and pathological conditions is also investigated.

2019 Findings

The circadian clock of P. vulgaris

The aim of our recent investigations in *P. vulgaris* is to understand the involvement of circadian oscillator genes in the mechanism of clock resynchronization by light. For this purpose, we studied in detail the rhythmic gene expression of two central oscillator genes, the morning-phased *PvLHY* and the evening-phased *PvTOC1* following exposure to continuous white light at various times of the photoperiod (Figure 1). Our results revealed that at each specific time of light application both genes displayed the same alteration in their rhythmic phase that is advance, delay or no change in regard to the pre-existing phase under the photoperiod. This coincidence shows that the two genes are interlocked and probably coordinated by a common mechanism. On the other hand, the rhythmic leaf movements showed a totally different synchronization pattern which indicates that this physiological process is not a direct output of the central oscillator (Galeou and Prombona, manuscript submitted for publication).

Furthermore, we investigated the role of the putative Evening Complex (EC) in *P. vulgaris*. In *Arabidopsis thaliana*, the EC is formed as a heterotrimer by the clock proteins LUX, ELF3 and ELF4 and regulates evening expressed clock genes. In protoplasts from bean primary leaf tissue the effect of the overexpression of the orthologue bean proteins PvLUX, PvELF3 and PvELF4 was investigated on LUC reporter constructs with the promoters of the evening expressed genes PvLUX, PvTOC1 and PvELF4. Our results showed that PvLUX has repressive activity which is not

influenced by the presence of the two other proteins PvELF3 and PvELF4. This is different from the findings in *A. thaliana*, and requires further investigation (Diploma thesis of V. Tomaropoulos).

Interaction of the circadian clock with oncogenesis

We constructed mutants of the oncoprotein c-MYC and the transactivation potential in the presence of its partner MAX is studied on circadian promoters.

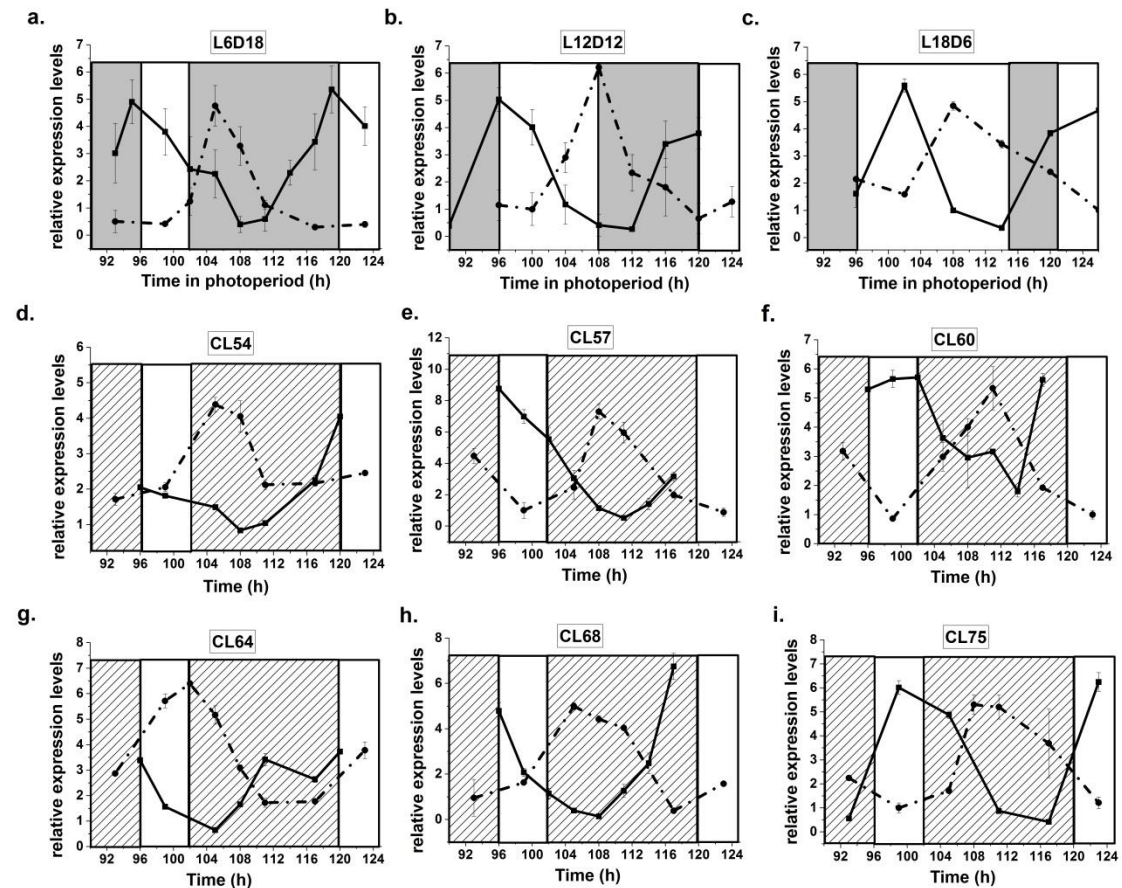


Figure 1: Resynchronization of the rhythmic expression of the central oscillator genes PvLHY (solid line) and PvTOC1 (dash-dot line) in *Phaseolus vulgaris*. Bean seedlings were grown in long night photoperiod (L6D18) and exposed to continuous light (CL) applied at different times of the photoperiod (CL54: beginning of scotophase, CL57: 3 hours after dusk, CL60: 6 hours after dusk, CL64: 10 hours after dusk, CL68: 14 hours after dusk and CL75: plants were kept in darkness for 3 hours after the dawn of the following day). a-c: white regions represent the day and grey the night of the photoperiod (L6D18=6 hours light and 18hours dark, L12D12=photoperiod of equal day-night length, L18D6=18 hours light and 6 hours dark); d-i: white regions represent subjective day and dashed subjective night.

Publications 2019

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. (2018) 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.

Conferences 2019

S. Mamoucha, V. Liapis, A. Prombona (2019) Antimicrobial effect of the essential oil from the plant species *Laurus nobilis L.*, 9th PANHELLENIC CONGRESS OF CLINICAL MICROBIOLOGY, Athens, Royal Olympic Hotel, 21-23 February 2019, oral presentation EA 39

S. Mamoucha, V. Liapis, A. Prombona (2019) Testing the antimicrobial effect of hydrodistillation products of different plant species, 45th ANNUAL PANHELLENIC MEDICAL CONGRESS, Athens, DIVANI CARAVEL HOTEL, 15-18 May, oral presentation no. 106

Mamoucha S., Liapis V., Prombona A. (2019) Antimicrobial activity of propolis and selected aromatic and medicinal plants 16th Conference of the Hellenic Botanical Society, 10-13 October, Athens, Oral presentation, Session IV.

Angeliki Galeou, Vasilios Tomaropoulos and Anastasia Prombona (2019) *In vitro* study of *Phaseolus vulgaris* circadian core clock elements, 70th HSBMB Annual Conference 29 Nov-1 Dec, Athens, Eugenides Foundation, Poster no 1

Education

Supervision and guidance of the Diploma student V. Tomaropoulos and of the summer practice students M. Pouloupoulou and E. Kokkinas.

Other activities in IB-A

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

Impact factor for 1 publication: 4.183

Citations 2019 (self-citations excluded): 25

Citations 2015-2019 (self-citations excluded): 92

h-factor: 8 (Scopus and Google Scholar)

Research Group: Microbial Molecular Genetics laboratory

Research Staff

Vicky Sophianopoulou, Research Director

Christos Gournas, Researcher

Ada Biratsi, Post-Graduate Fellow (PhD candidate)

Amalia Megarioti, Post-Graduate Fellow (PhD candidate)

Alexandros Valianatos, Post-Graduate Student (Master Thesis)

Spiros Gaitanos, Undergraduate Student (Diploma Thesis)

Tatiana Zakopoulou, Undergraduate Student (Diploma Thesis)

Eleftheria Giannioti, Undergraduate Student (Practical work)

Research Interests

Our group is primarily interested in the function, regulation and organization of the fungal plasma membrane (PM). The plasma membrane, as the boundary between the cell and its environment, is a platform for numerous functions. A major challenge is to understand how the PM coordinates these diverse processes while maintaining its barrier function, and the mechanisms underlay them. The general concept of our work is to understand how specific compartments/domains of the plasma membrane regulate their structure and function to promote the activity and /or trafficking of nutrient transporters, persistence of fungal cells, critical stress responses 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 elucidate the molecular mechanisms underlie detoxification of toxic amino acid analogues. L-Azetidine-2-Carboxylic Acid (AZC) is a toxic analogue of proline, produced by the flowering plant *Convallaria majalis* (valley lily), certain species of the genus *Polygonatum* and beets (*Beta vulgaris*). In nature, AZC has a protective role for the plants that produce it, and at the same time is a toxic substance for a multitude of organisms, including various bacteria, fungi and even mammals. Our studies targeted to understanding the molecular mechanism(s) underlie detoxification and catabolism of AZC in soil fungi.

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

2019 Findings

Study of the lateral compartmentalization of the plasma membrane:

In the context of the study of the molecular mechanism of endocytosis of eisosomal proteins, we obtained strong indications that the eisosomal proteins SurG and AnNce102 of *A. nidulans* follow different pathways for their vacuolar degradation in dormant conidiospores and in growing hyphae. More specifically, in dormant spores, the sorting of these proteins to vacuoles requires clathrin-

dependent endocytosis from the plasma membrane, while in growing hyphae direct sorting from the Golgi to the vacuole occurs.

In the context of the study of the role of eisosomes during quiescence, 1) it was shown that the quantity of the main eisosomal proteins Pil1, Lsp1 and Nce102 increases 3-5 fold in cells expressing markers of quiescent cells, while additional eisosomal proteins of unknown function are also induced (Fmp45, Ynl194c) (Figure 1A-C). The latter proteins require intact eisosomes in order to be protected from endocytosis in quiescent cells. Moreover, cells lacking Lsp1 show defective expansion of MCCs during quiescence, and this function probably involves the TORC1-regulated kinase Npr1. In total, the above results support that MCCs have an important role in quiescent cells. 2) the contribution of several transcription factors to the expression of Pil1 and Lsp1 was investigated. Results show that MCCs are induced in the presence of a non-fermentable carbon source and in the absence of glucose. The involvement of Mig1, a transcriptional repressor of gene expression in the presence of glucose, in the process is under investigation.

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

In the context of the study of the molecular mechanism underlying the detoxification of the toxic analogue of proline L-Azetidine-2-carboxylic acid (AZC) in *A. nidulans*, we measured the hyphal growth rate of several strains in the presence or absence of AZC, in submerged liquid cultures, using confocal microscopy. The results (Fig. 1D) show that strains lacking the AZC hydrolase, AzhA, show significantly reduced growth rates in the presence of AZC, while a double *azhAΔ ngn2Δ* (AZC acetyltransferase) shows dramatic reduction of the growth rate in AZC as sole nitrogen source. Only 20% of the spores of the strain were able to germinate. In total, these results indicate the high toxicity of AZC in the double deletion strain.

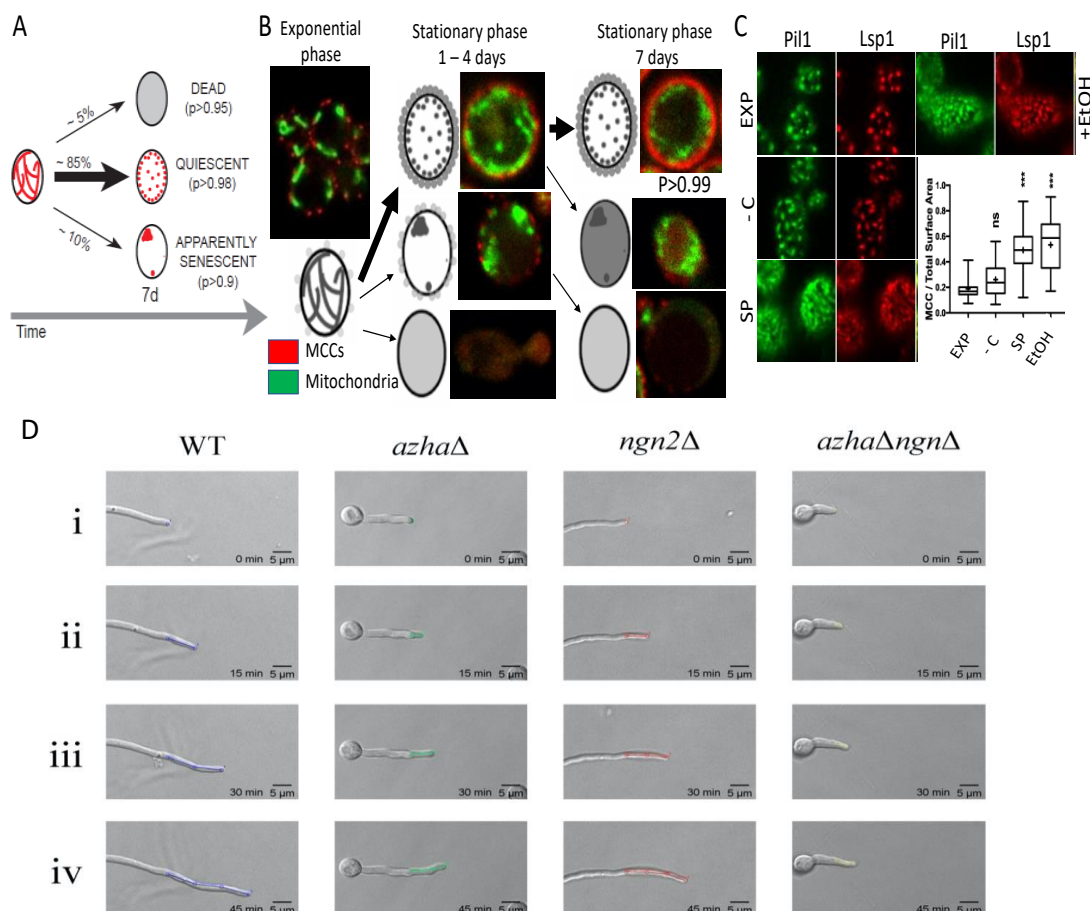


Figure 1. A) The morphology of the mitochondrial network is a reliable marker of cellular respiration and quiescence, and changes from network-like in the exponential phase, to cortical in Quiescent cells. Apparently senescent cells do not respire and possess globular mitochondria, while dead cells are non-fluorescent. **B)** Working model, based on our results, on the formation of Q cells (bold arrows). Following glucose exhaustion, a small percentage of cells never starts respiration, obtains globular mitochondria and never induces MCCs. These cells eventually die and become non-fluorescent. The majority obtain respiratory-active cortical mitochondria, and induce MCCs. Some of them eventually become senescent (globular mitochondria, Cytoplasmic Pil1), but the majority enters deep quiescence and obtains even more MCCs. **C)** Respiration is sufficient to trigger the expansion of MCCs. Induction of MCCs in stationary phase (SP) is not provoked by artificial carbon starvation (-C); the additional presence of a respiratory carbon source (ethanol, EtOH) is required. **D)** Growth rate of wt and mutant strains of *A. nidulans*, carrying single or double deletions of genes *azhA* (AZC-hydrolase) and *ngn2* (AZC-acetyl-transferase), the products of which are involved in the detoxification and the assimilation of AZC. Time-lapse confocal images (45 minutes total, 15 minutes interval) were used to study the growth rate of these strains. Strains were grown for 18h at 25 °C in submerged liquid cultures using Urea and AZC as nitrogen sources.

Publications in peer-reviewed journals

Athanasopoulos, A., André, B., Sophianopoulou, V. and Gournas, C. (2019). Fungal Plasma membrane domains. *FEMS Microbiology Reviews* (IF: 11.524)

Presentations in Conferences

G. Kapetanakis, E. Bodo, C. Gournas, M. Prévost, B. André, I. Georis. 2019. Characterization of three amino acid excretion proteins in yeast *Saccharomyces cerevisiae*. Emerging Applications of Microbes. Leuven, Belgium.

A. Megarioti, V. Sophianopoulou, B. André, C. Gournas. Eisosomes in Quiescence. International Conference on Yeast Genetics and Molecular Biology. 2019. Gothenburg, Sweden

E. Saliba, N.P. Guarini, M. Evangelinos, C. Gournas, F. Corrillon, I. Georis, B. André. Activation of TORC1 in Response to H⁺ Influx: Role of Pma1. International Conference on Yeast Genetics and Molecular Biology, 2019, Gothenburg, Sweden.

Other Scientific activities

Participation in Greek and international meetings and federations:

- Head of the Microbial Molecular Genetics lab of IB-A (2004-today) (V. Sophianopoulou).
- Member of the Advisory committee of the department of Biology, NKUA, for the PhD thesis of A. Biratsi (V. Sophianopoulou).
- Members of the Advisory committee of the department of Biology, NKUA, for the PhD thesis of A. Megarioti (V. Sophianopoulou, C. Gournas).
- Member of the Evaluation Committee for the recruitment of Collaborating Researchers at IB-A within the Industrial Research Fellowship Program of Stavros Niarchos at NCSR “Demokritos” (V. Sophianopoulou).
- Member of the Evaluation Committee for the recruitment of Post-graduate students within the Post-graduate Education Course on «Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products» at the Department of Chemistry, University of Patras (2018-2020) (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 Advisory Committee for the diploma thesis of T. Zakopoulou, Chemistry Department, University of Athens (V. Sophianopoulou, C. Gournas).
- Member of the Advisory Committee for the diploma thesis of S. Gaitanos, Chemistry Department, University of Athens (V. Sophianopoulou).

Participation in editorial boards of scientific journals:

- Member of the editorial board of Scientific Reports (Published by Springer Nature) (V. Sophianopoulou)
- Invitation to join the Editorial Board of International Journal of Molecular Sciences, as Topic Editor (V. Sophianopoulou).

Reviewing of grant applications:

- Ministry of Development and Investments - Support for researchers with emphasis on young researchers cycle B (ΕΣΠΑ 2014-2020) (V. Sophianopoulou)
- IKY State Scholarships Foundation (V. Sophianopoulou)
- Cyprus Research Promotion Foundation, Program “Excellence Hubs” (C. Gournas).

Referee of peer-review articles published in International Journals:

- (2) Biomolecules MDPI (V. Sophianopoulou).
- FEBS Journal, Wiley; Microorganisms, MDPI; Plant Gene, Elsevier (C. Gournas).

Other lectures or presentations of scientific content (except research conferences):

- Seminar at the Biomedical Research Foundation of the Academy of Athens, entitled: Starvation-protective plasma membrane domains in Quiescent cells of *Saccharomyces cerevisiae* (C. Gournas).
- Investigating the role of a starvation-protective membrane domain in quiescence. Fondation Santé 2019 Fellows Symposium. May 24-25, Athens, Greece (C. Gournas)

Distinctions and Awards

- Scholarship from the organizing committee for participation and poster presentation at the Conference on Yeast Genetics and Molecular Biology. 2019. Gothenburg, Sweden (A. Megarioti).

Training activities

Post-graduate Education Courses on:

- “Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products” at the Department of Chemistry, University of Patras (7 students, V. Sophianopoulou 3 hours, C. Gournas 2 hours).
- “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, V. Sophianopoulou 3 hours, C. Gournas 1 hour).
- “Molecular and Cellular Biology and Biotechnology”, Departments of Medicine and Biological Applications and Technologies, University of Ioannina, and IMBB (C. Gournas 1 hour).
- “Molecular Microbiology”, Department of Biology, University of Athens. (30 students, C. Gournas 2 hours)

Other activities at the IBA and the NCSR “D”

Participation in the Summer Camp of IBA (V. Sophianopoulou, C. Gournas, A. Biratsi, I. Theodorou)

Lecture at the Summer School of NCSR “D” entitled “Investigation the compartmentalization of the plasma membrane, aiming to develop a new generation of antifungal drugs (C Gournas).

Impact factors (for 1 publication): 11,524

Bibliographic references for 2019 (without self-citations):

- V. Sophianopoulou: 76
- C. Gournas: 106

Total citations 2015- 2019 (without self-citations):

- V. Sophianopoulou: 307
- C. Gournas: 318

h-index:

- V. Sophianopoulou: 19
- C. Gournas: 11

Current external funding

Grant entitled *Plasma membrane organization in quiescence*, by the Fondation Santé - Biomedical Research Grants. Scientific coordinator: Dr. C. Gournas.

Duration: 02/2019 - 06/2021

Total funding for the laboratory: 25.000 € (+ 25.000€)

Funding of the laboratory during 2019: 17.171,17€ €

Grant 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, cycle B). Scientific coordinator: Dr. C. Gournas. Academic advisor: Dr. V. Sophianopoulou.

Duration: 16 months

Total funding for the laboratory: 45.500 €

Funding of the laboratory during 2019: 0€

Research Group: Biophysics and Membrane Biotechnology

Research Staff

Kostas Stamatakis, Research Director

George C. Papageorgiou, Emeritus Researcher

Merope Tsimilli-Michael, Collaborating Scientist

Dimitris Vayenos, PhD candidate

Panayiotis-Ilias Broussos, PhD candidate

Aikaterini Giakoumidaki-Vogiatzi, Undergraduate student

Panayiotis Voulgaris, Undergraduate student

Chrysanthi Baxevani, Undergraduate student

Research Interests

Photosynthetic cyanobacteria are preferable candidates for the sequestration of large quantities CO₂ 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 CO₂ to produce high energy chemical compounds using sunlight. The rapidly growing cyanobacteria constitutes a very promising and CO₂ 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 (H₂) production by cyanobacteria through the process of anaerobic "dark fermentation" of the sucrose they accumulated under salinity stress.

(b) Terpenes are the largest group of secondary metabolites and are used by industry (production of drugs, cosmetics, food technology). Study of the production of terpenes from genetically modified strains of the cyanobacterium *Synechocystis* sp PCC 6813 (S6813) capable of producing terpenes. They are synthesized from acetyl-coenzyme-A (acetyl-CoA) or from glycolysis intermediates

(c) We study, also, the time dependent changes of chlorophyll *a* fluorescence (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.

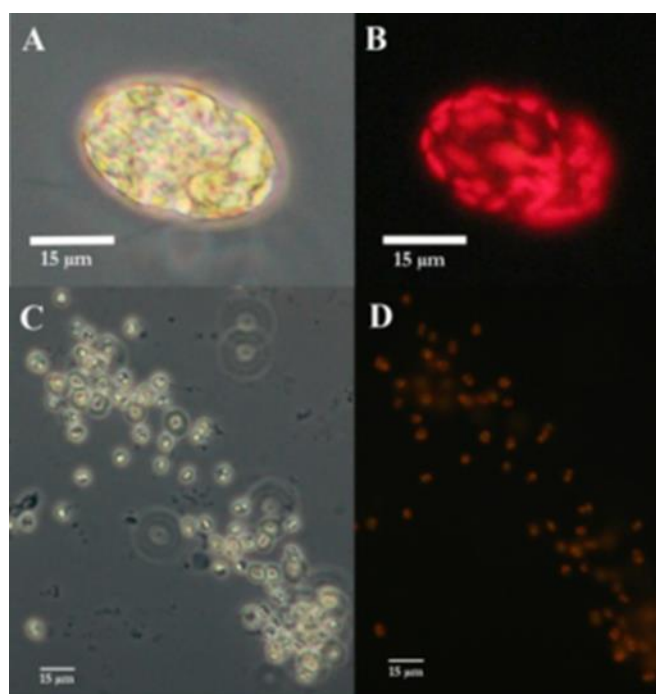
(d) We study the photosynthetic apparatus of the haptophyte *Phaeocystis antarctica* and of a novel Ross Sea dinoflagellate (RSD) that hosts *P. Antarctica* chloroplasts as kleptoplasts. Both algae are dominant in the phytoplankton of Ross Sea in Antarctica. Our research led to the discovery of the kleptoplasty.

(e) 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_o, 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.

2019 Findings

Light state transitions (STs) constitute 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.



(A) Ross Sea Dinoflagellate (RSD) and (C) haptophyte *Phaeocystis antarctica* (B) Fluorescence microscopy image of RSD and (D) fluorescence microscopy images of *Phaeocystis antarctica*

Bacterial attachment and colonization to hygiene sensitive surfaces, both public and nosocomial, as well as in food industry areas, poses a serious problem to human healthcare. Several infection incidents are reported, while bacterial resistance to antibiotics is increasing. Recently, novel techniques for the design of antibacterial surfaces to limit bacterial spreading have emerged, including bifunctional antibacterial surfaces with antifouling and bactericidal action. In this context, we have recently developed smart, universal, metal-sputtered superhydrophobic surfaces, demonstrating both bacterial repulsion and killing efficacy. Herein, we present the optimization process that led to the realization of these “hybrid” antibacterial surfaces. To this end, two bactericidal agents, silver and copper, were tested for their efficiency against Gram-negative bacteria, with copper showing a stronger bactericidal action. In addition, between two low surface energy coatings, the fluorinated-alkyl self-assembled chlorosilane layer from perfluorinated octyltrichlorosilane (pFOTS) solution and the fluorocarbon layer from octafluorocyclobutane

(C4F8) plasma were both approved for their anti-adhesive properties after immersion in bacterial solution. However, the latter was found to be more efficient when engrafted with the bactericidal agent in shielding its killing performance. Furthermore, the thickness of the plasma-deposited fluorocarbon layer was optimized, in order to simultaneously retain both the superhydrophobicity of the surface and its long-term bactericidal activity.

Original Publications in 2019

1. 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*, 1860, 1: 102-110.
2. Kefallinou, D., Ellinas, K., Speliotis, T., Stamatakis, K., Gogolides, E., Tserepi, A. (2019) Optimization of antibacterial properties of "hybrid" metal-sputtered superhydrophobic surfaces. *Coatings* 10, 25.
3. Govindjee, Papageorgiou, G.C., Govindjee R. (2019) Eugene I. Rabinowitch: A prophet of photosynthesis and of peace in the world. *Photos Research* 141, 143–150.

Original Publications in press 2020

1. Heliopoulos S. N., Kouzilos N. G., Papageorgiou S. K., Stamatakis K., Katsaros F. K. (2020) Viscose fabric functionalized with Copper and Copper Alginate treatment toward Antibacterial and UV blocking Properties. *Fibers and Polymers* (In Press) (IF: 1.439).
2. Vayenos D., Romanos Em. G., Papageorgiou G. C., Stamatakis K. (2020) The freshwater cyanobacterium *Synechococcus* sp. PCC7942 under salt stress: A cell factory for sucrose and hydrogen production. *Photosynth. Research* (In Press) (IF: 3.057).

Original publications in books

1. Stirbet A, Lazar D, Papageorgiou G, Govindjee (2019) Chlorophyll a fluorescence in cyanobacteria: Relation to photosynthesis. In: Mishra AN, Tiwari DN, Rai AN (eds) *Cyanobacteria: from basic science to applications*, Chapter 5. Elsevier Publishers Academic, Dordrecht, pp 79–130.

Articles included in Books and Volumes of Conferences Proceedings

1. Vayenos, D., George Romanos, G. Em., Papageorgiou, G.C., Stamatakis K. (2019) The freshwater cyanobacterium *Synechococcus* sp. PCC7942 under salt stress: A cell factory for sucrose and hydrogen production. *Proceedings of the 10th International Meeting "Photosynthesis and Hydrogen Energy Research for Sustainability – 2019"* June 23-28, 2019, St. Petersburg, Russia.

Member in Scientific committees

Member of the International Organizing Committee of the 10th International Meeting "Photosynthesis and Hydrogen Energy Research for Sustainability – 2019" June 23-28, 2019, St. Petersburg, Russia.

Impact factor (3 publications): 9.828

Citations in 2019 (without self-citations): 46 (Scopus), 53 (Web of Science) 62 (Google Scholar)

Total Citations in 2015 - 2019 (without self-citations): 246 (Scopus), 271 (Web of Science), 371 (Google Scholar)

h-factor: 13 (Scopus), 16 (Google Scholar)

PROGRAMME C

"STRUCTURAL AND COMPUTATIONAL BIOLOGY"

Research Group: Theoretical Biology and Computational Genomics

Research Staff

Yannis Almirantis, Research Director

Spyros Papageorgiou, Emeritus Scientist

Research Interests

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

- Deviations from randomness at the level of nucleotide n-tuplets 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.

2019 Findings

We studied the analogy between Noether's theorem (NT) and (Chargaff's) second parity rule (PR2), which is an approximative relation followed by most genomes. NT states that every differentiable symmetry of the action of a physical system has a corresponding conservation law. Examples are: translational invariance (symmetry) / linear momentum; rotational invariance / angular momentum; time invariance, where the corresponding conserved quantity is the total energy and several other couples of symmetries and conservation laws. PR2 states that the mean composition of each DNA strand follows the approximative equalities $A = T$ and $G = C$. Also, the corresponding mutational rates are equal, this last condition termed (Chargaff's) first parity rule.

NT involves only continuous symmetries. On the other hand, the inter-strand symmetry in the genome seems to be a (non-continuous) axial symmetry of order 2 (C₂). However, this is not directly related to the analogy we attempt to present here. What primarily interests here, is the symmetry between DNA strands in their functional and mutational dynamics. It is found that the PR2 equalities are more accurate as far as the two strands are more and more equivalent from functional and mutational point of view (i.e., as far as PR1 holds true).

We believe that the analogy we attempt to delineate here shed light onto both physical principles it concerns (i.e. NT and PR2). At a first place, it shows that, at least in one case, the connection between a symmetry and a conservation principle can hold outside the limits defined by the (mathematically strict) presuppositions of Noether's theorem. Further on, this is the first case where such a connection involves a symmetry which is approximative, that of the functional and mutational equivalence of the two genomic strands. Moreover, as one can easily document in the current literature and is shown by specific computational tools (e.g. ORILOC), the inverse relationship holds true, i.e. asymmetries found in specific regions / places in the inter-strand composition reveal functional genomic localizations, like starting points of replication (ori) etc.

Publications

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. [IF: 4.12]

Teaching

- Teaching (15H) of the course "An Introduction to Computational Genomics" in the framework of the "Post Graduate Specialisation Diploma" in Bioinformatics, Biology Department, NKUA.

- 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, NKUA.

Reviewer of scientific papers for: PLOS ONE, Mathematical Problems in Engineering, BMC Bioinformatics, Homeopathy, Scientific Reports.

Impact Factor (for 1 publication): 4.12

Citations 2018 (without self- citations): 57

Total Citations 2015-2019 (without self- citations): 242

h-factor: 14 (Scopus and Google Scholar)

Research Group: Laboratory of Designed Bioactive Molecules

Research Staff

Athanasios Papakyriakou, Senior Researcher

Anastasia Mpakali, Postdoctoral researcher

Georgios Mavridis, PhD candidate

Lykourgos Chiniadis, PhD candidate

Agoritsa Kalampaliki, Undergraduate student (*internship*)

Research interests

Study of the structure and dynamics of HLA complexes with extended antigenic peptides, with the aim to explore their stability against aminopeptidases ERAP1, ERAP2 and LAP.

Study the effect of a tetrapeptide binding at an allosteric pocket of the C-terminal domain of ERAP1 through dynamical network analysis of pathways connecting residues between the C-terminus residues and the catalytic site of the enzyme, with the aim to identify the role of the C-terminus of antigenic peptides.

Structure-based discovery of allosteric inhibitors of the aminopeptidase IRAP using the recently determined high resolution structures of ERAP1 with bound inhibitors.

Biophysical studies of LMTK3 kinase inhibition using small molecules and computational study of their interaction (collaboration with Prof. George Giamas, University of Sussex, UK).

Structure-based design of kinase inhibitors against sphingosine kinase isozymes SK1 and SK2 based on glycan moieties (collaboration with Prof. Barbara Richichi, University of Florence, Italy).

2019 Findings

We resolved the mechanism of antigen peptide selection by ERAP1 aminopeptidase based on crystallographic and enzymatic studies in conjunction with molecular dynamics simulations and dynamical network analysis of residues between the interacting C-terminus pocket and the catalytic site of the enzyme (Giastas P. et al. *PNAS* 2019).

Based on the crystal structure of the extracellular domain of $\alpha 9$ subunit of the nicotinic acetylcholine receptor (nAChR) in complex with the conotoxin RglA and using molecular dynamics calculations, we resolved at the atomic level the specificity of toxin binding at the interface of subunits $\alpha 9(+)/\alpha 9(-)$ or $\alpha 10(+)/\alpha 9(-)$, rather than $\alpha 9(+)/\alpha 10(-)$ (Giastas P. et al. *Front. Pharm.* 2019).

We completed the crystallographic study of Ru(II) complexes with potential cytotoxic activity bound to protein models (lysozyme and proteinase K), with the aim to investigate their selectivity for different protein sites of interactions (Chiniadis L. et al *J. Biol. Inorg. Chem.* 2020 *in press*).

We completed the publications reporting the design, synthesis and biochemical evaluation of aminopeptidase inhibitors (Tsoukalidou S. et al. *Bioorg. Med. Chem.* 2019), in addition to the study of the structure and dynamics of HLA-II complexes with extended antigenic peptides in collaboration with Prof. Andrew Godkin, Cardiff University, UK (MacLachan, B.J. et al *J. Biol. Chem.* 2019). We have contributed in the proteomics analysis of peptides presented by MHC-I in order to discover neoantigens in melanoma cells treated with ERAP1 inhibitors (Koumantou D. et al. *Cancer Immunol. Immunother.* 2019).

Publications

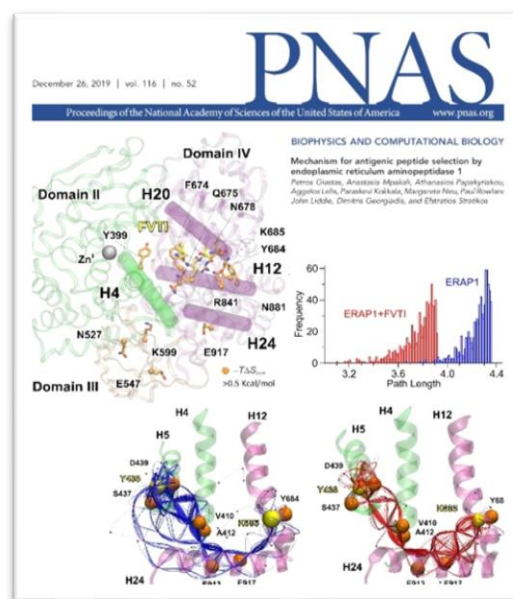
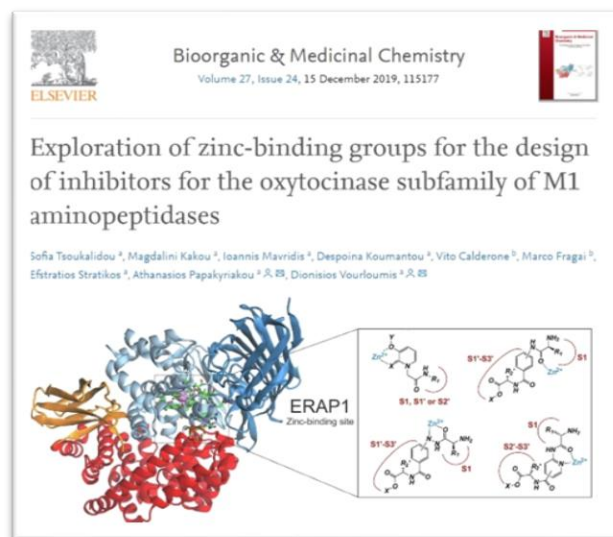
Giastas, P., Mpakali, A., Papakyriakou, A., Lelis, A., Kokkala, P., Neu, M., Rowland, P., Liddle, J., Georgiadis, D., Stratikos, E. (2019) Mechanism for antigenic peptide selection by endoplasmic reticulum aminopeptidase 1. *Proceedings of the National Academy of Sciences of the United States of America*, 116, 26709-26716.

Tsoukalidou, S., Kakou, M., Mavridis, I., Koumantou, D., Calderone, V., Fragai, M., Stratikos, E., Papakyriakou, A., Vourloumis, D. (2019) Exploration of zinc-binding groups for the design of inhibitors for the oxytocinase subfamily of M1 aminopeptidases. *Bioorganic and Medicinal Chemistry*, 27, 115177.

MacLachlan, B.J., Dolton, G., Papakyriakou, A., Greenshields-Watson, A., Mason, G.H., Schauenburg, A., Besneux, M., Szomolay, B., Elliott, T., Sewell, A.K., Gallimore, A., Rizkallah, P., Cole, D.K., Godkin, A. (2019) Human leukocyte antigen (HLA) class II peptide flanking residues tune the immunogenicity of a human tumor-derived epitope. *Journal of Biological Chemistry*, 294, 20246-20258.

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 Immunology, Immunotherapy*, 68, 1245-1261.

Zouridakis, M., Papakyriakou, A., Ivanov, I.A., Kasheverov, I.E., Tsetlin, V., Tzartos, S., Giastas, P. (2019) Crystal structure of the monomeric extracellular domain of $\alpha 9$ nicotinic receptor subunit in complex with α -conotoxin RgIA: Molecular dynamics insights into RgIA binding to $\alpha 9\alpha 10$ nicotinic receptors. *Frontiers in Pharmacology*, 10, 474.



Publications accepted in press

Mavridis G., Arya R., Domnick A., Zoidakis J., Makridakis M., Vlahou A., Mpakali A., Lelis A., Georgiadis D, Tampé R., Papakyriakou A., Stern L.J., and Stratikos E. (2020) A systematic re-examination of processing of MHCI-bound antigenic peptide precursors by ER aminopeptidase 1 *Journal of Biological Chemistry*, Mar 17, 2020 jbc.RA120.012976. doi:10.1074/jbc.RA120.012976 [IF: 4.1]

Chiniadis L., Bratsos I., Bethanis K., Karpusas M., Giastas P and Papakyriakou A. (2020) High-resolution crystal structures of a “half sandwich”-type Ru(II) coordination compound bound to hen egg-white lysozyme and proteinase K. *Journal of Biological Inorganic Chemistry*, published April 8, doi: 10.1007/s00775-020-01786-z [IF: 3.6]

Presentations in conferences

A. Papakyriakou, E. Scherer, A. Bailey, J. M. Werner, T. Elliott (2019) A comparative molecular dynamics and NMR study of H2-Db complex with a Sendai virus antigen reveals the high plasticity of the bound peptide. EMBO Workshop Antigen processing and presentation 10 (APP 10), 30 May – 02 June 2019, Paris, France.

A. Papakyriakou (2019) Structure-based virtual screening for drug-like allosteric inhibitors of IRAP. Insulin-Regulated Aminopeptidase – IRAP 2019, August 27–30, Nafplio, Greece.

Other scientific activities

Member of the Organizing Committee of the international conference Insulin-Regulated Aminopeptidase IRAP 2019, Nafplio, August 27–30, in collaborations with Dr. E. Stratikos, Dr. A. Chroni, supported by NCSR “Demokritos”. (<http://irap2019.org/>)

Member of the Scientific Committee for the evaluation of the Horizon-2020 Marie-Curie projects MSCA-IF-2019 (Remote Evaluator, Contract No. CT-EX2017D298493-101).

Member of the GSRT Scientific Committee for the evaluation of projects EREVNO-DIMIOURGO-KENOTOMO (Committee ID: B02YΦA03.)

Regular referee for the peer-reviews journal *Molecules*, *International Journal of Molecular Sciences*, *Pharmaceuticals* (MDPI).

Other scientific presentations or seminars:

1. A. Papakyriakou (2019) Computer-aided drug design. EU COST CHARME: Big data training school for life sciences, 4–8 March, Agricultural University of Athens, Greece.
2. A. Papakyriakou (2019) Structure-based design and virtual screening of small-molecule databases. OpenScreen GR meeting. 4th October, Aristotle University of Thessaloniki.

Participated at the 2019 Researcher’s Night, 27th September, Hellenic Cosmos Cultural Centre with Virtual Reality presentations of biomolecules and assisted by the two students, A. Kalampaliki and L. Chiniadis.

Educational Activities

Joint Postgraduate MSc Studies Program between IB-A, NCSR “D” and University of Patras, Molecular Pharmacology-Immunology, 2nd Semester 2019, 8 hours.

Other activities at IBA and NCSR “D”

Member of the Scientific Advisory Committee of the Technological Park “Lefkippos” of NCSR “D”

Impact factor (5 articles): 25.2

Heterocitations for 2019: 112

Heterocitations for 2015-2019: 515

h-factor: 20 (Google Scholar), 18 (Scopus)

Current funding

Project *ARIA* “Atomic Resolution Insight into the Antigen processing machinery, funded by the

H.F.R.I. Coordinator: Dr. A. Papakyriakou

Project duration: 11/10/2018-10/10/2021

Total funding: 180.000€

Funding for 2019: 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

Georgia Nigianni, Postgraduate Student

Maria-Aikaterini Daskalopoulou, Training Student

Maria Arfara, Training Student

Panayota Pantiora, Training Student

Olga Anestidou, Training Student

Research Interests

Development (design, synthesis, characterization, structural analysis, evaluation) of new compounds/agents of pharmacological interest for the diagnosis and/or treatment of diseases as well as for biotechnological and nanotechnological applications. Our main fields of research are Alzheimer's disease and cancer, and our tools are **NMR** and **Circular Dichroism (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 ($A\beta$) 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) and also targeted liposomes on the aggregation process of $A\beta$ is studied mainly with CD but also through the reduction of its toxicity in primary neurons (rescue effect).

2019 Findings

In 2019, the activity of the group in the utilization of natural products for the development of new bioactive compounds, continued, with the productive contribution of the postdoctoral collaborators D. Matiadis (organic synthesis), E. Halevas (complexation, nanoencapsulation) and B. Mavroidi (chemical analysis, biological evaluation). Characteristic examples include • synthesis of pyrazolo derivatives of monoketo curcuminoids and of their corresponding metal complexes with significant antifungal activity ($< 0.25 \mu\text{g/mL}$) and evaluation of selected derivatives for DNA

interaction • synthesis and crystallographic analysis of complexes of vanadium-curcumin and gallium-chrysin and encapsulation in cationic liposomic nanocarriers and magnetic nanoparticles as anticancer agents • synthesis and crystallographic analysis of copper-curcumin, copper-quercetin, copper-chrysin complexes and evaluation of antioxidant, genotoxic and cytostatic activity • synthesis and biological evaluation of novel hyper-branched dendrimeric nanocarriers with encapsulated artemisinin.

In 2019, following the Greek patent (OBI, #1009516), an international patent application (Patent Cooperation Treaty (PCT)) was filed regarding our findings on the benzothiazole and benzimidazole complexes with radioactive ^{99m}Tc and stable Re which present very significant penetration of the blood-brain barrier, and ideal properties for diagnosis (^{99m}Tc) and therapy (Re) of Alzheimer's disease (AD). In the same field of AD, the biological evaluation of derivatives of the natural indole isatin with CD, cellular assays, and electronic microscopy was submitted for publication, while their evaluation in 5xFAD transgenic mice as neuroprotective agents - through the insulin pathway - is in progress. Furthermore, the biological evaluation of phenylbenzothiazole-bearing liposomes targeting the blood-brain barrier as inhibitors of β -amyloid peptide aggregation was also completed. In the field of anticancer agents, the synthesis and evaluation of curcuminoids as photosensitizers in the photodynamic treatment of cancer in collaboration with NTUA was completed. At the stage of manuscript preparation is the synthesis and biological evaluation of ^{99m}Tc and Re complexes bearing phenylbenzothiazole derivatives as diagnostic/therapeutic tools for breast cancer.

Taking advantage of the IB-A infrastructure, our activity is also expanding to new areas through collaborations, with characteristic examples the: • CD study of live photosynthetic cells (Dr. K. Stamatakis, IB-A) • development of a protocol for imaging with confocal microscopy of nasal epithelia of patients with chronic sinusitis (Prof. E. Kirodimos, Medical School, UOA) • application of metabonomics in the study of the effectiveness of pesticides (Dr. K. Aliferis, Lecturer, Agricultural University, Athens) • development of q-NMR methods for application in the study of the purity of organic compounds, antibiotics, hormones, etc. (Chemical Metrology, General Chemical State Laboratory of Greece) • biological evaluation of nanomaterials with porphyrinoids and cyclodextrins for photodynamic tumor therapy with confocal microscopy and cytotoxicity studies (Dr. K. Yannakopoulou, INN).

Original articles published in 2019 in international journals after revision:

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., Pelecanou, M. (2019). Remarkable brain penetration of cyclopentadienyl $\text{M}(\text{CO})_3^+$ ($\text{M} = ^{99m}\text{Tc}$, 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)

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-yl-methyl-idene)aniline-κ2N,N']tricarbonylrhenium(I) hexa-fluorido-phosphate 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 (IF: 3.224)

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. *BBA-Bioenergetics*, 1860, 102-110 (IF: 4.45)

T. Tsoதாக, C. Triantis, C. Tsoukalas, A. Panagiotopoulou, A. Lazopoulos, S. Xanthopoulos, D. Psimadas, P. Bouziotis, M. Pelecanou, M. Papadopoulos, I. Pirmettis. (2019). Cysteine derivatized ^{99m}Tc-labeled fatty acids as β -oxidation markers. *Inorganics*, 7, 1-14 (IF: 1.90)

Original articles In Press for 2020:

Kazantzis, K. T., Koutsonikoli, K., Mavroidi, B., Zachariadis, M., Alexiou, P., Pelecanou, M., Politopoulos, K., Alexandratou, E., Sagnou, M. (2020). Curcumin derivatives as photosensitizers in photodynamic therapy: photophysical properties and in vitro studies with prostate cancer cells. *Photochem. Photobiol. Sci.* 19, 193-206 (IF: 2.408)

Halevas, E., Mavroidi, B., Antonoglou, O., Hatzidimitriou, A., Sagnou, M., Pantazaki, A. A., Litsardakis, G., Pelecanou, M. (2020). Structurally characterized gallium-chrysin complexes with anticancer potential. *Dalton Trans.* 49, 2734-2746 (IF: 4.052)

Ntatsi, G., Aliferis, K.A., Panagiotopoulou, A., Roupheal, Y., Savvas, D., (2020). Spiny chicory (*Cichorium spinosum* L.) ¹H NMR metabolomics dataset. *Data in Brief* 30, 105621-5 (IF: 0.970)

Matiadis, D., Mavroidi, B., Panagiotopoulou, A., Methenitis, C., Pelecanou, M. Sagnou, M. (2020). (E)-(1-(4-Ethoxycarbonylphenyl)-5-(3,4-dimethoxyphenyl)-3-(3,4-dimethoxystyryl)-2-pyrazoline: Synthesis, Characterization, DNA-Interaction, and Evaluation of Activity Against Drug-Resistant Cell Lines. *Molbank*, 1, M1114 (IF not available)

Salvanou, E. A, Stellas, D., Tsoukalas, C., Mavroidi, B., Paravatou-Petsotas, M., Kalogeropoulos, N., Xanthopoulos, S., Denat, F., Laurent, G., Bazzi, R., Roux, S., Bouziotis, P. (2020). A Proof-of-Concept Study on the Therapeutic Potential of Au Nanoparticles Radiolabeled with the Alpha-Emitter Actinium-225. *Pharmaceutics*. 12, E188 (IF: 4.773)

Kollatos, N., Mitsos, C., Manta, S., Tzioumaki, N., Giannakas, C., Alexouli, T., Panagiotopoulou, A., Schols, D., Andrei, G., Komiotis, D. (2020) Design, Synthesis, and Biological Evaluation of Novel C5-Modified Pyrimidine Ribofuranonucleosides as Potential Antitumor or/and Antiviral Agents. *Med Chem.* 16(3), 368-384 (IF: 2.53)

Halevas, E., Pekou, A., Papi, R., Mavroidi, B., Hatzidimitriou, A. G., Zahariou, G., Sanakis, Y., Litsardakis, D., Sagnou, M., Pelecanou, M., Pantazaki, A. A. (2020). Synthesis, physicochemical characterization and biological properties of two novel Cu(II) complexes based on natural products curcumin and quercetin. *J. Inorg. Biochem.* In press (IF: 3.224)

Matiadis D., Tsironis D., Stefanou V., Boussias S., Panagiotopoulou A., McKee V., Igglessi-Markopoulou O., Markopoulos J. (2020). Synthesis, biological evaluation and structure-activity relationship of novel 5-arylidene tetramic acid derivatives with antibacterial activity against methicillin-resistant *Staphylococcus aureus*. *Bioorg. Med. Chem. Lett.* In Press (IF: 2.448)

Sagnou, M., Novikov, F.N., Ivanovad, E.S., Alexiou, P., Stroylov, V.S., Titov, I.Y., Tatarskiyd, V.V., Vagidah, M. S., Pelecanou, M., Shtil, A.A., Chilov G.G. (2020). Novel Curcumin Derivatives as P-glycoprotein Inhibitors: Molecular Modeling, Synthesis and Sensitization of Multidrug Resistant Cells to Doxorubicin, *Eur. J. Med. Chem.* In Press (IF: 4.833)

Liolios, C., Shegani, A., Roupa, I., Kiritsis, C., Makarem, A., Paravatou-Petsotas, M., Pelecanou, M., Bouziotis, P., Papadopoulos, M., Kopka, K., Pirmettis, I. (2020). Synthesis, characterization and evaluation of ⁶⁸Ga labelled monomeric and dimeric quinazoline derivatives of the HBED-CC chelator targeting the epidermal growth factor receptor. *Bioorg. Chem.* In Press (IF: 2.793)

Impact Factor (for 7 publications): 22.464

Citations 2019 (without self-citations):

M. Pelecanou: 81

M. Sagnou: 67

A. Panagiotopoulou: 10

Total Citations 2015-2019 (without self-citations):

M. Pelecanou: 471

M. Sagnou: 300

A. Panagiotopoulou: 29

h-factor:

M. Pelecanou: 21 (Scopus and Google scholar)

M. Sagnou: 13 (Scopus and Google scholar)

A. Panagiotopoulou: 5 (Scopus and Google scholar)

Presentations at international conferences:

M. Ischyropoulou, I. Roupa, A. Papasavva, A. Shegani, M. Kaplanis, K. Makrypidi, C. Kiritsis, D. Ischyropoulos, Raptopoulou, V. Psycharis, A. Chiotellis, M. Pelecanou, I. Pirmettis, M. Papadopoulos (2019). New trans-[Re(SS)(isc)₂(CO)₂], [Re(SS)(isc)(P)(CO)₂] and [Re(SS)(P)₂(CO)₂], mixed ligand complexes. 23rd International Symposium on Radiopharmaceutical Sciences, Beijing, China, May 26-31, 2019.

Presentations at Greek Conferences:

D. Matiadis, B. Mavroidi, M. Pelecanou, M. Sagnou (2019). Novel curcuminoid analogues bearing pyrazolines: synthesis and biological evaluation. EFMC International Symposium on Advances in Synthetic and Medicinal Chemistry, September 1-5, 2019, Athens, Greece.

Ch. Alexopoulos, A. Georgopoulou, P. Giannikopoulou, E. Kakoulides, E. Stathoudaki, V. Schoina, A. Panagiotopoulou (2019). qNMR as a powerful tool for providing purity assessment and metrological traceability. 11th International Conference on Instrumental Methods of Analysis, (IMA 2019), September 22-25, 2019 Ioannina, Epirus, Greece.

B. Mavroidi, M. Sagnou, A. Shegani, M. Paravatou-Petsotas, I. Pirmettis, M. Papadopoulos, M. Pelecanou (2019). Biological Evaluation of a 2-(4'-Aminophenyl)benzothiazole Diagnostic Agent for Breast Cancer. 70th Panhellenic Conference of the Hellenic Society of Biochemistry and Molecular Biology (EEBMB2019), November 29 – December 01, 2019, Athens, Greece.

A. Kaminari, B. Mavroidi, A. Tzinia, M. Pelecanou, M. Sagnou (2019). Biological evaluation of new isatin derivatives as inhibitors of neurodegeneration by modulation of insulin signaling. 70th Panhellenic Conference of the Hellenic Society of Biochemistry and Molecular Biology (EEBMB2019), November 29 – December 01, 2019, Athens, Greece.

E. Halevas, B. Mavroidi, C. Kokotidou, A. Mitraki, M. Pelecanou, M. Sagnou (2019). Anticancer activity of artemisinin-loaded hyperbranched dendritic nanocarriers. 12th Panhellenic Conference of Chemical Engineering, May 29-31, 2019, Athens, Greece

M.K. Daskalopoulou, D. Matiadis, M. Sagnou, M. Pelecanou, T. Mavromoustakos, A. Panagiotopoulou (2019). Isolation, characterization and quantitation of curcuminoids. NMR studies in turmeric market products and pharmaceutical supplements. 12th Panhellenic Conference of Chemical Engineering, May 29-31, 2019, Athens, Greece

M-A Kakavoulia, M. Karakota, M. Kaloyianni-Dimitriadi, E. Halevas, M. Sagnou, G. Koliakos (2019). The effect of dendrimers and magnetic nanoparticles on human blood lymphocytes. 70th Panhellenic Conference of the Hellenic Society of Biochemistry and Molecular Biology (EEBMB2019), November 29 – December 01, 2019, Athens, Greece.

Patents approved in 2019:

A patent issued by the Hellenic Industrial Property Organization (OBI) "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" and depositors/inventors the National Centre for Scientific Research "Demokritos" and researchers M. Pelecanou (IB-A), M. Sagnou (IB-A), M. Papadopoulos (INRASTES), I. Pirmettis (INRASTES), B. Mavroidi (IB-A) and A. Shegani (INRASTES) (Patent #1009516 application filed in March 2018). In addition, an international patent application under the Patent Cooperation Treaty (PCT) "Tricarbonyl complexes of transition metals with benzo-heterocyclic derivatives of the cyclopentadienyl anion" has been filed with the same depositors/inventors (International application #PCT/EP2019/057235, September 2019).

Other scientific activities

Review of scientific publications:

Inorganic Chemistry, ACS (M. Pelecanou)

Molecules, Nutrients, International Journal of Molecular Science - MDPI and Letters in Drug Design & Discovery – Bentham (M. Sagnou)

Participation in lessons and other educational activities

Participation in the "Summer School 2019", NCSR "Demokritos" with the presentation "NMR Spectroscopy Laboratory for Liquid Samples; Principles and Applications of NMR Spectroscopy" (A. Panagiotopoulou)

Participation in "Summer Camp 2019" IB-A, NCSR "Demokritos": Scientific 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 for high school students "How well you know your mind? - We talk about addictions" which was held at NCSR "Demokritos" (M. Sagnou)

Lectures 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)

Member of the three-member committee of:

- Tsalouxiou Victoria, Postgraduate Program of the Faculty of Chemistry, Aristotle University of Thessaloniki. Title of thesis "Investigation of vanadium-curcumin complex as possible phosphatase inhibitors" (M. Sagnou)
- Kaplanai Entzis, Interdepartmental Postgraduate Program of the Faculty of Chemistry of the University of Patras "Chemical Biology". Title of thesis "Design and synthesis of innovative multipotent molecules with action on biological targets related to depression and cognitive disorders" (M. Sagnou)
- Rokopoulou Nikolaou, Interdepartmental Postgraduate Program of the Faculty of Chemistry of the University of Patras "Chemical Biology". Title of thesis "Design and synthesis of innovative multipotent molecules with SSRI action" (M. Sagnou)

Participation in IB-A other activities (committees, responsibilities, duties, etc.):

M. Pelecanou:

- Co-responsible (with M. Vlasi) 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"

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 2019: 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 2019: 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 2019: 4.000 €.

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 €

Proposals submitted in 2019 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, Graduate Associate

Research Interests

- Protein folding
- Sequence/structure relationships of amino-acid repeats / Role in protein-protein interactions
- Molecular dynamics of proteins
- Molecular dynamics simulations & development of related tools
- 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 2019

- With the aim to elucidate sequence/structure/function relationships of proteins linked to diseases (kinases in particular), in 2019 we continued our *in silico* structural studies of:

1) The tyrosine kinase Tyk2, which is related to various diseases. More precisely, in 2019 we expanded our previous molecular dynamics (MD) simulations (see Lesgidou et al 2018) of the wild type Tyk2 protein and of a Tyk2 variant linked to autoimmune diseases, to μ s-timescale. The large-scale (multiple-microseconds) MD simulations were performed in the National HPC facility-ARIS @GRNET (project ID: *KIN_IMMUN_MD*, approved: 29-11-2018, computational time granted: 900.000,0 core hours for 1 year). Analyses of the multiple- μ s MD trajectories, are currently in progress.

In addition, and in order to build on these studies, a new proposal to obtain additional computational time on ARIS @GRNET, was submitted in 2019 (approved in 29-11-2019) and additional computational resources of 1.500.000,0 core-hours were granted for another year.

2) The SRPK1 kinase, which we have also studied in the past (see Sellis et al 2012). More precisely, in 2019, using homology modeling, we constructed 3D-models of SRPK1 in complex with peptides from a human protein linked to carcinogenesis. Interaction of these two proteins was observed experimentally for the first time by our collaborators in the A. University of Thessaloniki (T. Giannakouros group). However, the details of this interaction at the atomic-level, are unknown. Towards this end, the initial 3D-models will be subsequently subjected to molecular dynamics simulations to test their validity.

In parallel, in 2019, we performed an *in silico* analysis of the amino-acid sequence of a less abundant isoform in humans, SRPK1a, which is formed from alternative splicing of the *SRPK1* gene and was also identified by our collaborators in AUTH. The *in silico* analysis supports the conservation of SRPK1a in mammals and provides information on the evolutionary history of the *SRPK1* gene, thus paving the way for future research probing into the contribution of SRPK1a to SRPK1 functions. Our *in silico* data were included in a work **published in Data in Brief** (Vlassi et al, Data in Brief, 2019).

- In 2019, an opinion article, survey of the status of Computational Biology in Greece and Cyprus, was **published in PLoS Comput Biol** in collaboration with other Scientists from the two counties (Chasapi et al, PLoS Comput Biol, 2019).

- Finally, in 2019, potential users continued to express interest in using new versions of the **GROMITA-GUI** we have previously developed in the lab (<http://gromita.bio.demokritos.gr>).

Publications 2019 in peer-reviewed journals:

Vlassi, M., Kyritsis, K. A., Vizirianakis, I. S., Giannakouros, T., Aivaliotis, M., Nikolakaki, E. (2019). Data on the expression of SRPK1a in mammals. *Data in Brief*, 25 (2019) 104210: 1-6. <https://doi.org/10.1016/j.dib.2019.104210>

Opinion article:

Chasapi A, Aivaliotis M, Angelis L, Chanalaris A, Iliopoulos I, Kappas I, Karapiperis C, Kyripides NC, Pafilis E, Panteris E, Topalis P, Tsiamis, G, Vizirianakis IS, Vlassi, M, Promponas VJ, Ouzounis CA (2019) Establishment of Computational Biology in Greece and Cyprus: Past, present, and future. *PLoS Comput Biol* 15(12): e1007532. <https://doi.org/10.1371/journal.pcbi.1007532>

Conference Proceedings

Apostolou, P, Mollaki, V, Fostira, F., Delimitsou, A, Vlassi, M, Kollia, P., Fountzilias, G, Konstantopoulou, I, Yannoukakos, D. Two novel CHEK2 large genomic rearrangements are associated with breast cancer predisposition. Abstract from the 50th European Society of Human Genetics Conference, Copenhagen, Denmark, May 27–30, 2017.

Published online in *European Journal of Human Genetics* (2019) 26:113–819 P12.064D

<https://doi.org/10.1038/s41431-018-0247-7>

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

Published online in *F1000Research* 2019, 8:364

<https://doi.org/10.7490/f1000research.1116510.1>

Congresses

N. Lesgidou and M. Vlassi (2019) Microsecond-scale molecular dynamics simulations of TYK2 kinase shed light on the structural consequences of a protective *TYK2* gene polymorphism against autoimmune diseases, 70th Annual Conference of the Hellenic Society of Biochemistry and Molecular Biology, 29 Nov-1 Dec 2019, Athens, Greece (Abstracts book p222).

Other Scientific Activities

- M.V.: Reviewer for the *Journal of Chemical Information and Modeling* (one article)
- Member of one evaluation committee for researcher promotion (BRFAA)
- M.V.: Member of the European Network **INSTRUCT-ERIC** (INSTRUCT: An integrated Structural Biology Infrastructure for Europe)
- M.V.: Member of the related National Research Infrastructure project: “INSTRUCT-EL, an initiative of Greek Researchers related to Structural Biology” The related RI “**INSPIRED: The National RIs on Integrated Structural Biology, Drug Screening efforts and Drug-target functional characterization**” is funded by the GSRT (funding approved: June2018, see *funding* section).

Educational Activities

✓ Supervision of the PhD Thesis of N. Lesgidou (Democritus University of Thrace, Dept of Molecular Biology & Genetics) entitled: “Structural and dynamics studies of proteins related to diseases using molecular dynamics simulations” (started: February 2019)

✓ Lecture entitled “Principles of X-Ray Crystallography: Applications in Structural Biology” in the framework of the post-graduate program: “Clinical Biochemistry – Molecular Diagnosis” (Depts. of Biology/Chemistry/Nursing, National & Kapodistrian University of Athens).

✓ Lecture entitled: “Protein Structure – Experimental & Theoretic approaches” in the framework of the post-graduate program: “Applied Biochemistry: Clinical Chemistry, Biotechnology, Pharmaceutical Products evaluation” co-organized by IB_A of NCSR “Demokritos” and the University of Patras”.

✓ Lecture entitled: “Protein Structure – Experimental & Theoretic approaches” in the framework of the post-graduate program: “Bioinformatics-Computational Biology” (Dept. of Biology, Kapodistrian University of Athens)

Other Activities at IBA & NCSR “D”

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

Member of various committees of NCSR “D”

Responsible for the operation of various common equipment of the IBA

Total Impact Factor 2019: 5.5

Citations 2019 (excluding self-citations): 29

Total citations 2015-2019 (excluding self-citations): 118

h-factor: 14

Funding-Projects

✓ *“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

Budget 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 2019: ~830.000 core hours

✓ Project entitled *“MD simulations of a kinase linked to autoimmune diseases. II* (project ID:KIN_IMMUNMD_II) in the framework of the 8th Call for Production Projects Accessing the supercomputer system ARIS @ GRNET (P.I.: M. Vlassi.).

Duration Dec 2019-Dec 2020

Total resources: 1.500.000,0 core-hours

CENTRAL PROJECTS

IBA

Beyond the hitherto described activities of each Lab, IBA's personnel were engaged in a series of central projects, funded by the supervising authority, i.e., the General Secretariat for Research and Technology (GSRT).

SANITURA

Almost all IBA's researchers (with the exception of those hired recently) participated in the project TARGET IDENTIFICATION AND DEVELOPMENT OF NOVEL APPROACHES FOR HEALTH AND ENVIRONMENTAL APPLICATIONS (acronym: SANITURA, MIS 5002514), belonging to the Action for the Strategic Development on the Research and Technological Sectors, 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). Coordinator of the project is the Director of IBA. Aim of the project is the support of IBA research activities falling into the National Research and Innovation Strategies (RIS), such as the delineation of disease mechanisms, the identification of biomarkers and novel treatment targets, the development of preclinical disease models, the discovery of bioactive molecules and natural products for pharmaceutical and cosmetic applications, and the design of technologies for suppressing the environmental footprint of the agro-food sector. The total budget for the project is 740.000 €, 148.000 € of which were distributed during 2019.

In this period SANITURA supported with salaries seventeen (17) external collaborators, who delivered approximately 90 person-months, while IBA's researchers provided approximately 42 person-months. Consumables were also purchased using SANITURA's funds, while a tender for the procurement of equipment is currently in progress. During 2019, SANITURA funded five publications in international peer-reviewed journals, as well as, five communications in national conferences.

OPENSREEN-GR



IBA coordinates the project AN OPEN-ACCESS RESEARCH INFRASTRUCTURE OF CHEMICAL BIOLOGY AND TARGET-BASED SCREENING TECHNOLOGIES FOR HUMAN AND ANIMAL HEALTH, AGRICULTURE AND THE ENVIRONMENT (acronym: OPENSREEN-GR, MIS 5002691), which is 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). Coordinator of the project is the Director of IBA. OPENSREEN-GR aims at the consolidation of a national infrastructure for medium to large-scale molecular target-based screening of existing libraries of synthetic small molecules, but also natural products. This infrastructure will provide the necessary equipment, as well as, trained personnel for implementing a vast array of bioactivity assessment methodologies. Beyond the identification of novel bioactive compounds, OPENSREEN-GR can proceed to their characterization, through studies of their biological effects and of the underlying molecular mechanisms, making use of a variety of model systems both *in vitro* and *in vivo*. These studies can also be combined with bioinformatics tools (*in silico*) for modeling the interactions of the bioactive compounds with their cellular targets, as well as, for analyzing structure-activity relationships (SAR). Apart from IBA, six other research and academic institutions are members of OPENSREEN-GR: Aristotle University of Thessaloniki, Democritus University of Thrace, University of Ioannina, National Hellenic Research Foundation, Biomedical Research Foundation of the Academy of Athens, and Agricultural University of Athens.

The total budget for IBA within the project is 899.600 €, 147.100 € of which were distributed during 2019. Eight IBA's researchers participated during this year in OPENSREEN-GR, providing approximately 18 research person-months. Moreover, four external collaborators were recruited,

delivering approximately 20 research person-months. During 2019 a call for tenders was published for upgrading the infrastructure, through the procurement of a state-of-the-art microplate analyzer, capable for reading absorbance, fluorescence, and chemiluminescence, equipped with dispenser, gas and temperature controllers, bright field imaging optics, and plate stacker. OPENSREEN-GR supported two publications by IBA researchers in international peer-reviewed journals within 2019.

Moreover, in 2019 the national infrastructure OPENSREEN-GR was connected to the corresponding European Research Infrastructure Consortium (ERIC) EU-OPENSREEN, through the implementation of the European project EU-OPENSREEN-DRIVE.

BIOIMAGING-GR



IBA is one of the eleven partners of the project A GREEK RESEARCH INFRASTRUCTURE FOR VISUALIZING AND MONITORING FUNDAMENTAL BIOLOGICAL PROCESSES (acronym: BIOIMAGING-GR, MIS 5002755), which is 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), and is coordinated by the Foundation for Research and Technology-Hellas (FORTH). Regarding IBA's part of the project, it aims at the optimal function of the Imaging Unit, consisting mainly in an inverted confocal / multiphoton microscope and two UV / visible microscopes (one upright and one inverted). Hence, this Unit is expected to contribute in the development of research collaborations for the *in vitro* identification and imaging of biomolecules, facilitating the study and delineation of biological mechanisms, cellular functions, biochemical pathways, as well as, the development of novel small molecules capable for selective interactions with the above molecular and cellular systems. Head of the IBA's part of the project is the Director of the Institute, while the scientific team comprises 14 more IBA researchers and an external collaborator, the Imaging Unit operator. The total budget for IBA within the project is 211.250 €, 57.000 € of which were distributed during 2019. This funding supported the salary of the Imaging Unit operator for 10 person-months, while the rest team members provided approximately 5 person-months. Moreover, BIOIMAGING-GR supported two publications by IBA researchers in international peer-reviewed journals within 2019.

INSPIRED



IBA is also member of the project THE NATIONAL RESEARCH INFRASTRUCTURES ON INTEGRATED STRUCTURAL BIOLOGY, DRUG SCREENING EFFORTS AND DRUG TARGET FUNCTIONAL CHARACTERIZATION (acronym: INSPIRED, MIS 5002550), which is 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), and is coordinated by the National Hellenic Research Foundation (NHRF). INSPIRED utilizes integrated approaches of Structural Biology and includes platforms for protein samples' preparation, their biophysical characterization, and the identification of their three-dimensional structures by means of X-ray crystallography, nuclear magnetic resonance (NMR) spectroscopy and *in silico* approaches. Main aim of INSPIRED is to ensure a functional management scheme for the existing national Structural Biology infrastructures, as well as, for the data generated from the corresponding approaches for the benefit of the scientific, technological and economic development of the country. INSPIRED comprises 14 partners (6 Research Institutes and 8 Universities), while NCSR "Demokritos" is involved through the relevant activities and infrastructures of three Institutes

(INN, IBA, and INRASTES) with a total budget of 220.000 €. IBA researchers with the relevant expertise are involved in research activities including protein sample purification / isolation, circular dichroism (CD) studies, NMR and *in silico* structural studies. The total budget for IBA activities includes 48.000 € for salaries of two research collaborators (30 person-months), as well as, 15.000 € for NMR spectrometers' maintenance. INSPIRED supported one publication by IBA researchers in an international peer-reviewed journal within 2019.



THE ROUTES OF BEE

Within 2019, the flagship national initiative entitled CREATION OF A NATIONAL RESEARCH NETWORK IN THE VALUE CHAIN OF "HONEY" (acronym: THE ROUTES OF BEE) was established as part of the 'Creation of national research networks in the value chains of "Olive", "Vineyard", "Honey" and "Livestock"', funded by the national section of GSRT's Programme of Public Investment. The project is coordinated by the Aristotle University of Thessaloniki and comprises 10 more research and academic partners, one of which is IBA. IBA's team is composed of 10 researchers and headed by the Director of the Institute. Within the framework of the characterization and promotion of the Greek Honey varieties, IBA researchers will implement studies of the intracellular antioxidant activity, as well as, of the atheroprotective and possible anti-cancer properties of selected honey samples of Greek origin, with a total budget amounting to 39.200 €.

SERVICE UNITS

- ✓ **LABORATORY FOR DOPING CONTROL AND METABOLIC STUDIES**
- ✓ **HUMAN TISSUE BANK**
- ✓ **EXPERIMENTAL ANIMAL FACILITY**
- ✓ **LASER CONFOCAL MICROSCOPY**
- ✓ **HISTOLOGY UNIT**
- ✓ **CIRCULAR DICHROISM (CD) LABORATORY**
- ✓ **ISOLATION, CHARACTERIZATION AND CULTURE OF STEM CELLS APPLICATIONS IN REGENERATIVE MEDICINE**
- ✓ **LABORATORY OF MOLECULAR DIAGNOSIS OF GENETIC DISEASES**
- ✓ **LABORATORY OF CELL-BASED ASSAY SYSTEMS AND BIOACTIVE COMPOUNDS**

LABORATORY FOR DOPING CONTROL AND METABOLIC STUDIES

Personnel

Dimitris Kletsas, Research Director, Institute Director, Administrative Director

Ioannis Angelis, Dr. Chemist, Scientific Director

Nassia Kioukia, Dr. Pharmacist

Polyxeni Kioussi, Dr. Chemist

Argyro Fraggaki, Dr. Chemist, Quality Manager

Stella Loui, Research Technician

Foteini Chlapana, Research Technician

Maria Vlahou, Administrative Officer

Maria Filippidou, Administrative Officer

Vassiliki Tzouvara, Administrative Officer

Maria Pavlaki, Supporting Personnel



Lab description – Scientific interests

Within 2019, according to the Law 4589/29-1-2019 and to the common Ministers' Decision 84397 (FEK 3201/21-8-2019) the Doping Control Laboratory of Athens (DCLA) was transferred to the Institute of Biosciences and Applications. The Laboratory was founded in 1986 and is located in the Olympic Athletic Center of Athens (OAKA) complex, in a dedicated three floor building, built for the doping control testing of the 2004 Olympic Games.

DCLA was accredited by the International Olympic Committee (IOC) in 1995 and later on (2000) by ESYD, the Greek accreditation body, according to the requirements of the International Standard ISO/IEC 17025:2005. DCLA is a WADA accredited laboratory since 2003, according to the International Standard of Laboratories. Furthermore, DCLA is accredited by the Association of Official Racing Chemists (AORC) in the field of anti-doping testing in horses.

In 1997, the DCLA performed the doping control of the World Championships in Athletics. After that, DCLA performed the doping control analyses of the athletes' samples during the 28th Summer Olympic Games in Athens. Also, DCLA has undertaken the analysis of doping control samples during the Mediterranean Games of Mersin (Turkey) in 2013.

DCLA has analyzed athlete's samples for a number of different NADOS and IFs such as the Greek Anti-doping Council (ESKAN), Cyprus Anti-Doping Authority (Cyprus NADO) (CYADA), Tunisian Anti Doping Agency (Tunisian NADO), Israel NADO, Turkish Anti-doping Committee, UEFA, FIBA, National Anti-Doping Commission of Albania (Albanian NADO), Federation Internationale de Volleyball (FIVB), Union Cycliste Internationale (UCI), Portugal NADO (ADoP), Anti-doping Centre of Bulgaria (Bulgarian NADO), National Anti-doping Organisation of Malta (NADO Malta). In the field of equine samples analyses, DCLA regularly analyses samples from the Jockey Club of Greece and the Hellenic Equestrian Federation.

DCLA is equipped with a high-quality infrastructure including, among others, GC (2), GC/MS (5), GC/C/IRMS, GC/TOF/MS, LC/TOF/MS, GC/HRMS (3), etc. Over the years, the members of the scientific staff have attended international meetings and symposiums such as the Manfred Donike Workshops and the USADA Symposium. Also, scientific staff have participated as international experts in the 20th Winter Olympic Games in Torino (Italy) in 2006, the 30th Summer Olympic Games in London (Great Britain) in 2012, the 22nd Winter Olympic Games in Sochi (Russia) and the 31st Summer Olympic Games, in Rio de Janeiro (Brazil).

DCLA, beyond sample analyses (within 2018 more than 3.000 samples have been analyzed), has undertaken a number of research programmes in the anti-doping research field, either partially funded by WADA or exclusively funded by OAKA. All projects have been conducted with the collaboration of external bodies, like governmental, university and WADA laboratories, in order to

ensure optimum scientific performance and results. The results of these projects have been published in peer-reviewed journals and presented in international anti-doping Workshops.

WADA inspection within 2018 led to a number of proposals to the Ministry as a prerequisite for the accreditation of the Laboratory. These led to the transfer of DCLA and its personnel to the IBA/NCSR “Demokritos”. NCSR “Demokritos” has assured from the Ministry of Culture a. the amount of 2.000.000 euros for purchasing state-of-the art analytical instruments and b. the amount of 1.280.000 euros for a period of three years as to cover functional expenses of DCLA, the recruitment of new personnel and the upgrading of its infrastructure.

The immediate goals of DCLA are the recruitment of new personnel, the upgrading of the research infrastructure, the accreditation by WADA and other organizations and the support of the Greek athletic community with doping control. In addition, major goal of the Laboratory is the upgrading of the research activity in the fields of chemical analysis and metabolic studies, in collaboration with the other laboratories of the Institute.

Publications

Chajistamatiou, A., Angelis, Y., Kiouisi, P., Tsiyou, M., Bakeas, E. (2019). Discrimination of tetryl samples by gas chromatography - isotope ratio mass spectrometry. *Forensic Chemistry*, 12, 42-45.

Articles accepted for publication within 2020

Fragkaki A.G., Petropoulou G., Athanasiadou I. Kiouisi P., Kioukia-Fougia N., Archontaki H., Bakeas E., Angelis Y.S. (2020). Determination of anabolic androgenic steroids as imidazole carbamate derivatives in human urine using liquid chromatography–tandem mass spectrometry. *Journal of Separation Science*, 43, 2154-2161 (IF: 2.878).

Sakellariou P., Kiouisi P., Fragkaki A.G., Lyris E., Petrou M., Georgakopoulos C. Angelis Y.S. (2020) Alternative markers for Methylnoretestosterone misuse in human urine. *Drug Testing and Analysis*, doi.org/10.1002/dta.2887 (IF: 2.903).

Sakellariou, P., Angelis, Y.S. (2020). Current methods of direct and indirect blood doping detection. *Pharmakeftiki Journal* (accepted). (IF: -)

HUMAN TISSUE BANK

Personnel

Helen Vavouraki, PhD, Senior Researcher- Scientific Responsible

Yiannis Ninios, PhD, Research Collaborator

Lydia Panagopoulou, MSc, Research Collaborator

Eleutherios Kosmidis, MSc, Scientific Collaborator

Zisis Miliotis, Undergraduate Student

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 Ministry of Health legislation 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. All the above activities comply with 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. It has gradually developed the necessary expertise in each procedure (procurement, tissue processing, irradiation sterilization and disposal of tissue grafts) involved in the Tissue Banking. In over 45 years of continuous operation, it has delivered more than 52.000 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.

During the last year, the Human Tissue Bank has participated and presented its products (Figure 1) in Dental congresses mainly, as follows:

- I) HAOMS 2019, 3rd Conference of Implants and Oral Surgery, organized by the Hellenic Association of Oral and Maxillofacial Surgery. Athens, January 24-26.
- II) International Congress “**MASTERMINDS 2**”, organized by the Greek Association of Medical and Dental Digital Technology **and** the Educational Company **OMNIPRESS**, Athens, May 17-17.
- III) 39th Panhellenic Dental Congress: “Personalised Medicine: From Diagnosis to Therapeutic Protocols” Heraklio Crete, October 24-26.

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.

Our research interests and activities are funded by:



Figure 1: Presentation of the Bank’s products in scientific congresses

- a) A Technological Research Project – Research, Development and Delivery of Tissue grafts - products of Tissue Repair, and
- b) A NSRF Research Project for the development of a new, specially designed bone graft to accompany the EPO patented TALOS, used in Neurosurgery (Figure 2)

Furthermore, we submitted a new proposal for the “development of new customized bone allograft using innovative digital technology”.

Our 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 (PhD theses).



Figure 2: Equipment which uses laser for the correct placement and cutting of the bone piece

2019 Findings

In 2019, we have collected tissues following the established tissue procurement regulations of the National and European Legislation. We have processed 134 femur heads from living donors and we have prepared and delivered 617 bone grafts to be used in Dentistry and Orthopedic Surgery. Moreover, we have delivered 13 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.

Other Activities for the Institute of Biosciences & Applications

Scientific Responsible of Human Tissue Bank.

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

Other Scientific Activities

Reviewer in the scientific Journals: 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

Research Proposals Assessor

Other Activities at the NCSR “DEMOKRITOS”

Member of the Health and Safety Committee of NCSR “DEMOKRITOS”

Educational activities

Joint MSc Programme “Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products”

Course: Tissue Banking-Development, Production and Quality Control of Tissue grafts.

June 2019

Current External Financing

NSRF Project 2014 – 2020:

Project title: TALOS-BIO - Development of a new, specially designed bone graft to accompany the EPO patented TALOS, used in Neurosurgery.

Duration: June 2018 – December 2020

Research Team: Y. Ninios, L. Panagopoulou, E. Kosmidis

Research Supervisor: H. Vavouraki

Overall payment: 188.800 €

Payment in 2019: 35.212 €

Citations 2019 (without self- citations): 7

Total Citations 2015-2019 (without self- citations): 66

h-factor: 9

EXPERIMENTAL ANIMAL FACILITY

Personnel

Dimitris Kletsas, Research Director, Scientific and Administrative Responsible

Giannis Zafeiropoulos, Laboratory Animal Technician

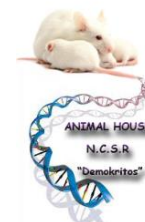
George Doulgeridis, Laboratory Animal Caretaker

Lykourgos Klamarias, Veterinarian

Laboratory Description

The Animal House has three facilities accredited according to the ΠΔ 56/2013 (A.Π. 310181/24-06-2019)

- Facility for Animal Reproduction: EL25BIObr019
- Facility for Animal Disposal: EL25BIOsup020
- Facility for Animal Experimentation: EL25BIOexp039



The animal facility during 2019 maintained and reproduced inbred strains of experimental animals. The following strains are currently available:

- Mice, strain CFW SWISS ALBINO
- Mice, strain NOD SCID (immunocompromised)- Developed within 2019
- Mice, strain SKH1 (hairless)
- Mice, strain C57Bl/6 (wild type and transgenic AD 5xFAD and TgMMP-9)
- Rats, strain WISTAR ALBINO
- Rabbits, strain New Zealand ALBINO

A **Unit of Aged Laboratory Animals** has been developed within 2019.

During 2019 the Animal Facility provided the following animals:

Users	Rats WISTAR	Mice SKH1	Mice CFW	Mice C57Bl/6J	Rabbits NZW	Mice SCID	Total
Institute of Biosciences and Applications	40	0	0	166	0	0	206
Institute of Nuclear & Radiological Sciences and Technology, Energy & Safety	37	0	403	25	2	261	728
External Users	194	6	2	62	0	0	264
Total	271	6	405	253	2	261	1.198

The operation 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, D. Mastellos, a representative from the the Veterinary Division of the Attica Prefecture -Substitutes: A. Tzinia, E. Livaniou, P. Sarris.

Committee for the Wellbeing of Laboratory Animals

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

During 2019:

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 animal colonies of the Facility have been renewed and new colonies (NOD 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 2019 and approved four (4) new research protocols.

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

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

The 3rd one-day Seminar for the users of the Facility has been organized.



ΕΘΝΙΚΟ ΚΕΝΤΡΟ ΕΡΕΥΝΑΣ
ΦΥΣΙΚΩΝ ΕΠΙΣΤΗΜΩΝ «ΔΗΜΟΚΡΙΤΟΣ»



ΕΚΤΡΟΦΕΙΟ ΠΕΙΡΑΜΑΤΟΖΩΩΝ

3^η ΗΜΕΡΙΔΑ ΕΚΤΡΟΦΕΙΟΥ ΠΕΙΡΑΜΑΤΟΖΩΩΝ

Τετάρτη 18/09/2019

Ωρα 10:00

Αμφιθέατρο IBE

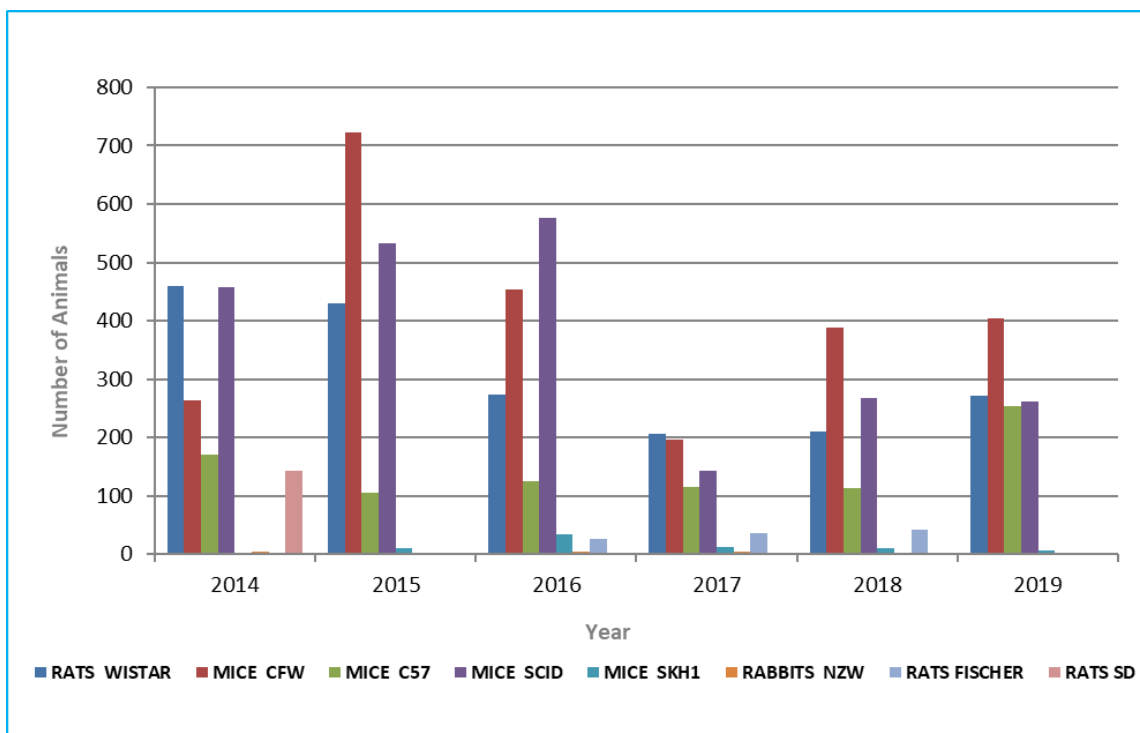
Πρόγραμμα:

- **10⁰⁰-10¹⁰ Δημήτρης Κλέτσας**
Διευθυντής Ινστιτούτου Βιοεπιστημών & Εφαρμογών ΕΚΕΦΕ «Δημόκριτος», Υπεύθυνος Εκτροφείου Πειραματοζώων.
«Εισαγωγή / Παρουσίαση Εκτροφείου Πειραματοζώων ΕΚΕΦΕ «Δημόκριτος»
- **10¹⁰-10⁴⁰ Νικόλαος Κωστομητσόπουλος**
Κτηνίατρος, Ειδικός Λειτουργικός Επιστήμονας Α' Βαθμίδας, Προϊστάμενος Μονάδας Ζωικών Προτύπων, Τόσημα Ιατροβιολογικών Ερευνών Ακαδημίας Αθηνών.
«Διαχείριση Μονάδας Ζωικών Προτύπων: Η Δεοντολογία στην Πράξη»
- **10⁴⁰-11¹⁰ Απόστολος Παπαλόης**
Διευθυντής Ερευνητικού, Εκπαιδευτικού και Πειραματικού Κέντρου ELPEN.
«Ποια δεδομένα έφερε η εφαρμογή της νέας νομοθεσίας στην Ελλάδα και διεθνώς»
- **11¹⁰-11⁴⁰ Παναγιώτης Ανδριόπουλος**
Κτηνίατρος, Περιφέρεια Αττικής - Διεύθυνση Αγροτικής και Κτηνιατρικής Πολιτικής.
«Αδειοδότηση πειραματικών πρωτοκόλλων»
- **11⁴⁰-12⁰⁰ Διάλειμμα**
- **12⁰⁰-12²⁰ Γιώργος Κουρούκλης**
Ειδικός Ιατρός Εργασίας, Διδάκτωρ Πανεπιστημίου Αθηνών.
«Διαδικασίες και μέτρα προστασίας των εργαζομένων με πειραματοζώα»
- **12²⁰-12⁴⁰ Λυκούργος Κλαμαριάς**
Κτηνίατρος, Υπεύθυνος Κτηνίατρος Εκτροφείου Πειραματοζώων ΕΚΕΦΕ «Δημόκριτος».
«Στοιχεία ανατομίας και φυσιολογίας μυών και επίμυων»
- **12⁴⁰-13⁰⁰ Παντελής Σαρρής**
Κτηνίατρος Αναπληρωτής Κτηνίατρος ΕΑΠ Εκτροφείου Πειραματοζώων ΕΚΕΦΕ «Δημόκριτος».
«Στοιχεία ανατομίας και φυσιολογίας κονίκλων»
- **13⁰⁰-13²⁰ Ευαγγελία Λιβανίου**
Ερευνητρια Α' Βαθμίδας, ΙΠΡΕΤΕΑ, ΕΚΕΦΕ «Δημόκριτος».
«Ανοσοποίηση κονίκλων και αιμοληψία»



Πληροφορίες - Επικοινωνία : Ι. Ζαφειρόπουλος (210-6503705) jzafiro@bio.demokritos.gr

DISPOSAL OF LABORATORY ANIMALS 2014-2019



LIGHT MICROSCOPY UNIT

Personnel

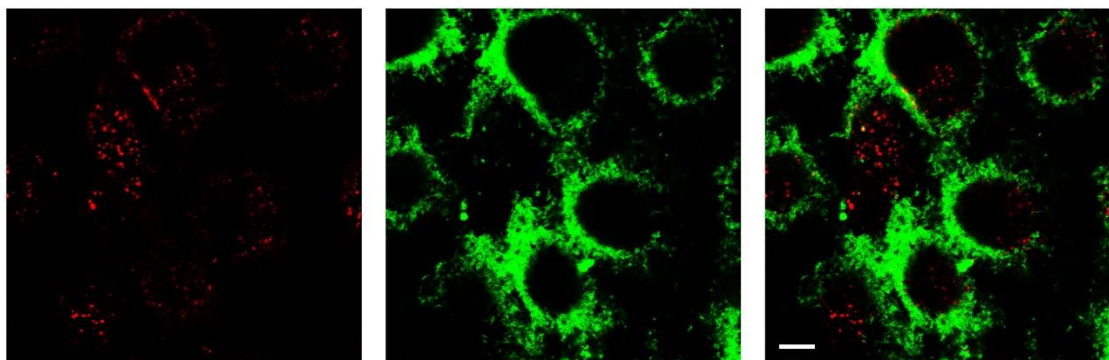
Dimitris Kletsas, Research Director, Director of IBA, Administrative and Scientific Responsible

Vassiliki Labropoulou, Senior Researcher

Haris Pratsinis, Senior Researcher

Marina Sagnou, Researcher

Alexandros Athanasopoulos, Research Assistant



Laboratory Description – Research interests - Progress:

The light microscopy unit of the Institute of Biosciences and Applications (IBA) 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 light microscopy unit is equipped with a Nikon E600 Confocal Microscope and a state-of-the-art Leica TCS SP8 multiphoton microscope, with a fully automated galvanometric stage. The system is accompanied by a climate chamber for the strict control of all environmental variables (humidity, temperature, CO₂, O₂, N₂).

The light microscopy unit offers 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 programs such as ImageJ / Fiji and Imaris (Bitplane))

Leica TCS SP8 MP



The light microscopy unit in the year 2019 recorded more than 470 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
- The study of the induction of genotoxic lesions and cell senescence
- The expression of specific proteins associated with mechanisms involved in age-associated diseases such as dyslipidemia, diabetes mellitus and Alzheimer's disease
- Functional characterization of opioid 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 light microscopy unit support the scientific work of the various research teams, contributing to scientific publications, doctoral theses and the development of collaborations among the users of the Unit. Moreover, the Unit actively supports the various NCSR "D" educational programs participating in presentations, demonstrations and workshops.

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

HISTOLOGY UNIT

Personnel

Dimitris Kletsas, Research Director, Director of IBA

Garyfalia Drossopoulou, Senior Researcher

Unit Infrastructure – Research Activities

The Histology Unit (HU) of the Institute of Biosciences and Applications (IBA) was established in 2019.

The HU aims to support a wide variety of research activities of IBA researchers and external collaborators. The HU focuses on the investigation and phenotypic analysis at the tissue level of human and animal model specimens that are related to several pathologies.

The HU is fully equipped to fulfill its purposes with chemicals, hoods, tissue processing and embedding equipment, 2 microtomes, a cryostat and a vibratome.

Users can perform tissue processing, embedding, sectioning and staining with a series of stains. IBA researchers can also be trained to use equipments like microtomes, cryostats or vibratomes. The unit can provide consultation on protocol set up and phenotype interpretation.

Our currently available main equipment:

Cryostat Leica CM1850



Embedding oven (Jouan Percision NAPCO)



Microtome Leica RM2135



Vibratome Leica VT1200S



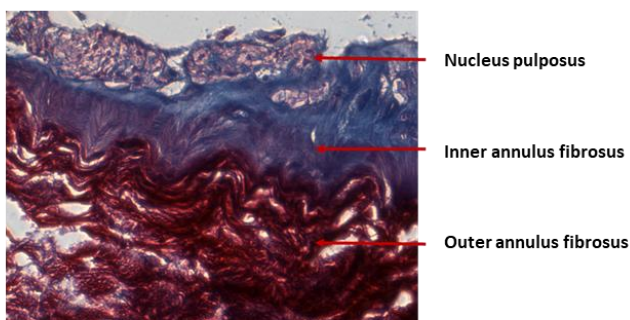
WaterBaths Leica



During 2019 in the Histology Unit of IBA, routine protocols were performed that involved the investigation of the following:

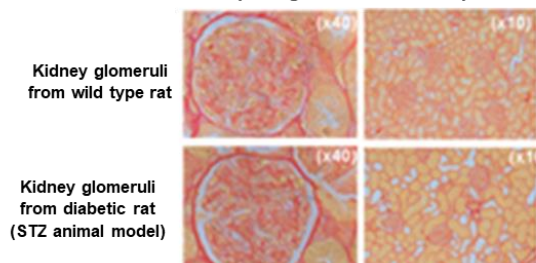
- Mode of action of liraglutide in the prevention of podocyte and β -cell apoptosis.
- Role of secreted conditioned media from human amniotic fluid mesenchymal stem/stromal cells in ameliorating the establishment and development of Diabetic Nephropathy.
- Intervertebral disc degeneration
- Skin ageing
- Cancer development in experimental animal models

Staining of intervertebral disc section

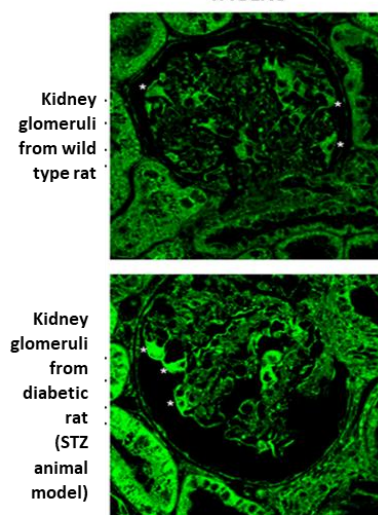


Cyan: Proteoglycans (Alcian Blue staining)
Red: Collagen (Sirius Red staining)

Sirius Red staining (collagen accumulation)



Immunofluorescence staining for TAGLN3



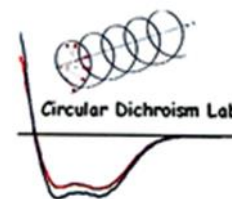
CIRCULAR DICHROISM (CD) LABORATORY

Personnel

Metaxia Vlassi, Research Director

Maria Pelecanou, Research Director

Angeliki Panagiotopoulou, Functional Research Scientist B'



User Committee

Dr. Metaxia Vlassi

Dr. Maria Pelecanou

Dr. Angeliki Chroni

Dr. Georgios Nounesis (INRASTES)

Dr. Efstratios Stratikos (INRASTES)

Laboratory Description - Object

The equipment of the Circular Dichroism Laboratory (CD) 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 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.

Achievements - Progress in 2019

The CD unit has been widely used since 1998 by research teams of NCSR "D" and other academic / research organizations from all over Greece, for structural analyzes and studies of interactions of biological macromolecules. It should be noted that the CD spectrophotometer 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 2019, as in previous years, the CD workshop has provided 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 National Technical University of Athens (Chemical Engineering Dept), the University of Patras, the University of Thessaloniki and the NHRF (Institute of Biology, Pharmaceutical Chemistry and Biotechnology). Income from the provision of services is solely used to cover the operation and repair needs of the 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) (funding approved in June 2018, for 3 years).

ISOLATION, CHARACTERIZATION AND CULTURE OF STEM CELLS APPLICATIONS IN REGENERATIVE MEDICINE

Personnel

Paraskevi Kitsiou, Senior Researcher (Admin)

Athina Tzinia, Senior Researcher

Garyfallia Drossopoulou, Senior Researcher

Laboratory Description – Research Objectives

The laboratory of Cell & Matrix Pathobiology focuses 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)

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, B¹ 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).

Progress achieved

During 2019, the laboratory focus 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.

Founding

The research activities of the laboratory of Cell & Matrix Pathobiology are founded by the company Biophylaxis, S.A.

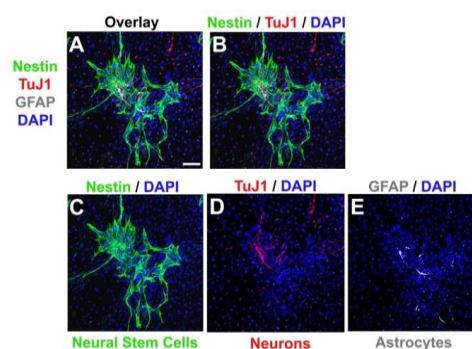


Figure 1: Culture of OECs results to enriched population of neural stem cells (NSC), as it appears from the use of appropriate indicators. These cells maintain the ability of proliferation and renewal.

LABORATORY OF MOLECULAR DIAGNOSIS OF GENETIC DISEASES

Personnel

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.

2019 Findings

During 2019, in our laboratory 3 families were tested for Nodular Sclerosis, free of charge.

LABORATORY OF CELL-BASED ASSAY SYSTEMS AND BIOACTIVE COMPOUNDS

Personnel

Dimitris Kletsas, Research Director

Harris Pratsinis, Senior Researcher

Eleni Mavrogatou, Researcher

Adamantia Papadopoulou, Postdoctoral Fellow

Maria Angelopoulou, Graduate Research Associate (MSc)

Anastasios Kouroumalis, Graduate Research Associate (MSc)

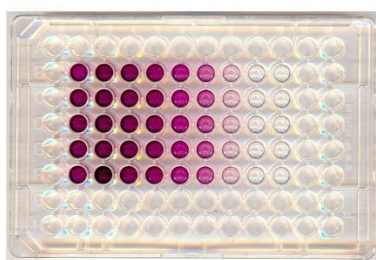
Description

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.

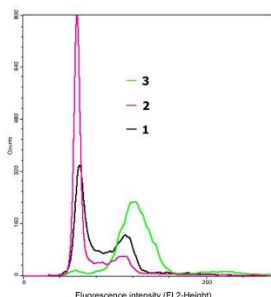
2019 Findings

During 2019, a new contract was signed between the service lab and the company AHB Group S.A. for the study of the effects of alkaline pH on human cell physiology, as well as, the effects of alkaline water on experimental animals.

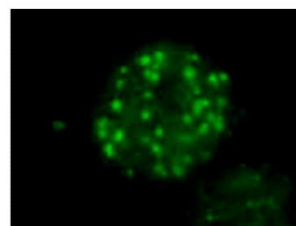
CYTOTOXICITY ASSESSMENT



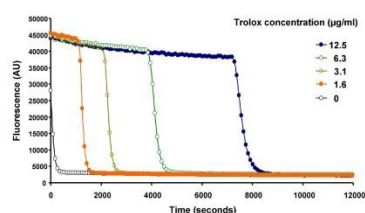
CELL-CYCLE ANALYSIS



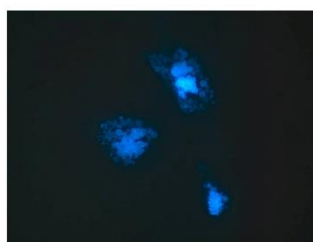
DNA DAMAGE ANALYSIS



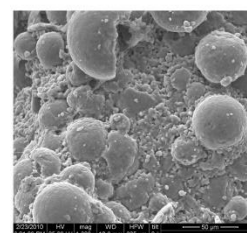
ANTIOXIDANT ACTIVITY ASSAY



STUDY OF APOPTOSIS



ORGANOTYPIC CELL CULTURES



EDUCATIONAL ACTIVITIES

EDUCATION

The Institute of Biosciences and Applications has continued the successful implementation of a variety of educational programs and activities in 2019, which include:

- a) the training of postdoctoral researchers,
- b) the training of undergraduate students and the supervision of postgraduate (PhD, MSc and diploma) students to successfully complete their project,
- c) the organization of postgraduate level courses and seminars,
- d) the participation of IBA researchers as lecturers in the Annual Summer School of NCSR “Demokritos” for undergraduate and graduate students,
- e) the organization of a “hands-on” Summer Camp for Lyceum students, and
- f) the participation in dissemination and science communication activities to promote science, inform the public on research activities in IBA and promote research careers to young people.

During 2019 **17** postdoctoral researchers were trained at IBA, while, **23** PhD students and **10** MSc students implemented their projects at the Institute under the supervision of IBA researchers.

In 2019, **2** graduate students completed their PhD theses and **4** students completed their Master’s theses successfully fulfilling their course requirements.

Moreover, **12** undergraduate students from Greek Universities performed their final year project at IBA. Additionally, **6** undergraduate students undertook research practice in IBA laboratories.

Additionally, IBA researchers participated as lecturers in various courses within the framework of Postgraduate Programmes of several Greek Universities:

- Lecture entitled «*Molecular mechanisms of carcinogenesis and pharmaceutical inhibition of selected therapeutic cellular targets*» in the framework of the Post-Graduate Specialization Diploma “*Drug development: Research, commercialization and accessibility*” (**Dr. G. Voutsinas**, Medical School, University of Athens)
- Lecture entitled “*Molecular mechanisms of carcinogenesis and pharmaceutical inhibition of selected therapeutic cellular targets*” in the framework of the Post-Graduate Specialization Diploma “*Applications of Biology in Medicine*” (**Dr. G. Voutsinas**, Department of Biology and Medical School, University of Athens)
- Lecture entitled “*G protein- coupled receptors in health and disease and drug development*” in the framework of the postgraduate course “*Molecular Basis of disease*” (**Dr. Z. Georgoussi**, Department of Biology, University of Athens)
- Lecture entitled “*G protein- coupled receptors in health and disease and drug development*” in the framework of the postgraduate course “*Molecular and Applied Physiology*” (**Dr. Z. Georgoussi**, Medical School, University of Athens)
- Course lecturing entitled “*Signaling of Neurotransmitter Receptors*” in the framework of the postgraduate course “*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 laboratory 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 Postgraduate Master's Degree "*Neoplastic Disease in Humans: Diagnosis, Modern Treatment and Research*" (**Dr. H. Pratsinis**, Medical School, University of Athens)
- Lecture entitled "*Cell Cycle: Checkpoints and Consequences for Normal Cellular Function when Cell Cycle Progress Dysfunctions*" in the framework of the course "*Cell cultures – Tissue cultures*" within the postgraduate programme "*Application of Biology in Medicine*" (**Dr. Th. Sourlingas**, Department of Biology & Medical School, University of Athens)
- Lecture entitled "*Alzheimer's Disease: a) diagnosis (clinical, laboratory, imaging), b) risk factors (genetics, age, sex, cardiovascular, trauma, depression, drugs etc.), c) recent data for the mechanisms of disease initiation and progress and therapeutic strategies*" in the framework of the Postgraduate Master's Degree "*Clinical Biochemistry-Molecular diagnosis*" (**Dr. A. Chroni**, Department of Chemistry, University of Athens)
- 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 "*Lateral organization of plasma membrane,*" in the framework of the Inter-Institutional Joint Post-Graduate Programme "*Molecular and Cellular Biology and Biotechnology*" (**Dr. C. Gournas**, Medical School & Dept. Biological Applications and Technologies, University of Ioannina and IMBB)
- Lecture entitled "*Lateral Compartmentalization and amino acid transporter endocytosis*" in the framework of the course "*Molecular Microbiology*" (**Dr. C. Gournas**, Dept. Biology, University of Athens)
- Teaching in the framework of the postgraduate program "*Bioinformatics*", the course "*Introduction to Computational Biology*" (**Dr. Y. Almirantis**, 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. Y. Almirantis**, Department of Biology, University of Athens)
- Lectures on "*Principles of X-Ray Crystallography: Applications in Structural Biology*" within the course "*Current biochemical and biophysical analytical methods*" 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)
- Lecture entitled "*Protein Structure – Experimental & Theoretic approaches*" in the framework of the postgraduate program "*Bioinformatics-Computational Biology*" (**Dr. M. Vlassi**, Department of Biology, University of Athens)

During 2019, the graduate students of the Institute participated in journal clubs and presented Research in Progress seminars (see list below). In addition, a series of seminars by invited speakers was held in IBA (see list below).

Moreover, in July 2019, within the framework of NCSR "Demokritos" Summer School, IBA researchers delivered a series of lectures on various frontier subjects of Biological interest (see list below)

In 2019 the joined **MSc Programme “Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products”** (ΦΕΚ 3923/2018) was successfully organized by the Department of Chemistry of the University of Patras and the Institute of Biosciences and Applications of NCSR "Demokritos". **9** postgraduate students were enrolled in this programme. The students attended courses at the 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**
 - Lecture entitled “*Functional testing of organs and endocrine glands*” (**Dr. G. Drossopoulou**)
 - Lecture entitled “*Chemical ecology: Applications of bioactive secondary metabolites of natural origin*” (**Dr. M. Konstantopoulou**)
 - Lecture entitled “*Methods for the analysis and study of proteins, lipids and carbohydrates*” (**Dr. A. Chroni**)
- **Advanced Biochemistry**
 - Lecture entitled “*Protein Structure – Experimental & Theoretic approaches*” (**Dr. M. Vlassi**)
 - Lecture entitled “*Signaling pathways of G protein-coupled receptors in health and disease and drug development*” (**Dr. Z. Georgoussi**)
 - Lecture entitled “*Transcription factors (CREB, CREM, NF-kB, AP-1, STAT), identification methods for transcription factors activation*” (**Dr. G. Drossopoulou**)
 - Lecture entitled “*Ca²⁺ signaling*” (**Dr. E. Mavrogonatou**)
 - Lecture entitled “*Signaling pathways of main cytokines and growth factors IL-1, TNF- α , TGF- β (SMAD proteins), PDGF, EGF, FGF*” (**Dr. D. Kletsas**)
 - Lecture entitled “*Extracellular matrix interaction with cells*” (**Dr. H. Pratsinis**)
 - Lecture entitled “*Lateral compartmentalization and function of plasma membrane: eisosomes and transmembrane transporters*” (**Dr. V. Sophianopoulou & Dr. C. Gournas**)
- **Molecular Pharmacology – Immunology**
 - Lecture entitled “*«Opioid analgesics [morphine, morphine derivatives, analgesic receptor theory, agonists and antagonists, encephalines and endorphins, receptor mechanisms (μ , κ , δ and σ receptors)»*” (**Dr. Z. Georgoussi**)
 - Lecture entitled “*Pharmaceutical activity on the receptors (the role of the receptor, neurotransmitters and hormones, receptors, signal transduction, receptor structural rearrangements, agonists and antagonists design, representative agonists, reverse antagonists, desensitization and sensitization, tolerance and addiction, cellular receptors, types and subtypes of receptors)*” (**Dr. Z. Georgoussi & Dr. Papakyriakou**)
 - Lecture entitled “*Pharmaceutical activity on enzymes (binding interactions, competitive and non-competitive inhibitors, allosteric inhibitors, the catalytic role of enzymes, enzyme regulation, isoenzymes, pharmaceutical applications of inhibitors (antimicrobial, antiviral and human enzyme inhibitors)*” (**Dr. Papakyriakou & Dr. M Sagnou**)
 - Lecture entitled “*«Structure and function of nucleic acids (DNA structure, anti-DNA drugs, RNA, anti-RNA drugs, drugs derived from nucleic acid structural motifs, molecular biology and genetic engineering)*” (**Dr. Papakyriakou & Dr. M Sagnou**)
 - Lecture entitled “*The adrenergic neuronal system (the adrenergic system, adrenergic receptors, adrenergic transducers, catecholamine biosynthesis and metabolism, neurotransmission, drug-targets, adrenergic binding area, structure-activity-relationships, agonists, antagonists of adrenergic receptors, other drugs affecting adrenergic transduction)*” (**Dr. Papakyriakou**)
 - Lecture entitled “*The RNAi as a defence mechanism against insect viruses*” (**Dr. L. Swevers & Dr. V. Labropoulou**)
- **Molecular and Cellular Biology – Molecular Biotechnology**

- Lecture entitled “*Development, Production and testing of tissue grafts*” (**Dr. H. Vavouraki**)
- Lectures entitled “*Recombination and hybridization*”, “*Which part of eukaryotic genome is transcribed and translated*”, “*DNA mapping*”, “*Structure and function of genes*”, “*Sequence vectors, expression vectors*”, “*Molecular carcinogenesis*”, “*Rare diseases*” (**Dr. G. Voutsinas**)
- Lectures entitled “*Strain selection, genetic recombination*”, “*Vectors - DNA (plasmids, cosmids, phages)*”, “*Cloning vectors*”, “*Methods of transfection and recombination of genetic information*” (**Dr. C. Gournas**)
- Lecture entitled “*Diabetes – Diabetic nephropathy: Current therapeutic approaches*” (**Dr. G. Drossopoulou**)
- Lecture entitled “*Cellular senescence as an anti-aging therapeutic target*” (**Dr. D. Kletsas**)
- Lecture entitled “*Flow cytometry*” (**Dr. E. Mavrogonatou**)
- Lecture entitled “*Methods for the evaluation of cytotoxicity-cytostatic activity*” (**Dr. H. Pratsinis**)
- Lecture entitled “*DNA organisation, histones and chromatine function*” (**Dr. Th. Sourlingas**)
- Lecture entitled “*Viral DNA replication, prokaryotic and eukaryotic cell*”, “*Synthetic DNA, cDNA, gene libraries*” (**Dr. V. Sophianopoulou**)
- Lecture entitled “*Bacteriophage expression system: generation of recombinant viral vectors, via homologous recombination and delocalization*” (**Dr L. Swevers & Dr. V. Labropoulou**)
- Lecture entitled “*Cardiavascular diseases and current therapeutic approaches*” (**Dr. A. Chroni**)

Furthermore, in 2019 the IBA researcher **Dr. Z. Georgoussi** participated for another year in the joined MSc Programme “**Athens International Master’s Programme in Neurosciences**” (ΦΕΚ 3802/2018).

In 2019 the Institute, for the second year organized the **2nd Summer Camp for Lyceum** students after the overwhelming success, comments and increased demand obtained in 2018. This two-week hands-on educational programme (24/6/2019 – 5/7/2019), was attended by **19** pupils from various schools of Attiki and other municipals, included a well-structured schedule of visits to the Institute's laboratories, an overview of the Institute’s research activities and active participation in hands-on projects. Moreover, theoretical familiarization on laboratory techniques used for biochemical, molecular and cellular biology studies was also achieved. 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 period, the students presented their results to IBA members, as well as to their teachers and parents. The IBA researchers who acted as instructors in this Summer Camp were: **Drs G. Drossopoulou, Z. Georgoussi, P. Kitsiou, D. Kletsas, M. Konstantopoulou, V. Labropoulou, E. Mavrogonatou, A. Papakyriakou, M. Pelecanou, H. Pratsinis, A. Prombona, M. Sagnou, V. Sophianopoulou, L. Swevers, A. Tzinia, H. Vavouraki, G. Voutsinas.**

Finally, **Dr. H. Pratsinis** and **Dr. A. Prombona** continued to provide guided tours and institute presentations to highschool and undergraduate students.



ΔΗΜΟΚΡΙΤΟΣ
DEMOKRITOS

24 ΙΟΥΝΙΟΥ - 5 ΙΟΥΛΙΟΥ 2019

**ΘΕΡΙΝΑ
ΕΠΙΣΤΗΜΟΝΙΚΑ
ΕΡΓΑΣΤΗΡΙΑ**
ΓΙΑ ΜΑΘΗΤΕΣ ΛΥΚΕΙΟΥ
ΣΤΟ ΙΝΣΤΙΤΟΥΤΟ
ΒΙΟΕΠΙΣΤΗΜΩΝ & ΕΦΑΡΜΟΓΩΝ

Πληροφορίες: <http://bio.demokritos.gr/el/announcements/173-summercamp>
Τηλ. 210 650 3582, E-mail: summercamp@bio.demokritos.gr



COMPLETION/AWARD OF DOCTORAL THESES IN 2019

GRADUATE STUDENT	DOCTORAL THESIS TITLE	IBA SUPERVISOR	UNIVERSITY
Christina Golfiopoulou	Structural and functional characterization of naturally occurring apoA-I mutants - analysis of HDL atheroprotective properties	A. Chroni	Department of Chemistry, University of Athens
Aggeliki Delimitsou	Functional evaluation of variations with unknown clinical significance and characterization of new gene mutations involved in hereditary breast-ovarian cancer	G. Voutsinas	School of Medicine, University of Athens

COMPLETION OF MASTER THESES IN 2019

GRADUATE STUDENT	TITLE OF MSc THESIS	IBA SUPERVISOR	UNIVERSITY
Konstantina Katrini	<i>Study of the HDL function on patients suffering from acute ischemic stroke</i>	A. Chroni	Department of Chemistry, University of Athens
Eva Pateraki	<i>The effect of pharmaceutical intervention on the intervertebral disk cellular homeostasis</i>	D. Kletsas	Department of Biology, University of Athens
Anna Santorinaiou	<i>The effect of thymosin peptides on human dermal fibroblasts</i>	D. Kletsas/ H. Pratsinis	Department of Pharmacy, University of Athens
Asimina Fotopoulou	<i>The importance of cellular senescence in the expression of extracellular matrix components of stromal fibroblasts</i>	D. Kletsas	Department of Chemistry, University of Athens

IBA LECTURES' CONTRIBUTION TO THE 2019 SUMMER SCHOOL

DATE	SPEAKER	TITLE
1/7/2019	Dr. D. Kletsas IBA, NCSR "Demokritos"	The multiple roles of cell senescence in tissue homeostasis
1/7/2019	Dr. L. Swevers IBA, NCSR "Demokritos"	A novel CRISPR/Cas technology and gene editing
1/7/2019	Dr. A. Choni IBA, NCSR "Demokritos"	Cardiovascular disease: causes and therapeutic approaches
1/7/2019	Dr. G. Drossopoulou IBA, NCSR "Demokritos"	Renal diseases: Could regenerative medicine contribute to therapeutic approaches?
3/7/2019	Dr. G. Gournas IBA, NCSR "Demokritos"	Exploring plasma membrane compartmentalization to develop a new generation of antifungal drugs
3/7/2019	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
3/7/2019	Dr. H. Pratsinis IBA, NCSR "Demokritos"	<i>In vitro</i> studies of natural and synthetic bioactive products

SEMINAR PROGRAMME 2019 OF THE GRADUATE STUDENTS INSTITUTE OF BIOSCIENCES & APPLICATIONS

DATE	SPEAKER	TITLE
12/6/2019	Ch. Mountaki IBA, NCSR "Demokritos"	α -Sheet secondary structure in amyloid β -peptide drives aggregation and toxicity in Alzheimer's disease
12/6/2019	P. Pallaki IBA, NCSR "Demokritos"	Alternative RGS4 cell signaling pathways in the neuronal development and homeostasis
19/6/2019	C. Karoussiotis IBA, NCSR "Demokritos"	Autophagy: The role of κ -opioid receptor
18/7/2019	A. Kouroumalis IBA, NCSR "Demokritos"	Study of the effect of the environment on gene expression and function of intervertebral disc cells
18/7/2019	N. Manikas IBA, NCSR "Demokritos"	The olfactory stimulation from plant aroma as a tool for garden design

SEMINAR PROGRAMME 2019 OF INVITED SPEAKERS INSTITUTE OF BIOSCIENCES & APPLICATIONS

DATE	SPEAKER	TITLE
12/4/2019	Assis. Prof. Nikolaos Balatsos Dep. Biochemistry & Biotechnology, Univ. Thessalia	A poly (A)-specific ribonuclease in RNA biology: a trilogy in cancer and circadian rhythms
13/5/2019	Prof. Nektarios Tavernarakis Medical School, Univ of Crete	Autophagy as a regulator of mitochondrial homeostasis against aging and neurodegeneration

COLLECTIVE DATA

SUMMARIZED DATA ON THE PRODUCTIVITY OF SCIENTIFIC PROGRAMMES

	P R O G R A M M E			I N S T I T U T E
	A	B	C	
Researchers & functional scientific personnel	11	7	6	25 ^a
Technical Specialists	1	1	-	7 ^b
Collaborating & Emeritus Scientists	3	1	1	5
Postdoctoral Fellows	6	7	4	17
PhD candidates	12	7	4	23
MSc students	8	1	1	10
Graduate Research Associates	7	1	1	14 ^c
Undergraduate and other training students	7	9	5	23 ^d
Administrative and Technical Support	-	-	-	13
Total Personnel	56	34	22	137
Publications in Peer-Reviewed Journals	16	15	15	46
Cumulative Impact Factor in Peer-Reviewed Journals	74.632 (16)	55.978 (15)	57.284 (15)	187.894 (46)
Proceedings in Conferences	2	1	1	4
Total Publications	18	16	16	50
Citations	1539	609	356	2511 ^e
International Patents	-	-	1	1
Greek Patents	-	-	1	1
Presentations to International Conferences	17	12	4	33
Presentations to Greek Conferences	17	7	7	31
Total Presentations to Conferences	34	19	11	64

^aOne Scientist of the Human Tissue Bank included

^bFour technical specialists (PhD) of the Laboratory for Doping Control and Metabolic Studies and one technical specialist (PhD) of the Light Microscopy Unit included

^cOne graduate research associate of the Experimental Animal Facility and one graduate research of the Human Tissue Bank included

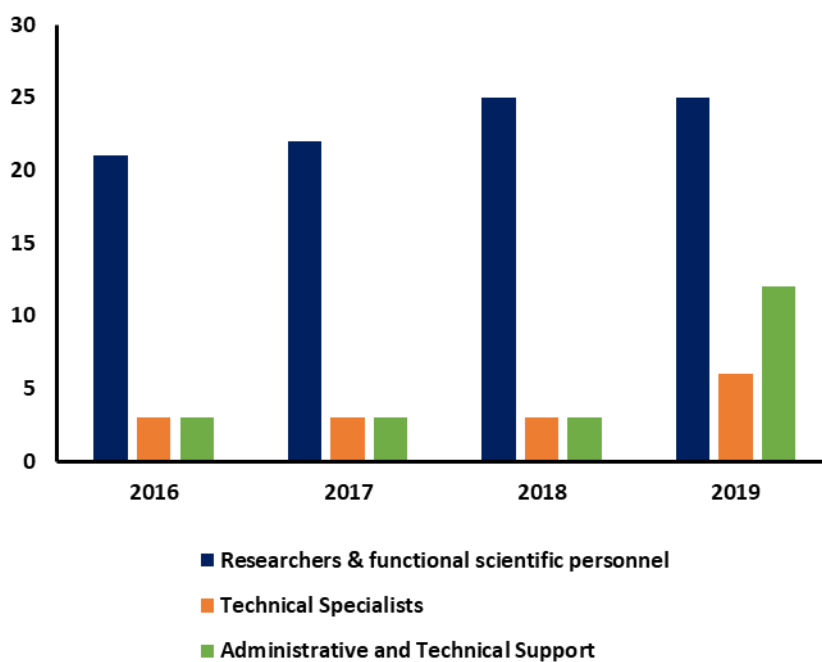
^dOne student of the Human Tissue Bank included

^eOne common publication between programmes B and C and one publication of the Laboratory for Doping Control and Metabolic Studies included

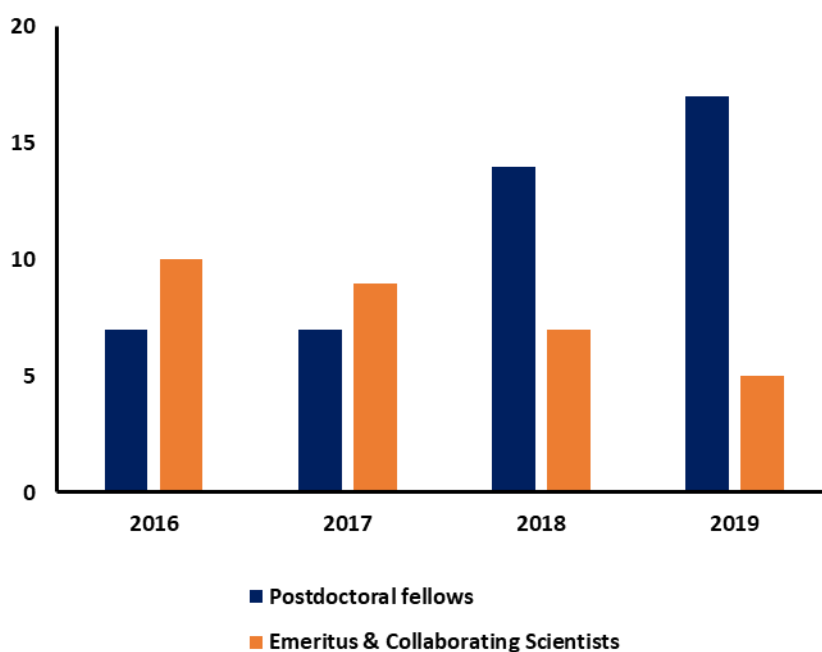
^fCitations of the Human Tissue Bank included

CHANGES OF IBA STAFF DURING 2016-2019

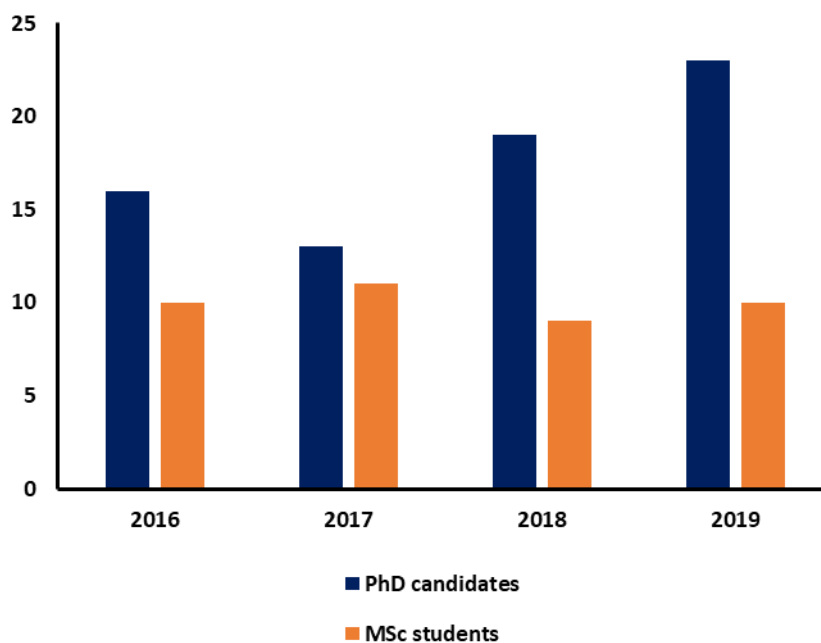
Tenured Staff



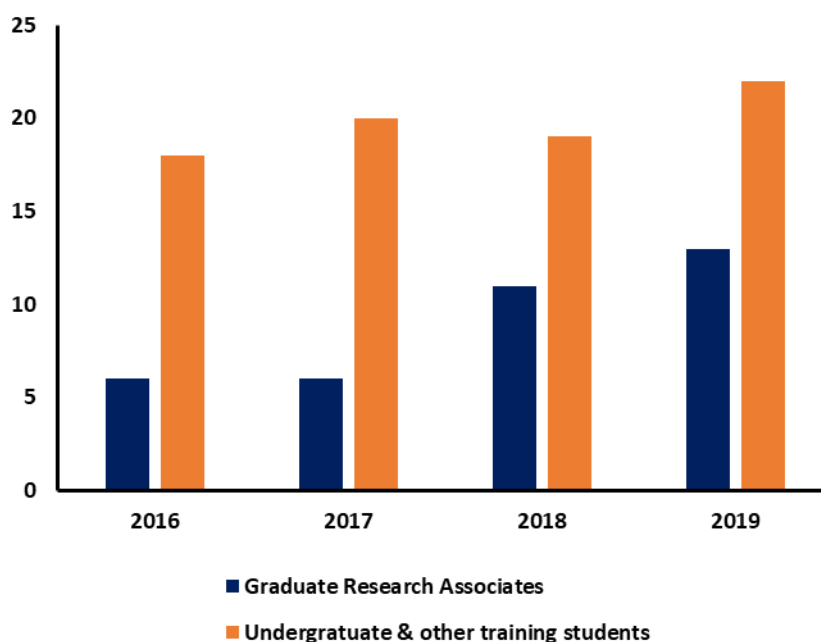
Postdoctoral fellows/ Collaborating Scientists



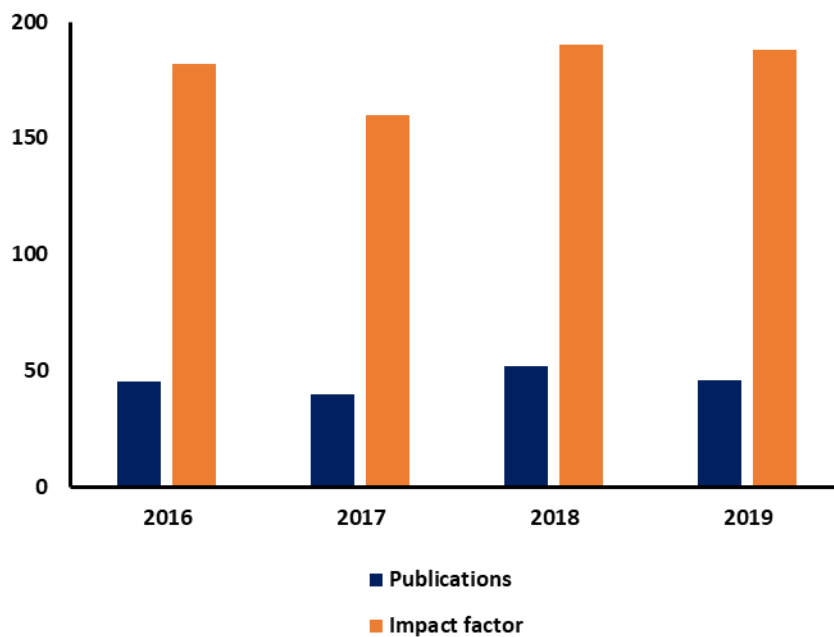
PhD candidates and MSc students



Undergraduate & other training students



Publications in peer-reviewed Journals and cumulative impact factor during 2016-2019



Citations 2016-2019

