DEMOKRITOS
NATIONAL CENTRE FOR SCIENTIFIC RESEARCH

IB-A
NCSR DEMOKRITOS

INSTITUTE OF BIOSCIENCES & APPLICATIONS

ANNUAL REPORT 2022

NATIONAL CENTRE FOR SCIENTIFIC RESEARCH

"DEMOKRITOS"

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ANNUAL REPORT 2022

AGIA PARASKEVI

NOVEMBER 2023

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ORGANISATION CHART-
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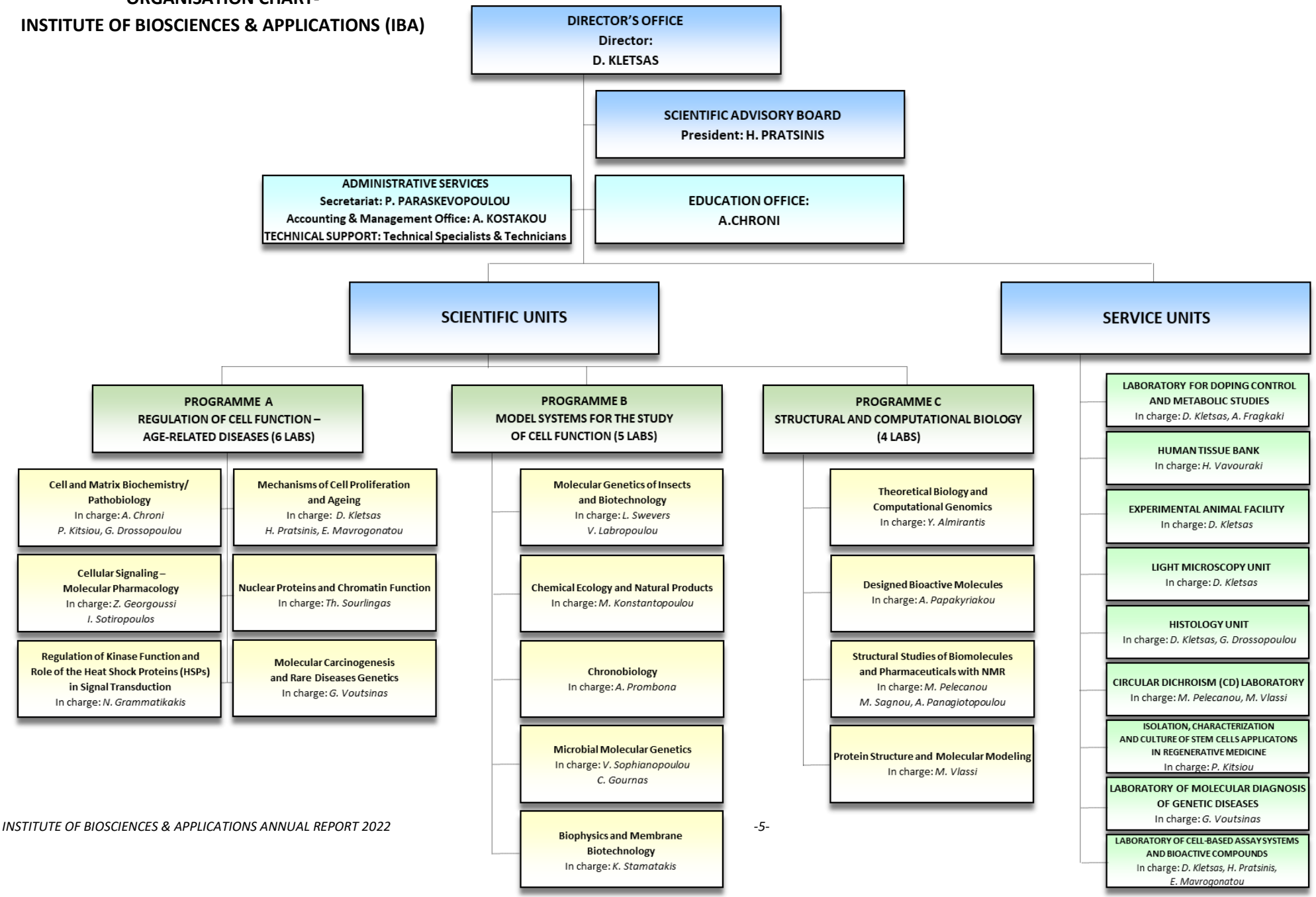

IBA PERSONNEL

DIRECTOR

Kletsas Dimitris	Dr. Biologist

SCIENTIFIC STAFF

Research Directors

Almirantis Yannis	Dr. Theoretical Biologist
Chroni Angeliki	Dr. Chemist
Georgoussi Zafiroula-Iro	Dr. Biochemist
Kletsas Dimitris	Dr. Biologist
Konstantopoulou Maria	Dr. Biologist
Pelecanou Maria	Dr. Pharmacist
Sophianopoulou Vassiliki	Dr. Molecular Biologist, Microbiologist
Stamatakis Konstantinos	Dr. Biologist
Swevers Luc	Dr. Biologist
Vlassi Metaxia	Dr. Physicist-Crystallographer
Voutsinas Gerassimos	Dr. Biologist

Senior Researchers

Grammatikakis Nikolaos	Dr. Molecular Biologist
Drossopoulou Garyfalia	Dr. Biologist
Kitsiou Paraskevi	Dr. Biologist
Labropoulou Vassiliki	Dr. Biochemist
Papakyriakou Athanasios	Dr. Chemist
Pratsinis Harris	Dr. Chemist
Prombona Anastasia	Dr. Molecular Plant Biologist
Sourlingas Thomae	Dr. Biologist
Vavouraki Helen	Dr. Pharmacist

Researchers

Gournas Christos	Dr. Biologist
Mavrogonatou Eleni	Dr. Biologist
Sagnou Marina	Dr. Biologist/Chemist
Sotiropoulos Ioannis	Dr. Biologist

Functional Scientific Personnel

Panagiotopoulou Angeliki	Dr. Biochemist

TECHNICAL SPECIALISTS

Angelis Yiannis	Dr. Chemist
Athanasopoulos Alexandros	Dr. Biologist
Avgeris Socratis	Technologist (MSc)
Fragkaki Argyro	Dr. Chemist
Kioukia-Fougia Athanasia	Dr. Pharmacist
Kiousi Polyxeni	Dr. Chemist
Stefanou Dimitra	Agronomist
Soukou Foteini	Dr. Biologist

ADMINISTRATIVE & TECHNICAL SUPPORT

Chlapana Foteini	Research Technician
Doulgeridis George	Laboratory Animal Caretaker
Filippidou Maria	Administrative Officer
Kostakou Athanasia	Administrative & Financial Officer
Loui Stella	Technologist
Paraskevopoulou Panagiota	Secretary
Pavlaki Maria	Supporting Personnel
Tzouvara Vassiliki	Administrative Officer
Tselia Milena	Administrative & Technical Support
Vlahos Panayiotis	Network Administrator (MSc)
Vlahou Maria	Administrative Officer
Zafeiropoulos Giannis	Laboratory Animal Technician

EMERITUS & COLLABORATING SCIENTISTS

Scientists	**IBA Researcher**
Iatrou Kostas (Dr. Biochemist & Molecular Biologist) – *Emeritus*	Georgoussi Z.
Papageorgiou Spyros (Dr. Physicist) – *Collaborating*	Almirantis Y.
Sekeri Kalliope (Dr. Biochemist) – *Collaborating*	Sourlingas Th.
Tzinia Athina (Dr. Biochemist) – *Collaborating*	Chroni A.

POSTDOCTORAL FELLOWS

Fellow	**IBA Researcher**
Christoforidis Christoforos	Kletsas D.
Dioli Chrysoula	Sotiropoulos I.
Galeou Angeliki	Prombona A.
Georgiadou Dafni	Chroni A.
Gkolfinopoulou Christina	Chroni A.
Karamanou Konstantina	Kletsas D.
Kolliopoulou Anna	Swevers L.
Kouroumalis Anastasios	Kletsas D.
Kythreoti Georgia	Iatrou K.
Mavroidi Barbara	Pelecanou M.
Ninios Ioannis	Vavouraki E.
Papadopoulou Adamantia	Kletsas D.
Valanti Eftaxia-Konstantina	Chroni A.

GRADUATE RESEARCH ASSOCIATES

Research Associate	**IBA Researcher**
Betsi Petri-Christina (MSc)	Konstantopoulou M.
Goula Olga (BSc)	Kletsas D.
Halevas Eleftherios (PhD)	Pelecanou M.
Klamarias Lykourgos (Veterinarian)	Kletsas D.
Kosmidis Eleutherios (MSc)	Vavouraki H.
Leventis Minas (Dentist / Dental prosthetist)	Vavouraki H.
Makrigianni Amalia (MSc)	Kletsas D.
Mamoucha Stavroula (PhD)	Prombona A.

Matiadis Dimitris (PhD)	Sagnou M.
Panagopoulou Lydia (MSc)	Vavouraki H.
Paraskevopoulou Katerina (MSc)	Kletsas D.
Raptopoulos Dimitris (PhD)	Konstantopoulou M.
Sakellariou Panagiotis (PhD)	Kletsas D.
Sotiropoulou Nefeli-Sofia (MSc)	Konstantopoulou M.
Vassiliadis Orestis (Dentist / Dental prosthetist)	Vavouraki H.
Voudommatis-Stergiou Charalampos (MSc)	Vavouraki H.
Xue Qi (Ghent University)	Swevers L.

PhD CANDIDATES AND MSc STUDENTS

PhD candidate (University)	**Supervisor in IBA**
Adamopoulou Maria (Univ. of Copenhagen, Denmark) – *Completed*	Kletsas D.
Angelopoulou Maria (NKUA)	Kletsas D.
Athanasoulis Alexandros (NKUA)	Papakyriakou A.
Biratsi Ada (NKUA) – *Completed*	Sophianopoulou V.
Broussos Panayiotis (AUA)	Stamatakis K.
Dedemadi Anastasia-Georgia (NKUA)	Chroni A.
Farmaki Danae (NKUA)	Prombona A.
Fotopoulou Asimina (Univ. of Patras)	Kletsas D.
Karoussiotis Christos (NKUA)	Georgoussi Z.
Liakou Eleni (Univ. of Patras)	Kletsas D.
Lesgidou Nastazia (DUT)	Vlassi M.
Manikas Neoklis (AUA)	Konstantopoulou M.
Megalokonomou Anastasia (Univ. of Crete)	Sotiropoulos I.
Megarioti Amalia (NKUA)	Gournas C.
Mountaki Christina (NKUA) – *Completed*	Chroni A.
Pallaki Paschalina (NKUA) – *Completed*	Georgoussi Z.
Symeonof Alexandra (NKUA)	Georgoussi Z.
Tsimelis Efstathios (Univ. of Patras)	Kletsas D.
Vamvaka-Iakovou Anastasia (Univ. of Ioannina)	Sotiropoulous I.
Vayenos Dimitris (NTUA)	Stamatakis K.

MSc student (University)	**Supervisor in IBA**
Athanasopoulou Georgia (NKUA)	Sagnou M.
Christogianni Mariam (NKUA)	Kletsas D.
Dimozi Maria (NKUA)	Kletsas D.
Gerontidi Dimitra (NKUA)	Sotiropoulos I.
Gerostathis Spyros (Univ. of Patras)	Sophianopoulou V.
Giakoumidaki-Vogiatzi Aikaterini (AUA)	Stamatakis K.
Gratsia Eirini (Univ. of Crete)	Sotiropoulos I.
Karanikou Maria (Univ. of West. Macedonia) – *Completed*	Pratsinis H.
Kavellari Marina (Univ. of Patras)	Kletsas D.
Kavvoura Dafni-Alexandra (NKUA)	Pratsinis H.
Kypraiou Anastasia (Univ. of Patras)	Kletsas D.
Louka Konstantina – *Completed*	Kletsas D. / Mavrogonatou E.
Lymperopoulos Dimitris	Chroni A.
Manassakis George (Erasmus)	Konstantopoulou M.
Micha Asimina – *Completed*	Chroni A.

Michailidis Periklis (NKUA) – *Completed*	Voutsinas G.
Ntinou Nikolina (NKUA)	Sotiropoulos I.
Papadimitriou Georgia-Zeta (NKUA)	Sotiropoulos I.
Tsistraki Aikaterini (NKUA)	Sotiropoulos I.
Tsoukas Evangelos (Univ. of Patras)	Papakyriakou A.
Tzouanou Foteini (NKUA)	Georgoussi Z.

UNDERGRATUATE & OTHER TRAINING STUDENTS

Student (University)	**Supervisor in IBA**
Charisis Angelos (AUA) – *Completed*	Voutsinas G.
Doumani Anastasia (Univ. of Ioannina) – *Completed*	Voutsinas G.
Filippaki Myrto (AUA)	Prombona A.
Georgiou Eirini (NKUA)	Chroni A.
Kambani Lito (AUA) – *Completed*	Voutsinas G.
Kanaki Irini (AUA)	Sophianopoulou V.
Karakike Margarita (AUA)	Sourlingas T.
Katsirma Irini (AUA)	Sourlingas T.
Kavvadia Vassiliki (NKUA)	Mavrogonatou E.
Kechagia Soultana (AUA)	Papakyriakou A.
Kotsikou Zoe (NKUA)	Sotiropoulos I.
Koulouris Dimitris (NKUA)	Gournas C.
Makatsoris Christos (NKUA)	Sotiropoulos I.
Panagopoulou Konstantina (NKUA)	Voutsinas G.
Pappa Athina (Univ. of Patras)	Sotiropoulos I.
Paraskevas Sotirios (NKUA)	Sotiropoulos I.
Perpiniadis Vassilis (NKUA)	Gournas C.
Routsi Retzep (AUA)	Sophianopoulou V.
Sotiropoulou Anastasia (NKUA) – *Completed*	Mavrogonatou E.
Spanomaridi Stamatina-Faidra (AUA)	Swevers L.
Tammas Joseph (AUA)	Swevers L.
Trasani Georgia (NKUA)	Georgoussi Z.
Tsamadia Eleni (NKUA)	Georgoussi Z.
Tsoumalis Antonis (AUA)	Georgoussi Z.
Voulgari Lydia (NKUA) – *Completed*	Chroni A.

INTRODUCTION

The Institute of Biosciences and Applications (IBA) is one of the five Institutes of the National Centre for Scientific Research (NCSR) "Demokritos". The Centre, among the best in Greece and in Europe, is characterized by multidisciplinarity and the unique coexistence of different fields of science, as well as the collaboration among scientists of different disciplines, towards the promotion of science and innovation. The IBA focuses its research and developmental activities in various areas of life sciences and especially in the study of cellular function, with an emphasis on ageing and 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, that support the research efforts and provide advanced technological research services to the Public and Private Sectors, and the Society, in general.

Within 2022, there was a significant upgrading of Institute's research and developmental work, as shown by the significant increase of the quality of IBA researchers' publications. For this achievement I would like to congratulate the scientific, technical and administrative staff of the Institute. I would like to thank the Vice Director G. Voutsinas and the members of the Scientific Council (ESI) of the IBA H. Pratsinis (President), M. Konstantopoulou, A. Papakyriakou, L. Swevers and G. Voutsinas (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 A. Chroni and the Deputy M. Sagnou for the upgrading of the education within IBA.

After several years, within 2022 the Institute has been evaluated by an external Committee, appointed by the General Secretary of Research and Innovation. The Committee with Prof. E. Gavathiotis (Albert Einstein College of Medicine) as President and Prof. P. Giannakakou (Weill Cornell Medical College), Prof. E. Lolis (Yale University), Prof. P. Poulicacos (Icahn School of Medicine at Mount Sinai) and Prof. A. Tsirigos (New York University) as Members, visited IBA and its infrastructures, met with the researchers, the students and the whole personnel and had the opportunity to be informed about the achievements of the Institute and the plan for the period to come. The report of the Committee was highly commendable and justifies the efforts of the members of the Institute and is a great boost for the further upgrading of the IBA.

During the last year the implementation of central projects of IBA, such as the EU-funded project EU-OPENSCREEN-DRIVE, of the national research infrastructures OPENSCREEN-GR, BIOIMAGING and INSPIRED, as well as of the national emblematic action "Creation of the National Network on the Value of Honey" has continued, along with the further upgrading of the Laboratory for Doping Control and Metabolic Studies in an effort to be re-accredited by the World AntiDoping Agency (WADA). The implementation of these projects, as well as of the other funded projects that have been recruited by the Institute members have attracted a large number of young scientists and have further strengthened the research and development effort of the IBA.

This year, our colleague Athina Tzinia has been retired. The Institute is thanking her for her work, her fruitful collaborations, her contribution to the ESI and, in general, for all her efforts aimed at upgrading the IBA.

During 2022, the long tradition of IBA on postgraduate education has been continued and 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 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 has continued, as well as the participation of the IBA in the IPEP "Athens International School for Neurosciences" and the IPEP "Stem Cells and Regenerative Medicine" with the University of Thessaloniki. 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.

For all the above, I would like to warmly thank all the members of the IBA for their essential and multifaceted contribution to the smooth operation and development of the Institute.

Dimitris Kletsas, PhD
IBA Director
November 2023

PROGRAMME A

“REGULATION OF CELL FUNCTION – AGE-RELATED DISEASES”

Research Group: Cell Signalling and Molecular Pharmacology

Research Staff
Zafiroula-Iro Georgoussi, Research Director
Ioannis Sotiropoulos, Researcher
Chrysoula Dioli, Postdoctoral researcher
Paschalina Pallaki – *PhD obtained in 2022*
Christos Karoussiotis, PhD student
Alexandra Symeonof, PhD student
Anastasia Vamvaka-Iakovou, PhD student
Anastasia Megalokonomou, PhD student
Foteini Tzouanou, Master student
Nikolina Ntinou, Master student
Zeta-Georgia Papadimitriou, Master student
Dimitra Gerontidi, Master student
Eirini Gratsia, Master student
Aikaterini Tsirtsaki, Master student
Georgia Trasani, Undergraduate student
Eleini Tsamadia Undergraduate student
Sotirios Paraskevas, Undergraduate student
Christos Makatsoris, Undergraduate student
Zoe Kotsikou, Undergraduate student
Athina Pappa, Undergraduate student
Antonis Tsoumalis, Undergraduate student

Kostas Iatrou, Emeritus Scientist
Georgia Kythreoti, Postdoctoral Fellow

Research Interests
The research activities of Dr Zafiroula (Iro) Georgoussi are focused on the elucidation of the regulatory mechanisms governing G protein-coupled receptors (GPCRs) signaling pathways. Emphasis is given on the mechanisms acting beyond the G protein paradigm 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 and are implicated in tolerance and dependence upon prolonged drug administration, pain, and emotional behaviors such as anxiety, depression and stress.

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

- The elucidation of novel signaling pathways and analysis of genes, transcription factors and proteins - whose function is altered upon opioid administration and are implicated in neuronal differentiation and outgrowth.
- The identification of why and how the activation of the opioid receptors induces the autophagic machinery in neurons under stress conditions
- The elucidation of the molecular mechanism of autophagy in neuronal plasticity under stress conditions in animal models upon opioid administration.
- 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.

The research work of Dr. Ioannis Sotiropoulos focuses on understanding the role of risk factors such as chronic (psychological) stress, gender, and chronic pain in the development of

Alzheimer's disease (AD), with particular emphasis on the relationship between AD and depression, a stress-related disorder. Combining studies in cells, animals, and humans, Dr. Sotiropoulos aims to elucidate the cellular mechanisms that regulate the Tau protein as a key molecule of neuroplasticity and neuropathology, while his recent studies focus on exosomes as mediators and biomarkers of brain pathology in AD.

Research Progress in 2022

Novel signal transduction pathways mediated upon opioid receptor activation: Given that the dynorphin / κ-opioid receptor (κ-OR) system plays a key role in modulating anxiety and stress related behaviors we identified using *in vitro* and *in vivo* studies a novel signaling pathway mediated by Gαio/ERK1,2 and p-CREB, via which activation of the κ-OR induces the autophagic machinery resulting in synaptosomal integrity changes in hippocampus (Figure 1A). Today, κ-OR antagonists such as aticaprant are in Phase III clinical trials as antidepressive drugs. In this respect, mice were subjected to unpredictable chronic stress, followed by administration of aticaprant and behavioral and molecular assessments were performed. We found that aticaprant produced an anxiolytic and antidepressant effect, reversed stress-induced impairments in long-term memory, and restored the stress-decreased levels of the autophagic markers beclin 1 and LC3II with concomitant alterations of specific hippocampal synaptic proteins providing evidence that autophagy could be a plausible mechanism via which aticaprant exerts its therapeutic effects as a putative "smart drug" to alleviate stress-related disorders.

Pharmacological characterization of bioactive compounds in cell-based throughput platforms: In the context of Dr Georgoussi's program under the acronym "NUTRIMED", funded by the Hellenic co-actions of Science and Innovation of the Republic Region of Attica (ESPA 2014-2020), in collaboration with IBA researchers, the Medical and Pharmaceutical Universities of Athens and the company INTERMED, isolated natural extracts from Greek medicinal plants were characterized as putative new antidepressant compounds that selectively bind to the κ-opioid and 5-HT1A serotonin receptors. Similar studies under the EU consortium «NORMOLIFE NETWORK» (collaboration with University of Catania), our group characterized the pharmacological profile of new bioactive compounds for pain management using specific cell-based assays.

Development of neuronal networks on graphene microelectrode nanostructures: Dr Georgoussi, in collaboration with Dr P. Dimitrakis of the INN Institute of NCSR" D", are developing neuronal cells on graphene nanoribbon interconnects. These studies aim in the design of biosensors that could allow to investigate cellular (electrical) responses and their plausible variations upon electrical or chemical stimuli.

Physiopathology, biomarkers and new therapeutic pathways in Alzheimer's disease: In the year 2022, Dr Sotiropoulos' team focused on the detailed characterization of the molecular basis of different risk factors of Alzheimer's disease (e.g., chronic psychological stress, chronic pain), their potential "footprint" on disease biomarkers, and the identification of new therapeutic molecules/compounds. Specifically, Dr Sotiropoulos' team a) monitored new molecular pathways through which chronic stress suppresses neurogenesis in the adult brain, b) the detrimental effect of chronic neuropathy (peripheral pain) on mechanisms of neuroplasticity and memory related to Tau protein and they initiation of Alzheimer's disease pathology, c) the proteomic content of brain exosomes and their biomarker potential for Alzheimer's disease brain pathology and its risk factors (eg chronic stress)- see scheme 1B).

Figure 1A

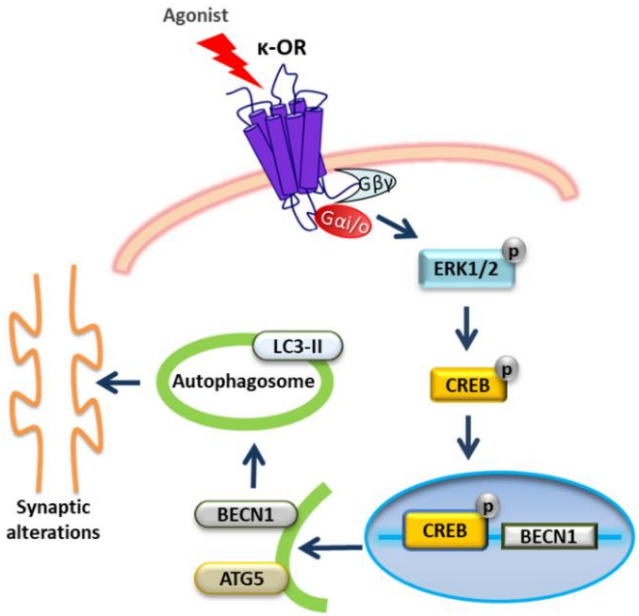

Figure 1B

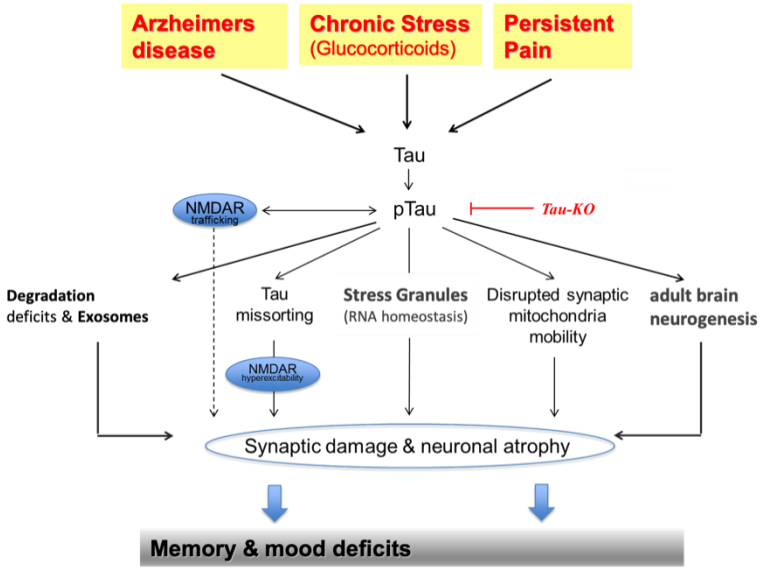

Figure 1A. *Schematic representation of a putative signaling pathway via which agonist-κ-OR activation triggers autophagy resulting in synaptic alterations. Agonist exposure of κ-OR in neuronal cells leads to ERK1, 2 phosphorylation mediated by Gi/o proteins. Activation of ERK1,2 subsequently phosphorylates CREB which in turn translocates to the nucleus to activate Becn1 gene expression. Upregulation of Beclin1 and Atg5 promotes the initiation of autophagy resulting in alterations of hippocampal synaptic proteins enriched in dendritic spines.*

Figure 1B. *Clinical and experimental studies suggest that chronic stress and chronic, persistent pain are a risk factors for Alzheimer's disease (AD), while depression, a stress-related disorder, appears to predispose to AD. Our research findings support common AD-related neurobiological mechanisms such as accumulation of pathological Tau and Tau-mediated inhibition/dysregulation of several important neuronal cell mechanisms e.g. protein degradation mechanisms (autophagy), damaged neurogenesis, loss of synapses/communication between neuronal cells in the brain.*

Publications

Karoussiotis C., Sotiriou A., Papavranoussi-Daponte D., Polissidis A.V., Symeonof A., Nikoletopoulou V. Georgoussi Z., (2022). "The role of κ-Opioid Receptor-induced autophagy is implicated in stress-driven synaptic alterations Front. Mol. Neurosci. 15: 1039135 (IF=6.261)

Monteiro F, Carvalho O, Sousa N, Silva FS, Sotiropoulos I*. "Photobiomodulation and visual stimulation against cognitive decline and Alzheimer's disease: a systematic review" Alzheimer & Dementia 2022 8(1):e12249 (IF= 7.09)

Gomes P, Tzouanou F, Skolariki K, Vamvaka Iakovou A, Noguera-Ortiz C, Tsirtsaki K, Waites L. C, Vlamos P, Sousa N, Costa-Silva B, Kapogiannis D, Sotiropoulos I*. "Extracellular Vesicles and Alzheimer's disease in the novel era of Precision Medicine: implications for disease progression, diagnosis and treatment" Exper Neurology 2022 Dec; 358:114183. (IF=5.6)

Guerreiro S, Guimarães M, Silva JM, Dioli D, Vamvaka-Iakovou A, Gomes P, Megalokonomou A, Campos-Marques C, Sousa N, Leite-Almeida H*, Sotiropoulos I* "Chronic pain causes Tau-dependent hippocampal pathology and memory deficits" Mol Psychiatry 2022 Sep 2. (IF=15.9)

Lopes M, Vieira de Castro J, Pojo M, Gonçalves CS, Martins EP, Coimbra B, Sotiropoulos I, Sousa N, Rodrigues AJ, Costa BM. "Chronic Stress does not influence the survival of mouse models of glioblastoma." Front Oncol 2022 Mar 25; 12:856210. eCollection 2022 (IF = 5.73)

Silveira-Rosa T, Mateus-Pinheiro A, Correia JS, Silva JM, Martins-Macedo J, Araújo B, Machado-Santos AR, Alves ND, Silva M, Loureiro-Campos E, Sotiropoulos I, Bessa JM, Rodrigues AJ, Sousa N, Patrício P, Pinto L. Suppression of adult cytogenesis in the rat brain leads to sex-differentiated disruption of the HPA axis activity Cell Prolif. 2022 Feb;55(2):e13165. (IF=8.75)

Articles in Press

Gomes P, Bodo C, Nogueras-Ortiz C, Samiotaki M, Chen M, Soares-Cunha C, Silva JM, Coimbra B, Stamatakis G, Santos L, Campos-Marques C, Panayotou G, Tzouanou F, Waites CL, Gatsogiannis C, Sousa N, Kapogiannis D, Costa-Silva B*, Sotiropoulos I*. "A novel isolation method for spontaneously released extracellular vesicles from brain tissue and its implications for stress-driven brain pathology" Cell Comm Sign 2023 21:35.

Articles published or in press (In Press) in proceedings of international conferences or other serial works, editing of publications of scientific books (e.g. conference proceedings, monographs, teaching texts or textbooks, etc.)

Georgoussi Z., Karoussiotis C., Sotiriou A., Papavranoussi-Daponte D., Polissidis A.V and Nikoletopoulou V., "Autophagy induction via κ-opioid receptor is implicated in stress driven synaptic alterations" FASEB J. 36, (S1).

Dioli C, Papadimitriou G, Megalokonomou A, Campos-Marques C, Sousa N, Sotiropoulos I*, "Chronic stress, depression and Alzheimer's disease: the triangle of oblivion" In: Vlamos P. (eds) GeNeDis 2022. Advances in Experimental Medicine and Biology, Springer, Cham. in press 2023.

Iatrou K., Kythreoti G., Thireou T., Karoussiotis C., Georgoussi Z., Zographos S., Liggri P., Michaelakis A., Schulz S. "Novel Anosmia-Inducing Compounds for Environmentally Friendly Mosquito Vector Control: Structural Determinants of ORco Ligands Antagonizing Odorant Receptor Function" Experimental Biology, FASEB J. 36, (S1) (poster).

International conferences

Georgoussi Z., Karoussiotis C., Sotiriou A., Papavranoussi-Daponte D., Polissidis A.V and Nikoletopoulou V., "Autophagy induction via κ-opioid receptor is implicated in stress driven synaptic alterations" Experimental Biology, Απρίλιος 2022, Philadelphia, USA, (poster)

Iatrou K., Kythreoti G., Thireou T., Karoussiotis C., Georgoussi Z., Zographos S., Liggri P., Michaelakis A., Schulz S. "Novel Anosmia-Inducing Compounds for Environmentally Friendly Mosquito Vector Control: Structural Determinants of ORco Ligands Antagonizing Odorant Receptor Function" Experimental Biology, Philadelphia, USA, Απρίλιος 2022 (poster)

Symeonof A., Karoussiotis C., Sotiriou A., Georgoussi Z. (2022). "The role of spinophilin in modulating the κ-opioid receptor signaling" 4GPCRnet Symposium, Leipzig, Germany, September 2022 (poster)

Sotiropoulos I "Lifetime stress on brain neuroplasticity and neuropathology: how can we model it?" - Blue Brain Workshop: Mouse neuronal morphologies in health and disease: reconstruction, analysis and modelling Geneve, Switzerland, (October 2022) – Invited Speaker

Sotiropoulos I "Exosomes and Alzheimer's disease in the new era of Precision Medicine" – International Society of Molecular Neurodegeneration – ISMND 2022, Athens, Greece (October 2022) – Invited Speaker

Sotiropoulos I "Chronic Stress & Exosomes: key players in progression and diagnosis of Alzheimer's disease" – Mediterranean Neuroscience Society 2022- Dubrovnik, Croatia (June 2022) – Symposium Organizer & Speaker

National conferences

Sotiropoulos I "Exosomes and psychological Stress: key players in initiation and progression of Alzheimer's disease brain pathology" – 7th Hellenic Dementia meeting, Portaria, Greece (November 2022) – Invited Speaker & Symposium organizer

Sotiropoulos I "Chronic stress and exosomes: key players in progression and diagnosis of Alzheimer's disease" – Hellenic Society of basic and Clinical Pharmacology, Arta, Greece (October 2022) – Invited Speaker

Other Scientific Activities

Participitaion in national and international scientific councils & oprganizations

Z. Georgoussi

President of the organizing Committee of the 8th ERNEST meeting of the European Cooperation in Science and Technology, COST-CA18133 "European Research Network on Signal Transduction (ERNEST)" *"GPCR structure and function: The present and perspectives for the future",* in the Orthodox Academy of Crete, Kolymbari, Krete.

National Representative, Intergovernmental Framework for European Cooperation in Science and Technology, COST-action- CA18133 entitled "European Research Network on Signal Transduction (ERNEST)".

Substitute National Representative, Intergovernmental Framework for European Cooperation in Science and Technology, EU–COST Action CA18240 entitled "ADHEsion GPCR Network: Research and Implementation Set the path for future Exploration" (Adher N' Rise).

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».

Co-coordinator of the course «Cellular and Molecular Neurosciences» 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.

Substitute member of the Ethics Committee of the NCSR "D"

Member of the evaluation Committee for the researchers of IBA

Substitute Member of the evaluation Committee for the recruitment of the Associate Professorship position, Department of Biochemistry, University of Thessaly

I. Sotiropoulos
Core member of the Hellenic Initiative against Alzheimer's Disease (HIAAD)

Member of Scientific Council of European College of Neuropsychopharmacology (ECNP)

Participation in editorial boards of scientific journals
Z. Georgoussi
Associate Editor Experimental Pharmacology and Drug Discovery (Frontiers in Pharmacology)

I. Sotiropoulos
Guest Editor of Special issue "Brain Metaplasticity" of scientific journal Neuroscience IBRO-Official Journal

Guest Editor of Special issue "Molecular and cellular mechanisms of Tauopathy" of scientific journal Neuroscience IBRO-Official Journal

Review Editor of scientific journal Frontiers in Neuroscience

Organization of scientific conferences
President of the organizing Committee of the 8th ERNEST meeting of the European Cooperation in Science and Technology, COST-CA18133 "*European Research Network on Signal Transduction (ERNEST*)" *"GPCR structure and function: The present and perspectives for the future"*, in the Orthodox Academy of Crete, Kolymbari, May 3-7 (Z. Georgoussi)

Member of the organizing committee of International Society of Molecular Neurodegeneration – ISMN 2022, Divani Acropolis, 10-13 October 2022, Athens, Greece (I. Sotiropoulos)

Participation in evaluation/reviewing committees of scientific proposals
Z. Georgoussi
Cyprus Research Promotion Foundation (RPF)

Operational Programme Competitiveness, Entrepreneurship and Innovation (EPAnEK)

Hellenic General Secretary for Research and Technology (GSRT)

State Scholarship Foundation (IKY)

I. Sotiropoulos
Grant evaluator of AAIC - Alzheimer Association International και του France Alzheimer

Reviewer in scientific Journals
Journal of Pharmacology and Experimental Therapeutics, Cellular Signaling, Neurophychopharmacology, Neuropharmacology, Journal of Neuroscience, BιoMed Cell Biology, Journal of Biological Chemistry, Letters in Drug Design & Discovery, Current Drug Discovery Technologies, CNS Neuroscience & Therapeutics, Neurochemisty, Frontiers in Neurosciences, Frontiers in Pharmacology (Z. Georgoussi)

EMBO Journal, Molecular Psychiatry, Aging Cell, Journal of Alzheimer's disease, Molecular Neurodegeneration, Neurobiology of Aging, Frontiers of Neuroscience, Neurobiology of Disease, Eur. Neuropsychopharmacology, Neuropharmacology, Eur. J. of Neuroscience (I. Sotiropoulos)

Others activities
Talks in general audience about the risk factors, the promising therapies ad societal impact of Alzheimer's disease (I. Sotiropoulos):
https://www.youtube.com/watch?v=urE_ctkYNVA
https://www.youtube.com/watch?v=5N5Ew7_VqZ0&t=7144s
https://www.youtube.com/watch?v=ykra5b1oORg

Scientific achievements and prizes
Paschalina Pallaki (PhD student of Dr Georgoussi) defensed her doctoral thesis entitled "*Alternative signaling pathways of opioid receptors implicated in genes expression during neurogenesis"* with Honours in the NKUA, Biology Department, July 2022.

Alexandra Symeonof (PhD student of Dr Georgoussi) was co-financed by Greece and the European Union (European Social Fund-ESF) through the Operational Programme «Human Resources Development, Education and Lifelong Learning» in the context of the Act "Enhancing Human Resources Research Potential by undertaking a Doctoral Research" Sub-action 2: IKY Scholarship Programme for PhD candidates in the Greek Universities» for the implementation of her doctoral thesis.

Teaching and other educational activities
Oral presentation in the 57th Summer School of NCSR "Demokritos" entitled "Opioid receptor signaling: Targeting new opioids", July 2022 (Z. Georgoussi)

Oral presentation in the 57th Summer School of NCSR "Demokritos" entitled "Chronic Stress and Exosomes as key "players" in progression and diagnosis of Alzheimer's disease (I. Sotiropoulos)

Z. Georgoussi
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".

Co-coordinator of the Syllabus course "Cellular and Molecular Neurosciences" of the "Athens International Master's Programme in Neurosciences".

Supervisor of the doctoral theses of the PhD students Pascalina Pallaki, Christos Karoussiotis, Alexandra Symeonof

Supervisor of the theses of the undergraduate students Georgia Trasani and Helen Tsamadia (Biology Department, NKUA)

Supervisor of the three-membered Consulting Committees of the Biology Department NKUA for the doctoral theses of the PhD students Pascalina Pallaki, Christos Karoussiotis, Alexandra Symeonof and Sofia Koutloglou

Supervisor of the three-membered Consulting Committees of the master students in the "Athens International Master's Program in Neurosciences" Fotini Tzouanou and Zeta Papadimitriou

Co-supervisor for the thesis of the master student in the "Athens International Master's Programme in Neurosciences" Fotini Tzouanou

Teaching in the NKUA Master Program "Athens International Master's Programme in Neurosciences" on "*Signaling of* N*eurotransmitter Receptors*" (19 hours)

Teaching in the NKUA Master Program "Molecular basis of Human Diseases" on "*G Protein Coupled Receptors in Health, Disease and new Drug Development*", Inter-departmental Master Program NKUA (30 hours)

Teaching in the Inter-constitutional and Inter-departmental Master Program in collaboration of the IBA of NCSR "D" and University of Patra's in "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Medicinal Products" on "*Cellular Signaling of Transmembrane Receptors- Molecular Pharmacology"* (12 hours)

I. Sotiropoulos
Teaching at the undergraduate course *«Human and Animal Physiology II»*, Department of Biology, University of Patras (94 students)

Teaching at the postgraduation (Master) course (14 hours, 16 students) *"Science of Stress and Promotion of Health "*, Medical School, National and Kapodistrian University of Athens

Teaching at the postgraduation (Master) course (4 hours, 20 students) "Applications of Biology in Medicine", Medical School, National and Kapodistrian University of Athens

Teaching at the postgraduation (Master) course (joined course between IBA & Department of Chemistry, University of Patras) *"Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Medicinal Products"* (2 hours, 16 students)

Teaching at the different postgraduation (Master) course (2-3 hours/pre course/ 20-25 students) in different Universities in Greece and abroad e.g. Athens Neuroscience Master (NKUA), Crete Neuroscience Master (UoC), Master of Neurodegenerative diseases (AUTH), Brain aging & pathology Master program (Univ. Coimbra, Portugal).

Main Supervisor of PhD students Anastasia Vamvaka Iakovou and Anastasia Megalokonomou.

Main supervisor and co-supervisor of Master thesis of students Georgia-Zeta Papadimitriou, Dimitra Gerontidi, Katerina Tsirtsaki, Nikolina Ntinou, Foteini Tzouanou, Lavrentia Grigoriadou (Biology Department and Medical School, University of Athens and University of Thessaloniki).

Other Activities in the Institute of Biosciences & Applications
Z. Georgoussi
Member of the working group of the National Roadmap Research Infrastructure "OPENSCREEN-GR: *An Open – Access Research Infrastructure of Target-Based Screening Technologies and Chemical Biology for Human and Animal Health, Agriculture and the Environment*" coordinated by the IBA.

Responsible scientist for the ultracentrifuges Beckman Coulter OPTIMA-MAX και L8-8OM and the Speed Vac, Savant of the IBA, NCSR "D"

I. Sotiropoulos
Deputy President of the Animal License Committee of Animal house of Institute of Biosciences & Applications, NCSR Demokritos.

Total Impact Factor for original publications in 2022
Z. Georgoussi: 6.261 (for 1 publication)
I. Sotiropoulos: 48.08 (for 7 publications)

Citations for 2022 (without self-citations)
Z. Georgoussi: 34
I. Sotiropoulos: 295

Citations for 2018-2022 (without self-citations)
Z. Georgoussi: 181

I. Sotiropoulos: 1710

h-factor
Z. Georgoussi: 19 (Scopus), 21 (Google Scholar)
I. Sotiropoulos: 23 (Scopus), 25 (Google Scholar)

Current External Funding
Z. Georgoussi
Coordinator of the program "Co-actions Science and Innovation in Hellenic Republic Region of Attica (ESPA 2014-2020), code ATTP4-0339288, code of action MIS 5185062 and title *"Food supplements with anxiolytic and antidepressive effect from Greek medicinal plants"*
Duration: 08/2022- 12/2023
Total Funding: 400,000 €
Total Funding for the lab: 155,000
Funding for 2022: 0 €

IKY Scholarship Programme for PhD candidates in the Greek Universities co-financed by Greece and the European Union (European Social Fund-ESF) through the Operational Programme "Human Resources Development, Education and Lifelong Learning" in the context of the Act "Enhancing Human Resources Research Potential by undertaking a Doctoral Research" Sub-action 2: IKY Scholarship Programme for PhD candidates in the Greek Universities» for studies entitled: *"The function of opioid receptors in the nervous system through the formation of specific protein complexes"*.
Duration: 05/2022-09/2023
Total Funding: 16000 €

Programme EU–COST Action CA18133 με τίτλο *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
Total Funding :164000 €
Funding for 2022: 0 €

Programme EU–COST Action CA18240 entitled *"ADHEsion GPCR Network: Research and Implementation Set the path for future Exploration" (Adher N' Rise)* as member and Substitute National Representative of the Management Committee
Duration: 11/2019- 11/2023
Total Funding: 120000 €
Funding for 2022: 0 €

Kostas Iatrou: Insect Physiology, Ethology and Applications

Research Staff
Georgia Kythreoti, Postdoctoral Fellow

Research Interests
Dr. Iatrou's current research interests focus on the discovery of natural volatile organic compounds (VOCs) causing anosmia to mosquitoes and thus preventing them from finding suitable hosts and transmitting infectious agents to them while obtaining blood meals from them. The selected target for the VOC-mediated disruption of mosquito odorant receptor function is the obligatory odorant co-receptor ORco. Specifically, Dr. Iatrou's research activities focus on the discovery of natural VOCs acting as antagonists of ORco using an *ex vivo* receptor

expression-activity detection platform. Large-scale expression of ORco is also carried out in order to deduce the structure of the ORco homomer and allow Artificial Intelligence-based discovery of new mosquito anosmia-causing molecules. This research aims at the reduction in the transmission of mosquito-borne infectious diseases to animal hosts including humans.

2022 Findings

In previous studies, we had used an insect cell-based (*ex vivo*) screening platform allowing the discovery of small molecules that inhibit the functionality of the obligatory co-receptor subunit of mosquito odor receptor heteromers and cause anosmia to targeted mosquitoes. The previous screening of small collections of volatile organic compounds (VOCs) of natural origin, resulted in the identification of 15 ORco antagonists acting as anosmic agents for mosquitoes. The experimental classification of the identified antagonists in orthosteric and allosteric classes allowed the design of a ligand-based pharmacophore capable of predicting the presence of ORco-specific orthosteric antagonists in available VOC collections (collaboration with Dr. Ada Thireou, Agricultural University of Athens). Following "training" of the pharmacophore with the experimentally confirmed antagonists and its optimization with specific combinations of structural parameters that minimized the selection of pseudo-positive antagonist ligands, the pharmacophore model was employed for the *in silico* screening of a new collection of as yet uncharacterized natural VOCs for the presence of ORco orthosteric antagonists. The experimental validation of the identified hits is currently in progress.

During the same period, we have also completed the generation of a new series of vectors for stable expression of N-terminally tagged ORco subunits in insect cells. The new vectors permit easy isolation of the tagged receptors by affinity chromatography and their processing to the authentic forms by digestion with a specific protease. Work to deduce to feasibility of producing the authentic subunits by digestion of the tagged forms while bound on the affinity matrix or after their elution from it is in progress. The ultimate goal of these studies is the isolation and structure determination of the authentic co-receptor channel, alone and in complex with selected antagonists, by X-ray crystallography or cryo-electron microscopy (collaboration with Dr. Spyros Zographos, National Hellenic Research Foundation).

International conferences

K Iatrou, G Kythreoti, T Thireou, C Karoussiotis, Z Georgoussi, SE Zographos, P Liggri, A Michaelakis, S Schulz (2022) Novel Anosmia-Inducing Compounds for Environmentally Friendly Mosquito Vector Control: Structural Determinants of ORco Ligands Antagonizing Odorant Receptor Function Annual Experimental Biology meeting (EB 2022), April 1-4, 2022, Philadelphia, PA, USA

Other Scientific Activities

Participation in Greek and international scientific bodies and organizations (in addition to participation as a member in scientific societies and organizations)

National Representative and Management Committee member for EU–COST Action CA18133 entitled "*European Research Network on Signal Transduction (ERNEST)".*

Participation in editorial boards of scientific journals

Member, Editorial Boards for "Sericologia", "Insect Biochemistry and Molecular Biology", "Archives of Insect Biochemistry and Physiology" και "Insects".

Reviewing of manuscripts in scientific journals

Reviewer of article submissions for "Insect Biochemistry and Molecular Biology", "Archives of Insect Biochemistry & Physiology", "Insects", "Pesticide Biochemistry and Physiology'.

Organization of scientific conferences or participation in organizing committees of conferences

2022-23: Member, Scientific Committee and co-Organizer of Session on *"Ecology and behavior",* XII European Congress of Entomology (ECE2023), Heraklion, Crete, Greece, October 16-20, 2023.
2022-23: Co-organizer, 8th meeting of the European Research Network on Signal Transduction (ERNEST8, COST No. ca18133) *"GPCR structure and function: The present and perspectives for the future"*, Orthodox Academy of Crete, Kolymbari, Crete, Greece, May 3-7, 2023.
Citations for 2022 (without self-citations): 169 (Scopus)

Total citations 2018-2022 (without self-citations): 872 (Scopus)

h-factor (from Scopus and Google scholar): 37 (Scopus), 48 (Google scholar)

Current External Funding
Programme entitled: *Identification of new insect olfactory and taste enhancers of natural or synthetic origin* funded by Inscent, Inc., USA
Programme duration: 2017-2023
Total programme funding (for the entire duration of the programme): 40.000€
Research groups participating in the programme: K. Iatrou, NCSR "D"
Scientific Supervisor: K. Iatrou
Funding of the Programme for 2022: 0€
Funding for 2022: 0€

Programme entitled: *3D-ORco: The structure of ORco, the odorant receptor co-receptor of mosquitoes* funded by Hellenic Foundation for Research and Innovation (HFRI)
Programme duration: 2020-2024
Total programme funding (for the entire duration of the programme): 180.000€
Research groups participating in the programme: Spyros Zographos, National Hellenic Research Foundation (NHRF) and K. Iatrou, NCSR "D"
Scientific Supervisor: K. Iatrou
Funding of the Programme for 2022: 90.000€ (to NHRF Special Accounts)
Funding for 2022: 30.000 € (from NHRF Special Accounts)

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
Konstantina Karamanou, Postdoctoral Fellow
Christophoros Christophoridis, Postdoctoral Fellow
Anastasios Kouroumalis, Postdoctoral Fellow
Asimina Fotopoulou, Graduate Student
Efstathios Tsimelis, Graduate Student
Eleni Liakou, Graduate Student
Maria Angelopoulou, Graduate Student
Maria Adamopoulou, Graduate Student – *PhD obtained in 2022*
Konstantina Louka, Collaborating Graduate Student (MSc) – *MSc obtained in 2022*
Anastasia Kypraiou, Collaborating Graduate Student (MSc) – *MSc obtained in 2022*
Marina Kavellari, Collaborating Graduate Student (MSc)
Maria Dimozi, Collaborating Graduate Student (MSc)
Dafni-Alexandra Kavvoura, Collaborating Graduate Student (MSc)
Maria Karanikou, Collaborating Graduate Student (MSc) – *MSc obtained in 2022*
Mariam Christogianni, Collaborating Graduate Student (MSc)
Vassiliki Kavvadia, Collaborating Undergraduate Student (BSc)
Anastasia Sotiropoulou, Trainee – *Training completed*

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 (such as γ or UV irradiation, oxidative stress, cytokines, etc.) - are investigated. The structural and functional characteristics of the senescent cell are studied at the transcriptional, translational/post-translational and epigenetic level. Especially, we are interested in the role of senescent cells, through their senescence-associated secretory phenotype (SASP), in the development of important age-related diseases, including 1. cancer progression, 2. intervertebral disc degeneration and manifestation of low back pain and 3. inherent skin ageing, as well as photoageing. In parallel, the effects of cellular senescence on the characteristics and function of mesenchymal stem cells are examined.

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.

2022 Findings

Main goal of the Laboratory is the study of the role of the senescent cell in the manifestation of age-related diseases. It has been established that UV irradiation is detrimental for the skin, causing damages that range from erythema and premature senescence to carcinogenesis. We studied the effect of UVB irradiation on the viability and premature senescence of human dermal fibroblasts. We showed that high UVB doses are cytotoxic, leading fibroblasts to apoptosis. Using selective inhibitors and siRNA molecules, we found that a number of biochemical pathways co-operate and contribute to the survival of human dermal fibroblasts: the EGFR/Akt axis and Nrf2 constitute an auxiliary mechanism, while the JNKs/ATM-p53 loop is indispensable for cytoprotection against UVB irradiation (Figure 1). We also studied the mechanism of premature senescence induction after serial exposures of human dermal fibroblasts to non-cytotoxic doses of UVB irradiation. We actually found that a subset of the exposed population avoids senescence, while RNA-seq anlaysis followed by functional experiments revealed that these cells constitute a distinct sub-population with traits in-between early-passage and senescent cells.

Furthermore, we studied the effect of senescence on the phenotype of adipose-derived mesenchymal stem cells (AdMSCs) and showed that senescent AdMSCs display a pro-inflammatory and catabolic phenotype, as well as a reduced ability towards osteogenic, adipogenic and chondrogenic differentiation.

In parallel, we examined epigenetic alterations of three human cell types (dermal fibroblasts and bone-marrow and adipose-derived mesenchymal stem cells), driven to senescence after replicative exhaustion or exposure to genotoxic stress in the form of ionizing radiation or doxorubicin. We showed that in terms of DNA methylation, replicatively senescent cells cluster separately from early-passage cells and cells driven to senescence by other senescence stimuli, suggesting the heterogeneity of senescent cells, leading possibly to a different outcome on the regulation of tissue homeostasis.

Low back pain constitutes one of the most important chronic age-related diseases, in the manifestation of which intervertebral disc degeneration is a critical parameter. Given the lack of vascularization in the intervertebral disc, we aimed to investigate whether improvement of the physiology of this tissue using pharmaceutical approaches is plausible. We showed that zoledronic acid, traditionally used to treat osteoporosis, compared to a vascularized tissue (the skin), shows a delayed, prolonged and at low concentrations accumulation in the periphery of the disc (annulus fibrosus) of rabbits, while it was not detected in the center of the disc (the nucleus pulposus). We are currently studying whether other pharmaceutical compounds with a different chemical composition display the same accumulation profile, to conclude if this constitutes a general characteristic of the particular tissue.

We also studied the expression of markers for osteogenic differentiation after the application of mechanical forces in orthodontics, as well as putative estrogenicity of orthodontic materials. Finally, we continued our research on the investigation of natural products and novel synthetic compounds with anti-cancer, anti-oxidant and cosmetic applications.

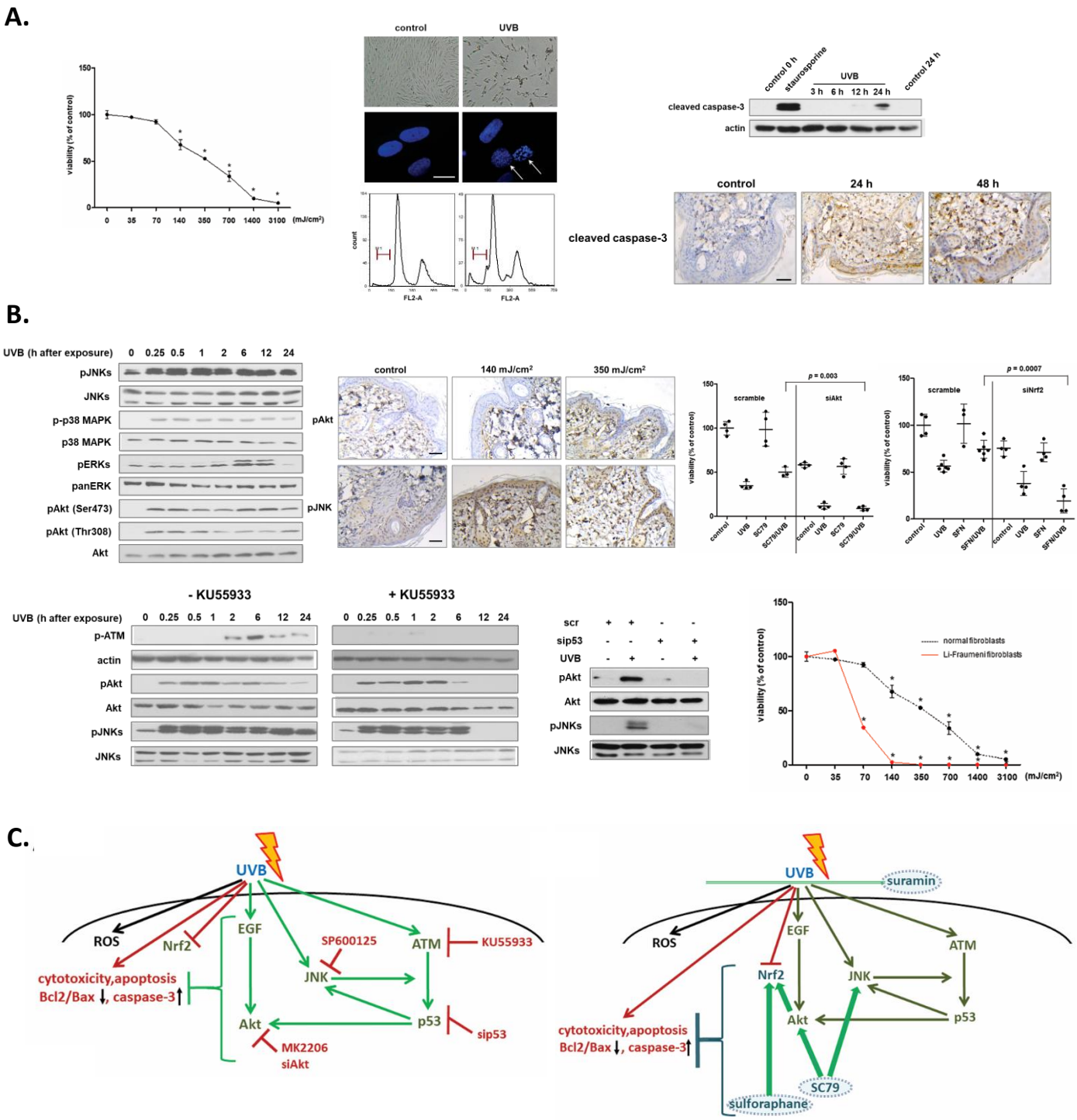

Figure 1: *A. High UVB doses lead human dermal fibroblasts to apoptosis. B. A number of biochemical pathways co-operate and contribute to the survival of human dermal fibroblasts, as revealed by selective inhibitors and siRNA approaches: the EGFR/Akt axis and Nrf2 constitute an auxiliary mechanism, while the JNKs/ATM-p53 loop is indispensable for cytoprotection from UVB irradiation. C. Proposed models of inherent responses and of the interaction between photoprotective molecules and inherent cellular machineries leading to an enhanced resistance of human dermal fibroblasts towards UVB irradiation [Mavrogonatou et al., Cell Death Dis. 2022 Jul 25;13(7):647].*

Publications

Mavrogonatou E, Angelopoulou M, Rizou SV, Pratsinis H, Gorgoulis VG, Kletsas D. (2022). Activation of the JNKs/ATM-p53 axis is indispensable for the cytoprotection of dermal fibroblasts exposed to UVB radiation. Cell Death Dis. 2022 Jul 25;13(7):647. (IF: 9.685)

Papadopoulou A, Kalodimou VE, Mavrogonatou E, Karamanou K, Yiacoumettis AM, Panagiotou PN, Pratsinis H, Kletsas D. (2022). Decreased differentiation capacity and altered expression of extracellular matrix components in irradiation-mediated senescent human breast adipose-derived stem cells. IUBMB Life. 2022 Oct;74(10):969-981. (IF: 4.709)

Karamanos N, Ricard-Blum S, Kletsas D. (2022). Extracellular matrix: The dynamic structural and functional network in health and disease. IUBMB Life. 2022 Oct;74(10):926. (IF: 4.709)

Christophoridis C, Kouroumalis A, Kletsas D. (2022). Accumulation of zoledronic acid in rabbit intervertebral discs. J Chromatogr B Analyt Technol Biomed Life Sci. 2022 May 1;1197:123229 (IF: 3.318)

Pratsinis H, Papageorgiou SN, Panayi N, Iliadi A, Eliades T, Kletsas D. (2022). Cytotoxicity and estrogenicity of a novel 3-dimensional printed orthodontic aligner. Am J Orthod Dentofacial Orthop. 2022 Sep;162(3):e116-e122. (IF: 2.711)

Vlachou F, Varela A, Stathopoulou K, Ntatsoulis K, Synolaki E, Pratsinis H, Kletsas D, Sideras P, Davos CH, Capetanaki Y, Psarras S. (2022). Galectin-3 interferes with tissue repair and promotes cardiac dysfunction and comorbidities in a genetic heart failure model. Cell Mol Life Sci. 2022 Apr 19;79(5):250. (IF: 9.234)

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Biczo A, Bereczki F, Koch K, Varga PP; Urban J, Fairbank J, Heywood C, Sivan S, Roberts S, Neidlinger-Wilke C, Kaprio J, Battie MC, Kletsas D, Ito K, Huyghe J, Brayda-Bruno M, Velikonja NK, Lazary A. (2022). Genetic variants of interleukin 1B and 6 are associated with clinical outcome of surgically treated lumbar degenerative disc disease. BMC Musculoskelet Disord. 2022 Aug 13;23(1):774. (IF: 2.562)

Papatsirou M, Diamantopoulos MA, Katsaraki K, Kletsas D, Kontos CK, Scorilas A. (2022). Identification of novel circular RNAs of the human protein arginine methyltransferase 1 (*PRMT1*) gene, expressed in breast cancer cells. Genes (Basel). 2022 Jun 24;13(7):1133. (IF: 4.141)

Madbouly EA, Lashine E-SM, Al-Karmalawy AA, Sebaiy MM, Pratsinis H, Kletsas D, Metwally K. (2022). Design and synthesis of novel quinazolinone-chalcone hybrids as potential apoptotic candidates targeting caspase-3 and PARP-1: *in vitro*, molecular docking, and SAR studies. New J Chem. 2022 October 5;46(46), pp. 22013-22029 (IF: 3.925)

Siderakou D, Zilelidou E, Poimenidou S, Paramithiotis S, Mavrogonatou E, Zoumpopoulou G, Tsipra I, Kletsas D, Tsakalidou E, Skandamis PN. (2022). *In vitro* virulence potential, surface attachment, and transcriptional response of sublethally injured *Listeria monocytogenes* following exposure to peracetic acid. Appl Environ Microbiol. 2022 Jan 25;88(2):e0158221. (IF: 5.005)

Kloukos D, Mavrogonatou E, Kletsas D, Makras P, Koukos G, Stavropoulos A, Katsaros C. (2022). Bone turnover markers in gingival crevicular fluid and blood serum of patients with fixed orthodontic appliances. Eur J Orthod. 2022 Aug 16;44(4):412-419. (IF: 3.131)

Temponeras I, Stamatakis G, Samiotaki M, Georgiadis D, Pratsinis H, Panayotou G, Stratikos E. (2022). ERAP2 inhibition induces cell-surface presentation by MOLT-4 leukemia cancer cells of many novel and potentially antigenic peptides. Int J Mol Sci. 2022 Feb 8;23(3):1913. (IF: 6.208)

Gioxari A, Amerikanou C, Nestoridi I, Gourgari E, Pratsinis H, Kalogeropoulos N, Andrikopoulos NK, Kaliora AC. (2022). Carob: A sustainable opportunity for metabolic health. Foods. 2022 Jul 20;11(14):2154. (IF: 5.561)

Kakali L, Giantikidis I, Sifakakis I, Kalimeri E, Karamani I, Mavrogonatou E, Kloukos D. (2022). Fluctuation of bone turnover markers' levels in samples of gingival crevicular fluid after orthodontic stimulus: a systematic review. Syst Rev. 2022 Jan 4;11(1):3. (IF: 3.136)

Articles in Press

Mourkioti I, Polyzou A, Veroutis D, Theocharous G, Lagopati N, Gentile E, Stravokefalou V, Thanos D-F, Havaki S, Kletsas D, Panaretakis T, Logothetis CJ, Stellas D, Petty R, Blandino G, Papaspyropoulos A, Gorgoulis VG. (2023). A GATA2-CDC6 axis modulates androgen receptor blockade-induced senescence in prostate cancer. J Exp Clin Cancer Res. 2023 (*in press*). (IF: 11.3)

Kwiatkowska KM*, Mavrogonatou E*, Papadopoulou A, Sala C, Calzari L, Gentilini D, Bacalini MG, Dall'Olio D, Castellani G, Ravaioli F, Franceschi C, Garagnani P, Pirazzini C, Kletsas D. (2023). Heterogeneity of cellular senescence: cell type-specific and senescence stimulus-dependent epigenetic alterations (* equal contribution). Cells. 2023 Mar 17;12(6):927. (IF: 7.666)

Kavvoura DA, Stefanakis MK, Kletsas D, Katerinopoulos HE, Pratsinis H. (2023). Biological activities of *Ceratonia siliqua* pod and seed extracts: A comparative analysis of two Cretan cultivars. Int J Mol Sci. 2023 (*in press*). (IF: 5.6)

Mavrogonatou E, Papadopoulou A, Pratsinis H, Kletsas D (2023). Senescence-associated alterations in the extracellular matrix: Deciphering their role in the regulation of cellular function. Am J Physiol Cell Physiol. 2023 (*in press*). (IF: 5.5)

Koutela A, Loudos G, Rouchota M, Kletsas D, Karameris A, Vilaras G, Zografos GC, Grypari IM, Dougenis D, Papalois AE. (2023). A novel experimental rat model for the *in vivo* assessment of myocardial ischemia based on single photon emission computed tomography. In Vivo. 2023 Mar-Apr;37(2):649-654. (IF: 2.406)

Lougiakis N, Sakalis N, Georgiou M, Marakos P, Pouli N, Skaltsounis AL, Mavrogonatou E, Pratsinis H, Kletsas D. (2023). Synthesis, cytotoxic activity evaluation and mechanistic investigation of novel 3,7-diarylsubstituted 6-azaindoles. Eur J Med Chem. 2023 Sep 13;261:115804. (IF: 6.700)

Articles published or in press (In Press) in proceedings of international conferences or other serial works, editing of publications of scientific books

Argyropoulou A, Lemus Ringele GB, Fotopoulou A, Nastos C, Papachristodoulou A, Stavropoulos G, Pratsinis H, Kletsas D, Kalpoutzakis E, Halabalaki M. (2022). Chemical and biological evaluation of plants from the Greek flora towards their use as cosmetics. Planta Med. 2022 Dec; 88(15): 1511-1512.

Koumantou D, Barnea E, Martin-Esteban A, Maben Z, Papakyriakou A, Kokkala P, Pratsinis H, Georgiadis D, Stern LJ, Admon A, Stratikos E. (2022). Chemical inhibition of ER aminopeptidase 1 as a tool for regulating the immunopeptidome of cancer cells. Mol. Immunol. 2022 Oct; 150: 221.

International conferences

Kletsas D. “Cellular senescence in tumor development”, Society for Free Radical Research - Europe (SFRR-E) Webinar “Cellular disfuction in cancer and ageing”, March 24, 2022, Virtual (invited speaker)

Kletsas D. “Effect of UVB on skin fibroblast homeostasis: from cell death to premature senescence” 10th International Conference on Oxidative Stress in Skin Medicine and Biology, September 12-15, Andros, Greece (invited speaker)

Mavrogonatou E., Papadopoulou A., Fotopoulou A., Liakou E., Karamanou K., Yiacoumettis A.M., Panagiotou P.N., Pratsinis H., Kletsas D. “Different stresses may lead to different senescent phenotypes: Implications in tissue homeostasis”, FEBS 2022 Advanced Course “Matrix Pathobiology, Signaling and Research Targets", May 05-10, Crete, Greece (invited speaker)

Kanioura A, Zeniou A, Petrou P, Papadopoulou A, Mavrogonatou E, Kletsas D, Tserepi A, Gogolides E, Kakabakos S. Adhesion, viability and differentiation of adipose tissue derived mesenchymal stem cells onto micro/nanostructured polystyrene substrates. 7th World Congress on Recent Advances in Nanotechnology (RAN'22), April 04-06, 2022, Virtual

Argyropoulou A, Lemus Ringele GB, Fotopoulou A, Nastos C, Papachristodoulou A, Stavropoulos G, Pratsinis H, Kletsas D, Kalpoutzakis E, Halabalaki M. Chemical and biological evaluation of plants from the Greek flora towards their use as cosmetics. 70th International Congress and Annual Meeting of the Society for Medicinal Plant and Natural Product Research (GA), August 28-31, 2022, Thessaloniki, Greece

Koumantou D, Barnea E, Martin-Esteban A, Maben Z, Papakyriakou A, Kokkala P, Pratsinis H, Georgiadis D, Stern LJ, Admon A, Stratikos E. Chemical inhibition of ER aminopeptidase 1 as a tool for regulating the immunopeptidome of cancer cells. 18th European Meeting on Complement in Human Disease (EMCHD), September 26-29, 2022, Bern, Switzerland

National conferences

Papatsirou M, Kletsas D, Scorilas A, Kontos C. Identification of alternatively spliced, circular transcripts (circRNAs) of the *PRMT1* gene in breast cancer cell lines, using targeted nanopore sequencing. 72nd Congress of the Hellenic Society of Biochemistry and Molecular Biology, December 02-04, 2022, Patras

Louka K, Mavrogonatou E, Kletsas D. The role of oxidative stress in the high osmolality-induced upregulation of calcium-activated chloride channel regulator 2 in nucleus pulposus intervertebral disc cells. 72nd Congress of the Hellenic Society of Biochemistry and Molecular Biology, December 02-04, 2022, Patras

Papadopoulou A, Kalodimou VE, Mavrogonatou E, Karamanou K, Yiacoumettis AM, Panagiotou PN, Pratsinis H, Kletsas D. Decreased differentiation capacity and altered expression of extracellular matrix components in irradiation-mediated senescent human breast adipose-derived stem cells. 72nd Congress of the Hellenic Society of Biochemistry and Molecular Biology, December 02-04, 2022, Patras

Fotopoulou A, Angelopoulou M, Pratsinis H, Mavrogonatou E, Kletsas D. A subset of human skin fibroblasts exposed to UVB radiation can escape premature senescence. 72nd Congress of the Hellenic Society of Biochemistry and Molecular Biology, December 02-04, 2022, Patras

Mavrogonatou E, Angelopoulou MT, Rizou SV, Pratsinis H, Gorgoulis VG, Kletsas D. A functional JNKs/ATM-p53 loop is necessary for the protection of dermal fibroblasts against UVB-induced apoptosis. 72nd Congress of the Hellenic Society of Biochemistry and Molecular Biology, December 02-04, 2022, Patras

Kavvoura DA, Stefanakis MK, Kletsas D, Katerinopoulos HE, Pratsinis H. The carob of Crete: Chemotaxonomic and bioactivity studies in *Ceratonia siliqua* samples of Cretan origin. 72nd Congress of the Hellenic Society of Biochemistry and Molecular Biology, December 02-04, 2022, Patras

Papadopoulou A, Krikoni L, Gkolfinopoulou C, Tananaki C, Chroni A, Pratsinis H, Kletsas D. Greek honey biological activities: comparative analysis of samples from various botanical and geographic origins. 72nd Congress of the Hellenic Society of Biochemistry and Molecular Biology, December 02-04, 2022, Patras

Karamanou K, Fotopoulou A, Lemus Ringele GB, Kalpoutzakis E, Argyropoulou A, Mavrogonatou E, Stavropoulos G, Halabalaki M, Pratsinis H, Kletsas D. *In vitro* screening of extracts from the Greek flora as a basis for the development of innovative cosmeceuticals. 72nd Congress of the Hellenic Society of Biochemistry and Molecular Biology, December 02-04, 2022, Patras

Other Scientific Activities

Participation in Greek and international scientific bodies and organizations

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

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

Representative of the Hellenic Society for Biochemistry and Molecular Biology in the Council of the Federation of the European Biochemical Societies (FEBS) (D. Kletsas)

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

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

Member of the Evaluation Committee for GRAMMER European Spine Journal Award (D. Kletsas)

Evaluator/Expert of research proposals and funded actions of the General Secretariat for Research and Innovation (GSRI) (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", "Journal of Orthopaedic Research Spine", "Antioxidants", "Matrix Biology" and "Matrix Biology Plus" (D. Kletsas)

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

Reviewer board member of the Journal "International Journal of Molecular Sciences" and Review Editor for Craniofacial Biology and Dental Research of the Journal "Frontiers in Physiology" (E. Mavrogonatou)

Organization of scientific conferences or participation in conference organizing committees

Member of the Scientific Committee of the 10th International Cenference on Oxidative Stress in Skin Medicine and Biology, September 12-15, Andros, Greece (D. Kletsas)

Reviewing of manuscripts in scientific journals

European Spine Journal (3), Mechanisms of Ageing and Development, Biogerontology, Experimental Gerontology (3), Aging Cell, Tissue Engineering, Antioxidants (D. Kletsas)

Advanced Science, Antioxidants, Arabian Journal of Chemistry, Chemistry & Biodiversity, Cosmetics, European Journal of Pharmacology (2), FEBS Journal, Frontiers in Bioengineering,

International Journal of Molecular Sciences (3), Journal of Cellular and Molecular Medicine, Marine Drugs (2), Molecular Biology Reports, Pharmaceuticals (2), Rejuvenation Research (2) (H. Pratsinis)

Biomedicine and Pharmacotherapy (2), International Journal of Molecular Sciences (11), American Journal of Orthodontics & Dentofacial Orthopedics (8), Cancers, Antioxidants (2), Vaccines (2), Applied Biosciences and Bioengineering, Clinical, Cosmetic and Investigational Dermatology (2), Frontiers in Endocrinology (E. Mavrogonatou)

Educational Activities

Member of the special interinstitutional 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)

Supervision of the PhD theses of Asimina Fotopoulou, Efstathios Tsimelis, Eleni Liakou, Maria Angelopoulou and Maria Adamopoulou (D. Kletsas)

Supervision of the theses for the acquisition of a Master's degree of Konstantina Louka, Marina Kavellari, Anastasia Kypraiou, Mariam Christogianni and Maria Dimozi (D. Kletsas)

Supervision of the theses for the acquisition of a Master's degree of Dafni-Alexandra Kavvoura and Maria Karanikou (H. Pratsinis)

Co-Supervision of the thesis for the acquisition of a Master's degree of Konstantina Louka (E. Mavrogonatou)

Supervision of the thesis for the acquisition of a Bachelor's degree of Vassiliki Kavvadia (E. Mavrogonatou)

Supervision of the trainee Anastasia Sotiropoulou (E. Mavrogonatou)

"*In vitro* studies of natural and synthetic bioactive products", 57th NCSR "Demokritos" Summer School, 1 hour, 100 students (H. Pratsinis)

"Cell biology of the degenerated and aged intervertebral disc", 57th NCSR "Demokritos" Summer School, 1 hour, 100 students (E. Mavrogonatou)

"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)

"Regenerative medicine in intervertebral discs", Post-graduate Master's Degree "Stem cells and regenerative medicine", Aristotle University of Thessaloniki, 1 hour, 20 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, 25 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, 1 hour, 25 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, 13 students (D. Kletsas, H. Pratsinis and E. Mavrogonatou)

Invited talk entitled "Cellular senescence: A new target for the development of antiageing therapies" in the framework of the educational seminar of Secondary Education Teachers "Natural Sciences: Advancements and Perspectives" organized by École Franco-Hellénique Des Ursulines (02/04/2022) (D. Kletsas)

Instructor of the science lab "Protein electrophoresis in the school environment" in the framework of the educational seminar of Secondary Education Teachers "Natural Sciences: Advancements and Perspectives" organized by École Franco-Hellénique Des Ursulines (02/04/2022) (E. Mavrogonatou)

Member of examination committees for PhD, MSc and BSc theses
Maria Adamopoulou concluded her PhD thesis entitled "Genetic engineering of intervertebral disc cells using CRISPR-Cas9" in Biotech Research & Innovation Centre (BRIC), Faculty of Health and Medical Sciences, University of Copenhagen (Scientific Co-Supervisor D. Kletsas, Member of the three-member examination committee H. Pratsinis)

Konstantina Louka concluded her MSc thesis entitled "The role of oxidative stress in the high osmolality-induced CLCA2 up-regulation in intervertebral disc cells" in the framework of the Master's Degree Programme "Applications of Biology in Medicine" in the Department of Biology, University of Athens. The thesis was unanimously accepted and awarded the degree "Excellent" (Scientific Supervisor D. Kletsas, Member of the three-member examination committee E. Mavrogonatou)

Maria Karanikou concluded her MSc thesis entitled "Towards an Application of Plant Derived Vesicular Material on Human Cells: Cytotoxicity and Cells' Proliferation Studies" in the framework of the Master's Degree Programme "Biomedical Engineering" in the Department of Mechanical Engineering, University of Western Macedonia. The thesis was unanimously accepted and awarded the degree "Excellent" (Scientific Co-Supervisor and member of the three-member examination committee H. Pratsinis)

Member of the examination committee of the PhD thesis of Christina Kyriakopoulou entitled "Biochemical and cell study of the effect of EGFR-mediated signaling on the morphology, functional properties and stemness of breast cancer cells with differential ERs expression" in the Department of Chemistry, University of Patras (D. Kletsas)

Member of the examination committee of the PhD thesis of Vassiliki-Ioanna Mpoka entitled "Exploitation of Greek flora for the discovery of antioxidant and skin-whitening natural compounds based on HPTLC and CPC techniques" in the School of Pharmacy, University of Athens (D. Kletsas)

Other Activities in IBA and in NCSR "Demokritos"
D. Kletsas:
Director of IBA & Member of the Board of NCSR "Demokritos"
Vice-President of the Board of NCSR "Demokritos"
Member of the Committee for Research Exploitation in NCSR "Demokritos"
Scientific and Administrative Responsible of the Experimental Animal Facility
Administrative Responsible of the Laboratory for Doping Control and Metabolic Studies

Scientific and Administrative Responsible of the Light Microscopy Unit and the Histology Unit

H. Pratsinis:
President of the Scientific Board of IBA
Responsible for the conducted tours in the Institute of Biosciences and Applications of NCSR "Demokritos"
Member of the Research Exploitation Committee for the commercial exploitation of IBA researchers' patents
Member of the Committee for the monitoring of the renovation procedure of the central building of IBA
Member of the Evaluation Committees for the evaluation of candidates for temporary staff positions (projects 12551 and 12259 of ELKE, NCSR "Demokritos") and receipt of deliverables (project 12388)

E. Mavrogonatou:
Organization of the teaching and examination schedule of the course "Molecular & Cellular Biology-Molecular Biotechnology" course in the framework of the Inter-Institutional Joint Post-Graduate Programme between the Institute of Biosciences and Applications and the University of Patras "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" (Spring semester)
Member of the Committee for the accomplishment of an open electronic competition for deliverables' supply in the framework of the implementation of project E-12426
Member of the three-member evaluation committee for the evaluation of candidates for temporary staff positions in the framework of the implementation of project E-12584
Substitute member of the three-member evaluation committee for the evaluation of candidates for temporary staff positions in the framework of the implementation of project E-12545

Total Impact Factor for original publications in 2022
D. Kletsas (for 12 publications): 58.868
H. Pratsinis (for 7 publications): 42.033
E. Mavrogonatou (for 5 publications): 25.666

Citations 2022 (without self-citations)
D. Kletsas: 838
H. Pratsinis: 308
E. Mavrogonatou: 221

Total Citations 2018-2022 (without self-citations)
D. Kletsas: 3954
H. Pratsinis: 1220
E. Mavrogonatou: 810

h-factor
D. Kletsas: 50 (Scopus), 58 (Google Scholar)
H. Pratsinis: 33 (Scopus), 37 (Google Scholar)
E. Mavrogonatou: 21 (Scopus), 22 (Google Scholar)

Current External Funding
Project entitled "Development of innovative cosmeceuticals based on the greek flora (CosmAGE)" (Τ2ΕΔΚ-02583, MIS 5070022), co-financed by the European Regional Development Fund of the European Union and Greek national funds through the Operational Program Competitiveness, Entrepreneurship and Innovation, under the call RESEARCH –

CREATE – INNOVATE
Scientific Supervisor: Dr. D. Kletsas
Duration: 2020-2023
Total programme funding (for the entire duration of the programme): 229.999,99 €
Funding of the lab for 2022: 29.963,57 €

Project entitled “Development of a value chain for the Greek "wild rose" (*Rosa canina L.*) applying good agricultural practices for the production of cosmetic raw materials via innovative green extraction processes (Green_Wild_ ROSE.gr)” (Τ2ΕΔΚ-02333, MIS 5131416), co-financed by the European Regional Development Fund of the European Union and Greek national funds through the Operational Program Competitiveness, Entrepreneurship and Innovation, under the call RESEARCH – CREATE – INNOVATE
Scientific Supervisor: Dr. D. Kletsas
Duration: 2021-2023
Total programme funding (for the entire duration of the programme): 200.000,00 €
Funding of the lab for 2022: 0 €

Project entitled “Effect of secreted factors from 3D printed aligners on human gingival fibroblasts and epithelial cells”, financed by the University of Zurich (Clinic of Orthodontics and Pediatric Dentistry)
Scientific Supervisor: Dr. D. Kletsas
Duration: 2021-2023
Total programme funding (for the entire duration of the programme): 7.136,49 €
Funding of the lab for 2022: 0 €

Project entitled “In vitro assessment of combinations of known senotherapeutics for their potential application in the prevention and/or treatment of intrinsic and ultraviolet radiation-induced skin ageing”, financed by UNI-PHARMA Pharmaceutical Laboratories S.A.
Scientific Supervisor: Dr. D. Kletsas
Duration: 2021-2023
Total programme funding (for the entire duration of the programme): 25.000,00 €
Funding of the lab for 2022: 16.600,00 €

Current External IBA Funding
Project entitled “Ensuring long-term sustainability of excellence in chemical biology within Europe and beyond (EU-OPENSCREEN-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 (for the entire duration of the programme): 16.875,00 €
Funding for 2022: 0 €

Project entitled “The Routes of Bee”, funded by the General Secretariat for Research and Innovation (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: 2017-2021
Total programme funding (for the entire duration of the programme): 39.200,00 €
Funding for 2022: 19.600,00 €

Project entitled “Laboratory for Doping Control”, funded by the Ministry of Culture and Sports

Scientific Supervisor: Dr. D. Kletsas
Duration: 2020-2023
Total programme funding (for the entire duration of the programme): 1.200.000,00 €
Funding for 2022: 0 €

Project entitled “Upgrading of the Analytical Equipment of the Laboratory for Doping Control”, funded by the General Secretariat for Research and Innovation
Scientific Supervisor: Dr. D. Kletsas
Duration: 2019-2022
Total programme funding (for the entire duration of the programme): 2.000.000,00 €
Funding for 2022: 466.008,00 €

Research Group: Nuclear Proteins and Chromatin Function

Research Staff
Thomae Sourlingas, Senior Researcher B' Grade
Irini Katsirma, Undergratuate Student
Margarita Karakike, Undergratuate Student
Kalliope Sekeri, Research Collaborator, Retired A' Grade

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.

2022 Findings

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, but not H3 dimethylation, increase significantly. Of great interest was the finding that while the levels of the H1.0 subtype increase in the presence of sodium butyrate, for the first time we see another effect, which has not been previously reported. We observe a statistically significant decrease in H1.3. The levels of the H1.5 subtype, associated with closed heterochromatin, do not change. H1.0 has been well-studied, but not H1.3. Thus, these results are of special significance. It is also important that these 2 subtypes (H1.0 and H1.3) that were

found to be affected by this inhibitor are related to chromatin regulatory functions, while H1.5, which was found not to be affected, is associated with closed inactive, heterochromatin. Histone H3 dimethylation which was also found to remain unaffected in the presence of this drug, is also associated with closed heterochromatin. It is noted that the increase of H1.0 with the simultaneous decrease of H1.3 in the presence of butyrate is observed only in the leukemic cell lines. Sodium butyrate does not affect the protein levels of physiological lymphocytes. This was also associated with butyrate-induced mortality rates. In lymphocytes we do not observe an increase in mortality, in contrast to NB4 and Molt4 cells where we have a statistically significant decrease in viability in the presence of this HDAC inhibitor. These results suggest that these histone epigenetic factors may be used as biomarkers of the efficacy of HDACIs in therapeutic regimens.

Articles that have been accepted for publication

Xydous M., Chrysanthoy-Piterou M., Panagiotopoulou C., Kloukina-Pantazidou I., Havaki S., Dedemadi A-G., Kontaxakis V.P., Kollias C., Angelopoulos E., Sekeri-Pataryas K.E., Prombona A., and T.G. Sourlingas. Alterations in the levels of an H1 DNA linker histone subtype in peripheral blood leukocytes from schizophrenia patients are linked with this disorder. Journal of Biological Research Thessaloniki 2022. (IF: 2.576).

Educational Activities

Withn IBA:

"DNA organization, histones and chromatin function" within the framework of the course "Molecular and Cell Biology – Molecular Biotechnology" of the Bi-Institutional Graduate Masters' Program, "Applied Biochemistry, Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products", Institute of Biosciences and Applications and University of Patras (2 hours, 13 students).

Outside IBA:

"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 (3 hours, 19 students).

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 that have been acquired by funds from the Demokritos budget.

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.

Citations 2022 (without self-citations): 10

Total citations 2018-2022 (without self-citations): 113

h-factor: 11 (Scopus), 14 (Google scholar)

Research Group: Cell & Matrix Biochemistry/Pathobiology

Research Staff
Angeliki Chroni, Research Director
Paraskevi Kitsiou, Senior Researcher
Garyfalia Drossopoulou, Senior Researcher
Christina Gkolfinopoulou, Postdoctoral Fellow
Dafni Georgiadou, Postdoctoral Fellow
Eftaxia-Konstantina Valanti, Postdoctoral Fellow
Christina Mountaki, PhD student – *PhD obtained in 2022*
Anastasia Georgia Dedemadi, PhD student
Asimina Micha, MSc student – *MSc obtained in 2022*
Dimitris Lymperopoulos, MSc student
Lydia Voulgari, Diploma student – *BSc obtained in 2022*
Eirini Georgiou, Diploma student

Research Interests

1. ***Molecular mechanisms of dyslipidemias and atherosclerosis***
   A) Elucidation of the biological and pathological functions of apolipoproteins and lipoproteins in relation to atherosclerosis, with particular emphasis on the study of the structure-function relationship of apoA-I and other proteins associated with high-density lipoprotein (HDL).
   B) Characterization of changes in composition and atheroprotective functions of HDL from patients with increased cardiovascular risk for the identification of novel biomarkers of cardiovascular risk.

2. ***Molecular mechanisms of Alzheimer's disease***
   A) Elucidation of the molecular mechanisms underlying the role of apoE4, the major risk factor for Alzheimer's disease, amyloid peptide beta (Aβ), tau protein, neuroinflammation and cholesterol homeostasis in disease pathogenesis.
   B) Examination of the neuroprotective activity of natural products and pursue of therapeutic strategies aiming at the correction of the pathogenic properties of apoE4 in Alzheimer's disease.

3. Diabetes Mellitus and Diabetic Nephropathy
   A) Study of pancreatic β-cell survival mechanisms in diabetic conditions:
      i) Cross talk between nephrin and survival signaling pathways in pancreatic insulin producing beta cells.
      ii) Study of the effect of liraglutide (a human GLP-1 analogue) on islet β-cell survival signaling 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).
      ii) Role in prevention and/or treatment of diabetic nephropathy in isolated rat glomeruli and animal models. Interactions with signaling pathways that regulate podocyte survival.

2022 Findings

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

Proprotein Convertase Subtilisin/Kexin type 9 (PCSK9) plays an important role in the pathophysiology of atherosclerosis and has been associated with increased cardiovascular risk. PCSK9 binds to the LDL lipoprotein and its inhibition, with novel drugs, lowers plasma LDL-cholesterol levels. The relationship of PCSK9 with another lipoprotein, the HDL, has not be

thoroughly studied. We showed that PCSK9 can inhibit the atheroprotective properties of HDL related to the maintenance of endothelial function. This finding highlights further the importance of PCSK9 inhibition for protection against atherosclerosis and the development of cardiovascular disease (Dafnis et al, J. Lipid Res. 2023).

2. *Molecular mechanisms of Alzheimer's disease*

Alzheimer's disease (AD) is associated with brain amyloid-β (Aβ) peptide accumulation and neuroinflammation. Currants, a low glycemic index dried fruit, display pleiotropic neuroprotective effects in AD. We examined how diet enriched in Corinthian currants administered to the AD mice model 5xFAD affects Aβ levels and neuroinflammation in comparison to control diet or sugar-matched diet containing glucose/fructose. Our findings suggested that a short-term currant consumption from 5xFAD mice at the early stages of the disease, reduces Aβ42 levels and inhibits neuroinflammation as compared to sugar-matched or control diet. A long-term intake though of a glucose/fructose-containing diet such as currant-supplemented diet results on detrimental effects regarding neuroinflammation. The impact of chronic intake of low levels of sugars on brain health and AD is largely unexplored and current findings create new questions on the effects and molecular mechanisms of chronic intake of natural sugar-containing products on brain function. Since synaptic and neuronal loss is largely irreversible in the late stages of AD pathogenesis, any disease-modifying dietary interventions should be considered early before the onset of severe neurodegeneration (Dafnis et al, Mol. Neurobiol. 2023).

3. Diabetes Mellitus and Diabetic Nephropathy

A) In mouse pancreatic β-cells (βTC-6), nephrin signaling promotes cell survival. High glucose concentration down-regulates nephrin signaling without affecting nephrin expression. Our results demonstrated that in cultured βTC6 cells, high glucose led to increased expression of PKCα accompanied by enhanced nephrin internalization and suggest that glucose-induced impairment of nephrin-mediated signaling could be partly explained by decreased availability of β-cell surface nephrin. It is possible that nephrin internalization serves as an ignition spark for impaired β-cell signaling in long-standing hyperglycemia.

B) Diabetic nephropathy (DN) is a major chronic complication in diabetic subjects. Treatment of DN by pharmacological means has many limitations. Our results demonstrated the promising and beneficial effects of cell therapy approaches. Mesenchymal stem cells isolated from human amniotic fluid (AF-MSC) were differentiated in insulin-producing cells (iPCs) through administration of Exendin-4 (glucagon-like protein-1 receptor agonist) and/or Liraglutide. iPCs were capable of secreting insulin and expressing characteristic markers such as nephrin. Secreted condition media (CM) from iPCs, at different stages of differentiation have been isolated and analyzed in order to verify their anti-apoptotic potential.

Publications

Dafnis I., Mountaki C., Fanarioti E., Mastellos D. C., Karvelas M., Karathanos V. T., Tzinia A., Dermon C. R. and Chroni A. Temporal Pattern of Neuroinflammation Associated with a Low Glycemic Index Diet in the 5xFAD Mouse Model of Alzheimer's Disease. Mol. Neurobiol. 59, 7303-7322 (2022) (IF 5.686)

Dafnis I., Tsouka A. N., Gkolfinopoulou C., Tellis C. C., Chroni A. and Tselepis A. D. PCSK9 is minimally associated with HDL but impairs the anti-atherosclerotic HDL effects on endothelial cell activation. J. Lipid Res. 63, 100272 (2022) (IF 6.676)

Valanti E. K., Dalakoura-Karagkouni K., Fotakis P., Vafiadaki E., Mantzoros C. S., Chroni A., Zannis V., Kardassis D. and Sanoudou D. Reconstituted HDL-apoE3 promotes endothelial cell migration through ID1 and its downstream kinases ERK1/2, AKT and p38 MAPK. Metabolism 127, 154954 (2022) (IF 13.934)

Kardassis D., Thymiakou E. and Chroni A. Genetics and regulation of HDL metabolism. Biochim. Biophys. Acta Mol. Cell. Biol. Lipids 1867, 159060 (2022) (IF 5.228)

Published or in press articles in international conferences' proceedings or other volumes

Gkolfinopoulou C., Bourtsala A. and Chroni A. Identification of molecules that correct structural and functional defects of naturally-occurring pathogenic apoA-I mutants. *Atherosclerosis*, 355: e151 (2022).

Tsouka A.N., Dafnis I., Tellis C.C., Gkolfinopoulou C., Chroni A. and Tselepis A.D. PCSK9 is differentially distributed among HDL subpopulations. *Atherosclerosis*, 355: e154 (2022).

Dedemadi A.G., Gkolfinopoulou C. and Chroni A. Screening for small molecules that enhance the enzyme activity of human paraoxonase 1 in serum. *FEBS Open Bio*, 12 (Suppl. S1): 149 (2022).

Chernyaeva L., Ratti G., Teirilä L., Rankka U., Fudo S., Pelkonen A., Korhonen P., Leskinen K., Keskitalo S., Salokas K., Christodoulopoulou C., Crompton K.E., Varjosalo M., Malm T., Leinonen V., Chroni A., Saavalainen P., Meri S., Wollman A.J., Nissilä E. and Haapasalo K. Isoform-specific binding of apolipoprotein E to complement factor H alters amyloid-β-mediated neurotoxicity in vitro and in vivo. *Mol. Immunol.* 150: 147 (2022).

International conferences

Gkolfinopoulou C, Bourtsala A. and Chroni A. Identification of molecules that correct structural and functional defects of naturally-occurring pathogenic apoA-I mutants. *90th European Atherosclerosis Society Congress,* 22-26 May 2022, Milan, Italy

Tsouka A.N., Dafnis I., Tellis C.C., Gkolfinopoulou C., Chroni A. and Tselepis A.D. PCSK9 is differentially distributed among HDL subpopulations. *90th European Atherosclerosis Society Congress,* 22-26 May 2022, Milan, Italy

Dedemadi A.G., Gkolfinopoulou C. and Chroni A. Screening for small molecules that enhance the enzyme activity of human paraoxonase 1 in serum. *46th FEBS Congress*, 9-14 July 2022, Lisbon, Portugal

Chernyaeva L., Ratti G., Teirilä L., Rankka U., Fudo S., Pelkonen A., Korhonen P., Leskinen K., Keskitalo S., Salokas K., Christodoulopoulou C., Crompton K.E., Varjosalo M., Malm T., Leinonen V., Chroni A., Saavalainen P., Meri S., Wollman A.J., Nissilä E. and Haapasalo K. Isoform-specific binding of apolipoprotein E to complement factor H alters amyloid-β-mediated neurotoxicity in vitro and in vivo. *18th European Meeting on Complement in Human Disease (EMCHD)*, 26-29 August 2022, Bern, Switzerland

Dafnis I., Mountaki C., Fanarioti E., Mastellos D. C., Karvelas M., Karathanos V. T., Tzinia A., Dermon C. R. and Chroni A. Chronic effects of a low glycemic index diet in neuroinflammation in the 5xFAD mouse model of Alzheimer's disease. *International Society for Molecular* Neurodegeneration (*ISMND) 2022 Meeting,* 10-12 October 2022, Athens, Greece

National conferences

Dedemadi A. G., Gkolfinopoulou C., Nikoleri D., Nikoloudaki M., Sidiropoulos P., Bertsias G. and Chroni A. Improvement of atheroprotective properties of HDL in patients with Systemic lupus erythematosus after belimumab treatment. *10th Congress of the Hellenic Atherosclerosis Society*, 1-3 December 2022, Athens (2nd Prize for oral presentation)

Papadopoulou A., Krikoni L., Gkolfinopoulou C. Tananaki C., Chroni A., Pratsinis H. and Kletsas D. Greek honey biological activities: comparative analysis of samples from various botanical and geographic origins. *72nd Annual Conference of the Hellenic Society for Biochemistry and Molecular Biology*, 2-4 December 2022, Patras

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: 1) Chairman of the Management Committee of Working Group on the Pathophysiology of Atherosclerosis, Hellenic Atherosclerosis Society, 2) Alternate Member of the General Assembly of the Hellenic Foundation for Research and Innovation, 3) Member of WG1 of COST Action CA21153 (AtheroNET).

G. Drossopoulou: Member of the workgroup "Kidney function and Diabetes Mellitus" of the Hellenic Society of Nephrology.

Participation in editorial boards of scientific journals

A Chroni: 1) Editorial board member, Atherosclerosis Plus, Elsevier; 2) Associate editor, Frontiers in Cardiovascular Medicine - Lipids in Cardiovascular Disease; 3) Associate editor, Frontiers in Genetics

Reviewing of manuscripts in scientific journals

Arteriosclerosis, Thrombosis, & Vascular Biology, BBA-Molecular and Cell Biology of Lipids, Atherosclerosis, Scientific Reports, PLOS ONE, Neurochemistry International, International Journal of Molecular Sciences, Bioscience Reports, Atherosclerosis Plus, MedComm, Therapeutic Advances in Chronic Disease (A Chroni)

Current Diabetes Reviews, PLoS ONE, Recent Patents on Endocrine, Metabolic & Immune Drug Discovery (P. Kitsiou)

Current Diabetes Reviews, Journal of Nephrology, PLoS ONE, Nutrients, International Journal of Environmental Research and Public Health, American Journal of Nephrology (G. Drossopoulou)

Other lectures or presentations of scientific content (except from presentations at scientific conferences)

A. Chroni

1) "Quantity or quality? The myth of "good" cholesterol", Joint Seminar Series in Biotechnology, Biosciences and Biomedical Research organized by the University Research Center of Ioannina (Institute of Biosciences), the Foundation for Research and Technology-Hellas (Biomedical Research Institute) and the Inter-institutional Interdepartmental Program of Postgraduate Studies in Molecular and Cellular Biology and Biotechnology, 15 April 2022, Ioannina
2) "Inflammation and Atherosclerosis: from pathophysiology to therapeutic interventions" 15th Summer School of the Hellenic Atherosclerosis Society. 1-2 July 2022, Athens
3) "a) HDL cholesterol: Reassessment of its clinical significance. b) The role of apolipoprotein E in lipid homeostasis in circulation and tissues" Webinar series on "Atherosclerosis and Cardiovascular disease" organized in the framework of ELIDEK project entitled "Lifestyle and cardiovascular disease: From pathophysiological mechanisms to clinical practice" (CARDIOLIFE), 22 September 2022
4) "Recombinant protein expression in *E. coli*: Options, Approaches and Paradigms", 4th CAPSTONE-ETN Summit, 19-21 October 2022, Athens
5) "Dyslipidemia: the great enemy of heart and blood vessels", Free University of the Municipality of Halandri, 12 December 2022, Halandri, Attiki

Awards and Distinctions

PhD candidate Christina Mountaki was awarded the Akoyunoglu Award of the Institute of Biosciences and Applications, NCSR "Demokritos"

The PhD candidate Anastasia Georgia Dedemadi received the 2nd Prize for Oral Presentation at the 10th Congress of the Hellenic Society of Atherosclerosis, 1-3 December 2022, Athens

Educational Activities

A. Chroni

Member of the Inter-Departmental Committee and Faculty in the joined MSc Programme "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" of the Department of Chemistry of the University of Patras and of the Institute of Biosciences and Applications of NCSR Demokritos

Lecturer 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: "Cardiovascual disease and current therapeutic approaches" (2 h - 9 students), Course: "Molecular & Cellular Biology-Molecular Biotechnology"
Title of lecture: "Methods for analysis and characterization of proteins, lipids and hydrocarbons" (2 h-9 students), Course: "Biochemical Analysis- Clinical Biochemistry"

Guest lecturer in graduate course "Clinical Chemistry", "Clinical Biochemistry-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 – 25 students)

Chair of PhD Advisory Committee of C. Mountaki and A. G. Dedemadi at the Department of Chemistry, University of Athens
Christina Mountaki defended her PhD thesis at the Department of Chemistry of the University of Athens (November 2022). Title of thesis: "The role of apolipoprotein E in the pathogenesis of Alzheimer's disease: effect of naturally occurring compounds on the structure and function of apoE".

MSc supervisor for A. Micha and D. Lymperopoulos, "Clinical Biochemistry-Molecular Diagnostics" Graduate Program, University of Athens

Participation in the three-member Examination Committee for the evaluation of thesis of A. Micha for obtaining a MSc in Clinical Biochemistry-Molecular Diagnostics from the University of Athens
Asimina Micha defended her MSc thesis at the University of Athens (February 2022). Title of thesis: "Relationship between apolipoprotein E4 and lipid transport in the brain with Alzheimer's disease pathogenesis".

Diploma thesis supervision for undergraduate students L. Voulgari and E. Georgiou of the Chemistry department, University of Athens
Lydia Voulgari presented her Diploma thesis at the Department of Chemistry of the University of Athens (June 2022). Title of thesis: " Study of serum PON1 activity in the mouse model of Alzheimer's disease 5xFAD in relation to the age of mice and diet with Corinthian raisins".

Member of PhD Advisory Committee of a) E. K. Valanti at the School of Medicine, University of Athens, b) C. Mahalia at the Chemistry Department, University of Athens and c) A. Papagianni at the School of Medicine, Aristotle University of Thessaloniki.

Participation in the seven-member Examination Committee for the award of a Doctoral Degree from the School of Medicine of the University of Athens to E. K. Valanti.

G. Drossopoulou
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 – 13 students). Lectures on “Biochemical Analysis – Clinical Biochemistry).

Guest lecturer in MSc postgraduate program “Molecular and Applied Physiology”, Medical School, University of Athens “Regulation of Apoptosis in disease progression: Is it desirable or must be avoided?” October 2022 (3 hours lecture - 28 students)

Guest lecturer in MSc postgraduate course Clinical Biochemistry – Molecular Diagnostics, Unit: Physiology Chapters, Department of Biology, National and Kapodistrian University of Athens, “Metabolic Syndromes – Diebetes Mellitus and its complications”. (3 hours – 23 students)

4) Undergraduate research projects in collaboration with Department of Biomedical Sciences (Deree College, American College of Greece)

Other Activities in IBA and in NCSR “Demokritos”
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”.

Member of Special Committee for the utilization of research findings, NCSR “Demokritos”

G. Drossopoulou
Member of the committee for gender equality “Equality”, of NCSR Demokritos.

Coordinator of the Histology unit, NCSR Demokritos

Other scientific activities
Evaluation of abstracts for the annual conference of the Hellenic Atherosclerosis Society (A. Chroni)

Total Impact Factor for original publications in 2022
A. Chroni: 31.524

Citations 2022 (without self-citations)
A. Chroni: 174 (Scopus)
P. Kitsiou: 42 (Scopus)
G. Drossopoulou: 63 (Scopus)

Total Citations 2018-2022 (without self-citations)
A. Chroni: 768 (Scopus)
P. Kitsiou: 161 (Scopus)
G. Drossopoulou: 341 (Scopus)

h-factor
A. Chroni: 25 (Scopus),30 (Google Scholar)
P. Kitsiou: 11 (Scopus, Google Scholar)
G. Drossopoulou: 14 (Scopus), 15 (Google Scholar)

Current External Funding

Project entitled: Complementary neuroprotective action of currant as a natural dietary supplement. Highlighting the mechanisms of action of currant using animal models of neurodegenerative diseases funded by the Ministry of Economy and Development of Greece/ NSRF 2014-2020, Action "RESEARCH-CREATE-INNOVATE"
Programme duration: 2018-2022
Scientific Supervisor: A. Chroni
Total lab funding (for the entire duration of the programme): 188.000 €
Funding of the lab for 2022: 5.000 €

Project entitled: New therapies aiming to improve the atheroprotective and immunomodulatory properties of HDL for the treatment of autoimmune and cardiovascular diseases funded by the Ministry of Economy and Development of Greece/ NSRF 2014-2020, Action "RESEARCH-CREATE-INNOVATE"
Programme duration: 2020-2023
Scientific Supervisor: A. Chroni
Total lab funding (for the entire duration of the programme): 250.000 €
Funding of the lab for 2022: 80.000 €

Project entitled: The National Research Infrastructures on Integrated Structural Biology, Drug, Screening, Efforts and Drug Target Functional Characterization-INSPIRED funded by the Ministry of Economy and Development of Greece/ NSRF 2014-2020, Action "Reinforcement of the Research and Innovation Infrastructure"
Programme duration: 2018-2023
Scientific Supervisor: G. Nounessis as Principal Investigator for NCSR Demokritos and A. Chroni as team member
Total lab funding (for the entire duration of the programme): 16.000 €
Funding of the lab for 2022: -

Project entitled: *Training experts in antigen processing to deliver new drug prototypes for cancer and autoimmune diseases* funded by the European Commission, H2020, Marie Skłodowska-Curie Innovative Training Networks (ITN)
Programme duration: 2021-2024
Scientific Supervisor: E. Stratikos as Scientific Supervisor for NCSR Demokritos and A. Chroni as Deputy Scientific Supervisor
Total funding for NCSR Demokritos (for the entire duration of the programme): 486.035 €
Total lab funding (for the entire duration of the programme): 30.000 €
Funding of the lab for 2022: 10.000 €

Project entitled: Lifestyle and cardiovascular disease: From pathophysiological mechanisms to clinical practice- CARDIOLIFE funded by the Hellenic Foundation for Research & Innovation (ELIDEK), Action "Science and Society" - "Research, Innovation and Dissemination Hubs"
Programme duration: 2020-2023
Scientific Supervisor: A. Chroni
Total lab funding (for the entire duration of the programme): 2.800 €
Funding of the lab for 2022: 400 €

Project entitled: Nephroprotective role of Vitamin D3 funded by AENORASIS SA
Programme duration: 2017-2022
Scientific Supervisor: G. Drossopoulou
Funding of the lab for 2022: 13.825 €

Research Group: Molecular Carcinogenesis and Rare Disease Genetics

Research Staff

Gerassimos Voutsinas, Research Director (Researcher A')
Periklis Michailidis, Graduate student – *MSc obtained in 2022*
Konstantina Panagopoulou, Undergraduate student
Angelos Charisis, Undergraduate student – *Practical internship completed*
Anastasia Doumani, Undergraduate student – *Practical internship completed*
Lito Kambani, Undergraduate student – *Practical internship completed*
Socratis 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. Pathogenesis and molecular analysis of human genetic diseases

2022 Findings

Organismal and Cellular Stress Responses upon Disruption of Mitochondrial Lonp1 Protease: Cells engage complex surveillance mechanisms to maintain mitochondrial function and protein homeostasis. LonP1 protease is a key component of mitochondrial quality control and has been implicated in human malignancies and other pathological disorders. Here, we employed two experimental systems, the worm Caenorhabditis elegans and human cancer cells, to investigate and compare the effects of LONP-1/LonP1 deficiency at the molecular, cellular, and organismal levels. Deletion of the lonp-1 gene in worms disturbed mitochondrial function, provoked reactive oxygen species accumulation, and impaired normal processes, such as growth, behavior, and lifespan. The viability of lonp-1 mutants was dependent on the activity of the ATFS-1 transcription factor, and loss of LONP-1 evoked retrograde signaling that involved both the mitochondrial and cytoplasmic unfolded protein response (UPRmt and UPRcyt) pathways and ensuing diverse organismal stress responses. Exposure of worms to triterpenoid CDDO-Me, an inhibitor of human LonP1, stimulated only UPRcyt responses. In cancer cells, CDDO-Me induced key components of the integrated stress response (ISR), the UPRmt and UPRcyt pathways, and the redox machinery. However, genetic knockdown of LonP1 revealed a genotype-specific cellular response and induced apoptosis similar to CDDO-Me treatment. Overall, the mitochondrial dysfunction ensued by disruption of LonP1 elicits adaptive cytoprotective mechanisms that can inhibit cancer cell survival but diversely modulate organismal stress response and aging.

Publications

Taouktsi E., E. Kyriakou, S. Smyrniotis, F. Borbolis, L. Bondi, S. Avgeris, E. Trigazis, S. Rigas, G.E. Voutsinas, P. Syntichaki (2022) Organismal and cellular stress responses upon disruption of mitochondrial LONP1 protease, Cells 2022, 11, 1363. (IF: 6.600)

Other Scientific Activities

Reviewer of research articles for Cancers (4 articles), and PeerJ (Peer Journal, 1 article).

Educational Activities

Periklis Michailidis presented his Master Dissertation entitled "Crosstalk of signal transduction pathways after induction of dysfunction in cancer cell mitochondria and endoplasmic reticulum" (October 2021), at the Department of Biology, National and Kapodistrian University of Athens, Greece.

Konstantina Panagopoulou is performing the experimental work for her Dissertation entitled "Signal transduction after induction of dysfunction in cancer cell mitochondria", to be presented at the Department of Biology, National and Kapodistrian University of Athens, Greece. The work is in progress.

Angelos Charisis has started the experimental work for his Dissertation entitled "Mitochondrial and cytoplasmic signal transduction after induction of hypoxia in cancer cells", to be presented at the Department of Biotechnology, Agricultural University of Athens, Greece. The work is in progress.

Practical laboratory internships of Angelos Charisis, Anastasia Doumani and Lito Kambani have been successfully completed.

Lecture entitled "Molecular mechanisms of carcinogenesis and pharmacological inhibition of selected cellular targets for therapy", Common Post-Graduate Program "Applied Biochemistry" of the Dept of Chemistry, University of Patras, and the Institute of BioSciences and Applications, NCSR "Demokritos", April 18, 2022 (number of attendants: 13 students, teaching hours: 2).

Teaching of the undergraduate course: “Introduction to Molecular Biology” (3 semesters), American College of Greece (Deree College), Agia Paraskevi Attikis, January - December 2022 (number of attendants: 50 students, teaching hours: 138).

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 26, 2022, Athens (number of attendants: 80 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 13, 2022, Athens (number of attendants: 20 students, teaching hours: 3).

Two lectures entitled "Signaling pathways involved in cell immortalization - Wnt, Hippo, p53" and "Signaling pathways evading tumor suppressor messages pRB, p53, APC, BRCA1-2, PTEN, WT1-WT2, NF1-NF2", Post-Graduate Program "Neoplastic Disease in Man", Department of Medicine, National and Kapodistrian University of Athens, November 25, 2022, Athens (number of students: 22, teaching hours: 2).

Other Activities at the Institute of Biosciences and Applications and NCSR “Demokritos”

In charge for the operation of 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".

Acting Director of IBA (January 1, 2022, until March 2, 2022).

Deputy Director of IBA (March 7, 2022, until March 6, 2023).

Member of the Research Council of the Institute (ESI) (January 1, 2022 – December 31, 2022).

Member of the Research Committee of NCSR “Demokritos” (January 1, 2022 – May 9, 2022).

Member of the Certification Committee for the Scientific Part of the Flagship Action Projects to Combat the SARS-CoV-2 virus (January 1, 2022 – December 31, 2022).

Member of 6 Evaluation Committees for recruitment of scientific collaborators at IBA [Projects E12476 (04/04/2022 - 03/07/2023), Openscreen (30/05/2022), E12555 (26/07/2022), E12510 (07/09/2022), E10565 (25/10/2022), E12515 (22/12/2022)].

Committee member of the Open Online Competition for Provision of Consumables of the CosmAGE project - E12426 (07/07/2022).

Committee member for the Approval of the Implementation Report of project MIS 5047829 (30/11/2022).

Committee member for Receipt of Consumables through the Open Online Competition ΟΠΣ 5070022 for the project E12426 (14/10/2022).

Committee member for Receipt and Guaranteed Operation of Equipment, Contract 015/2021-138 (26/07/2022).

Committee member for Election of a new Regular Member for the Research Council of the Institute (ESI IBA) (02/03/2022).

Total Impact Factor for original publications in 2022 (for 1 publication): 6.600

Number of citations for 2022 (without self-citations): 87

Number of citations 2018-2022 (without self-citations): 423

h-factor: 21

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
Qi Xue, Graduate Research Collaborator
Joseph Tammas, Trainee
Stamatina-Faidra Spanomaridi, Trainee
Dimitra Stefanou, Technical Specialist

Research Interests

(1) Analysis of small RNA (miRNA, siRNA, piRNA) pathways in Lepidoptera. Development of methods for improvement of RNAi efficiency in lepidopteran insects. Development and improvement of methods for screening of molecules, mainly antimicrobial peptides (AMPs), with antiviral properties.
(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.

2022 Findings

Viral-like particles for efficient dsRNA delivery to insect pests

Fusions of the capsid shell protein of Cypovirus with GFP were used to generate fluorescent VLPs of which the structure was confirmed by electron microscopy. Fluorescent VLPs could be loaded with dsRNA by the dis-assembly/re-assembly strategy and were used to monitor the uptake by lepidopteran cell lines and midgut tissue of the silkworm *ex vivo*. In addition, a second VLP platform, based on *Drosophila* X virus (DXV), was generated. Fluorescent DXV-based VLPs were efficiently loaded by dsRNA and could mediate gene silencing in *Drosophila* S2 cells and induce toxicity in larvae of the spotted wing drosophila, a notorious fruit pest Collaboration with Qi Xue and Clauvis Taning, Gent University).

A screening system for the identification of compounds that interfere with the protein translation mechanism of picornaviruses.

The screening system is based on a double reporter gene assay that consists of firefly luciferase (used for normalization) and renilla luciferase of which the translation is controlled by the internal ribosomal entry site (IRES) of Cricket paralysis virus (*Dicistroviridae*). RNAi and over-expression experiments identified the translation initiation factors eIF4A and Rack1 as proviral factors while the regulator of nonsense transcripts UPF1 had antiviral effects. Experiments will be extended to see whether small molecule drugs can affect CrPV infection in cell lines and silkworm larvae.

Piwi proteins as antiviral and proviral factors

Over-expression and RNAi experiments established that Argonaute proteins of the Piwi subclass (Siwi, Ago3) have an antiviral function during infections with RNA viruses (collaboration with Dulce Santos and Jozef Vanden Broeck, KULeuven, Belgium). Unexpectedly,

however, it was found that Piwi proteins act as proviral factors during baculovirus (DNA virus) infections (collaboration with Min Feng, South China Agricultural University).

Publications

Jiang L., Yu, X.-Q., Swevers, L. (2022). Editorial: Novel Insights Into Insect Antiviral Immunity. Front. Immunol. 12, 740989. (IF = 8.787)

Samantsidis, G.-R., Denecke, S., Swevers, L., Skavdis, G., Geibel, S., Vontas, J. (2022). Identification of Helicoverpa armigera promoters for biotechnological applications. Insect Biochem. Mol. Biol. 142, 103725. (IF = 4.421)

Feng, M., Swevers, L., Sun, J. (2022). Hemocyte Clusters Defined by scRNA-Seq in Bombyx mori: In Silico Analysis of Predicted Marker Genes and Implications for Potential Functional Roles. Front. Immunol. 13:852702. (IF = 8.787)

De Schutter, K., Verbeke, I., Kontogiannatos, D., Dubruel, P., Swevers, L., Van Damme, E.J.M., Smagghe, G. (2022). Use of cell cultures *in vitro* to assess the uptake of long dsRNA in plant cells. In Vitro Cell. Dev. Biol. – Plant 58, 511–520. (IF = 2.273)

Ren, F., Yan, J., Kontogiannatos, D., Wang, X. Li, J., Swevers, L., Sun, J. (2022). Characterization of virus-like particles assembled by co-expression of BmCPV capsid shell protein and large protrusion protein. Int. J. Biol. Macromol. 209, 1656–1664. (IF = 8.025)

Kolliopoulou, A., Kontogiannatos, D., Mazurek, D.J. Prifti, I., Christopoulou, V.-M., Labropoulou, V., Swevers, L. (2022). Analysis of luciferase dsRNA production during baculovirus infection of Hi5 cells: RNA hairpins expressed by very late promoters do not trigger gene silencing. Front. Insect Sci. 2, 959077. (IF = N/A)

Zhang, M., Fei, S., Xia, J., Wang, Y., Wu, H., Li, X,, Guo, Y., Swevers, L., Sun, J. Feng, M. (2022) Sirt5 Inhibits BmNPV Replication by Promoting a Relish-Mediated Antiviral Pathway in *Bombyx mori*. Front. Immunol. 13, 906738. (IF = 8.787)

Santos, D., Verdonckt, T.W., Mingels, L., Van den Brande, S., Geens, B., Van Nieuwerburgh, F., Kolliopoulou, A., Swevers, L., Wynant, N., Vanden Broeck, J. (2022). PIWI Proteins Play an Antiviral Role in Lepidopteran Cell Lines. Viruses 14, 1442. (IF = 5.818)

Samantsidis, G.R., Fotiadou, M., Tzavellas, S., Geibel, S., Nauen, R., Swevers, L., Denecke, S., and Vontas, J. (2022). Functional characterization of putative ecdysone transporters in lepidopteran pests. Insect Biochem. Mol. Biol. 2022 151, 103830. (IF = 4.421)

Articles in Press

Wu, H., Xia, J., Fei, S., Wang, Y., Zhang, M., Guo, Y., Li, X., Swevers, L., Sun, J., Feng, M. (2023). BmCH25H, a vertebrate interferon-stimulated gene (ISG) homolog, inhibits BmNPV infection dependent on its hydroxylase activity in *Bombyx mori*. Insect Sci. 30, 321-337. (IF = 3.605)

Xia, J., Fei, S., Wu, H., Yang, Y., Yu, W., Zhang, M., Guo, Y., Swevers, L., Sun, J., Feng, M. (2022). The piRNA pathway is required for nucleopolyhedrovirus replication in Lepidoptera. Insect Sci. 2022 Dec 10. (IF = 3.605)

Liang, Y., Wang, T., Yang, W., Chen, Z., Li, Q., Swevers, L., and Liu, J. (2023). Silencing of the immune gene BmPGRP-L4 in the midgut affects the growth of silkworm (*Bombyx mori*) larvae. Insect Mol. Biol. 2023 Jan 27. (IF = 3.424)

Santos, D., Feng, M., Kolliopoulou, A., Taning, C.N.T., Sun, J., Swevers, L. (2023). What Are the Functional Roles of Piwi Proteins and piRNAs in Insects? Insects 14, 187. (IF = 3.141)

Ren, F., Yan, J., Wang, X., Xie, Y., Guo, N., Swevers, L., Sun, J. (2023). Peptidoglycan recognition protein S5 of *Bombyx mori* facilitates the proliferation of *Bombyx mori* Cypovirus 1. J. Agric. Food Chem. 71, 6338-6347. (IF = 5.895)

Xue, Q., Swevers, L., Taning, C.N.T. (2023). Plant and insect virus-like particles: Emerging nanoparticles for agricultural pest management. Pest Manag. Sci. 2023 Apr 27. (IF = 4.462)

International conferences

Swevers, L., Kolliopoulou, A., Kontogiannatos, D., Ren, F., Sun, J. (2022). Viral-like particles for dsRNA delivery. XXVI International Congress of Entomology, 17-22 July, Helsinki, Finland

National conferences

Swevers, L., Kolliopoulou, A., Kontogiannatos, D., Mazurek, A.J., Prifti, I., Christopoulou, V.-M., Labropoulou, V. (2021). Analysis of dsRNA production during baculovirus infection. 71st National Conference Hellenic Society of Biochemistry and Molecular Biology, 26-28 November 2021, Athens.

Kontogiannatos, D., Kolliopoulou, A., Swevers, L. (2021). Viruses and viral-like particles for delivery of RNAi in insects. 71st National Conference Hellenic Society of Biochemistry and Molecular Biology, 26-28 November 2021, Athens.

Other scientific activities

Participation in editorial boards of scientific journals

Member of the Editorial Board of the scientific journals: “Archives of Insect Biochemistry and Physiology”, “Journal of Insect Science”, “Frontiers in Insect Science”, “Frontiers in Plant Science” and “Virus Research”. Guest Associate Editor for special issue in the journal “Insects” with title “RNAi in Insects” (L. Swevers)

Participation in committees for the evaluation of research proposals

L Swevers: Expert for the funding agencies “Agence Nationale de la Recherche (ANR)” (France), “Research Foundation Flanders (FWO)” (Belgium) and “National Science Centre” (Poland).

Reviewing of manuscripts in scientific journals

“Agronomy”, “Archives of Insect Biochemistry and Physiology” (3x), “BMC Genomics” (2x), “BMC Genomics” (2x), “Entomologia Generalis” (2x), “Environmental Pollution”, “Frontiers in Forests and Global Change” (2x), “Frontiers in Immunology” (2x), “Frontiers in Microbiology”, “Frontiers in Physiology”, “Frontiers in Plant Sciences” (4x), “Heliyon”, “Insect Biochemistry and Molecular Biology” (7x), “International Journal of Molecular Sciences” (5x), “Insect Science” (4x), “Insects” (5x), “Journal of Pest Science” (2x), “Journal of Cellular Physiology”, “Journal of Insect Physiology” (2x), “Journal of Invertebrate Pathology”, “Pesticide Biochemistry and Physiology” (2x), “PLoS ONE”, “Pest Management Science” (7x), “Scientific Reports” (2x), “Virus Research” (2x) (L. Swevers)

Participation in teaching courses and other educational activities

Inside IBA

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)

- L. Swevers: Molecular Pharmacology – Immunology: lecture with title: “Nucleic Acid-based Drugs” (4 hours, 13 students)
- V. Labropoulou: Molecular and Cellular Biology – Molecular Biotechnology: lecture with title “The Baculovirus Expression System” (2 hours, 13 students)

Outside IBA

L. Swevers:

- Lecture of 30 min with title: “PIWI-associated RNAs and the regulation of stem cell function and transposon silencing” at the Summer School of NCSR “Demokritos”.

  Member of the 7-member evaluation committee of PhD thesis of George-Rafael Samantsidis with title “Innovative methods for insect pests control and insecticide resistance management”, Department of Biology, University of Crete & Institute of Molecular Biology and Biotechnology, Foundation of Research and Technology - Hellas.

Other Activities in IBA and in NCSR “Demokritos”
Member of the Scientific Board of the Institute (L. Swevers)

Total Impact Factor for original publications in 2022
L. Swevers: 51.319 (for 9 publications)

Citations for 2022 (without self-citations)
L. Swevers: 357
V. Labropoulou: 60

Total citations 2018-2022 (without self-citations)
L. Swevers: 1637
V. Labropoulou: 219

h-factor
L Swevers: 36 (Scopus), 43 (Google Scholar)
V. Labropoulou: 14 (Scopus), 17 (Google Scholar)

Current External Funding
Project entitled: Characterization of extracellular RNA-signals and their role in antiviral immunity in insects funded by FWO – Vlaanderen G093119N (Belgium)
Programme duration: 1/2019-12/2022
Total programme funding (for the entire duration of the programme): 700.800 €
Research groups participating in the programme: K.U.Leuven (Belgium), Gent University (Belgium), IBA
Scientific Supervisor: J. Vanden Broeck, supervisor for team in Greece: L. Swevers
Funding for 2022: 175.200 €
Funding of the lab for 2022: 0 €

Project entitled: Viral-like Particles for Increased Delivery of RNAi in Insects (VLP-RNAi, 785) funded by Hellenic Foundation for Research & Innovation (“1st Announcement of research projects H.F.R.I. for the support of faculty members and researchers and the supply of research equipment of great value")
Programme duration: 02/2020-02/2023
Total programme funding (for the entire duration of the programme): 152.000 €
Research groups participating in the programme: South China Agricultural University, IBA
Scientific Supervisor: L. Swevers
Funding for 2022: 45.778 €
Funding of the lab for 2022: 45.778 €

Research Group: Chemical Ecology and Natural Products

Research Staff
Maria Konstantopoulou, Research Director
Dimitris Raptopoulos, Graduate Research Associate
Neoklis Manikas, PhD candidate
Petri-Christina Betsi, Graduate Research Associate
Nefeli-Sofia Sotiropoulou, Graduate Research Associate
George Manassakis, MSc student Erasmus

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 semiochemicals acting as attractants/repellants for insects and technologies for their application in pest control. Advanced semiochemical slow-release systems based on biodegradable (membranes, nanomaterials) and environmentally-friendly materials.

Development of biocides of biological origin (Biological Control Agents. BCAs) and methods/technologies of application, aiming to incorporating 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.

2022 Findings
Within the framework of the OLEFINE (OLEaginous yeast platforms for FINE chemicals) and PHERA (Pheromones for Row crop Applications) HORIZON 2020 programs, the following tasks were completed: i) production of insect sex pheromones by biotechnological methods using yeast platforms and ii) validation of the homology of produced biopheromones to those produced by chemical synthesis. A study of the electro-physiological response (using EAG electro-antenography and GC-EAD gas chromatograph-coupled electro-antenography) of male insect antennae to substances produced by fermentation was carried out. In addition, behavioral bioassays were performed on male insects in a wind tunnel using a camera recording system. In order to test the activity of biopheromones, field experiments were carried out in two regions of Greece, which verified their homology in relation to chemically produced ones.In particular, i) population monitoring experiments were carried out, ii) mating disruption experiments were conducted on *Helicoverpa armigera* using a flowable biopolymer formulation of the sex pheromone in caulking gun cartridges and applied by means of a UAV (Figure 1) and iii) using new hydrodegradable dispenser on *Plutella xylostella*. Research on developing systems for the release of semiochemicals by encapsulating them in non-toxic,

biodegradable and environmentally friendly matrices endowed with enhances protection characteristics of the semiochemicals from UV irradiation, oxidation etc.

Identification of infochemicals and other bioactive metabolites of natural origin (Biological Control Agents, BCAs) for their use as "smart" insecticides (“bio-rational” insecticides). Effect of secondary metabolites of *Pistacia lentiscus* and *Mucor hiemalis* (strain SMU-21) on the viability of insect larvae of crop pests of great economic importance like *Lobesia botrana* and *Plutella xylostella*.

Participation in the NutriMED project which aims at the development and production of innovative phytotherapeutic products-nutritional supplements with anxiolytic and anti-depressant action of Greek medicinal plants in collaboration with Dr. Z. Georgousi.

Participation as a member of the three-member scientific committee in the Opti new -AromaQ project funded by the Cyprus Research and Innovation Foundation as part of the Excellence Hubs (Bridge Programs) action. The main objectives of the project are to identify properties of medicinal/aromatic plants and improve the quality, nutritional value and storage capacity of fresh and dry products aiming to support the competitiveness of SMEs.

The study of the psychophysiological approach to olfactory stimuli of therapeutic gardens in collaboration with the School of Medicine and the Agricultural University of Athens was continued.

The study of the semiochemicals involved in the chemical communication of Lepidopteran insects carried out in the framework of the MSc internship between the laboratory and the Plant Sciences Group/Biosystematics Group of Wageningen University with an ERASMUS grant has been completed and presented at Wageningen University.

In addition, colonies of five economically important crop pests are maintained in the laboratory to be used in electrophysiology and behavioral experiments.

Figure 1

Publications

Dasenaki, I.; Betsi, P.-C.; Raptopoulos, D.; Konstantopoulou, M.. Insecticidal Effect of *Pistacia lentiscus* (Anacardiaceae) Metabolites against *Lobesia botrana* (Lepidoptera: Tortricidae). Agronomy 12, 755 (IF: 3.7).

Jani A, Exner A, Braun R, Braun B, Torri L, Verhoeven S, Murante AM, Van Devijvere S, Harrington J, Ochoa A, Marchiori GDL, Defranceschi P, Bunker A, Barnighausen T, Sanz Sanz E,

Napoleone C, Verger EO, Schader C, Roklov J, Stegeman I, Tonello S, Pederson R, Kristensen NH, Smits T, Wascher D, Voshol P, Kaptejins A, Nesrallah S, Kjorven O, DeClerck F, Biella C, Gjorgjioska MA, Tomicic A, Ferreira Oliveira AT, Bracco S, Estevens S, Rossi L, Laister G, Ro˙zalska A, Jankuloski B, Hurbin C, Jannic M, Steel F, Manbaliu E, De Jager K, Sfetsos A, Konstantopoulou M, Kapetanakis P-A, Hickersberger M, Chi□ard E and Woolhead C (2022) Transitions to food democracy through multilevel governance. Frontiers in Sustainable Food Systems, 6, 1039127. (IF=5.005).

Chrysargyris, A.; Skaltsa, H.; Konstantopoulou, M. Medicinal and Aromatic Plants (MAPs): The Connection between Cultivation Practices and Biological Properties. Agronomy 2022, 12, 3108. (IF=3.7).

National conferences

Koutsoumpeli, E., Betsi P.Ch., Raptopoulos, D., and Konstantopoulou M.A. Biologically produced pheromones for *Helicoverpa armigera* and *Ostrinia nubilalis*. 19ο Panhellenic Entomological Congress, Agrinio, 23-27 May 2022, Abtract: 158-159.

Dasenaki I., Betsi P.Ch, Koutsoumpeli E., και Konstantopoulou M.A.: Insecticidal effect of *Pistacia lentiscus* (Sapindales: Anacardiaceae) and *Mucor hiemalis* strain (SMU-21) metabolites on the *Lobesia botrana* (Lepidoptera: Tortricidae) larvae*,* 19ο Panhellenic Entomological Congress, Agrinio, 23-27 May 2022, Abtract: 111-112.

Other Scientific Activities

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

President of the Union of Greek Researcher

Member og the Scientific Committee of XII European Congress of Entomology, 16-20/10/2023, Crete Greece

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, Agronomy, Journal of Environmental Management

Topic Editor του Open Access Journal Insects

Review Editor for Chemical Ecology in Frontiers in Ecology and Evolution

Special Issue Editor of Special Issue of Agronomy: "Medicinal and Aromatic Plants (MAPs): The Connection between Cultivation Practices and Biological Properties"

Special Issue Editor of Special Issue of Agronomy: “Biocontrol Effects of Natural Metabolites on Insect Pests”

Scientific distinctions and awards

The presentation: Dasenaki I., Betsi P.Ch, Koutsoumpeli E., και Konstantopoulou M.A.: Insecticidal effect of *Pistacia lentiscus* (Sapindales: Anacardiaceae) and *Mucor hiemalis* strain (SMU-21) metabolites on the *Lobesia botrana* (Lepidoptera: Tortricidae) larvae*,* at the 19ο Panhellenic Entomological Congress was awarded the 1st prize of the Scientific Committie of the Congress.

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

Invited Speaker in Erasmios Hellenic-German School in the context of Professional Orientation: "Leadership and Overcoming Crisis", 28/2/2023.

Invited Speaker in Seminar gaining of skills for the effective implementation of Action Plans for Gender Equality (GEPA) in Research Institutions» organized from Hellenic Foundation for European & Foreign Policy (ELIAMEP), 2/12/2022.

Presentation entitled "Gender Equality Action Plan 2022-2024, NCSR "D", at the NCSR "D" Committee in the Gender Equality Committee event 21/11/2022.

Other activities in IBA
Member of the Scientific Advisory Board (ESI) of the Institute.

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

Researcher and Specialist Functional Scientist representative in NCSR "Demokritos" Board of Directors.

Member of the Gender Equality Committee of NCSR "D".

Total Impact Factor for original publications in 2022: 12,405 (for 3 publications)

Citations for 2022 (without self-citations): 102

Total citations 2018-2022 (without self-citations): 512

h-factor: 16 (Scopus), 20 (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 30/06/2022
Total program funding: 441.311 €
Laboratory Funding for2022: 105.153,64 €

Project entitled *Bio Based Industries Joint Undertaking, PHERA "Pheromones for Row crop Applications*" (Horizon 2020, Subcontractor) funded by EU, and Scientific responsible Dr. M. Konstantopoulou.
Duration: 1/1/2020 – 31/12/2023
Total program funding: 45.000 €
Laboratory Funding for 2022: 20.000 €

Project entitled *Food systems that support transitions to hEalthy And Sustainable dieTs* (Horizon Europe) funded by EU, and Scientific responsible Dr. M. Konstantopoulou.
Duration: 01/07/2022-30/06/2027
Total program funding: 74.312,50 €
Laboratory Funding for2022: 26.009,38 €

Project entitled *Opti new -AromaQ Identification of Medicinal/Aromatic Plants properties and improving quality, nutritive value and storability of fresh and dry products to support SME competitiveness* funded from The Research and Innovation Foundation Programmes for Research, Technological Development and Innovation, CYPRUS and Scientific responsible Dr. M. Konstantopoulou.
Duration: 01/04/2022-31/03/2024
Total program funding: 8.000 €
Laboratory Funding for 2022: 0 €

Project entitled *Nutritional supplements with anti-anxiety and anti-depressant properties from Greek pharmaceutical plants* funded from Region of Attica, «Synergeies Research and Innovation in Region of Attica» (ESPA 2014-2020) and Scientific responsible Dr Z. Georgoussi.
Duration: 04/08/2022-31/12/2023
Total program funding: 155.000 €
Laboratory Funding for 2022: included in the budget of the SR.

Research Group: Chronobiology

Research Staff

Anastasia Prombona, Senior Researcher
Angeliki Galeou, Postdoctoral Fellow (IKY scholarship)
Danae Farmaki, PhD student
Myrto Filippaki, Trainee Student
Stavroula Mamoucha, Graduate Research Collaborator

Research Interests

The research projects of our laboratory explore the gene expression regulation and the function of the circadian oscillator components in *Phaseolus vulgaris* and in mammalian cell culture systems under physiological and pathological conditions.

The function of the plant circadian clock

Our studies on the plant circadian clock focus on gene expression analysis and regulation of *P. vulgaris* clock and clock-controlled genes under physiological conditions and during infection of the plant with pathogenic bacteria (*Pseudomonas syringae* pathovar *phaseolicola*). We also explore the phytoprotection from infection by the use of bioactive compounds.

Interaction of the mammalian circadian clock with pathological conditions

We are interested in elucidating the molecular mechanisms involved in the interaction of the circadian clock and the cell cycle in cancer. The role of the transcription factor/oncoprotein c-MYC in the regulation of circadian clock genes and the effect of pharmacological treatment of cancer cell lines on cell cycle progression, apoptosis and metastasis are investigated.

2022 Findings

The function of the plant circadian clock

In order to explore the transcriptional changes that occur in the first line defense of the plant species *Phaseolus vulgaris* during *Pseudomonas syringae* infection, the cultivar red kidney and the pathovar *phaseolicola* were utilized. Work with other species has shown that the initial defense relies on the production of reactive oxygen species (ROS) and involves two types of enzymes: the oxidases that are transmembrane proteins and the peroxidases that are localized in the apoplastic space. We have studied the time-dependent gene expression of all nine *P. vulgaris* oxidases (respiratory burst oxidase homologs, PvRBOHA-PvRBOHI) and of the peroxidase FBP1 (French bean peroxidase 1), which is well studied for its activity during bacterial infection. Our results have shown that the circadian clock is involved in the pre- and the post-invasive defense of the *P. vulgaris* plant species. The three oxidases *PvRBOHB, PvRBOHC and PvRBOHD* are induced to higher levels following infection. The two genes *PvRBOHC* and *PvRBOHD* are pre-invasively rhythmically expressed, but following infection they abolish the oscillations in steady-state mRNA levels. *PvRBOHB*, on the other hand, has under physiological conditions very low expression levels that post infection are acutely highly induced (>100X) with no detectable rhythmicity. Our results indicate that specific oxidases have pre-invasively a role that is clock-dependent, but the active defense following infection evolves clock-independently. In contrast to the oxidases, the *FBP1* peroxidase gene is clock-regulated pre- and post-invasively. In this case, the active defense induces higher expression levels that remain rhythmic at the same phase. Thus, the circadian clock is involved in the preventive and the active defense of *P. vulgaris* against *P. syringae*. These experiments were performed by Dr. A. Galeou (postdoctoral IKY scholarship) and the Diploma student C. Stefanatou.

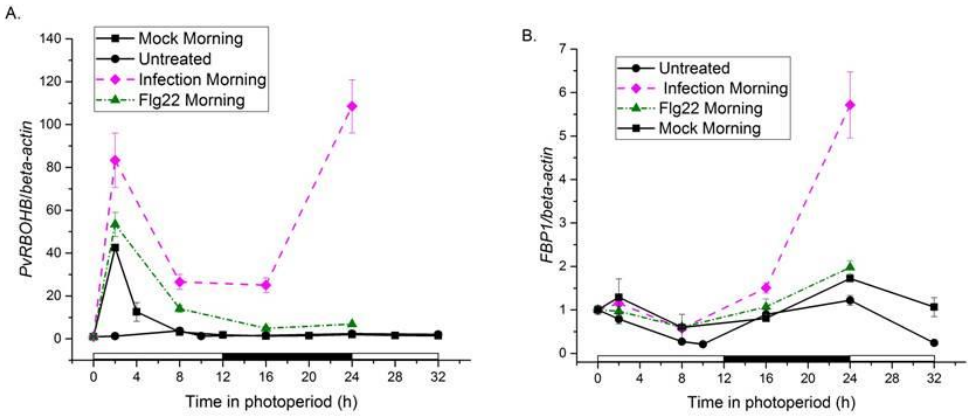


Figure 1: *Response of Phaseolus vulgaris to infection with Pseudomonas syringae pathovar phaseolicola (Psp) is partly dependent on the circadian clock. Primary leaves from plants grown in photoperiod with 12 hours light and 12 hours darkness (white and black bars below the graphs) were infiltrated in the morning with bacteria (Infection Morning) or the elicitor flg22 (Flg22 Morning) or water (Mock Morning) and samples also from untreated leaves were collected every four hours for a total duration of 32 hours. A. The oxidase PvRBOHBgene responds acutely to all treatments, but Psp infection causes the highest increase in expression levels with no rhythmicity. B. The peroxidase FBP1 gene displays rhythmic expression that following Psp infection is significantly enhanced and retains the same phase with peak in the morning.*

Interaction of the circadian clock with pathological conditions

In this project the idea is to target the dysfunctional circadian clock of cancer cells with the aim to achieve the recession of the malignant condition. To achieve this, we have utilized a modulator of the cryptochrome function in a pharmacologically compatible concentration (EC_{50}) and have studied its anticancer properties in three cancer cell lines. Our results indicate that, depending on the genetic background, cell cycle inhibition, autophagy and apoptosis are induced. The role of circadian clock components in these processes is under investigation. These experiments constitute part of the PhD thesis work of D. Farmaki.

Articles in Press

Galeou, A., Stefanatou, C., Prombona, A. (2023) Circadian clock-dependent and -independent response of *Phaseolus vulgaris* to *Pseudomonas syringae*. Physiological and Molecular Plant Pathology 124,101944 (IF: 2.741)

Xydous, M., Chrysanthou-Piterou, M., Panagiotopoulou, C., (...), Prombona, A., Sourlingas, T.G. (2023) Alterations in the levels of an H1 DNA linker histone subtype in peripheral blood leukocytes from schizophrenia patients are linked with this disorder. Journal of Biological Research (Greece)
30,1 (IF: 2.576).

National conferences

S. Mamoucha, V. Liapis, A. Prombona (2022) Medicinal plant species: histological localization of bioactive compounds and medicines of plant origin. 48th Annual Panhellenic Medical Conference, Athens Medical Society, Divani Caravel Hotel – Athens 12 – 14 May, oral presentation no. 23, General Medicine

A. Galeou, S. Mamoucha, A. Prombona (2022) Combating Pseudomonas by the use of *Laurus nobilis* essential oil. 20th Panhellenic Phytopathological Conference, 3 - 6 October, Porto Palace Hotel, Thessaloniki, poster no. 117-Bioacrive compounds

S. Mamoucha, V. Liapis, A. Prombona (2022) Propolis: a biotechnological approach screening for antibacterial activity, 72nd HSBMB Congress, 2 – 4 December, Conference and Cultural Centre, University of Patras, Patras, Greece, short talk ST42

D. Farmakis, D. J. Stravopodis, A. Prombona (2022) Pharmacological modulation of the Circadian Clock affects oncogenic characteristics of pancreatic cancer cell lines, 72nd HSBMB Congress, 2 – 4 December, Conference and Cultural Centre, University of Patras, Patras, Greece, poster P9

Educational activities
Outside IBA
Talk in the 57th Summer School of NCSR "Demokritos" with the title: Biological Circadian Clock and Cancer

Other activities in IB-A
Responsible person for educational demonstrations to vising school classes.

Citations for the year 2022 (without self citations): 22

Citations for the years 2018-2022 (without self citations): 145

h-index: 9

Current External Funding
Project entitled: "The circadian clock in the defence and the phytoprotection of the plant *Phaseolus vulgaris* during the infection with *Pseudomonas syringae*" funded by IKY "Reinforcement of Postdoctoral Researchers - 2nd Cycle" (MIS-5033021), Operational Program "Human Resources Development, Education and Lifelong Learning" of National Scholarship Foundation (IKY) (Scholarship contract number: 2019-050-0503-18278)
Programme duration: 16.2.2020-15.2.2022
Total programme funding (for the entire duration of the programme): 26.400,0 €
Research groups participating in the programme: Chronobiology
Scientific Supervisor: Anastasia Prombona
Funding for 2022: 1.650 €
Funding of the lab for 2022: 1.650 €

Research Group: Microbial Molecular Genetics

Research Staff
Vicky Sophianopoulou, Research Director
Christos Gournas, Researcher
Ada Biratsi, Postgraduate Fellow – *PhD obtained in 2022*
Amalia Megarioti, Postgraduate Fellow (PhD candidate)
Spiros Gerostathis, Postgraduate (MA candidate)
Vassilis Perpiniadis, Undergratuate Student
Dimitris Koulouris Undergratuate Student
Retzep Routsi (Practical undergraduate)
Irini Kanaki (Practical undergraduate)

Research interests
Our group's fundamental research focuses on:

1. 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 physiological processes. A major effort is to understand how the PM coordinates these diverse processes and the mechanisms underlay them. Our studies aimed at identifying and/or characterize the molecular mechanisms by which eisosomes, specific compartments of the fungal plasma membrane, regulate the homeostasis of the plasma membrane, the persistence of fungal cells, and how these processes are related to long-term survival and fungal pathogenicity. (I. Vangelatos et al., 2010; C. Scazzocchio et al., 2011; A. Athanasopoulos et al., 2013, A. Athanasopoulos et al., 2015; Gournas et al, 2018; Athanasopoulos et al., 2019). In this context, we recently added the *in vivo* evaluation of specific dendritic nanoparticles as drug delivery systems and /or antifungal agents.

Medium and long-term objectives: identification of new pharmaceutical targets and future development of highly-targeted antifungals.

2. Elucidate the molecular mechanisms underlie detoxification of toxic amino acid analogues from different microorganisms, including pathogenic fungi, using the opportunistic pathogenic fungus *Aspergillus nidulans* as model system. L-Azetidine-2-Carboxylic Acid (AZC) is a proline toxic analogue produced by certain plants to protect them since is toxic for a multitude of organisms, including various bacteria, fungi and mammals.

Medium and long-term objectives: design novel antifungals to protect crops of nutritional and economic significance.

3. Regulation and structure/function analysis of amino acid transporters. Transporters are essential in nutrient and drug uptake, and involved in nutrition, signaling, neurotransmission & cell communication. Transporter malfunction is linked with >50 human genetic diseases and in phenomena of drug or antibiotic resistance. Understanding transporter function, specificity determination, trafficking to the plasma membrane is essential to understand transporter physiology

Medium and long-term objectives: identification of new targets for novel therapies and antimicrobials.

2022 Findings
1. Eisosomes in quiescent yeast cells were shown to be induced as it was shown for *A. nidulans* quiescent conidiospores (Vangelatos et al., 2010, DOI: 10.1128/EC.00087-10), promoting their long-term viability. The protective role of eisosomes is related to the stabilization of eisosome-

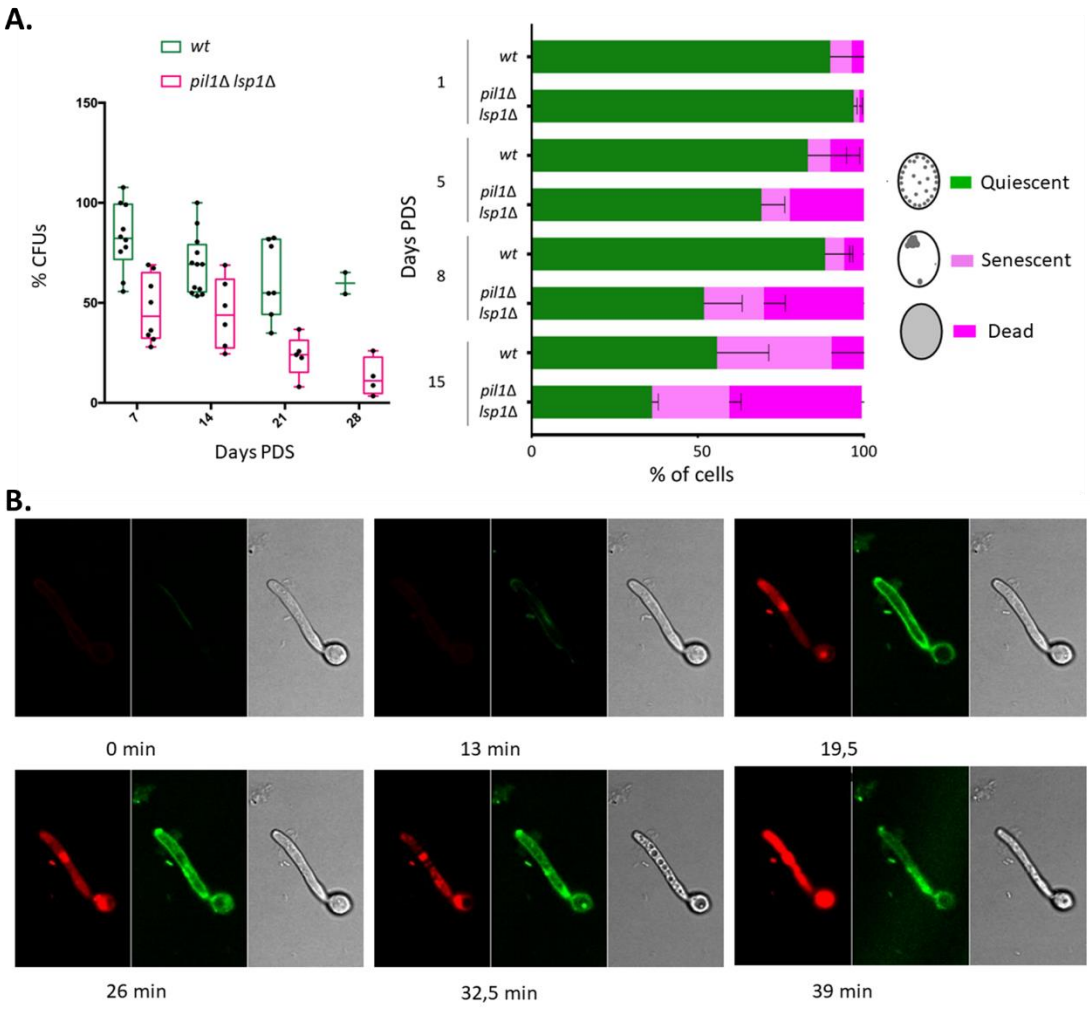


Figure: *A. Eisosomes are required for the long-term survival and the maintenance of quiescence. B. Representative confocal microscopy images of A. nidulans germlings showing the time-course distribution of GPEI-FITC (10μg/mL) compared to that of PI (red).*

hosted enzymes (FLPs: Flavodoxin-like proteins) with ubiquinone oxidoreductase activity. Ubiquinol, a reduced form of ubiquinone, as a strong lipophilic antioxidant reduces peroxidized lipids. In collaboration with Dr. Fröhlich, targeted lipidomic analysis showed that in the absence of either eisosomes or FLPs, quiescent yeast cells accumulate peroxidized phospholipids. Genetic data support that FLPs are essential for the protection of quiescent yeast cells from lipid peroxidation, acting in parallel with glutathione peroxidases (GPXs). A mutant yeast strain deleted in both FLPs and GPX-coding genes undergoes cell death upon addition of polyunsaturated fatty acids (PUFAs), which is rescued by the lipophilic antioxidant α-tocopherol or by iron chelators, thus displaying the typical features of ferroptosis, a non-apoptotic cell death. Recent data in mammals (Doll et al., 2019, DOI: 10.1038/s41586-019-1707-0) indicate that the quinone reductase FSP1 prevents lipid peroxidation and ferroptosis. With *in silico* approaches, homologues of human FSP1 were identified in *A. nidulans*, the proteins FspA & B. (Megarioti et al., 2023; Ferroptosis-Protective Membrane Domains in Quiescence under revision).

2. In *A. nidulans*, the antifungal properties and subcellular localization of hyperbranched polymeric nanoparticles of polyethyleneimine (PEI) and two of their derivatives (QPEI, GPEI),

resulting from the substitution of the terminal amino groups of the polymer with different functional groups, were studied (in collaboration with Drs. Sideratou & Dr. Tsiourvas). Our results indicate that the nanoparticles localize firstly to the membrane and then to the interior of both quiescent conidiospores and developing germlings. Growth assays showed that nanoparticle concentrations with low toxicity in the order of μM and close to the determined minimum inhibitory concentration (MIC), with the lowest MIC attributed to PEI, are able to inhibit germination of both quiescent spores and germlings. Confocal microscopy experiments at these concentrations indicate that the nanoparticles cause growth inhibition and cell death of fungal cells by increasing the permeability of the plasma membrane (S. Gerostathis, Master's thesis).

3. The α-arrestin Art2 was identified as essential for the endocytosis of Can1 in yeast cells during stationary phase. In addition, regions at the amino-terminal end of the transporter involved in endocytosis were identified (V. Perpiniadis, Diploma thesis).

International conferences

S. Gaitanos, A. Biratsi, A. Athanasopoulos, C. Gournas and V. Sophianopoulou. Endocytosis of the tetraspan eisosome-resident proteins: a developmentally regulated membrane-remodeling mechanism. Abstract of the 31st Fungal Genetics Conference, 15-20 March 2022. Asilomar, Pacific Grove, CA, USA

S. Gaitanos, A. Athanasopoulos, C. Gournas and V. Sophianopoulou. Endocytosis of the tetraspan eisosome-resident proteins: a developmentally regulated membrane-remodeling mechanism. EMBO Workshop on Membrane transporters as essential elements of cellular function and homeostasis. 23-27 August 2022 Chania Crete.

A. Megarioti, T. Zakopoulou, A. Athanasopoulos, B. André, V. Sophianopoulou, C. Gournas (2022) Lipid peroxidation-protective plasma membrane domains in quiescence. Yesterday, May 13, 2022, Brussels Belgium.
A. Megarioti, A. Athanasopoulos, B. André, V. Sophianopoulou, C. Gournas (2022). Lipid peroxidation-protective plasma membrane domains in quiescence. EMBO workshop “Membrane transporters as essential elements of cellular function and homeostasis”. August 23-27, 2022, Chania, Greece.

National conferences

A. Megarioti, A. Athanasopoulos, B. André, F. Fröhlich, V. Sophianopoulou, C. Gournas (2022). Lipid peroxidation-protective plasma membrane domains in quiescence. 72nd Conference of the Hellenic Society for Biochemistry & Molecular Biology, December 2-4, 2022, Patras, Greece.

Gerostathis S., Athanasopoulos A., Gournas C., Panagiotaki K., Tsiourvas D., Sideratou Z. and Sophianopoulou V., 2022. Antifungal effect and cellular localization of hyperbranched polymer nanoparticles in *Aspergillus nidulans.* Poster in the 72nd Conference of the Hellenic Society for Biochemistry & Molecular Biology, December 2-4, 2022, Patras, Greece.

Other Scientific activities

Participation in Greek and international scientific bodies and organizations (in addition to participation as a member in scientific societies and organizations)

Head of the Microbial Molecular Genetics lab of IB-A (2004-today) (V. Sophianopoulou)

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

Members of the Advisory Committee of the Biology Department, University of Athens, for the PhD thesis of A. Megarioti (V. Sophianopoulou, C. Gournas (supervisor))

Members of the Advisory Committee of the Biology Department, University of Athens, for the PhD thesis of P. Georgiou (C. Gournas)

Members of the Advisory Committee of the Biology Department, University of Athens, for the PhD thesis of G. M. Sagia (C. Gournas)

Member of the Advisory Committee & supervisor for the Master thesis of S. Gerostathis, Chemistry Department, University of Patras (V. Sophianopoulou)

Member of the Advisory Committee of the Biology Department, University of Athens for the Diploma thesis of D. Koulouris (C. Gournas)

Member of the Advisory Committee of the Biology Department, University of Athens for the Diploma thesis of V. Perpiniadis (C. Gournas)

Supervisor of the Practical training of the undergraduate student Irini Kanaki from the Agricultural University of Athens (18/07/22-16/09/22) (V. Sophianopoulou)

Supervisor of the Practical training of the undergraduate student Retzep Routsi from the Agricultural University of Athens (18/07/22-16/09/22) (V. Sophianopoulou)

Member of the examining committee for the assessment of the doctoral thesis of Aggeliki-Maria Dionisopoulou, Department of Biology, University of Athens (C. Gournas)

Member of the examining committee for the assessment of the doctoral thesis of Claudia Manuela Pinto Barata Antunes, University of Minho, Portugal (C. Gournas)

Member of the Co-ordination Committee of the Post-graduate Education Course (MSc) on "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" at the Department of Chemistry, University of Patras (2018-2022) (V. Sophianopoulou)

Member of the Special Interdepartmental Committee of the Post-graduate Education Course (MSc) on "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" at the Department of Chemistry, University of Patras and Institute of Biosciences and Applications NCSR "D" (2018-2022) (V. Sophianopoulou)

Member of the Complaints and Objections Management Committee of the of the Post-graduate Education Course (MSc) on "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" at the Department of Chemistry, University of Patras and Institute of Biosciences and Applications NCSR "D" (2022) (V. Sophianopoulou)

Regular member of the Electoral Body for the tenure of Assistant Professor, University of West Attica, School of Health and Welfare Sciences (V. Sophianopoulou)

Regular member of the Electoral Body for the tenure of Full Professor, School of Veterinary Medicine, Aristotle University of Thessaloniki (V. Sophianopoulou)

Deputy member of the Evaluation Committee for the tenure of Assistant Professor, of the School of Health Sciences, Department of Biochemistry & Biotechnology University of Thessaly (V. Sophianopoulou)

Presentation of the Microbial Molecular Genetics Lab achievements (2018-2021) in the context of the Evaluation of Institutes and Laboratories of the GSRI (V. Sophianopoulou).

Invitation as a member of the Editorial Board of Scientific Reports to participate with 2 other members as Quest Editor in the Collection on Fungal Evolution and Diversity (V. Sophianopoulou).

Reviewing of manuscripts in scientific journals

Biomolecules (MDPI), Journal of Fungi (MDPI), International Journal of Molecular Sciences X 2 (MDPI) (V. Sophianopoulou)

The EMBO Journal (EMBO press); Molecular Microbiology (Wiley); Traffic (Wiley); Journal of Cell Science, (The Company of Biologists); Frontiers in Microbiology (Frontiers); Frontiers in Cell and Developmental Biology (Frontiers); Food microbiology (Elsevier); Scientific Reports (Nature portfolio) (C. Gournas)

Participation in editorial boards of scientific journals

Member of the Editorial Board of Scientific Reports (Published by Springer Nature) (2016-today) (V. Sophianopoulou)

Member of the Editorial Board of Methods & Protocols (MDPI Publishers) (2021-today) (V. Sophianopoulou)

Handling the evaluation of 1 manuscript of Scientific Reports as Editorial Board Member (V. Sophianopoulou)

Other lectures or presentations of scientific content (except from presentations at scientific conferences)

A. Biratsi. A highly conserved mechanism for the detoxification and assimilation of the toxic phytoproduct L-azetidine-2-carboxylic acid in Aspergillus nidulans. MSc Seminar Program "Mycopat", Dept. of Forest Mycology and Plant Pathology, Uppsala Biocentrum, Sweden (28/04/2022) (Invited speaker)

Scientific awards and distinctions

1st prize for oral presentation at the 72nd Conference of the Hellenic Society for Biochemistry & Molecular Biology (A. Megarioti)

2022 Akoyounoglou Award from IBA (A. Megarioti)

Educational activities

Post-graduate Education Courses on:

Inside IBA

"Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" at the Department of Chemistry, University of Patras (10 students, V. Sophianopoulou 3 hours, C. Gournas 2 hours).

Outside IBA

"Molecular Biology: Systemic and in silico Approaches", a Graduate Mandatory Course of the Interdisciplinary (Faculty of Biology & Medical School, University of Athens). Two - Years Graduate Program "Applications of Biology in Medicine" (20 students, 4 hours V. Sophianopoulou).

Other scientific activities

In the context of a career orientation course of Danae Portokalaki, a 1st year Biology student at the University of Claude Bernard Lyon 1 in France, we interviewed her as scientists working in scientific field in which the student plans to work in the future (V. Sophianopoulou, C. Gournas).

Other activities in IBA and in NCSR "D"

Lecture at the 57th Summer School of NCSR "D" entitled "Study plasma membrane compartmentalization to develop a new generation of antifungal drugs targeting non-growing pathogenic fungi" (V. Sophianopoulou, C. Gournas).

Citations for 2022 (without self-citations)
V. Sophianopoulou: 67
C. Gournas: 87

Total citations 2018-2022 (without self-citations)
V. Sophianopoulou: 413
C. Gournas: 547

h-factor
V. Sophianopoulou: 19 (Scopus), 20 (ResearchGate)
C. Gournas: 15 (Scopus), 15 (Google Scholar)

Current external funding

Grant entitled "The organization of the fungal plasma membrane in the quiescent state"
Duration: 06/22-08/23
IKY PhD scholarship to A. Megarioti
Total funding: 15000 €

Grant entitled "Determination of peroxidised lipid species in Quiescent cells of *Saccharomyces cerevisiae*"
Duration: 06/2022-08/2022
EMBO short fellowship to A. Megarioti to visit the lab of Prof. Fröhlich, at Osnabrück University, Germany
Total funding: 10000 €

Research Group: Biophysics and Membrane Biotechnology

Research Staff

Kostas Stamatakis, Research Director

Dimitris Vayenos, Graduate student (PhD candidate)

Panagiotis Broussos P, Graduate student (PhD candidate)

Ekaterini Giakoumidaki-Vogiatzi, Graduate student (MSc)

Research Interests

Photosynthetic cyanobacteria are preferable candidates for the sequestration of large quantities CO_2 from the atmosphere because they can grow in extreme or/and specified environmental conditions (temperature, pressure, salinity, pH, chemical composition) and are capable of binding CO_2 to produce high energy chemical compounds using sunlight. The rapidly growing cyanobacteria constitutes a very promising and CO_2 emission-free source for biofuels production which can substitute for other carbon-dependent natural sources of energy. The production and accumulation of sucrose in cyanobacteria is connected to their adaptation to extreme environmental conditions. Our research addresses the following themes:

(a) We investigate the production of hydrogen (H_2) production by cyanobacteria through the process of anaerobic "dark fermentation" of the sucrose they accumulated under salinity stress.

(b) 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 ($\mathbf{F_{Chla}}$), or fluorescence induction, in cyanobacteria, giving emphasis to the distribution of the electronic excitation to the reaction centers of photosystem I (PSI) and photosystem II (PSII), as an indicator of protective mechanism against the destructive effects of the reactive oxygen species (ROS) that are produced during photosynthesis.

(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_0, the initial value of F_{Chla} kinetic trace (OJIP), upon a transition from darkness to continuous light of cyanobacteria. Since cyanobacteria are gram negative, we can use them as a guide for antibacterial assay.

2022 Findings

In compliance with circular economy and sustainability principles, novel wastewater treatment processes based on microalgae and/or cyanobacteria cultivation should be developed and applied. The lack of fundamental design and operational parameters hinders upscaling and implementation of such phototrophic wastewater treatment processes. In this regard, the present study sheds light on the dimensioning of a *Synechococcus elongatus* PCC 7492 (*S*7942) cultivation photobioreactor for nitrogen removal from different salinity wastewaters and for biomass-derived added value products. To attain photobioreactor dimensioning, *S*7942' s *cell productivity*, nitrates removal rate and *specific nitrates utilization* rates were calculated based

on experimental data under non-favorable growth conditions of limited lighting (5 to 30 μmol m^{-2} s^{-1}). Chlorophyll *a* and phycocyanin concentrations, as well as biomass nitrogen content were measured to assess nitrogen assimilation in relation to salinity. Under conditions of limited lighting, *S*7942' s *cell productivity* ranged from 43.7 to 20.0 mgVSS L^{-1} d^{-1}. Increasing salinity up to the obtained threshold value of 450 mmolNaCl L^{-1}, *specific nitrogen utilization* rate ranged from 0.140 to 0.286 mgNO3_N $mgVSS^{-1}$. The resulting photobioreactor volume is 10 to 20 times larger compared to an activated sludge denitrification reactor, thus does not hinder the application of the proposed process. Given an optimal *cell productivity* obtained by applying light intensity of 150 μmol m 2 s 1, photobioreactor volume can be at the same order of magnitude (1.5 to 4 times larger). In contrast to activated sludge denitrification reactors, the volume of *S*7942 photobioreactor remains relatively constant regardless of the wastewater salinity. The study promotes the implementation of phototrophic wastewater treatment processes contributing to GHGs emission mitigation, resources recovery, as well as added value products and green energy obtainment.

We present here our adventures in research in photosynthesis with George C. Papageorgiou (1933–2020) focusing on George's initiative in the discovery of the protective effects of glycine betaine on the oxygen-evolving photosystem II complex. We end with a brief description of research on glycine betaine-synthesizing transgenic cyanobacteria. Two of us, Norio Murata (in Japan) and Kostas Stamatakis (in Greece), and all our collaborators, have the highest respect for George, and we miss him and our intense discussions with him on various topics of photosynthesis research.

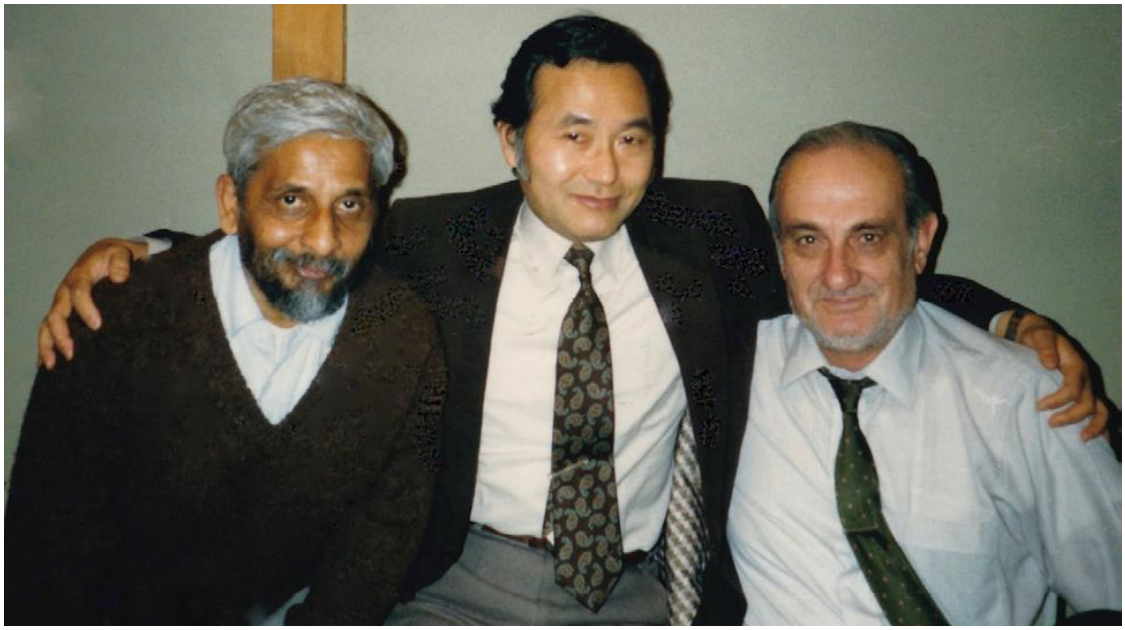


Figure 1: *Three talents of the glycine betaine research team. P.S. Mohanty (left), N. Murata (center), G.C. Papageorgiou (right). Taken at the National Institute for Basic Biology (NIBB), Okazaki, Japan, 1990.*

Publications

Murata, N., Stamatakis K. (2022) George C. Papageorgiou and the protective role of glycine betaine in activation and stabilization of the oxygen-evolving photosystem II complex. Photosynthetica 60 (1): 21-24 (IF 3.189)

Samiotis, G., Stamatakis, K., Amanatidou, E (2022). Dimensioning of Synechococcus elongatus PCC 7492 cultivation photobioreactor for valorization of wastewater resources Chemical Engineering Journal 134895, (IF 13.273)

Other Scientific Activities

Organization of scientific conferences or participation in conference organizing committees

Member of the International Organizing Committee of the International Meeting "Photosynthesis and Hydrogen Energy Research for Sustainability"

Educational Activities

Outside IBA

Invitation from the Department of Chemical Engineering of the Polytechnic School of the University of Western Macedonia as a member of the seven-member examination committee, which was appointed by decision of the Assembly of the Department of Chemical Engineering in No. 102/17-10-2022, for the examination of the doctoral thesis of the PhD candidate Mr. Georgios Samiotis, on the subject *"Wastewater treatment and valorization coupled with cyanobacterium Synechococcus elongatus PCC 7942 cultivation*"

Total Impact Factor for original publications in 2022: 16.462

Citations for 2022 (without self-citations): 84 (Scopus), 115 (Google Scholar)

Total citations 2018-2022 (without self-citations): 387 (Scopus), 454 (Google Scholar)

h-factor: 15 (Scopus), 17 (Google Scholar)

Current External Funding

Partnership and Cooperation Agreement (NSRF) 2014-2020, European Regional Development Fund (ERDF) Development of New Innovative Energy Technologies of Low Carbon Footprint for the Enhancement of Excellence in the Region of Western Macedonia - SUB-PROJECT 01_UoWM, MIS code 5047197 of The Operational Program "Competitiveness, Entrepreneurship & Innovation" (EPAnEK) co-financed by Greece and the European Union.
Scientific Supervisor: Prof. Amanatidou Elisavet.
Financial support: 10.000 €

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.

2022 Findings
Heaps' or Herdan's law is a linguistic law describing the relationship between the vocabulary/dictionary size (type) and word counts (token) to be a power-law function. Its existence in genomes with certain definition of DNA words is unclear partly because the dictionary size in genome could be much smaller than that in a human language. We define a DNA word in a genome as a DNA coding region that codes for a protein domain (CRCPD). Using human chromosomes and chromosome arms as individual samples, we establish the existence of Heaps' law in the human genome within limited range. Our definition of words in a genomic or proteomic context is different from that in large language models for DNA or protein sequences where words are usually short. Although an approximate power-law distribution of protein domain sizes due to gene duplication and the related Zipf's law are well known, their translation to the Heaps' law in CRCPD is not automatic. Several other animal genomes are shown to also exhibit range-limited Heaps' law with our definition of DNA words for CRCPD, though with various exponents, partially depending on their level of complexity. Investigation

of Heaps' law and its exponent value could provide an alternative narrative of reusage and redundancy of protein domains, creation of new protein domains, etc. from a linguistic perspective.

Publications

Nikolaidis M., Papakyriakou A., Chlichlia K., Markoulatos P., Oliver S.G., Amoutzias G.D. (2022) Comparative Analysis of SARS-CoV-2 Variants of Concern, Including Omicron, Highlights Their Common and Distinctive Amino Acid Substitution Patterns, Especially at the Spike ORF. Viruses, 14(4), 707. [IF: 5.8]

Papakyriakou A.*, Mpakali A., Stratikos E. (2022) Can ERAP1 and ERAP2 Form Functional Heterodimers? A Structural Dynamics Investigation. Frontiers in Immunology, 20(13) art. No. 863529. [IF: 8.8]

Vourloumis D, Mavridis I, Athanasoulis A, Temponeras I, Koumantou D, Giastas P, Mpakali A, Magrioti V, Leib J, van Endert P, Stratikos E,* Papakyriakou A.* (2022) Discovery of Selective Nanomolar Inhibitors for Insulin-Regulated Aminopeptidase Based on α-Hydroxy-β-amino Acid Derivatives of Bestatin. Journal of Medicinal Chemistry, 65(14):10098-10117. [IF: 8.0]

Giastas P., Papakyriakou A., Tsafaras G., Tzartos S.J., Zouridakis M. (2022) Structural Insights into the Role of β3 nAChR Subunit in the Activation of Nicotinic Receptors. Molecules, 27(14), 4642. [IF: 4.9]

Grigalavicius M., Ezzatpanah S., Papakyriakou A., Raabe T.T.H., Yannakopoulou K., Theodossiou T.A. (2022) 5-ALA Is a Potent Lactate Dehydrogenase Inhibitor but Not a Substrate: Implications for Cell Glycolysis and New Avenues in 5-ALA-Mediated Anticancer Action. Cancers (Basel), 14(16), 4003. [IF: 6.6]

Giarimoglou N., Kouvela A., Maniatis A., Papakyriakou A., Zhang J., Stamatopoulou V., Stathopoulos C. (2022) A Riboswitch-Driven Era of New Antibacterials. Antibiotics (Basel), 11(9), 1243. [IF: 5.2]

da Silva R.L., Papakyriakou A., Carmona A.K., Spyroulias G.A., Sturrock E.D., Bersanetti P.A., Nakaie C.R. (2022) Peptide inhibitors of angiotensin-I converting enzyme based on angiotensin (1-7) with selectivity for the C-terminal domain. Bioorganic Chemistry, 129, 106204. [IF: 5.3]

Kintos D.P., Salagiannis K., Vazoura V., Wittrien T., Papakyriakou A., Nikolaropoulos S.S., Behrends S., Topouzis S., Fousteris M.A. (2022) Design, synthesis and biological evaluation of new 3,4-dihydroquinoxalin-2(1H)-one derivatives as soluble guanylyl cyclase (sGC) activators. Heliyon, 8(11), e11438. [IF: 3.8]

Georgiadis D., Skoulikas N., Papakyriakou A., Stratikos E. (2022) Phosphinic Peptides as Tool Compounds for the Study of Pharmacologically Relevant Zn-Metalloproteases. ACS Pharmacology Translational Science, 5(12), 1228-1253. [IF: 5.1]

Other Scientific activities

Reviewer of scientific papers for: Mathematical Problems in Engineering, BMC Bioinformatics, Homeopathy.

Educational Activities

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

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

Total Impact Factor for original publications in 2022: 4.2

Citations 2022 (without self- citations): 104

Total Citations 2018-2022 (without self-citations): 411

h-factor: 16 (Scopus)

Research Group: Designed Biomolecules Research Lab

Research Staff
Athanasios Papakyriakou, Senior Researcher
Alexandros Athanasoulis, PhD Student
Evangelos Tsoukas, MSc Student
Soultana Kechagia, Undergraduate Student

Research Interests
Design and synthesis of M1 family aminopeptidase inhibitors, and discovery of allosteric inhibitors of insulin-regulated aminopeptidase (IRAP) guided by the structure. Design of biologically active compounds based on the structure of beta-adrenergic receptors (collaboration with Prof. Barbata Richichi, University of Florence, Italy). Study of the structure and molecular dynamics of acetylcholine receptors in complexes with toxins (collaboration with Dr. P. Giasta, University of Athens), as well as the interaction of natural and non-natural peptide substrates in the angiotensin-converting enzyme (ACE, in collaboration with Prof. G. Spiroulias and Prof. Ed Sturrock, University of Cape Town). Study of the structure and interaction of the LMKT3 kinase–inhibitor complex using biophysical and computational methods (collaboration with Prof. G. Giamas, University of Sussex, UK). Discovery of allosteric phosphatase inhibitors through virtual screening of small organic compound libraries (collaboration with Dr. D. Kletsas, Prof. G. Spiroulias, Dr. P. Giasta).

2022 Findings
Significant progress has been made in the synthesis of M1 family aminopeptidase inhibitors by the PhD candidate Alexandros Athanasoulis, who succeed in preparing new compounds that target ERAP2 ERAP2 selectively. Moreover, he designed and prepared inhibitors for the homologous, but functionally distinct, M1 aminopeptidases APN and APA. The work, which made a substantial contribution with basic inhibitors of ERAP1 and IRAP, was accepted in a high-impact pharmaceutical chemistry journal (J. Med. Chem. 2022).

The structural study of the heterodimeric ERAP1/ERAP2 complex was carried out using computational methods in conjunction with a major experimental effort to co-express the dimeric complex by the post-doctoral researched Dr. A. Bakali (H.F.R.I). However, all these efforts did not yield the desired amount of heterodimer for further studies, therefor an article presenting only the computational work has been published (Frontiers in Immunology, 2022).

The collaboration with Dr. P. Giasta for the study of the dynamics and the role of β3 subunit of nicotinic acetylcholine receptors (nAChR) was completed and published in an open-access journal (Molecules 2022), as well as the collaboration with Prof. G. Giamas with the publication on the discovery and characterization of a new LMTK3 kinase inhibitor (Int. J. Mol. Sci. 2023).

Another study on the activity of 5-aminolevulinic acid (5-ALA) with lactate dehydrogenase in glycolysis, a collaboration with Dr. Th. Theodosiou, Oslo University Hospital and Dr. K. Giannakopoulou (INN) led to some very promising results for 5-ALA as candidate in anticancer therapy (Cancers, 2022).

The design of beta-adrenergic receptor ligands in collaboration with Prof. B. Richichi and the ERASMUS+ master's student Luca Landini was completed; an article on work was accepted at a respectable medicinal chemistry journal (Eur J Med Chem, 2023).

A collaborative study (Prof. Ed Sturrock, University of Cape Town and Prof. G.A. Spyroulias, University of Patras) on the two angiotensin-converting enzyme (ACE) subunits in complex with synthetic peptides acting as selective inhibitors has been presented with a full article at Bioorg. Chem. 2022.

Another significant contribution was the co-authoring of two review articles, one related to the structure and function of small molecules acting on bacterial ribonucleases (Prof. K. Stathopoulos, Antibiotics, 2022), and another on the role of phosphinic peptides as inhibitors of Zn metalloproteases (Prof. D. Georgiadis, ACS Pharm. Trans. Sci. 2022).

Publications

Mavridis, G., Mpakali, A., Zoidakis, J., Makridakis, M., Vlahou, A., Kaloumenou, E., Ziotopoulou, A., Georgiadis, D., Papakyriakou, A., Stratikos, E. (2021) The ERAP1 active site cannot productively access the N-terminus of antigenic peptide precursors stably bound onto MHC class I. Scientific Reports, 11 (1), art. no. 16475. [IF: 4.4]

Chiniadis, L., Giastas, P., Bratsos, I., Papakyriakou, A. (2021) Insights into the Protein Ruthenation Mechanism by Antimetastatic Metallodrugs: High-Resolution X-ray Structures of the Adduct Formed between Hen Egg-White Lysozyme and NAMI-A at Various Time Points. Inorganic Chemistry, 60, 10729-10737. [IF: 5.2]

Temponeras, I., Chiniadis, L., Papakyriakou, A., Stratikos, E. (2021) Discovery of selective inhibitor leads by targeting an allosteric site in insulin-regulated aminopeptidase. Pharmaceuticals, 14 (6), art. no. 584. [IF: 5.9]

Cilibrasi, C., Ditsiou, A., Papakyriakou, A., Mavridis, G., Eravci, M., Stebbing, J., Gagliano, T., Giamas, G. (2021) LMTK3 inhibition affects microtubule stability. Molecular Cancer, 20 (1), art. no. 53. [IF: 27.4]

Lepore, A., Choy, P.M., Lee, N.C.W., Carella, M.A., Favicchio, R., Briones-Orta, M.A., Glaser, S.S., Alpini, G., D'Santos, C., Tooze, R.M., Lorger, M., Syn, W.-K., Papakyriakou, A., Giamas, G., Bubici, C., Papa, S. (2021) Phosphorylation and Stabilization of PIN1 by JNK Promote Intrahepatic Cholangiocarcinoma Growth. Hepatology, 74 (5), 2561-2579. [IF: 17.4]

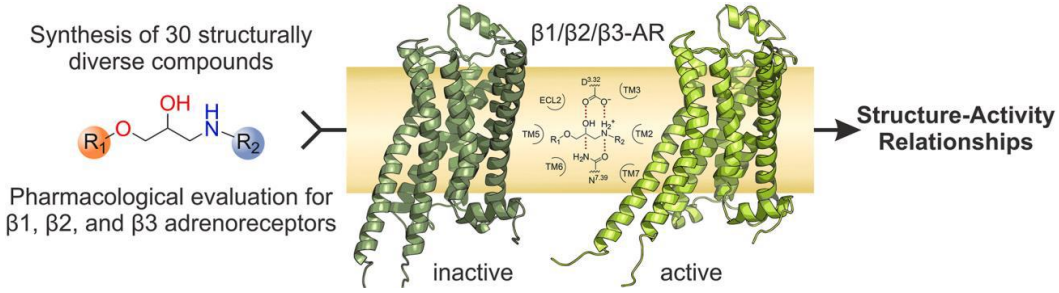
Kalampalidis, A., Peppas, A., Schnakenburg, G., Papakyriakou, A., Tsoupras, A., Zabetakis, I., Philippopoulos, A.I. (2021) Antithrombotic and antiplatelet activity of an organometallic rhodium(I) complex incorporating a substituted thieno-[2,3-d]-pyrimidine ligand: Synthesis, structural characterization, and molecular docking calculations. Applied Organometallic Chemistry, 35 (6), art. no. e6210. [IF: 4.1]

Articles in press

Andreou A., Papakyriakou A., Zervou M.I., Goulielmos G.N., Eliopoulos E.E. (2023) Is the Association of the Rare rs35667974 IFIH1 Gene Polymorphism With Autoimmune Diseases a Case of RNA Epigenetics? Journal of Molecular Evolution, 91(2), 204-213. [IF: 4.0]

Agnarelli A., Lauer Betrán A., Papakyriakou A., Vella V., Samuels M., Papanastasopoulos P., Giamas C., Mancini E.J., Stebbing J., Spencer J., Cilibrasi C., Ditsiou A., Giamas G. (2023) The Inhibitory Properties of a Novel, Selective LMTK3 Kinase Inhibitor. International Journal of Molecular Sciences 24(1), 865. [IF: 6.2]

Tricomi J., Landini L., Nieddu V., Cavallaro U., Baker J.G., Papakyriakou A.*, Richichi B.* (2023) Rational design, synthesis, and pharmacological evaluation of a cohort of novel beta-adrenergic receptors ligands enables an assessment of structure-activity relationships. European Journal of Medicinal Chemistry 246, 114961. [IF: 7.1]



International conferences

A. Athanasoulis, I. Temponeras, E. Stratikos, A. Papakyriakou (2022) Optimization and structure-activity relationships of α-hydroxy-β-amino acid based inhibitors of M1 aminopeptidases, Athens Conference on Advances in Chemistry (acac2022), June 26–July 1, 2022, Athens, Greece.

J. Tricomi, A. Papakyriakou, U. Cavallaro, J. Baker, B. Richichi (2022) Exploring The Binding Ligand Space of β-Adrenergic Receptors: How to do it and why it is important. International Summer School on Organic Synthesis (ISOS 2022), June 12–16, 2022, Gargnano (BS), Italy.

A. Papakyriakou (2022) Beyond the single structure: Computational Molecular Dynamics. 4th CAPSTONE summit, October 18–21, 2022, University of Athens, Greece.

Other Scientific Activities

Member of the Evaluation Committee of research proposals submitted within the framework of basic and applied research in Health Sciences by the Latvian Council of Science, Sep.-Dec. 2022.

Elected member of the Board – Treasurer of the Hellenic Crystallographic Association (HeCrA) and member of the European Peptide Society (EPS).

Member of the editorial team of the journals Frontiers in Immunology (Associate Editor for Antigen Presenting Cell Biology) and International Journal of Molecular Sciences (Topical Advisory Panel Member). Regular reviewer of scientific publications in the journals Molecules, International Journal of Molecular Sciences, Biomedicines, Nutrients, Pharmaceuticals, and Marine Drugs (MDPI), as well as in Frontiers in Immunology and Frontiers in Chemistry (Frontiers).

Educational activities

Interdepartmental Program for Postgraduate Studies of IBE and the Department of Chemistry, University of Patras; Molecular Pharmacology, 2nd semester 2022 (4 hours), Courses: "*Drugs acting on receptors», «Drugs acting on enzymes»,* and *«The adrenergic nervous system – structure-activity relationships of agonists and antagonists»* for 12 students.

Other Activities in IBA and in NCSR "Demokritos"

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

Total Impact Factor for original publications in 2022: 53.5

Citations for 2022 (without self-citations): 183

Total citations 2018-2022 (without self-citations): 877

h-factor (from Scopus and Google scholar): 24 (Scopus), 28 (Google Scholar)

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, Graduate Research associate
Eleftherios Halevas, Graduate Research associate
Georgia Athanasopoulou, Postgraduate 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 nano-technological applications. Our main fields of research are Alzheimer's disease (AD) and cancer, and our tools are NMR and CD spectroscopies for structural and molecular interaction studies, combined with methodologies of organic synthesis, complexation/labeling, encapsulation, and biological evaluation of the new compounds/agents in appropriate systems. Biological evaluation includes in vitro studies of interaction with biomolecules, biochemical/microscopic/cellular assays in cancer and primary cell lines, as well as in vivo evauation in experimental animals in collaboration with INRASTES.

Recently, our research activity focuses on:

- pharmacophoric molecules/bioactive natural products (including 2- (4'-aminophenyl)benzothiazole, curcumin, isatin, flavonoids etc), derivatives of these molecules with improved pharmacological properties, as well as their complexes (with copper, palladium, platinum, zinc, nickel, etc) with dual/combined activity from the pharmacophore-ligand and the metal. The compounds of interest are studied either free or encapsulated in nanostructures (nanoparticles, liposomes) for increased bioavailability and targeted transport and release.
- 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. Within the same framework, development of agents suitable for ^{18}F labeling labeling for PET imaging.
- photochemicall active molecules as photosensitizers in the photodynamic treatment of cancer and as tracers of cellular processes.
- inhibitors of the aggregation of β-amyloid peptide (Aβ) of Alzheimer's disease to toxic oligomeric and polymeric forms. The effect of natural products and synthetic organic molecules, on the aggregation process of Aβ is studied mainly with Circular Dichroism (CD) but also through the reduction of its toxicity in primary neurons (rescue effect).
- application of quantitative NMR (qNMR) methods in the determination of purity of organic compounds and the composition of mixtures, as well as metabolomics NMR analysis for the characterization/classification of oils, wines, natural extracts etc.

2022 Findings
The use of natural products and known pharmacophoric structures in the preparation of novel bioactive compounds constitutes the major goal of our activities and continued successfully during 2022. Representative examples include • synthesis of novel pyrazolo-pyridines with affinity for amyloid plaques of AD • synthesis of isatin derivatives with multimodal activity

against AD • development of novel dendrimeric hyperbranched nanocarriers with encapsulated remdesivir, a clinically used anti-COVID-19 drug, aiming at developing an inhalable suspension for clinical use • development of colloidal albumin as curcumin nanocarrier in collaboration with the National Hellenic Research Foundation • study of *Rosmarinus officinalis* extracts as aryl hydrocarbon receptor inhibitors in collaboration with the University of Athens.

Within the framework of Industrial Scholarships (B. Mavroidi) from the Stavros Niarchos Foundation and in collaboration with the company PharmaGnose SA, the photoprotecting capacity of various bioactive natural products from the Greek flora (pure compounds or extracts) against skin cell lines is studied for cosmetic and medical applications. In 2022, extracts from mountain tea (*Sideritis clandestina*, *Sideritis syriaca*, *Sideritis scardica*), olive leaves (*Olea europaea*), rose petals (*Rosa damascena*) and from the shrubby plant *Cistus creticus* were shown to have strong antioxidant and photoprotecting activity against UV-A irradiation with extremely low, if any, cytotoxicity.

In continuation of the study of benzothiazole and benzimidazole complexes with the radioactive cyclopentadienyl ^{99m}Tc and the stable Re, which exhibit remarkable blood-brain barrier penetration and properties that make them ideal for diagnosis (^{99m}Tc) and therapy (Re) of CNS diseases, the results of the evaluation of their activity against brain cancer cells (IC_{50} value of the order of 1 μM against the U-251 MG glioblastoma cell line, superior to that of temozolomide, the clinically used chemotherapeutic) were published. In the area of AD, in vivo experiments on the 4-month administration of the Re complexes in transgenic 5xFAD mice, recognized AD models, have been completed and a significant reduction of the amount of toxic Aβ oligomers and of the Amyloid Precursor Protein (APP) levels, as well as a concomitant significant increase of levels of Insulin-degrading enzyme (IDE, known to cleave Aβ) in the mouse brain, was observed. The results are of high scientific impact and the manuscript is in preparation.

In recent years our activity is expanding to new areas and collaborations taking advantage of the IB-A infrastructure with characteristic examples: • fluorescence confocal microscopy study on the staining of systemic light chain amyloidosis for diagnostic applications (in collaboration with Prof. I. Andreadou, School of Pharmacy & Prof. Efstathios Kastritis, Medical School, University of Athens) • CD studies on the aggregation of light chain amyloid proteins responsible for systemic amyloidosis (in collaboration with Prof. I. Andreadou, School of Pharmacy, University of Athens) • Study on the effect of pesticides on native and cultivated plants of the Greek flora applying metabolomic NMR techniques (in collaboration with Assist. Prof. K. Aliferis, Agricultural University of Athens) • Study of the degree of purity of organic compounds and determination of veterinary drug traces by means of quantitative NMR (qNMR) (in collaboration with Dr. E. Kakoulidis, Chemical Metrology Lab, General Chemical State Laboratory) • Fluorescence confocal microscopy study of porphyrin-β-cyclodextrin nanomaterials for anticancer photodynamic therapy (in collaboration with Dr. K. Yannakopoulou, NCSR "Demokritos").

Publications

Panagiotakis, S., Mavroidi, B., Athanasopoulos, A., Charalambidis, G., Coutsolelos, A.G., Paravatou-Petsotas, M., Pelecanou, M., Mavridis, I.M., Yannakopoulou, K. (2022). Unsymmetrical, monocarboxyalkyl meso-arylporphyrins in the photokilling of breast cancer cells using permethyl-β-cyclodextrin as sequestrant and cell uptake modulator. Carbohydr. Polym. 275, 118666 (IF: 10.25)

Vidali, V.P., Nigianni, G., Athanassopoulou, G.D., Canko, A., Mavroidi, B., Matiadis, D., Pelecanou, M., Sagnou, M. (2022). Synthesis of Novel Pyrazolo[3,4-b]pyridines with Affinity for β-Amyloid Plaques. MolBank, 1, M1343 (IF: 0.54)

Mavroidi, B., Kaminari, A., Makrypidi, K., Shegani, A., Bouziotis, P., Pirmettis, I., Papadopoulos, M., Sagnou, M., Pelecanou, M. (2022). Biological evaluation of complexes of cyclopentadienyl M(CO)3+ (M = Re, 99mTc) with high blood–brain barrier penetration potential as brain cancer agents. Investig. New Drugs, 40, 497-505 (IF: 3.85)

Halevas, E., Mavroidi, B., Kaplanis, M., Hatzidimitriou, A.G., Moschona, A., Litsardakis, G., Pelecanou, M. (2022). Hydrophilic bis-MPA hyperbranched dendritic scaffolds as nanocarriers of a fully characterized flavonoid morin-Zn(II) complex for anticancer applications. J. Inorg. Biochem. 232, 111832 (IF: 4.155)

Matskou, K., Kisaoglan, B., Mavroidi, B., Pelecanou, M., Zoumpanioti, M., Matis, I., Xenakis, A. (2022). Inducing the formation of a colloidal albumin carrier of curcumin. JCIS Open, 6, 100051 (IF: 8.128)

Matiadis, D., Fountzoula, C., Trapali, M., Karkalousos, P., Sagnou, M. (2022). Naked-eye colorimetric cyanide detection by monocarbonyl analogue of curcumin, J. Mol. Struct., 1268, 133677 (IF: 3.842)

Mavroidi, B., Kaminari, A., Matiadis, D., Hadjipavlou-Litina, D., Pelecanou, M., Tzinia, A., Sagnou, M. (2022). The Prophylactic and Multimodal Activity of Two Isatin Thiosemicarbazones against Alzheimer's Disease In Vitro. Brain Sci. 12, 806. (IF: 3.333)

Kakavoulia, M. A., Karakota, M., Kaloyianni, M., Halevas, E., Sagnou, M., Galliou, P. A., Koliakos, G. (2022). The cytotoxicity effect of a bis-MPA-based dendron, a bis-MPA-PEG dendrimer and a magnetite nanoparticle on stimulated and non-stimulated human blood lymphocytes. Toxicology in vitro: an international journal published in association with BIBRA, 82, 105377. (IF: 3.685)

Mamalis, D., Panagiotopoulou, A., Couladouros, E. A., Tzeli, D., Vidali, V. (2022). A DFT study towards the amide cis-trans isomerization process of the myc-max inhibitor mycro 3 and its photophysical properties; synthesis and NMR studies of the trans-conformation. Chemistry Select, 7, 257. (IF:2.307)

Kallimanis, P., Chinou, I., Panagiotopoulou, A., Soshilov, A., He, G., Denison, M., Magiatis, P. (2022). Rosmarinus officinalis L. leaf extracts and their metabolites inhibit the aryl hydrocarbon receptor (AhR) activation in vitro and in human keratinocytes: potential impact on inflammatory skin diseases and skin cancer. Molecules, 27(8), 2499. (IF: 4.927)

Dermitzaki, D., Panagiotopoulou, A., Pissas, M., Sanakis, Y., Psycharis, V., Raptopoulou, C. (2022). Synthesis, Crystal Structures and Magnetic Properties of Trinuclear {Ni2Ln} (LnIII = Dy, Ho) and {Ni2Y} Complexes with Schiff Base Ligands. Crystals, 12(1), 95 (IF: 2.589)

Kiritsis, C., Shegani, A., Makrypidi, K., Roupa, I., Lazopoulos, A., Panagiotopoulou, A., Triantopoulou, S., Paravatou-Petsotas, M., Pietzsch, H.J., Pelecanou, M., Papadopoulos, M., Pirmettis, I. (2022). Synthesis and preclinical evaluation of rhenium and technetium-99m "4 + 1" mixed-ligand complexes bearing quinazoline derivatives as potential EGFR imaging agents. Biorg. Med. Chem. 73, 117012. (IF: 3.641)

Halevas, E., Mavroidi, B., Kokotidou, C., Moschona, A., Sagnou, M., Mitraki, A., Litsardakis, G., Pelecanou, M. (2022). Remdesivir-loaded bis-MPA hyperbranched dendritic nanocarriers for pulmonary delivery. J. Drug Deliv. Sci. Technol. 75, 103625 (IF: 5.062)

Articles in Press

Mavroidi, B., Sagnou, M., Halevas, E., Mitrikas, G., Kapiris, F., Bouziotis, P., Hatzidimitriou, A.G., Pelecanou, M., Methenitis, C. (2023). A tridentate Cu(II) complex with a 2-(4'-aminophenyl)benzothiazole derivative: crystal structure and biological evaluation for anticancer activity. Inorganics. 11, 132 (IF: 3.149)

Panagiotakis, S., Mavroidi, B., Athanasopoulos, A., Bugnicourt-Moreira, L., Regagnon, T., Gonçalves, A-R., Boukos, N., Grigalavicius, M., Theodossiou, T-A., Berg, K., Ladaviere, C., Pelecanou, M., Yannakopoulou, K. (2023). Small anticancer drug release by light: photochemical internalization of porphyrin-β-cyclodextrin nanoparticles. Carbohydr. Polym. 306, 120579 (IF: 10.25)

Makrypidi, K., Kiritsis, C., Roupa, I., Triantopoulou, S., Shegani, A., Paravatou-Petsotas, M., Chiotellis, A., Pelecanou, M., Papadopoulos, M., Pirmettis, I. (2023). Evaluation of Rhenium and Technetium-99m Complexes Bearing Quinazoline Derivatives as Potential EGFR Agents. Molecules. 28, 1786 (IF: 4.927)

Halevas, E., Mavroidi, B., Pelecanou, M., Hatzidimitriou A.G. (2022). Structurally characterized copper complexes of flavonoid naringenin with antioxidant potential. Inorg. Chim. Acta. 546, 121325 (IF: 2.545)

Pantiora, P., Furlan, V., Matiadis, D., Mavroidi, B., Perperopoulou, F., Papageorgiou, A., Sagnou, M., Bren, U., Pelecanou, M., Labrou, N. (2022). Monocarbonyl curcumin derivatives as potent inhibitors against human glutathione transferase P1-1. Antioxidants, 12, 63 (IF: 7.675)

Articles published or in press (In Press) in proceedings of international conferences or other serial works, editing of publications of scientific books (e.g. conference proceedings, monographs, teaching texts or textbooks, etc.)

Nikolaou, P. E., Georgoulis, A., Liacos, C., Makridakis, M., Efentakis, P., Baltatzis, G., Mavroidi, B., Pelecanou, M., Vlachou, A., Terpos, E., Vorgias, C. E., Dimopoulos, M. A., Kastritis, E., Andreadou, I. Understanding the molecular mosaic of cardiotoxicity of light chains in plasma cell dyscrasias and cardiac light chain amyloidosis with the use of patient derived full-length light chains. In “European Heart Journal Supplements” (Roberto Ferrari ed.), vol. 43, pp. 2987, Oxford University Press, Oxford, United Kingdom, UK, 2022

Nikolaou, P. E., Georgoulis, A., Liacos, C., Efentakis, P., Baltatzis, G. E., Makridakis, M., Mavroidi, B., Pelecanou. M., Vlachou, A., Terpos, E., Vorgias, C. E., Dimopoulos, M. A., Kastritis, E., Andreadou, I. Investigation of the cardiotoxicity of full-length light chains derived from patients with cardiac light chain amyloidosis, multiple myeloma and monoclonal gammopathy of undetermined significance. In “Journal of Molecular and Cellular Cardiology” (Rong Tian ed.), vol. 173, pp. 153, Elsevier, Amsterdam, Netherlands, NL, 2022

Mavroidi, B., Thoma, E., Argyropoulou, A., Skaltsounis, A. L., Pelecanou. M. Plants of the Greek Flora as photoprotective cosmeceuticals. In “Planta Medica” (Oliver Kayser ed.), vol. 88, pp. 212, Georg Thieme Verlag KG, Stuttgart, Germany, DE, 2022

International conferences

E. Halevas, B. Mavroidi, A. Hatzidimitriou, M. Pelecanou, G. Litsardakis (2022). Novel fluorescent mitochondrial-targeting liposomal drug-delivery system of Ga(III)-naringenin complex for anticancer applications. 19th International Conference on Nanosciences & Nanotechnologies (NN21) July 5-8, 2022, Thessaloniki, Greece

B. Mavroidi, E. Thoma, A. Argyropoulou, A-L Skaltsounis, M. Pelecanou (2022). Plants of the Greek Flora as photoprotective cosmeceuticals. 70th International Congress and Annual Meeting of the Society for

Medicinal Plant and Natural Product Research (GA), August 28-31, 2022, Thessaloniki, Greece

E. Halevas, B. Mavroidi, A. G. Hatzidimitriou, G. Litsardakis, M. Pelecanou (2022). Bis-MPA hyperbranched dendritic nanocarriers of a structurally characterized flavonoid morin-Zn(II) complex with antioxidant and anticancer potential. 70th International Congress and Annual

Meeting of the Society for Medicinal Plant and Natural Product Research (GA), August 28-31, 2022, Thessaloniki, Greece

B. Mavroidi, M. Sagnou, A. Shegani, I. Pirmettis, M. Papadopoulos and Maria Pelecanou (2022). Remarkable blood-brain barrier penetrating diagnostics & therapeutic agents for central nervous system pathologies. Athens Conference on Advances in Chemistry - acac2022, 26/06/2022 to 01/07/2022, Athens, Greece

Al. Magiakos, R. Pappa, El. Efthimiadou, B. Mavroidi, M. Pelecanou, M. Paravatou-Petsotasc, C. Methenitis (2022). DNA/BSA Interaction and in vitro biological evaluation of Ru(II) complex with a derivative of 1,10-phenanthroline. Athens Conference on Advances in Chemistry - acac2022, 26/06/2022 to 01/07/2022, Athens, Greece

P. E. Nikolaou, A. Georgoulis, C. Liacos, M. Makridakis, P. Efentakis, G. Baltatzis, B. Mavroidi, M. Pelecanou, A. Vlachou, E. Terpos, C. E. Vorgias, M. A. Dimopoulos, E. Kastritis, I. Andreadou (2022). Understanding the molecular mosaic of cardiotoxicity of light chains in plasma cell dyscrasias and cardiac light chain amyloidosis with the use of patient derived full-length light chains. European Society of Cardiology (ESC) Congress August 26-29, 2022, Barcelona, Spain

National conferences

P. E. Nikolaou, A. Georgoulis, C. Liacos, M. Makridakis, P. Efentakis, G. Baltatzis, B. Mavroidi, M. Pelecanou, A. Vlachou, E. Terpos, C. E. Vorgias, M. A. Dimopoulos, E. Kastritis, I. Andreadou (2022). Cardiac light chain amyloidosis and cardiac involvement: Investigation of cardiotoxicity of light chains in vitro και in vivo. 33rd Panhellenic Hematology Congress, 9-12 November, 2022, Thessaloniki, I. Vellidis Conference Center - HELEXPO

P. Giannikopoulou, E. Kakoulidis, E. Skotidaki, E. Stathoudaki, V. Schoina, H. Alexopoulos, A. Panagiotopoulou (2022). Purity of organic compounds: the case of bisphenol-A. 8th Metrology Conference. July 1-2, Thessaloniki, Aristotle University Research Dissemination Centre (KE.D.E.A.), Greece

M. Pelecanou (2022) New molecules for the diagnosis and monitoring of AL amyloidosis. Scientific Conference on Plasma Cell Dyscrasias: Newer Data, February 10-12, 2022, Athens, Caravel Hotel

Other Scientific Activities

Publication Reviewing activity

Inorganic Chemistry - ACS (M. Pelecanou)

Letters in Drug Design & Discovery, Medicinal Chemistry, Bioorganic Medicinal Chemistry Letters, PLOS ONE, Pharmaceuticals, Molecules, Catalyst, Inorganics, Int J Mol Struct, Foods, Cancers, Archiv der Pharmazie (M. Sagnou)

Materials, Metals, Molecules, MDPI (A. Panagiotopoulou)

Educational activities

Inside IBA

Lecturing in the Bi-Institutional Program of Graduate Studies, a collaboration of the Chemistry Department of the University of Patras with IB-A of the NCSR “Demokritos” entitled “Applied Biochemistry: Clinical Chemistry, Biotechnology, Validation of Pharmaceutical Drugs”. Molecular Pharmacology – Special topics (A’ semester) – Structure and function of nucleic acids – DNS structure/DNA targeting drugs/RNA structure/RNA targeting drugs/nucleic acid targeting drugs/ molecular biology and genetic engineering) (B’ Semester). – 10 students (M. Sagnou)

Other activities in IBA

M Pelecanou

- Co-responsible (with M. Vlassi) for the operation of the circular dichroism spectrometer (CD) at IB-A. (E-11811, Provincial Council No. 515, 12/6/2013)
- Co-responsible (with L. Leondiadis, INRASTES) for the operation of the NMR Laboratory of NCSR "Demokritos" (Internal Project E-10949, Provincial Council No. 305, 1/3/2002)

M. Sagnou

- Member of the BIOIMAGING-GR monitoring group within the framework of the Infrastructure Roadmap together with H. Pratsinis, V. Lambropoulou
- Deputy education responsible

A. Panagiotopoulou

- Functional support/operation of the CD spectropolarimeter and the 250 MHz and 500 MHz NMR spectrometers and Provision of Specialized Scientific Services
- Deputy Scientific Responsible of the Internal Project E-10949 for the Specific Scientific Service providing/ liquid NMR Laboratory of NCSR "Demokritos"
- Responsible for the Blood Bank of NCSR "Demokritos"

Other Activities

Evaluator of the Hellenic Accreditation System (ESYD) according to ISO 17025 regarding the accreditation of Analytical Laboratories (A. Panagiotopoulou).

Total Impact Factor for publications in 2022

Maria Pelecanou: 38.959
Marina Sagnou: 31.234
Angeliki Panagiotopoulou: 13.464

Citations in 2022 (without selfcitations)

Maria Pelecanou: 210 (Scopus)
Marina Sagnou: 181 (Scopus)
Angeliki Panagiotopoulou: 37 (Scopus)

Total citations during 2018-2022 (without self-citations)

Maria Pelecanou: 637 (Scopus)
Marina Sagnou: 500 (Scopus)
Angeliki Panagiotopoulou: 35 (Scopus)

h-factor (Scopus)

Maria Pelecanou: 25
Marina Sagnou: 19
Angeliki Panagiotopoulou: 8

Current External Funding

Project entitled: Greek Pharmaceutical Plants for Photoprotection, funded by Stavros Niarchos Foundation and PharmaGnose S.A. within the framework of the Industrial Scholarship Program NCSR “Demokritos” - Stavros Niarchos Foundation
Duration: 3 years 2020-2023
Collaborating teams: Dr. A. Argiropoulou, PharmaGnose S.A
Scientific Responsible: M. Pelecanou
Industrial Scholarship Fellow: Dr. B. Mavroidi
Total Program Funding: 65.459,88 €
Funding of the lab for 2022: 21.819,96€

Project entitled: Innovative Radiopharmaceuticals with Fluoride-18: Research, Development and Introduction to the Greek Market for Diagnosis / Progression of Major Diseases with PET (BIOPET), funded by EREVNO-DIMIOURGO-KENOTOMO with I. Pirmettis (INRASTES, NCSR "D") as scientific coordinator. Responsible for IB-A: M. Pelecanou
Duration: 3 years 2017-2020
Collaborating teams: NCSR “Demokritos”, BIOKOSMOS SA
Total Program Funding: 998.075€
Funding of the lab for 2022: 10.000 €

Project entitled: Novel 99mTc complexes as AL amyloidosis radiodiagnostic tracers (SPECT-AL), funded by Johnson & Johnson Innovation, QuickFire Challenge: Improving Detection of AL Amyloidosis (IDEA) s with Professor E. Kastritis (School of Medicine, NKUA) as scientific coordinator.
Responsible for IB-A: M. Pelecanou and M. Sagnou
Duration: 1 year, 2021-2022
Collaborating teams: NCSR “Demokritos” (IB-A and INRASTES), School of Medicine & Department of Pharmacy, NKUA
Total Program Funding: 250.000 $
Funding of the lab for 2022: 30.000 €

Project entitled: Qualitative and quantitative upgrading of olive oil production in Messinia area of Peloponnese through the development of a modern plant protection program against the disease “anthracnose” of olives, funded by Agricultural Development Program (RAP) 16.1-16.2.
Duration: 3 years 2022-2025
Collaborating teams: Dr. K. Aliferis AUA, NILEAS Agricultural Cooperative, GAIA EPICHEIREIN
Scientific Responsible: A. Panagiotopoulou
Total Program Funding: 144.933,52€
Total Funding of the lab: 15.792,13€

Research Group: Protein Structure and Molecular Modeling

Research Staff
Metaxia Vlassi, Research Director
Nastazia-Lemonia Lesgidou, PhD student

Research Interests

- Protein folding
- Protein interactions. Sequence/structure relationships of amino-acid repeats / Role in protein-protein interactions
- Molecular dynamics of proteins
- Molecular dynamics simulations and their analysis, development of related tools
- Kinases
- Intrinsically disordered proteins

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

2022 Findings
With the aim of elucidating sequence/structure-function relationships of proteins and kinases in particular, in 2022 we built on, and expanded our previous in *silico* structural studies of:

1) the tyrosine kinase Tyk2, which is associated with various diseases including autoimmune diseases and cancer. More specifically, in 2022, we extended MD simulations, up to 6 μs, on various forms of the catalytic domain of the wild type Tyk2 and of variants either associated with diseases or emerged from analyses of MD trajectories obtained in previous years using the National HPC-system ARIS @GRNET. An application for additional computing resources to use ARIS was submitted to GRNET (January 2022) in the framework of the "*12th Call for ARIS Project Access*". The proposal was approved in March 2022 (granted resources: 1.400.000,0 core-hours for one year)
2) the SRPK1 kinase, which we have also studied in the past, and of its interaction with a protein linked to carcinogenesis that has been observed experimentally (biochemically) by our collaborators (T. Giannakouros' group, Aristotle University of Thessaloniki). More specifically, in 2022, MD simulations of various SRPK1-peptide complexes, modelled in the past, were extended to longer time-scales (1.5 μs). These simulations were carried out using a 64-core server available in the lab.
3) Moreover, in 2022 we developed a specialized protocol for analysis of MD trajectories aiming at identifying dynamic profiles and dynamics-driven allosteric communications during MD simulations. Comparative analyses of dynamic profiles between the wild type protein and its variants are expected to shed light on dynamics-function relationships, especially in the case of lack of obvious conformational changes. Application of this analysis protocol on both Tyk2 and SRPK1 MD simulations, is in progress.

In addition, in 2022, potential end-users continued to express interest to use the **GROMITA-GUI** we have previously developed in the lab (http://gromita.bio.demokritos.gr).

Other Scientific Activities
Member of the ad hoc three-membered evaluation committee for the appointment of an Associate Researcher (one position) in the Institute of Chemical Biology of the Hellenic Research Foundation, Athens, Greece

Member of the National Research Infrastructure project: "***INSPIRED:*** *The National RIs on Integrated Structural Biology, Drug Screening efforts and Drug-target functional*

characterization" is funded by NSRF 2014-2020 and co-financed by Greece (GSRT) and the European Union (European Regional Development Fund) (funding approved: June 2018). Role of MV: member of the group of Scientists of the NCSR "Demokritos" node and responsible for the *in silico* structural studies of the node.

Member of the group of Scientists of the NCSR "Demokritos" node of the ***ELIXIR-GR*** National Research Infrastructure.

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 in IB-A & NCSR "D"
In charge (with Dr. M. Pelecanou) of the Circular Dichroism (CD) service unit of IBA.
Member of various committees of NCSR "D"

Citations 2022 (excluding self-citations): 24

Total citations 2018-2022 (excluding self-citations): 165

h-factor: 16 (Scopus)

Current External Funding
"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 the NCSR "Demokritos" node and responsible for the in silico structural studies of the node) (Coordination: NHRF).
Duration: Sept 2018 – Sept 2022
Total Budget (revised) for the computational activities of the NCSR "D" node: 51.730,0€.
Budget 2022 for the group: 14.220 €

Project entitled *"Microsecond-scale MD simulations of a tyrosine kinase linked to autoimmune diseases_III*". *Acronym/project ID:* KIN_IMMUNMD_III in the framework of the *10th Call for Production Projects Accessing the supercomputer system ARIS* @ GRNET (P.I.: M. Vlassi.)
Duration: March 2021-March 2022
Total computing resources: 1.900.000,0 core-hours
Computing resources for 2022: 400.000,0 core-hours

Project entitled *"Using microsecond-scale MD simulations to elucidate sequence -dynamics-function relationships of a tyrosine kinase linked to autoimmune diseases IV*". *Acronym/project ID:* KIN_IMMUNMD_IV in the framework of the *12th Call for Production Projects Accessing the supercomputer system ARIS* @ GRNET (P.I.: M. Vlassi.)
Submitted
Duration: March 2022-March 2023
Total computing resources: 1.400.000,0 core-hours
Computing resources for 2022: 1.050.000,0 core-hours

CENTRAL PROJECTS
IBA

Beyond the hitherto described activities of each Lab, part of IBA's personnel were engaged in the following central projects:

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.

THE ROUTES OF BEE

During 2022, the flagship national initiative entitled CREATION OF A NATIONAL RESEARCH NETWORK IN THE VALUE CHAIN OF "HONEY" (acronym: THE ROUTES OF BEE) was finalized. This 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 and was coordinated by the Aristotle University of Thessaloniki. Ten more partners were involved, including IBA, participating in the initiative with a team of ten researchers headed by the Institutes' Director. Within the framework of the characterization and promotion of the Greek Honey varieties, studies of the intracellular antioxidant activity, as well as, of the atheroprotective and possible anti-cancer properties of selected honey samples of Greek origin were implemented in IBA, with a total budget amounting to 39,200 €.

EU-OPENSCREEN-DRIVE

The European project Driving forward long-term Sustainability of Excellence in Chemical Biology within Europe and beyond (acronym: EU-OPENSCREEN-DRIVE) was also continued during 2023. The project is coordinated by the European Research Infrastructure Consortium (ERIC) EU-OPENSCREEN, while 34 more partners are involved, from 15 European Union countries (or associated states). The project was selected for funding within the framework of the call H2020-INFRADEV-2018-2020/H2020-INFRADEV-2018-1 (Grant Agreement: 823893) with a total budget of 2.485.600,80 €, from which 16.875 € were allocated to IBA. The involvement of IBA is based on the fact that it coordinated the National Research Infrastructure OPENSCREEN-GR, which has the same object with the ERIC EU-OPENSCREEN. Aim of the project is the support of EU-OPENSCREEN through dissemination activities targeting possible users, as

well as, through the enhancement of the collaborations among the project partners. EU-OPENSCREEN-DRIVE is very important for IBA, keeping the communication channels with EU-OPENSCREEN open until the final integration of OPENSCREEN-GR into the ERIC.

Three more central projects were finalized within 2021: an action for the Strategic Development on the Research and Technological Sectors entitled TARGET IDENTIFICATION AND DEVELOPMENT OF NOVEL APPROACHES FOR HEALTH AND ENVIRONMENTAL APPLICATIONS (acronym: SANITURA, MIS 5002514), and two actions in the framework of the Reinforcement of the Research and Innovation Infrastructure: 1) AN OPEN-ACCESS RESEARCH INFRASTRUCTURE OF CHEMICAL BIOLOGY AND TARGET-BASED SCREENING TECHNOLOGIES FOR HUMAN AND ANIMAL HEALTH, AGRICULTURE AND THE ENVIRONMENT (acronym: OPENSCREEN-GR, MIS 5002691), and 2) A GREEK RESEARCH INFASTRUCTURE FOR VISUALIZING AND MONITORING FUNDAMENTAL BIOLOGICAL PROCESSES (acronym: BIOIMAGING-GR, MIS 5002755). All three projects were 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 they were supervised by the Director of IBA. The implementation of all three projects was very successful, with very high budget absorption rates and remarkable production of publications in peer-reviewed scientific journal and communications in scientific conferences. Moreover, the infrastructure acquired during these projects is now fully operational for the benefit of IBA’s personnel, as well as, of external users.

Figure 1: *Parts of the laboratory equipment of the National Research Infrastructure OPENSCREEN-GR coordinated by IBA*

SERVICE UNITS

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

LABORATORY FOR DOPING CONTROL AND METABOLIC STUDIES

Personnel
Dimitris Kletsas, Institute Director,
Laboratory Administrative Director
Argyro Fragkaki, PhD Chem, Laboratory Scientific Director
Aimilia Makrygianni, MSc Chem, Quality Manager
Ioannis Angelis, PhD Chem, Analyst
Athanasia Kioukia-Fougia, PhD Pharm, Analyst
Polyxeni Kiousi, PhD Chem, Analyst
Christoforidis Christoforos, PhD Chem, Analyst
Olga Goula, Chemist, MSc student, Analyst
Paraskevopoulou Katerina, Chem Eng, PhD student, Analyst
Sakellariou Panagiotis, PhD Biol, Analyst
Tsimelis Efstathios, Med Technol, PhD student, Analyst
Fotini Chlapana, Technician
Stella Loui, Technician
Maria Fillipidou, Secretary
Maria Vlachou, Secretary
Maria Pavlaki, Support personnel
Vassiliki Tzouvara, Support personnel

Research Interests
The main mission of the Doping Control Laboratory of Athens (DCLA) is to control human samples and horses for the existence of doping compounds. For this reason, it has all the appropriate infrastructure and know-how. At the same time, DCLA has undertaken many anti-doping research projects, either partially funded by the World Anti-Doping Agency (WADA) or anti-doping organizations, such as the Cyprus Anti-Doping Authority (Cyprus Anti-Doping Agency, CYADA) or exclusively funded by the previous host organization (OAKA). The results of these studies have been published in peer-reviewed international journals and presented at international anti-doping conferences. In addition, several diploma theses, either master's or doctoral level, have been conducted at DCLA's facilities with its scientific staff as supervisors in collaboration with local universities.

DCLA is constantly interested in the development of scientific research in the field of human and equine doping control, improving existing methods of detecting prohibited substances or developing new ones, as well as conducting metabolic studies. Among the future research goals of the Laboratory is the strengthening of its research activities by interacting with other laboratories of IBE in the characterization of molecules, protein and metabolic studies in combination with studies in cellular systems and experimental animals.

Progress in 2022
In April 2022, the Laboratory submitted an application to be be re-accredited by WADA, collecting the necessary documentation in accordance with the prerequisites of the international organization. DCLA was appointed the status of WADA's candidate lab in September 2022, after a meeting of WADA's executive committee.

DCLA maintained its accreditation by the National Accreditation System (ESYD) according to ISO17025 in the fields of human and equine doping control and by the Association of Official Racing Chemists (AORC) in the field of equine doping control.

Services were provided through an annual contract for the analysis of biological samples (urine and blood) to the Hellenic Equestrian Federation (HEF).

Tenders for the purchase of new analytical instruments have been completed: two GC-MS/MS (qqq), one GC-IRMS and one HPLC. The procedures for installing the instruments by the respective companies and training users of the above analytical instruments have been completed.

Training of the corresponding staff was carried out by an external instructor in proteomics procedures using nano-LC (30/5-4/6/2022).

Validation of analytical methods continued with the aim of re-accreditation of the Laboratory by WADA in the field of doping control of athletes.

Procedures for the urgent procurement of reference materials and consumables worth approximately €30,000 have been initiated.

Actions were taken to protect the security and storage of electronic documents through the installation of a new back-up system in collaboration with the IT manager of the IBE.

Contacts continued with the technical service of the "Demokritos" EKEFE for the maintenance of the building infrastructure (restoration of UPS operation, fire detection/fire safety system, safety nets/irons on windows, electrical work, support for the good operation of refrigeration/freezer devices, maintenance of premises).

A four-month (March-June 2022) internship was carried out by a student from the University of Western Attica, related to preparation procedures of human and equine biological samples for the detection of prohibited substances.

Research activities in the framework of a research program funded by WADA and a research program in collaboration between the Laboratory and the Institute of Nanoscience and Nanotechnology (INN) of the "Demokritos" ERC, continued normally. EEN staff continued their research activity to publish their research results in scientific journals or conferences.

Publications

Pitsinos E.N., Angelis S.A., Petrou M. Structure revision and chemical synthesis of ligandrol's main bishydroxylated long-term metabolic marker. Org. Biomol. Chem. 20, 9112-9116 (2022). (IF: 3.2).

Wagener F, Guddat S, Gorgens C, Angelis YS, Petrou M, Lagojda A, Kuhne D, Thevis M. Investigations into the elimination profiles and metabolite ratios of micro-dosed selective androgen receptor modulator LGD-4033 for doping control purposes. *Anal Bioanal Chem* 414, 1151–1162 (2022). (IF: 4.3).

HUMAN TISSUE BANK

Personnel

Helen Vavouraki Senior Researcher, Scientific Responsible
Yiannis Ninios, Postdoctoral Fellow
Lydia Panagopoulou, Graduate Research Associate (MSc)
Charalampos Voudommatis-Stergiou, Graduate Research Associate (MSc)
Eleutherios Kosmidis, Graduate Research Associate (MSc)
Milena Tselia, Administrative / Technical Support
Minas Leventis, Graduate Research Associate, Dentist / Dental prosthetist
Orestis Vassiliadis, Graduate Research Associate, Dentist / Dental prosthetist

Laboratory Description – Research Interests

A) Development activity

Human Tissue Bank of NCSR "DEMOKRITOS" is one of the first legislated laboratories of the Center, always mentioned in the laws of the Ministry of Health regarding transplantations. The main objective of the Bank includes the collection of various human tissues, their processing and the production of grafts to be used in Regenerative Medicine and Reconstructive Surgery.

It is licensed as a Tissue and Cell Bank by the Greek Ministry of Health (European Code GR013836). We follow 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, the recommendations of IAEA. Member of the European Association of Tissue Banks, it is the only bank of its kind in Greece, applying its "knowhow" in the processing of a great variety of human tissues and its expertise that has gradually developed in each procedure (procurement, tissue processing, irradiation sterilization and disposal of tissue grafts). In over 47 years of continuous operation, it has delivered more than 55.000 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.

B) Research activity

The Tissue Bank's research interests are mainly focused on the study of the activity of the produced grafts, the optimization of the production methods, the process of new types of tissues, the development of new techniques and new graft products. Its research activities are therefore based on collaborations with universities and healthcare institutions, in order to promote Public Health by launching improved products, publishing original papers and participating in doctorate degrees (Ph.D. theses).

Progress in 2022

In 2022, despite the problems entrained by the SARS-CoV-2 pandemic especially in Hospitals, HTB managed to collect adequate tissues from collaborating hospitals. More precisely, we have processed femur heads from 372 living donors and we have produced and delivered 905 bone grafts to be used in Dentistry and Orthopedic Surgery. Meanwhile, we have processed 12 cranium grafts from Neurosurgery Depts.

Moreover, we have worked towards the design of research and development of new innovative tissue grafts like bone grafts in putty form, and new protocols for the processing of human amnion. The new products will comply with the recent demands of Regenerative Medicine.

The paste (putty) is a new pharmaceutical form of allografts that includes components other than bone substance, such as special excipients, hyaluronic acid, antibiotics, possibly growth factors and / or BMPs. The desired result is the creation of a stable mesh that can be bio-absorbed at the required rate, leading to the creation of new living bone that progressively replaces it.

Our Laboratory aim is to study the development of an original formulation based on the assay of different combinations of excipients and other substances at various concentrations, in order to select the one that provides a composition (pharmacoform) with the desired properties, e.g. physical form, grain size, malleability and plasticity. Since in the international bibliography, there are differences in the effectiveness of bone regeneration of various products that are marketed, and have been attributed to the method of processing bone substance by different banks, the stage of processing of the relevant bone allograft (lyophilized or not, demineralized or not) that will participate in the preparation of the paste, is particularly studied. The parallel use of demineralized and non-demineralized bone material presupposes the production of demineralized cancellous bone in accordance with the protocol previously studied at the Bank. The form (solution or powder), and the concentration of the added hyaluronic acid were examined so that the product obtained had the desired pharmaceutical properties (paste viscosity, homogeneity and malleability). Studies are ongoing to finalize the concentrations of the various components.

The team also worked towards research and development of new protocols for the preparation of membrane grafts from fetal membranes, with multiple applications. The new products will meet the modern needs of Reconstructive Regenerative Medicine for safety and effectiveness, reduction of surgical and recovery time, utilization of additional materials, better application and use.

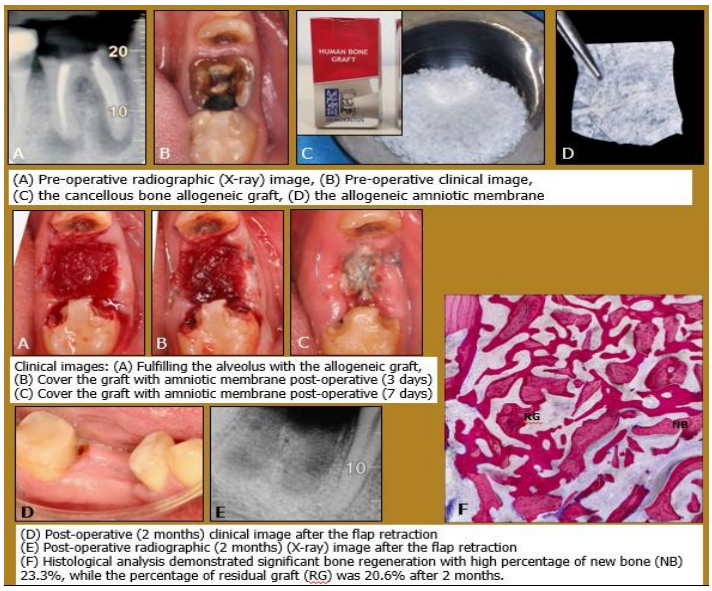
Scientific collaboration with hospitals, University labs, etc., has resulted in the processing of new types of tissues, the application of new optimized techniques and the production of improved and customized products, e.g. for child facial Surgery.

Announcements /Participation in Congresses/Fairs

HAOMS 2022, Annual Congress of the Hellenic Society of Oral and Maxillofacial Surgery on: Directed bone regeneration in implantology (3-4 /6/2022, Athens)

Orestis Vassiliadis, Eleni Vavouraki, Charalambos Voudommatis, Ioannis Ninios, Minas Leventis
Human Tissue Bank, IBA, NCSR “DEMOKRITOS”.
"Preservation of the alveolar crest using spongy allograft and human amniotic membrane. Cases report." 40th Anniversary Panhellenic Dental Congress, 6-8 /10/2022, Athens

I. Ninios, L. Panagopoulou, E. Kosmidis and H. Vavouraki
"Development of a new innovative bone allograft for application in the TALOS system. Clinical applications in Neurosurgery."
12th Panhellenic Conference of the Hellenic Society of Biomaterials, Athens, 15-17/12/2022



Online participation / attendance of Workshops/Events/Conferences
Innovation and Start-ups in Greece Feb 2, 2022 06:30 PM Athens, diaNEOsis

Public Procurement of Innovation in Health Horizon Europe, The EU Research and Innovation Program, 2/2/2022

Women in Bio-Sciences Hellenic Society of Biochemistry and Molecular Biology, Feb 23, 2022 Athens

"Initiatives and New Financial Tools to Support Research and Entrepreneurship" PRAXI/FORTH Network, 9/2/2022

Workshop entitled "Artificial Intelligence: Applications and Ethical Challenges" Research Ethics Committee of NCSR "Demokritos" March 23, 2022

Other Scientific Activities
Reviewer in the international journal CELL AND TISSUE BANKING (Springer).

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

Member of the Scientific / Organizing Committee of the 12th Conference of the Hellenic Society of Biomaterials.

Member of the NSRF Project Certification/Verification Committee RESEARCH-CREATE-INNOVATE / PSKE T2EDK-03546.

Scientific Coordinator of YGEIA Innovations, spinoff of NCSR "D", for the exploitation of the Lab expertise in the field of Human Tissue Grafts.

Member of the European Commission for the establishment of a single European code of nomenclature and characterization of tissues and cells.

Member of the European Network of Inspectors of Tissue and Cell Banks

Member of the Board (treasurer) of the Hellenic Society of Biomaterials

Continuous Cooperation/expert with the Ministry of Health and the National Transplant Organization

Research Proposals Assessor

Other Activities in NCSR "DEMOKRITOS"
Quality Manager of the Lab, according the ISO 9001/2015

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

Final Verification of the NSRF Program 2014-2020, RESEARCH - CREATE - INNOVATE, entitled: TALOS-BIO (2018-2022)

Participation in Projects
Erasmus + entitled: SCIence outreach: The exemple of BIObanks in Europe (SCIBIOEU). 2022-1-EL01-KA220-HED-000088145

Erasmus entitled: Colibri Women
Women in Business: Interviews with Women Entrepreneurs.

Educational activities
Joint MSc Program "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products", May 2022
Course: Research and Development of Tissue Grafts

Participation of the Lab in the Center Education Program for the visitors/students

Member of the Advisory Committee/Supervision of the postgraduate thesis during the Postgraduate Program: "Biomedical and Molecular Sciences in the Diagnosis and Treatment of Diseases", of the Democritos University of Thrace, Department of Medicine/TEITH.

Citations 2022 (without self- citations):4

Total Citations 2018-2022 (without self- citations): 31

h-factor: (Scopus, Google scholar): 10

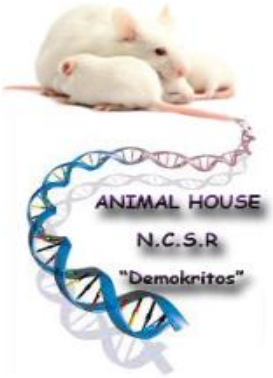
Current External Funding
The funding of the Human Tissue Bank is implemented by research programs and private resources

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 of the Institute of Biosciences and Applications of the National Centre for Scientific Research "Demokritos" is one of the first organized and specialized Laboratories for the breeding and disposal of small laboratory animals in Greece. Aim of the Animal House is the breeding and disposal of small laboratory animals to be used in research and development of new technologies, as well as for educational purposes. The Animal House functions in compliance with the national and international standards of facilities for laboratory animals and covers the most recent demands for research conducted on animal models.

The facility of the Animal House of the Institute of Biosciences and Applications of the National Centre for Scientific Research "Demokritos" includes units of reproduction, disposal and use (experimentation) of laboratory animals. The Committee for the Evaluation of Research Protocols and the Committee for the Wellbeing of Laboratory Animals, the continuously educated personnel, the up-to-date infrastructure, the accreditation of the Quality Management System according to ISO 9001:2015, the program for the control and assurance of the animals' health, as well as the organization of educational seminars, guarantee the quality of the services provided.

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

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

Animal strains

The animal facility during 2022 maintained and reproduced the following strains:

1. Mice, strain CFW SWISS ALBINO
2. Mice, strain NOD SCID (immunocompromised)
3. Mice, strain SKH1 (hairless)
4. Mice, strain C57Bl/6
5. Rats, strain WISTAR ALBINO
6. Rabbits, strain New Zealand ALBINO
7. Colonies of aged mice and rats are also available

During 2022, the Animal House supplied the following laboratory animals:

Users	Rats WISTAR	Mice SKH1	Mice CFW	Mice C57Bl/6J	Rabbits NZW	Mice SCID	Total
IBA	0	0	35	71	0	6	112
INRASTES	42	0	324	0	0	93	459
External users	144	62	0	269	40	20	535
Total disposal of laboratory animals	186	62	359	340	40	119	1.106

The operation of the Animal House, according to ΠΔ 56/2013, is supported by the following Committees:

Committee for the Evaluation of the Research Protocols - (Α.Π. 310295-24/06/2019)

Members: D. Kletsas, L. Klamarias, D. Mastellos, a representative from the Veterinary Division of the Attica Prefecture.

Substituting Members: I. Sotiropoulos, E. Livaniou, P. Sarris.

Committee for the Wellbeing of Laboratory Animals - (Α.Π. 310181-24/06/2019)

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

D. Kletsas is a substitute member of the National Committee for the wellbeing of laboratory animals.

During 2022

The Animal House regained accreditation of the Quality Management System to ELOT EN ISO 9001:2015.

Required health examinations of the animals of the Animal House were carried out in domestic and foreign specialized laboratories.

Building and mechanical upgrading of the facility and equipment of the Animal House continued.

The required laboratory animal procedure permissions were approved and issued, nine (9) protocols for animal experimentation were modified, renewed and executed in the Facility of Use of EL25BIOexp039.

The annual microbiological and chemical test of EYDAP water was carried out and the necessary certificates were received.

The contract with the company "LOCATE ITS" of the telemetry control system was renewed, for the recording, surveillance and immediate restoration of the mechanical equipment of temperatures and fresh air flow on a 24-hour basis.

An air purification device was installed in the common areas of the Animal House.

The breeding-disposal of the New Zealand (NZW) rabbit colony was extended to external users on order.

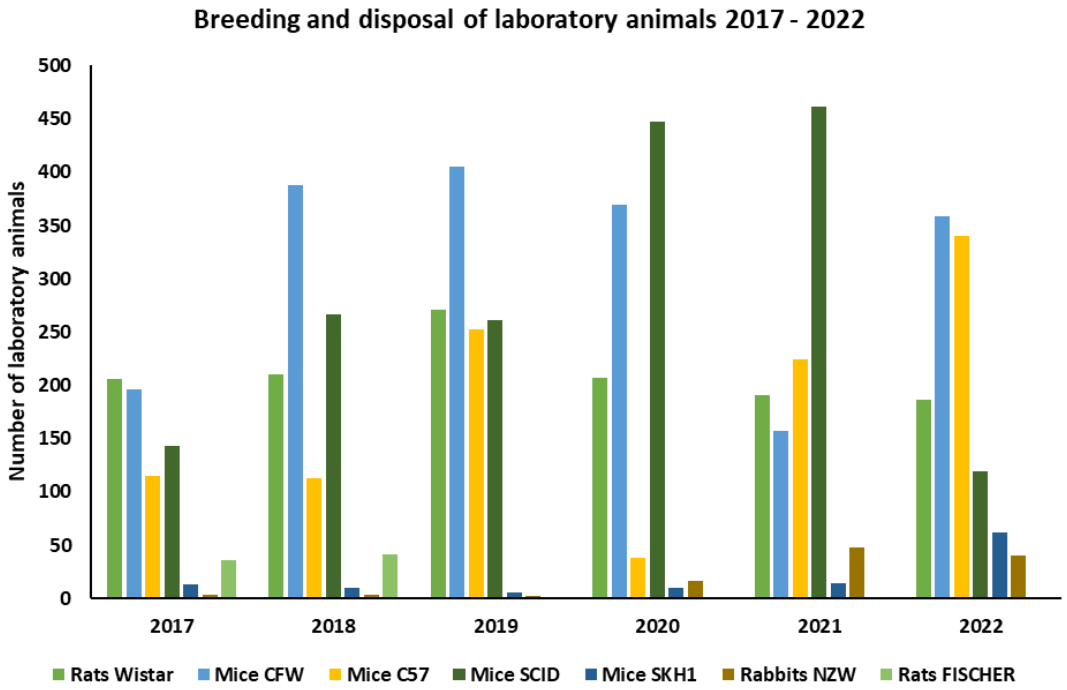
The personnel of the Animal House assisted in the handling of the animals, performed administrations, immunizations, blood samplings, etc., instructed methods and techniques on the animals, participated in the execution of the experimental protocols of the Facility of Animal Experimentation and generally provided any assistance and information requested, either within the Center or in collaboration with other institutions and sectors.

The personnel of the Animal House followed several educational seminars.

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

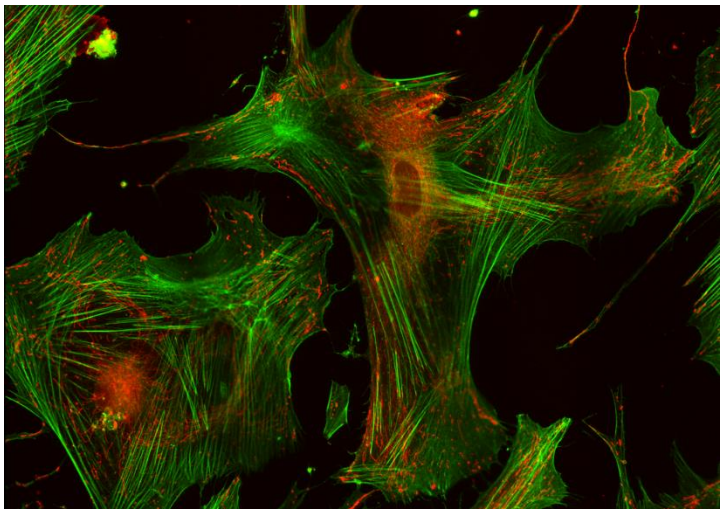
The Colony of Aged Animals has been enriched with new species.

Contracts were concluded with collaborating companies, research centers and institutions for the disposal and experimentation of animal models.



LIGHT MICROSCOPY UNIT

Personnel
Dimitris Kletsas, Research Director, Institute Director, Scientific and Administrative Responsible
Vassiliki Labropoulou, Senior Researcher
Harris Pratsinis, Senior Researcher
Marina Sagnou, Researcher
Alexandros Athanasopoulos, Research assistant



Laboratory Description – Progress during 2022
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 "Demokritos", 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, CO_2, O_2, N_2).

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)
- Cell/tissue Colocalization analysis
- Calcium imaging
- Differential Interference Contrast (DIC) microscopy (known as Nomarski microscopy)
- Image processing and analysis (with specialized software programss uch as ImageJ / Fiji and Imaris (Bitplane)

Leica TCS SP8 MP

During 2022 the light microscopy unit recorded 250 operating hours, many of which have been collaborations with external research centers and universities. The unit collaborated with research teams from the IBA 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 cellular senescence
- The expression of specific proteins associated with mechanisms involved in age-associated diseases such as dyslipidemia, diabetes mellitus and Alzheimer's disease
- Functional characterization of opioid receptors
- Imaging and cellular identification of new dendrimers, liposomal preparations and nanostructures for the transport of bioactive substances
- Imaging of biofilms 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 “Demokritos” educational programs participating in presentations, demonstrations and workshops, for all educational grades.

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

HISTOLOGY UNIT

Personnel
Dimitris Kletsas, Research Director, Institute Director, Admistrative Responsible
Garyfalia Drossopoulou, Senior Researcher, Scientific responsible

Laboratory Description – Research Interests
The Histology Unit (HU) of the Institute of Biosciences and Applications (IBA) was established in 2019 and is housed in an especially formed site, in the basement of the cental building of the Institute.

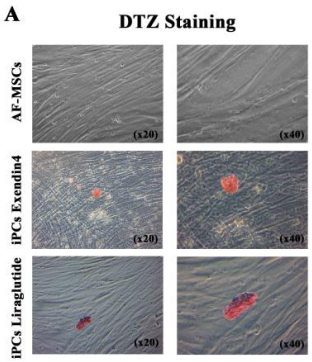
The HU supports the scientific work of several research groups and focuses on the investigation and phenotypic analysis at the tissue level of human and animal model specimens that are related to several pathologies, many of which derive from the Experimental Animal Facility of IBA.

The HU is fully equipped with hoods, tissue processing and embedding equipment, microtome, a cryostat and a vibratome, as well as all small necessary equipment.

Users can perform tissue processing, embedding, sectioning and staining with a series of stains. IBA researchers can also be trained to use selected equipment and then be able to acquire their own tissue sections. The unit can support protocol set up and application.

During 2022 IBA HU, participated in research protocols regading the following:

- The mode of action of liraglutide on the survival of glomerular podocytes β-pancreatic cells.
- Role of secreted conditioned media from human amniotic fluid mesenchymal stem/stromal cells in ameliorating the establishment and development of Diabetic Nephropathy.
- Differentiation of insulin producing cells (IPCs) by mesenchymal stem cells
- Intervertebral disc degeneration
- Skin ageing
- Cancer development in experimental animal models



The main equipment of IBA HU consists of:

Cryostat Leica CM1850

Microtome Leica

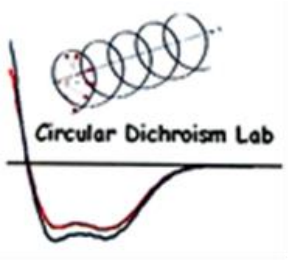
Vibratome Leica

Water Baths Leica

Embedding oven (Jouan Percision)

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)

Laboratory Description - Object
The equipment of the Circular Cichroism 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.
- Monitoring conformational changes of biological macromolecules under different conditions
- Comparative structure-thermal stability studies of proteins under various conditions

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

Progress in 2022
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 2022, as in previous years, the CD Lab has supported research projects of at least 10 groups of the 3 participating NCSR "D" Institutes (IB-A, INRASTES, INN) and other Greek academic

institutions, such as the National and Kapodistrian University of Athens (Pharmaceuticals, and Chemistry Depts), the University of Patras (Biology Dept), the Aristotle University of Thessaloniki (Chemistry Dept), the University of Thessaly (Biochemistry & Biotechnology Dept) and the Agricultural University of Athens (Biotechnology Dept). Income from the provision of services is solely used to cover the operation and repair needs of the spectrophotometer.

The CD Laboratory is part of 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).

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

Personnel
Paraskevi Kitsiou, Senior Researcher (Administrative responsible)
Garyfallia Drossopoulou, Senior Researcher

Laboratory Description – Research Interests

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

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

In addition, the laboratory has been expanded in isolation and culture of stem cells emanating from olfactory mucous, in collaboration with Dr. O. Trohatou and the Biomedical Research Foundation Academy of Athens (BRFAA, Dr A. Charonis and Dr P. Politis), as well as with Dr Pedro Escada, Dr José Pratas-Vital (Hospital de Egas Moniz, Centro Hospitalar de Lisboa, Ocidental, Lisbon, Portugal), Dr. Ch. Gogo (NKUA, Attikon Hospital, B' Neurosurgical Clinic, President of the Hellenic OMA Groups). Olfactory tissue is of key importance, given that it contains neuronal tissue which regenerates quickly due to its high content in stem cells.

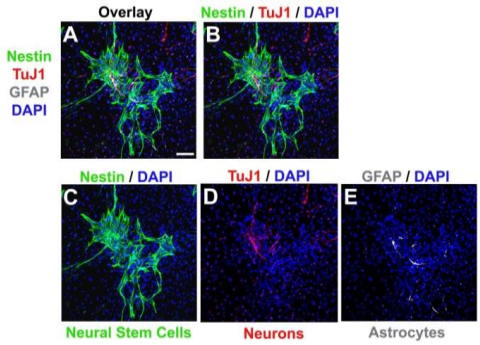


Figure: *Culture of OECs results to enriched population of neural stem cells (NSC), as it appears from the use of appropriate indicators. These cells maintain the ability of proliferation and renewal.*

Progress in 2022

During 2022, the laboratory was implicated in the isolation and culture of mesenchymal stem cells from mouse fat tissue. Characterization of the above-mentioned cells was achieved by the use of flow cytometry.

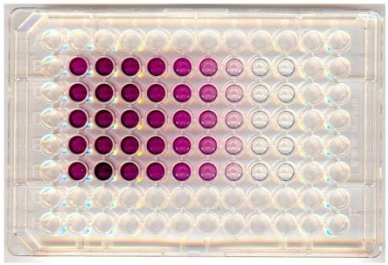
LABORATORY OF CELL-BASED ASSAY SYSTEMS AND BIOACTIVE COMPOUNDS

Personnel
Dimitris Kletsas, Research Director
Harris Pratsinis, **Senior Researcher**
Eleni Mavrogonatou, **Researcher**
Adamantia Papadopoulou, Post-doctoral Fellow

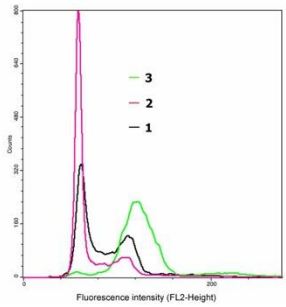
Description
The activities of the Laboratory comprise the isolation of primary somatic or mesenchymal stem cells, and the development of the appropriate cell assay systems for the evaluation of synthetic or natural bioactive products regarding their wound healing, anti-ageing, and anti-cancer properties.

2022 Findings
During 2022, the service lab continued its collaboration with the company UNI-PHARMA SA for the study of compounds with putative senolytic or senomorphic activity, as well as with the Clinic of Orthodontics and Pediatric Dentistry, Institute of Oral Biology at the Center of Dental Medicine, University of Zurich for the implementation of *in vitro* biocompatibility studies. In addition, in collaboration with the company Korres Natural Products SA, bioactivity assays of plant extracts were conducted.

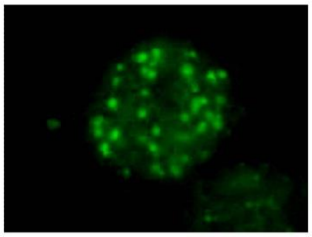
CYTOTOXICITY ASSESSMENT



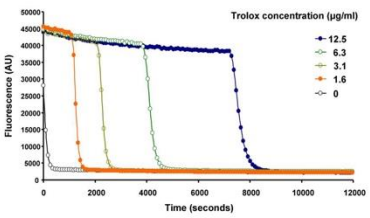
CELL-CYCLE ANALYSIS



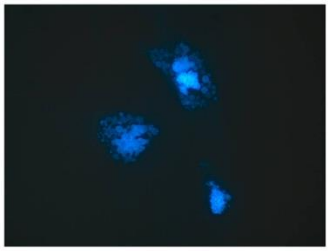
DNA DAMAGE ANALYSIS



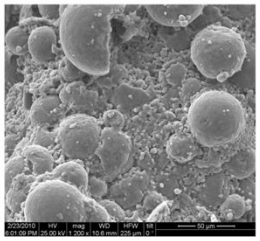
ANTIOXIDANT ACTIVITY ASSAY



STUDY OF APOPTOSIS



ORGANOTYPIC CELL CULTURES



EDUCATIONAL ACTIVITIES

EDUCATION

The Institute of Biosciences and Applications continued the successful implementation of a variety of educational programs and activities in 2022, 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 projects,
c) the organization of postgraduate level seminars,
d) the participation of IBA researchers in courses and lectures within the framework of postgraduate programs of several Greek Universities,
e) the participation of IBA researchers as instructors in the Annual Summer School of NCSR "Demokritos" for undergraduate and graduate students,
f) the organization of a summer camp with hands-on experiments for high school students and
g) 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 2022, **12** postdoctoral researchers were trained at IBA, while **20** PhD students and **21** MSc students carried out their research projects at the Institute under the supervision of IBA researchers.

In 2022, **4** students completed their PhD theses and **4** students completed their Master's theses successfully.

Moreover, **15** undergraduate students from Greek Universities performed their final year project at IBA, while **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" (***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" (**G. Voutsinas**, Department of Biology and Medical School, University of Athens)*

*Two lectures entitled "Signaling pathways involved in cell immortalization - Wnt, Hippo, p53" and "Signaling pathways evading tumor suppressor messages pRB, p53, APC, BRCA1-2, PTEN, WT1-WT2, NF1-NF2", Post-Graduate Program "Neoplastic Disease in Man" (**G. Voutsinas**, Department of Medicine, National and Kapodistrian 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" (**Z. Georgoussi**, Department of Biology, University of Athens)*

*Course lecturing entitled "Signaling of Neurotransmitter Receptors" in the framework of the postgraduate course "Athens International Master's Programme in Neurosciences" (**Z. Georgoussi**, Department of Biology, University of Athens)*

*Teaching at the postgraduation (Master) course (14 lectures) "Stress Science and Health Promotion", (**I. Sotiropoulos**, Medical School, National and Kapodistrian University of Athens)*

*Teaching at the postgraduation (Master) course (4 lectures) "Applications of Biology in Medicine", (**I. Sotiropoulos**, Department of Biology and Medical School, National and Kapodistrian University of Athens)*

*Teaching at different postgraduation (Master) courses in different Universities in Greece and abroad, e.g., Athens Neuroscience Master (Univ. of Athens), Crete Neuroscience Master (Univ. of Crete), Neuroscience & Neurodegenerative disorders (Univ. of Thessaloniki), Brain aging & pathology Master program (Univ. Coimbra, Portugal) (**I. Sotiropoulos**)*

*Lecture entitled "Cell senescence and carcinogenesis" in the framework of the postgraduate course entitled "Thoracic oncology", (**D. Kletsas**, Medical School, University of Athens)*

*Lecture entitled "Cell senescence and tissue homeostasis" in the framework of the postgraduate course "Physiology" (**D. Kletsas**, Medical School, University of Athens)*

*Lecture entitled "Cell senescence and tissue homeostasis" in the framework of the postgraduate course "Cosmetology" (**D. Kletsas,** Department of Pharmacology, University of Athens)*

*Lecture entitled "Cell senescence: Molecular mechanisms and role in tissue homeostasis" (**D. Kletsas**, Harokopio University)*

*Teaching in the framework of the postgraduate course "Applied Biomechanics and Biomaterials in Orthopaedics" (**D. Kletsas**, Medical School, University of Athens)*

*Lecture entitled "Regenerative medicine in intervertebral discs" in the framework of the postgraduate course "Stem cells and regenerative medicine" (**D. Kletsas**, School of Medicine, Aristotle University of Thessaloniki)*

*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" (**D. Kletsas, H. Pratsinis** and **E. Mavrogonatou**, Department of Biology and Medical School, 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" (**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 postgraduate programme "Application of Biology in Medicine" (**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 the Postgraduate Master's Degree "Clinical Biochemistry-Molecular diagnosis" (**A. Chroni**, Department of Biology, Chemistry and Nursing, 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" (**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" (**G. Drossopoulou**, Department of Biology, University of Athens)*

*Lecture entitled "Organization and Function of fungal plasma membrane," in the framework of the Post-Graduate Programme "Applications of Biology in Medicine" (**V. Sophianopoulou,** Medical School & Dept. Biology, University of Athens)*

*Teaching in the framework of the postgraduate program "Bioinformatics", the course "Introduction to Computational Biology" (**Y. Almirantis**, Department of Biology, University of Athens)*

*Teaching in the framework of the postgraduate program "Clinical Biochemistry-Molecular Diagnostics", the course "Introduction to Computational Biology" (**Y. Almirantis**, Departments of Biology, Chemistry and Nursing, University of Athens)*

*Lectures on "Principles of X-Ray Crystallography: Applications in Structural Biology" in the framework of the postgraduate program entitled "Clinical Biochemistry – Molecular Diagnosis" (**M. Vlassi,** Department of Biology, Chemistry & Nursing, University of Athens)*

*Lecture entitled "Protein Structure – Experimental & Theoretical approaches" in the framework of the postgraduate program "Bioinformatics-Computational Biology" (**M. Vlassi,** Department of Biology, University of Athens)*

As part of the education of postgraduate students, seminars were held by external speakers, which are presented below. There were also presentations by the postgraduate students of the Institute regarding their research progress, which are also presented in detail below.

In addition, in July 2022, as part of the "Summer School" of the NCSR "Demokritos", the Institute of Biosciences & Applications took part in a series of lectures by the Institute's scientists on modern biological topics. The participation of the scientific staff of the Institute of Biosciences & Applications in these courses is presented in detail below.

In 2022 13 more postgraduate students were enrolled in the MSc Programme **"Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products"** organized by the Department of Chemistry of the University of Patras and the Institute of Biosciences and Applications of NCSR "Demokritos". The students attended courses at the University of Patras and IBA and currently 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"* **(*G. Drossopoulou*)**
  - Lecture entitled "*Chemical ecology: Applications of bioactive secondary metabolites of natural origin"* **(*M. Konstantopoulou*)**
  - Lecture entitled *"The drug development roadmap. From bench to clinic"* **(*M. Sagnou*)**
  - Lecture entitled *"Methods for the analysis and study of proteins, lipids and carbohydrates"* **(*A. Chroni*)**
- **Advanced Biochemistry**
  - Lecture entitled *"Protein Structure – Experimental & Theoretical approaches"* **(*M. Vlassi*)**
  - Lecture entitled *"Signalling of* G protein-coupled receptors, trimeric G proteins, cAMP pathway, protein kinase A" **(*Z. Georgoussi*)**
  - Lecture entitled "*Transcription factors (CREB, CREM, NF-kB, AP-1, STAT), identification methods for transcription factors activation"* **(*G. Drossopoulou*)**
  - Lecture entitled "*Ca^{2+}signaling*" (***E. Mavrogonatou***)
  - Lecture entitled *"MAP kinases (ERK1,2, JNKs, p38)"* **(*D. Kletsas*)**
  - Lecture entitled *"Signaling pathways of main cytokines and developmental factors IL-1, TNF-α, TGF-β (SMAD proteins), PDGF, EGF, FGF"* **(*H. Pratisnis*)**
  - Lecture entitled "*Lateral compartmentalization and function of plasma membrane: eisosomes and transmembrane transporters*" (***V. Sophianopoulou*** & ***C. Gournas***)
- **Molecular Pharmacology – Immunology**
  - Lecture entitled *"Viral immunology and pharmacology focusing on SARS-Cov-2 and COVID-19"* (***L. Swevers***)

- Lecture entitled *"Enzymes, receptors and drugs"* (***A. Papakyriakou***)
- Lecture entitled *"DNA: structure, function and drug binding"* (***M. Sagnou***)
- Lecture entitled *"GPCRs in health, disease and new drugs production"* (***Z. Georgoussi***)
- Lecture entitled *"Novel therapeutic dimensions in Alzheimer's disease: etiopathology, biomarkers and new targets"* (**I. Sotiropoulos**)

- **Molecular and Cellular Biology – Molecular Biotechnology**
  - Lecture entitled *"Research and Development of tissue grafts"* **(*E. Vavouraki*)**
  - Lecture entitled *"Molecular mechanisms of carcinogenesis and pharmaceutical inhibition of selected cell targets for therapy"* **(*G. Voutsinas***)
  - Lecture entitled *"Cloning vectors"* (***C. Gournas*)**
  - Lecture entitled *"Diabetis – Diabetic nephropathy: Current therapeutic approaches"* **(*G. Drossopoulou*)**
  - Lecture entitled *"Cellular senescence as an anti-aging therapeutic target"* **(*D. Kletsas*)**
  - Lecture entitled *"Flow cytometry"* **(*E. Mavrogonatou*)**
  - Lecture entitled *"Methods for the evaluation of cytotoxicity-cytostatic activity"* **(*H. Pratsinis*)**
  - Lecture entitled "*DNA organisation, histones and chromatin function"* **(*Th. Sourlingas*)**
  - Lecture entitled *"DNA replication in prokaryotic and eukaryotic organisms"* **(V. Sophianopoulou)**
  - Lecture entitled *"Baculovirus expression system"* **(*B. Labropoulou*)**
  - Lecture entitled *"Cardiavascular diseases and current therapeutic approaches"* **(*A. Chroni*)**

COMPLETION OF MASTER THESES IN 2022

POSTGRADUATE STUDENT	TITLE OF MSc THESIS	IBA SUPERVISOR	UNIVERSITY
Karanikou Maria	*Applications of vesicles of plant-derived material to human cells: cytotoxicity and cell proliferation studies*	H. Pratsinis	Dept. of Mechanical Engineering, Univ. of Western Macedonia
Louka Konstantina	*Role of oxidative stress in high osmolarity-induced upregulation of CLCA2 channel in intervertebral disc cells*	D. Kletsas / E. Mavrogonatou	Dept. Biology, University of Athens
Micha Asimina	*Relationship of apolipoprotein E4 and brain lipid transport with Alzheimer's disease*	A. Chroni	Dept. Biology, University of Athens
Michailidis Periklis	*Crosstalk of stress response pathways after respiratory chain complex I inhibition in cancer cells*	G. Voutsinas	Dept. Biology, University of Athens

COMPLETION/AWARD OF DOCTORAL THESES IN 2022

PhD STUDENT	TITLE OF DOCTORAL THESIS	IBA SUPERVISOR	UNIVERSITY
Adamopoulou Maria	*Genetic engineering of intervertebral disc cells using CRISPR-Cas9*	D. Kletsas	Biotech Research & Innovation Centre, Faculty of Health and Medical Sciences, Copenhagen Univ.
Mountaki Christina	*The role of apolipoprotein E in the pathogenesis of Alzheimer's disease: effect of naturally occurring molecules on apoE structure and function*	A. Chroni	Dept. Chemistry, University of Athens
Biratsi Ada	*Study of the genes responsible for the detoxification of L-azetidine-2-carboxylic acid and its catabolism in Aspergillus nidulans*	V. Sophianopoulou	Dept. Biology, University of Athens
Pallaki Paschalina	*Alternative pathways of opioid receptor signaling involved in gene expression during neurogenesis*	Z. Georgoussi	Dept. Biology, University of Athens

IBA LECTURES' CONTRIBUTION TO THE 2022 SUMMER SCHOOL

DATE	SPEAKER	TITLE
15/7/2022	**Dr. L. Swevers**	piRNAs in the regulation of stem cell function and the silencing of transposable elements (transposons)
15/7/2022	**Dr. A. Prombona**	Biological clock and Cancer
15/7/2022	**Dr. E. Mavrogonatou**	Cell biology of inetervertebral disc degeneration and ageing
15/7/2022	**Dr. H. Pratsinis**	In vitro studies of natural and synthetic bioactive products
15/7/2022	**Dr. C. Gournas**	Exploring plasma membrane compartmentalization to develop a new generation of antifungal drugs targeting non-growing pathogenic fungi
15/7/2022	**Dr. Z. Georgoussi**	Opioid receptor cell signaling: targeting novel opioids
15/7/2022	**Dr. I. Sotiropoulos**	Chronic stress and exosomes in Alzheimer's disease

2022 INVITED SPEAKERS SEMINARS

DATE	SPEAKER	TITLE
13/1/2022	**Prof. Patricia ROUSSELLE** CNRS, Lyon, France	Cell / microenvironment cross talk and tissue repair
20/1/2022	**Dr. Maria dM. Vivanco** CIC bioGUNE, Spain	Breast cancer heterogeneity and resistance to therapy
27/1/2022	**Prof. Maurizio Onisto** Dept. of Biomedical Sciences University of Padova, Italy	Heparanase in Extracellular Matrix (ECM) remodeling during tumor progression and fibrosis
3/2/2022	**Prof. Liliana Schaefer** Institute of Pharmacology, Goethe University, Frankfurt/Main, Germany	Interplay of biglycan with its receptors in inflammation and autophagy
10/2/2022	**Prof. Alberto Passi** University of Insubria, Department of medicine and Surgery, Italy	When simplicity meets complexity: the biology of hyaluronan

COLLECTIVE DATA

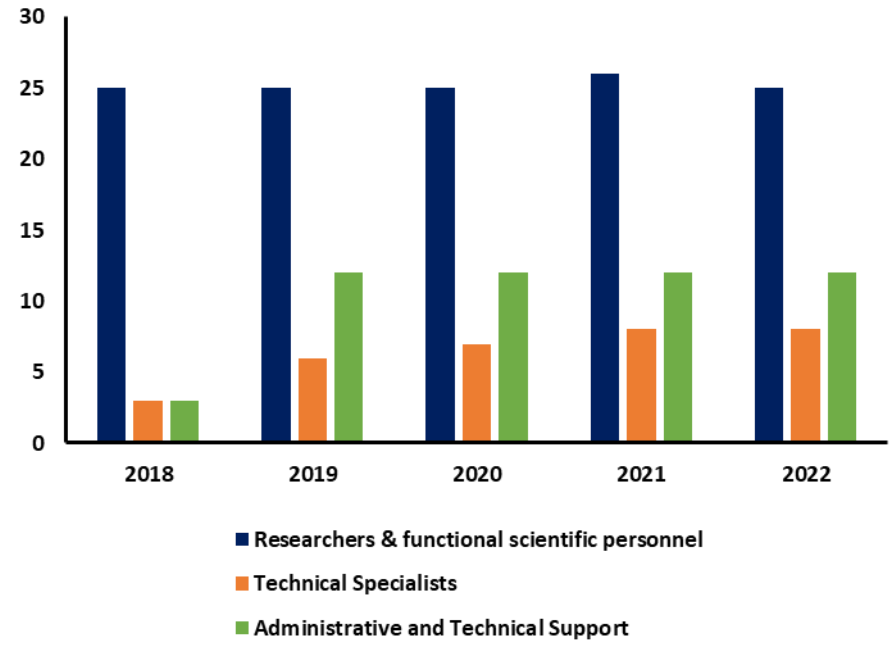
SUMMARIZED DATA ON THE PRODUCTIVITY OF SCIENTIFIC PROGRAMMES

	PROGRAMME			
	A	**B**	**C**	**INSTITUTE**
Researchers & functional scientific personnel	11	7	6	25[a]
Technical Specialists	1	1	-	8[b]
Collaborating & Emeritus Scientists	3	1	0	6[c]
Postdoctoral Fellows	8	2	1	12[d]
PhD candidates	12	6	2	20
MSc students	16	3	2	21
Graduate Research Associates	6	5	2	16[e]
Undergraduate and other training students	18	7	1	26
Administrative and Technical Support	-	-	-	12
Total Personnel	**75**	**32**	**14**	**146**
Publications in Peer-Reviewed Journals	**26**	**14**	**24**	**66[f]**
Cumulative Impact Factor in Peer-Reviewed Journals	**220.098**	**80.186**	**141.357**	**449.141[f]**
Proceedings in Conferences	**8**	**-**	**3**	**11**
Total Publications				**77**
Citations	**2241**	**779**	**728**	**4191[g]**
International Patents	**-**	**-**	**-**	
Greek Patents	**-**	**-**	**-**	
Presentations in International Conferences	**18**	**5**	**9**	**32**
Presentations in International Conferences	**12**	**7**	**2**	**21**
Total Number of Presentations in Conferences	**30**	**12**	**11**	**56[h]**

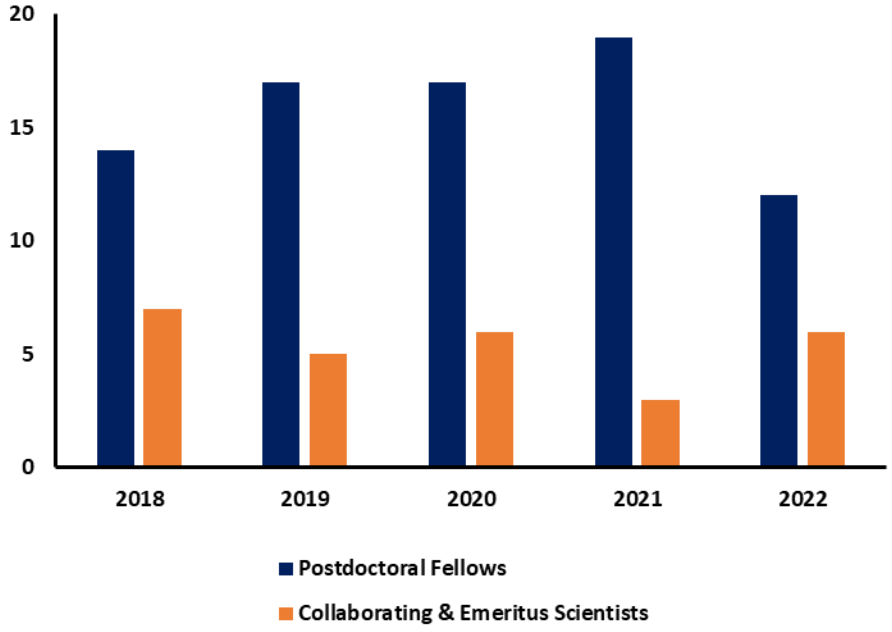
[a] 1 Scientist of the Human Tissue Bank included
[b] 4 Technical Specialists of the Laboratory for Doping Control and Metabolic Studies and 2 Technical Specialists of the National Infrastructure OPENSCREEN-GR included
[c] 2 Collaborating Scientists of the Human Tissue Bank included
[d] 1 Postdoctoral Fellow of the Human Tissue Bank included
[e] 3 Graduate Research Associates of the Human Tissue Bank included
[f] 2 Publications of the Laboratory for Doping Control and Metabolic Studies included
[g] Citations of the the Laboratory for Doping Control and Metabolic Studies and the Human Tissue Bank included
[h] 3 Participations of the Human Tissue Bank in Greek Conferences included

CHANGES IN IBA STAFF DURING 2018-2022

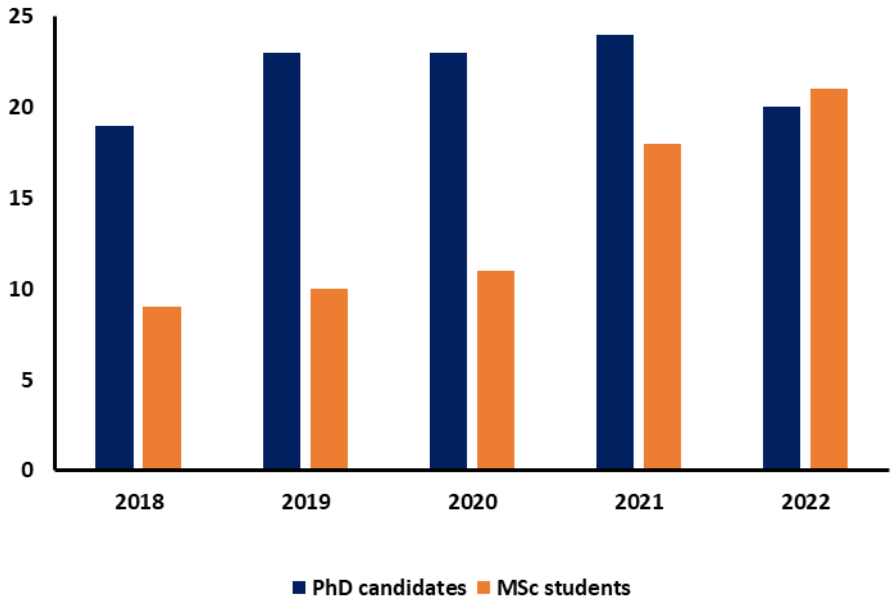
Tenured Staff



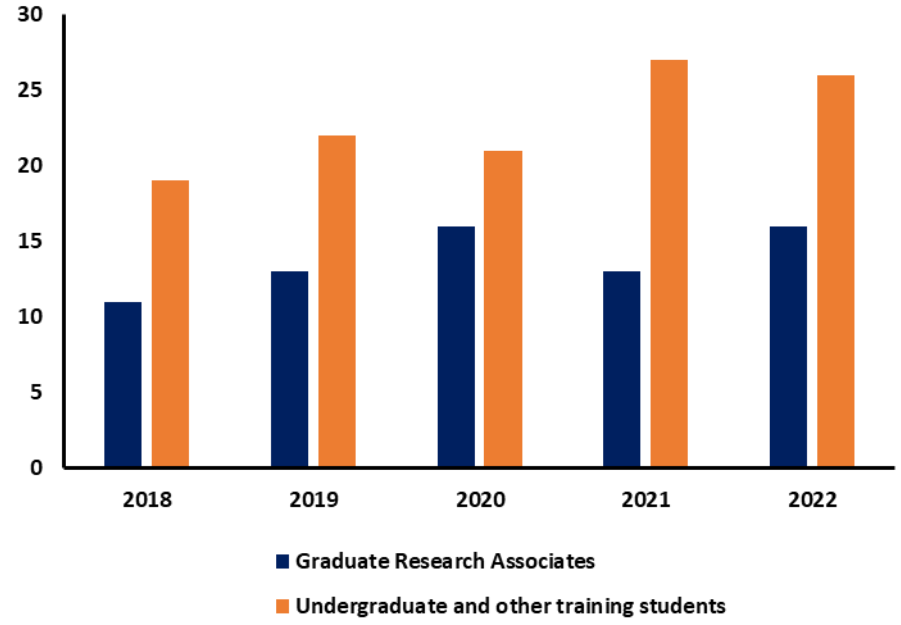
Postdoctoral fellows/ Emeritus & Collaborating Scientists



PhD candidates / MSc students

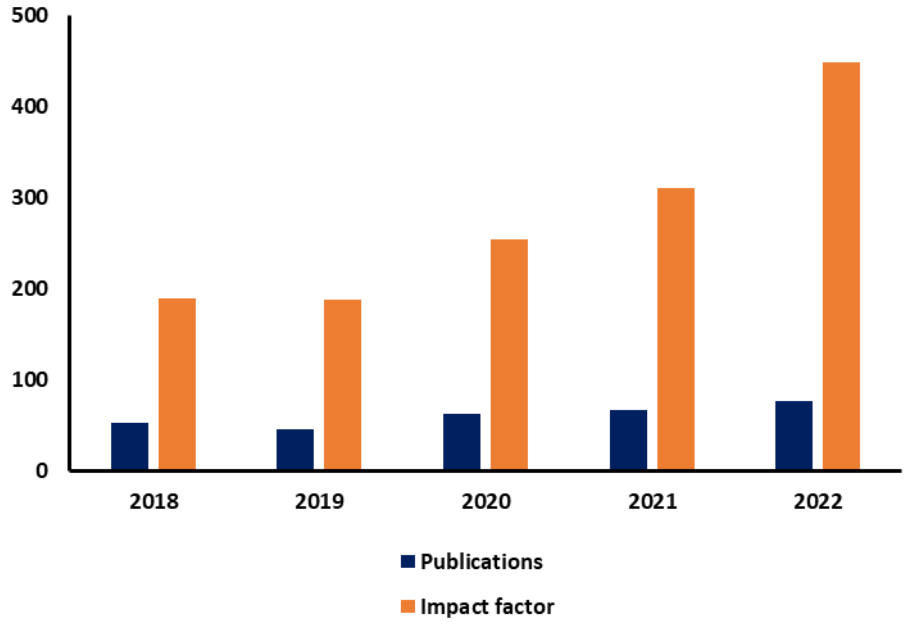


Undergratuate & other training students



QUALITATIVE AND QUANTITATIVE DATA ON IBA PUBLICATIONS DURING 2018-2022

Publications in peer-reviewed Journals / Cumulative impact factor



Citations