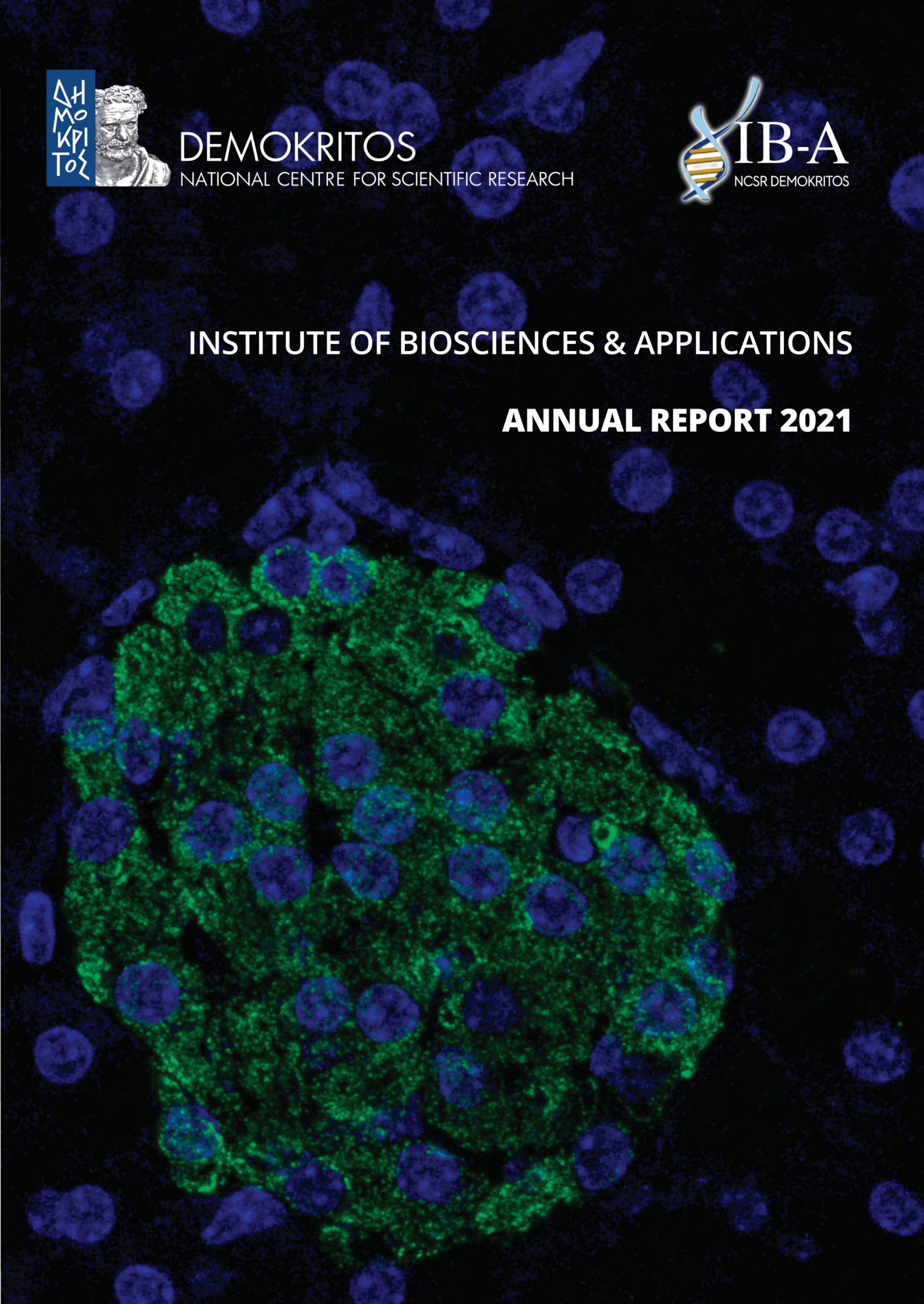
DEMOKRITOS
NATIONAL CENTRE FOR SCIENTIFIC RESEARCH

IB-A
NCSR DEMOKRITOS

INSTITUTE OF BIOSCIENCES & APPLICATIONS

ANNUAL REPORT 2021



NATIONAL CENTRE FOR SCIENTIFIC RESEARCH

"DEMOKRITOS"

INSTITUTE OF BIOSCIENCES & APPLICATIONS

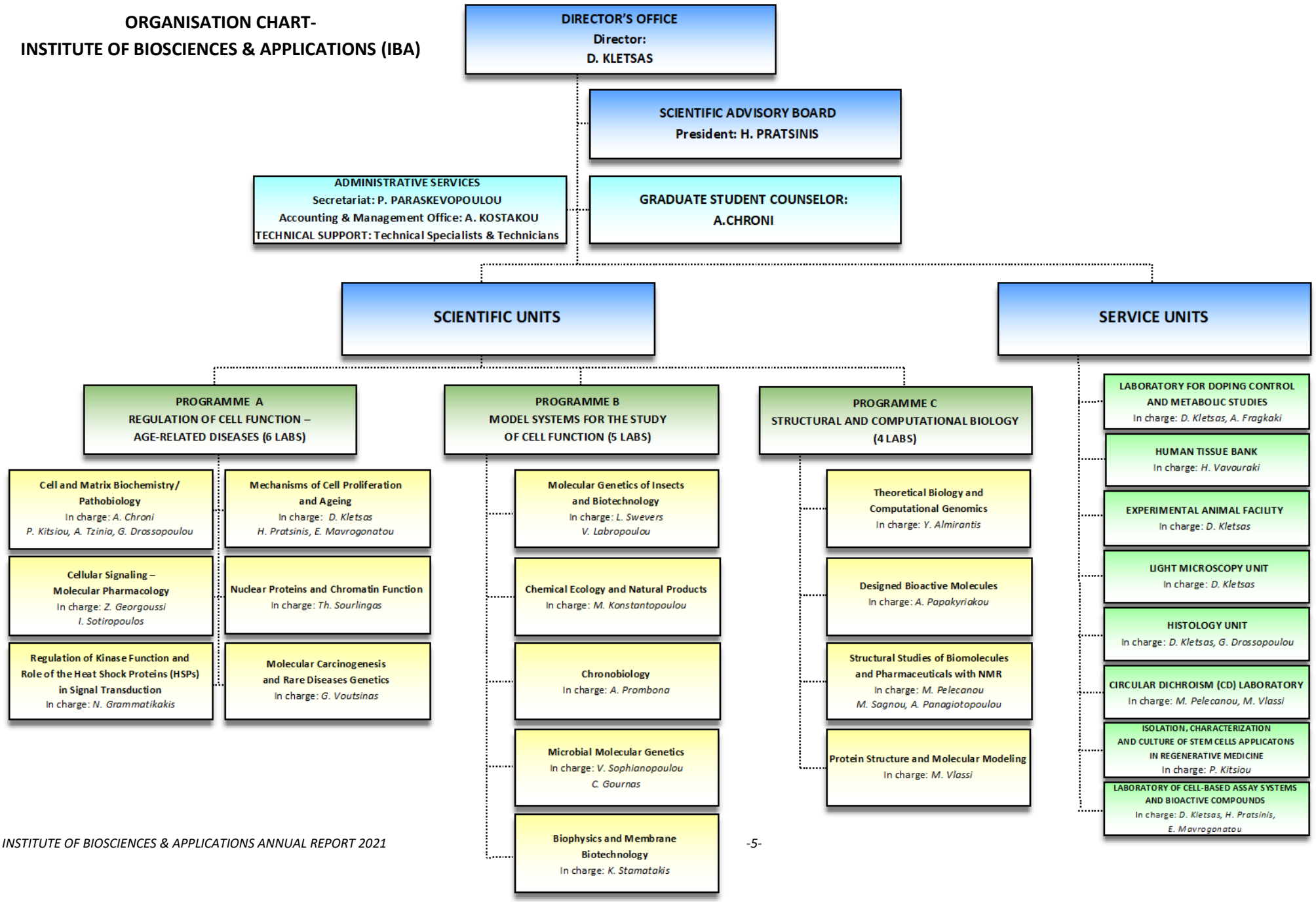
ANNUAL REPORT 2021

AGIA PARASKEVI

OCTOBER 2022

TABLE OF CONTENTS

ORGANISATION CHART-
INSTITUTE OF BIOSCIENCES & APPLICATIONS (IBA)



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
Tzinia Athina	Dr. Biochemist
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 Nassia	Dr. Pharmacist
Kiousi Polyxeni	Dr. Chemist
Stefanou Dimitra	Agronomist

Soukou Foteini	Dr. Biologist
Yiannakas Nikolaos	Biologist

ADMINISTRATIVE & TECHNICAL SUPPORT

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

POSTDOCTORAL FELLOWS

Fellow	**IBA Researcher**
Christoforidis Christoforos	Kletsas D.
Dioli Chrysoula	Sotiropoulos I.
Galeou Angeliki	Prombona A.
Gkolfinopoulou Christina	Chroni A.
Halevas Eleftherios	Sagnou M.
Kaminari Archontia	Tzinia A.
Kaplanis Michalis	Pelecanou M.
Karamanou Konstantina	Kletsas D.
Karanikou Maria	Chroni A.
Kolliopoulou Anna	Swevers L.
Kontogiannatos Dimitrios	Swevers L.
Kouroumalis Anastasios	Kletsas D.
Koutsoumpeli Eleni	Konstantopoulou M.
Kythreoti Georgia	Iatrou K.
Matiadis Dimitris	Pelecanou M.
Mavroidi Barbara	Pelecanou M.
Mpakali Anastasia	Papakyriakou A.
Ninios Ioannis	Vavouraki E.
Papadopoulou Adamantia	Kletsas D.

GRADUATE RESEARCH ASSOCIATES

Research Associate	IBA Researcher
Betsi Petri-Christina (MSc)	Konstantopoulou M.
Dasenaki Ioanna (MSc)	Konstantopoulou M.
Goula Olga	Kletsas D.
Klamarias Lykourgos (Veterinarian)	Kletsas D.
Kosmidis Eleutherios	Vavouraki H.
Kryoni Lyda	Chroni A.
Makrigianni Amalia (MSc)	Kletsas D.
Michailidis Periklis	Voutsinas G.
Panagopoulou Lydia (MSc)	Vavouraki H.
Pantiora Panagiota	Pelecanou M.
Paraskevopoulou Katerina	Kletsas D.
Raptopoulos Dimitris (PhD)	Konstantopoulou M.
Sakellariou Panagiotis (PhD)	Kletsas D.
Smyrniotis Stefanos	Voutsinas G.
Valanti Effie	Chroni A.

PhD CANDIDATES AND MSc STUDENTS

PhD candidate (University)	Supervisor in IBA
Adamopoulou Maria (Univ. of Copenhagen, Denmark)	Kletsas D.
Angelopoulou Maria (NKUA)	Kletsas D.
Athanasoulis Alexandros (NKUA)	Papakyriakou A.
Biratsi Alda (NKUA)	Sophianopoulou V.
Broussos Panayiotis (AUA)	Stamatakis K.
Chiniadis Lykourgos (AUA)	Papakyriakou A.
Dedemadi Anastasia-Georgia (NKUA)	Chroni A.
Farmaki Danae (NKUA)	Prombona A.
Fotopoulou Asimina (Univ. of Patras)	Kletsas D.
Karoussiotis Christos (NKUA)	Georgoussi Z.
Krespa Jenny (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)	Chroni A.
Pallaki Paschalina (NKUA)	Georgoussi Z.
Papagiannis Achilleas (AUTH)	Chroni A.
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	Sagnou M.
Dimozi Maria (NKUA)	Kletsas D.
Gerontidi Dimitra	Sotiropoulos I.
Gerostathis Spyros (Univ. of Patras)	Sophianopoulou V.

Giakoumidaki-Vogiatzi Aikaterini (AUA)	Stamatakis K.
Kaplani Eleni (NKUA)	Kletsas D.
Kelemeni Marina – Gemma (Univ. of Patras)	Kletsas D.
Kypraiou Anastasia (Univ. of Patras)	Kletsas D.
Louka Konstantina	Konstantopoulou M.
Manassakis George	Konstantopoulou M.
Micha Asimina	Chroni A.
Ntinou Nikolina	Sotiropoulos I.
Papadimitriou Georgia-Zeta	Sotiropoulos I.
Stefanatou Chrysanthi	Prombona A.
Tsistraki Katerina	Sotiropoulos I.
Tsoukas Evangelos	Papakyriakou A.
Tzouanou Foteini	Georgoussi Z.
Valianatos Alexandros (NKUA)–*Dissertation completed*	Sophianopoulou V.

UNDERGRATUATE & OTHER TRAINING STUDENTS

Student (University)	**Supervisor in IBA**
Argyriou Minas (AUA)	Georgoussi Z.
Athanasouli Anna– *Dissertation completed*	Voutsinas G.
Bodi Labrina – *Dissertation completed*	Voutsinas G.
Fourmouzi Aikaterini-Maria	Sotiropoulos I.
Gaitanos Spiros (NKUA)	Sophianopoulou V.
Gerodimou Ioanna	Prombona A.
Ifanti Georgia-Despina (NKUA)	Gournas C.
Kechagia Soultana	Papakyriakou A.
Kostaloupi Elina	Pelecanou M.
Kyriakopoulou Christina (NKUA)	Georgoussi Z.
Landini Luca	Papakyriakou A.
Maraidonis Ioannis-Nektarios (NKUA)	Labroboulou V.
Oikonomou Chrysanthi-Andriani	Mavrogonatou E.
Panagopoulou Konstantina	Voutsinas G.
Papanagnou Dimitris (Univ. of Crete)	Georgoussi Z.
Pateli Amalia – *Dissertation completed*	Voutsinas G.
Perpiniadis Vasilis	Gournas C.
Prifti Izabela	Swevers L.
Simitsopoulou Despina	Prombona A.
Siountri Maria-Angeliki	Papakyriakou A.
Sourliotis George	Swevers L.
Theodorou Iliana	Sotiropoulos I.
Trazani Georgia (NKUA)	Georgoussi Z.
Tsakogias Iraklis (NKUA)	Georgoussi Z.
Tsigaras Marios	Prombona A.
Tsinidi Marialina	Mavrogonatou E.
Zakopoulou Tatiana (NKUA)	Sophianopoulou V.
Zerva Maritina	Georgoussi Z.

INTRODUCTION

The Institute of Biosciences and Applications (IBA) is one of the five Institutes of the National Centre for Scientific Research (NCSR) "Demokritos". The Centre, among the best in Greece and in Europe, is characterized by multidisciplinarity and the unique coexistence of different fields of science, as well as the collaboration among scientists of different disciplines, towards the promotion of science and innovation. Within this framework, the IBA focuses its research and developmental activities in various areas of life sciences and especially in the study of cellular function, with an emphasis on age-related diseases, on biotechnology and the environment, as well as on structural and computational biology. In addition, the Institute houses a considerable number of laboratories, some of them unique in Greece, providing advanced technological research services to the Public and the Private Sector.

Within 2021, despite the covid-19 pandemic, there was a significant upgrading of Institute's research and developmental work, as shown by the significant increase of the number and the quality of IBA researchers' publications. For this achievement I want to congratulate the researchers and the whole personnel of the Institute. I want to thank the Vice Director G. Voutsinas and the members of the Scientific Council of the IBA H. Pratsinis (President), M. Konstantopoulou, V. Labropoulou, A. Tzinia, 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.

The implementation of important programs for the function and upgrading of the infrastructure of the IBA continued within 2021. A special reference is needed to those colleagues who worked, in collaboration with all the members of the Institute (researchers, technical and administrative staff), for the implementation of these projects, namely SANITURA (Drs. V. Labropoulou and H. Pratsinis), OPENSCREEN-GR (Drs. K. Iatrou, A. Chroni, Z. Georgoussi, and H. Pratsinis), BIOIMAGING-GR (Drs. V. Labropoulou, H. Pratsinis, and M. Sagnou) and INSPIRED (Drs. A. Chroni, A. Panagiotopoulou, M. Pelecanou and M. Vlassi). The elaboration of the emblematic action "Creation of the National Network on the Value of Honey" and of the programme OPENSCREEN-DRIVE has also continued. The successful implementation of these projects, as well as of all the competitive grants the members of the IBA have attracted, increased significantly the number of young researchers, renewed the infrastructures and supported considerably the scientific and developmental effort of the Institute.

The upgrading of the Laboratory for Doping Control and Metabolic Studies continued, with the efforts of A. Fragaki (Scientific Director) and the scientific, technical and administrative personnel, aiming at the acquisition of the status of "Candidate Lab" from WADA. In this direction, the Lab has been financially supported by a Memorandum signed by the Deputy Minister of Sports and the Deputy Minister of Development, and upgraded its analytical infrastructure and attracted new scientific personnel.

Unfortunately, within 2021 we experienced the loss of three distinguished colleagues that played an important role in the development of the Institute, those of M. Argyraki-Vomvogianni, T. Kotsopoulou and G. Zervas. We will remember them with respect and affection.

During 2021, 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". In addition, in collaboration with the European Learning Laboratory for the Life Sciences of the European Molecular Biology Laboratory (EMBL) and the European Scientific Research Infrastructures network EU-OPENSREEN, a training course for secondary school biology teachers was organized with great success. Finally, the researchers of the IBA participated in the Summer School of NCSR "Demokritos", as well as in a number of activities for the dissemination of science to the general public. Congratulations to all colleagues participating in these activities.

Finally, I want to thank the IBA Administrative & Financial Officer Mrs. A. Kostakou and the Secretaries Mrs. M. Filippidou, Mrs. P. Paraskevopoulou and Mrs. M. Vlachou for their significant contribution to the orderly function of the Institute.

Dimitris Kletsas, PhD
IBA Director
October 2022

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 Student
Christos Karoussiotis, PhD student
Alexandra Symeonof, PhD student
Anastasia Vamvaka-Iakovou, PhD student
Anastasia Megalokonomou, PhD student
Tzeni Krespa, PhD student (έως 10/21)
Foteini Tzouanou, Master student
Nikolina Ntinou, Master student
Zeta-Georgia Papadimitriou, Master student
Dimitra Gerontidi, Master student
Aikaterini Tsirtsaki, Master student
Georgia Tsazani, Undergraduate student
Minas Argyrou, Undergraduate student
Dimitris Papanagnou, Undergraduate student
Maritina Zerva, Undergraduate student
Iraklis Tsakogias, Undergraduate student
Christina Kyriakopoulou, Undergraduate student
Aikaterini Fourmouzi, Undergraduate student
Iliana Theodorou, 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) signalling 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 signalling 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 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 2021

Alternative signal transduction pathways induced upon opioid receptor activation:

Autophagy: an unexplored mechanism of the opioid receptor function: Given that the dynorphin /κ-opioid receptor (κ-OR) system plays key role in modulating anxiety and stress related behaviors and that κ-OR antagonists are considered as important pharmacological targets for depressive disorders and anxiety-like behaviors we identified that specific κ-OR analogs induce the autophagic machinery. Our studies propose a novel signalling pathway involving Gαi/o proteins, ERK1,2 and the p-CREB which regulates the transcription of autophagic genes, leading to significant decreases of the synaptic proteins spinophilin, PSD-95 and SNAP-25 in hippocampus upon κ-OR activation (Figure 1A). Parallel studies have shown that spinophilin, is found in the autophagosomes and modulates κ-OR signalling by directly interacting with the receptor. Finally, we detected that in isolated synaptosomes from RGS4-/- mice specific autophagic markers are significantly reduced, with a concomitant decrease of spinophilin and other synaptosomal protein levels.

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

In the context of Dr Georgoussi's participation in the EU consortium «NORMOLIFE NETWORK» (collaboration with University of Catania), our group characterized using specific cell-based assays the pharmacological profile of new bioactive compounds. These compounds exert functional selectivity towards a specific opioid receptor pathway (biased agonism), thus providing new dimensions for the use of δ-opioid receptor analogs for pain management.

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.

Daylife Stress and its role in the pathophysiology of Alzheimer's disease: Although Dr Sotiropoulos joined the Institute in March 2021, his team includes 1 postdoctoral researcher, 2 PhD students and 5 postgraduate students while he published his research work in 7 scientific articles in high-impact scientific journals describing novel neuronal pathways through which chronic stress triggers the accumulation of Aβ and the formation of pathological forms of Tau protein, the two main molecules hallmarks of Alzheimer's disease brain (Figure 1B). In addition, Dr. Sotiropoulos has published (editor and author), a multidisciplinary book on Alzheimer's disease for the general public ("When Logic Chases Memory", University Crete Press). At the same time, he participated in public awareness events on Alzheimer's disease throughout the country. He also received the Alzheimer's International Best Mentor Award in Neurosciences 2021. Finally, he has been able to establish key collaborations with research laboratories in Greece that extend the analytical and technical capabilities of his team (e.g. Fleming Institute, Institute of Molecular Biology) and abroad (School of Medicine, Univ. Minho, Portugal – Columbia University, USA).

Figure 1A

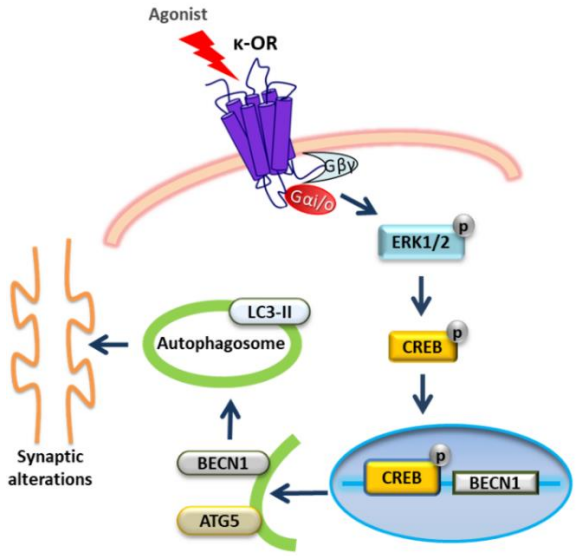


Figure 1B

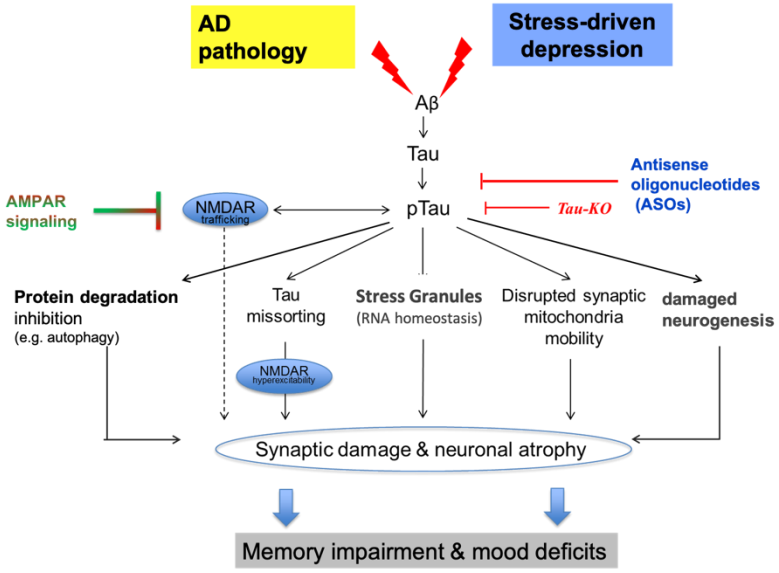


Figure 1A: *Schematic representation of a putative signalling pathway through which activation of the κ-opioid receptor with selective agonists induces the autophagic machinery and leads to synaptic alterations in hippocampal neurons under stress conditions.* ***Figure 1B.*** *Clinical and experimental studies suggest that chronic stress is a risk factor for Alzheimer's disease (AD), while depression, a stress-related disorder, appears to predispose to AD. Our research findings support chronic stress as a connecting parameter between the two diseases highlighting common neurobiological mechanisms such as accumulation of pathological Tau and inhibition/inhibition of several important neuronal cell mechanisms e.g. protein degradation mechanisms (autophagy), damaged neurogenesis, loss of synapses/communication between neuronal cells in the brain. In parallel, our studies focus on different therapeutic targets & tools, such as antinomic oligonucleotides (ASOs).*

Publications

Pasquinucci L., Parenti C., Georgoussi Z., Reina L., Tomarchio E. and Turnaturi R. (2021) *"LP1 and LP2: Dual-Target MOPr/DOPr Ligands as Drug Candidates for Persistent Pain Relief"*. Molecules 26, 4168. https://doi.org/10.3390/molecules26144168 (IF:4.411)

Dioli C., Patrício P, Pinto LG, Marie C, Morais M, Vyas S, Bessa JM, Pinto L, Sotiropoulos I* (2021) Adult neurogenic process in the subventricular zone-olfactory bulb system is regulated by Tau protein under prolonged stress. Cell Prolif. 54(7):e13027. Doi: 10.1111/cpr.13027 (IF= 8.75)

Zhuravleva V, Vaz-Silva J, Zhu M, Gomes P, Silva JM, Sousa N, Sotiropoulos I, Waites CL. (2021) Rab35 and glucocorticoids regulate APP and BACE1 trafficking to modulate Aβ production. Cell Death Dis. 12(12):1137. Doi: 10.1038/s41419-021-04433-w. (IF= 9.7)

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. (2021) Suppression of adult cytogenesis in the rat brain leads to sex-differentiated disruption of the HPA axis activity. Cell Prolif. 2021 Dec 30:e13165. Doi: 10.1111/cpr.13165. Online ahead of print. IF= (8.75)

Moosecker S, Pissioti A, Leidmaa E, Harb MR, Dioli C, Gassen NC, Yu S, Gazea M, Catania C, Anderzhanova E, Patchev AV, Kühne C, Stoffel R, Sotiropoulos I, Almeida OFX. (2021) Brain Expression, Physiological Regulation and Role in Motivation and Associative Learning of Peroxisome Proliferator-activated Receptor γ. Neuroscience. 479:91-106. Doi: 10.1016/j.neuroscience.2021.10.029. Epub 2021 Nov 8. IF= (3.7)

Amalric M, Pattij T, Sotiropoulos I, Silva JM, Sousa N, Ztaou S, Chiamulera C, Wahlberg LU, Emerich DF, Paolone G. (2021) Where Dopaminergic and Cholinergic Systems Interact: A Gateway for Tuning Neurodegenerative Disorders. Front Behav Neurosci. 15:661973. Doi: 10.3389/fnbeh.2021.661973. (IF= 3.6)

Monteiro F*†, Sotiropoulos I*†, Carvalho O, Sousa N and Silva FS. (2021) Multi-mechanical waves against Alzheimer's disease pathology: a systematic review. Transla Neurodegeneration 10(1):36. Doi: 10.1186/s40035-021-00256-z. (IF= 9.88)

Sotiropoulos I*, Trejo JL. (2021) Brain metaplasticity. Neuroscience 454 :1-2. Doi : 10.1016/j.neuroscience.2020.12.011. (IF= 3.7)

Articles in Press

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 *in press doi*: 10.1002/trc2.12249 (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 accepted. (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 *in press.* (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. Doi: 10.3389/fonc.2022.856210. eCollection 2022 (IF = 5.73)

Articles (published or in press) in scientific conferences or books

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 in Synaptic Alterations"*. *FASEB Journal* 34, S1, https://doi.org/10.1096/fasebj.2020.34.s1.02897

Sotiropoulos I, Papanikolopoulou K, Alexopoulos C. Skoulakis E. *"Why do I forget? Pathological features in Alzheimer's disease brain*" in the book entitled << Όταν η λογική κυνηγάει την μνήμη -¨When reasoning chases memory. The multidimensional threat of Alzheimer's disease in the 21st-century (in Greek) published by Crete University Press (2021);

Sotiropoulos I, Krokida St, Kokras N. "*Chronic stress, depression and Alzheimer's disease: the triangle of oblivion"* in the book entitled << Όταν η λογική κυνηγάει την μνήμη -¨When reasoning chases memory. The multidimensional threat of Alzheimer's disease in the 21st-century (in Greek) published by Crete University Press (2021);

Gravanis A, Charalampopoulos I, Machairaki V, Alexopoulos C, Tsarbopoulos A, Kapogiannis D, Sotiropoulos I. "*Nobel perspectives in the understanding and treatment of Alzheimer's disease*" in the book entitled << Όταν η λογική κυνηγάει την μνήμη -¨When reasoning chases memory. The multidimensional threat of Alzheimer's disease in the 21st-century (in Greek) published by Crete University Press (2021);

Sotiropoulos I, Lyketsos K, Machairaki V. *"Precision Medicine in Alzheimer's disease"* in the book entitled << Όταν η λογική κυνηγάει την μνήμη -¨When reasoning chases memory. The multidimensional threat of Alzheimer's disease in the 21st-century (in Greek) published by Crete University Press (2021)

Sotiropoulos I, Dalla C, Politis A, Lyketsos K. *"A novel global strategy against Alzheimer's disease?"* in the book entitled << Όταν η λογική κυνηγάει την μνήμη -¨When reasoning chases memory. The multidimensional threat of Alzheimer's disease in the 21st-century (in Greek) published by Crete University Press (2021)

Editing in books

Όταν η λογική κυνηγάει την μνήμη -¨When reasoning chases memory. The multidimensional threat of Alzheimer's disease in the 21st-century (in Greek) published by Crete University Press (2021); Editors: Ioannis Sotiropoulos & Christina Dalla.

International Conference Participation

Georgoussi Z., Karoussiotis C Sotiriou A., Papavranoussi-Daponte D., Polissidis A.V., Nikoletopoulou V. (2021). "The role of κ-opioid-induced autophagy in synaptic alterations" 5th General Meeting of the European Research Network on Signal Transduction. Bridging Perspectives and Neworking in Signal Transduction, Bari, Italy, October 2021 (invited speaker).

Christos Karoussiotis, Aggeliki Sotiriou, Alexia-Victoria Polissidis, Danae Papavranoussi-Daponte, Alexandra Symeonof, Vassiliki Nikoletopoulou and Zafiroula Georgoussi, "The role of κ-opioid receptor-induced autophagy in synaptic alterations" 1st International i-GPCRnet Meeting, Online Symposium, November 2021. (Oral presentation).

Ioannis Sotiropoulos (2021). Exosome secretion of Tau: a potential biomarker in Stress and Alzheimer's disease pathologies. Portuguese Society for Neuroscience 2021, 1-3 Dec, Coimbra, Portugal ((invited speaker).

Ioannis Sotiropoulos (2021). A novel method of spontaneously-released extracellular vesicles isolation from mouse and human brain, 3rd EuroTau conference, 14-16 October, Lille, France

National conference participation

Ioannis Sotiropoulos (2021) "Εξωσώματα και Χρόνιο στρες: κομβικοί παράγοντες στην εξέλιξη και διάγνωση της νόσου Αλτσχάιμερ» 2nd conference Εγκέφαλος & Νους, Νοv 2021 Athens, Greece

Ioannis Sotiropoulos (2021) Chronic Stress & Exosomes: key players in progression and diagnosis of Alzheimer's disease – 71o conference Hellenic Society of Molecular Biology & Biochemistry, Athens, Greece

Other Scientific Activities

Participitaion in national and international scientific councils & oprganizations

Z. Georgoussi

National Representative, Intergovernmental Framework for European Cooperation in Science and Technology, COST-action- CA18133 entitled "*European Research Network on Signal Transduction (ERNEST*)".
Alternate Member of the Research Ethics Committee of the NCSR "Demokritos"
Alternate 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».
Co-coordinator of the Syllabus "Cellular and Molecular Neuroscience of the «Athens International Master's Programme in Neurosciences».
Member of the evaluation committee for the MSc Students of the «Athens International Master's Programme in Neurosciences».
Member of the Research Consortium «*Normolife Network*" responsible for the identification of novel opioid compounds to alleviate pain.
Alternate Member of the evaluation Committee for the recruitment of the Associate Professorship position, Department of Biochemistry, University of Thessaly and Patras.
Member of the Evaluation Report Committee for the recruitment of Researcher of the Institute Pasteur

I. Sotiropoulos

Core members of the Hellenic Initiative against Alzheimer's Disease (HIAAD)
Member of the scientific broard 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 in Special Issue "Brain Metaplasticity" of scientific journal "Neuroscience IBRO-Official Journal"

Guest Editor in Special Issue “Molecular and cellular mechanisms of Tauopathy” of scientific journal “Neuroscience IBRO-Official Journal”
Review Editor of the scientific journal “Frontiers in Neuroscience”.

Organization of scientific conferences

I. Sotiropoulos

Member of the Organizing committee of “International Society of Molecular Neurodegeneration – ISMN 2022”, Divani Acropolis, 10-13 October 2022, Athens, Greece https://www.ismnd2022.com

Participation in evaluation/reviewing committees of scientific proposals

Z. Georgoussi

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

I. Sotiropoulos

Reviewer of scientific proposals of “AAIC – Alzheimer Association International” and “France Alzheimer”

Publication Reviewing activity

Z. Georgoussi

Reviewer at scientific journals: Journal of Neurochemistry, Journal of Pharmacology and Experimental Therapeutics, Cellular Signalling, Neuropharmacology, Journal of Neuroscience, BioMed Cell Biology, BioMed Research International, Journal of Biological Chemistry, Letters in Drug Design & Discovery, Current Drug Discovery Technologies, CNS Neuroscience & Therapeutics, Neurochemisty, Nature Neuroscience, Frontiers in Neurosciences, Frontiers in Pharmacology.

I. Sotiropoulos

Reviewer at different scientific journals: e.g. 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.

Others activities (besides participation in scientific conferences/meetings)

I. Sotiropoulos

Talks for the general audience about the therapeutic efforts and trials as well as the societal impact of Alzheimer’s disease:
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

Prizes and Awards

I. Sotiropoulos

Alzheimer International Best Mentor Award in Neurosciences 2021

Teaching and Educational activities

inside IBE:

I. Sotiropoulos

Speaker at «56^{o} Summer School» of NCSR Demokritos 2021

Outside IBE:

Z. Georgoussi

Member of the Educational Committee of the International Masters course in Neurosciences entitled "*Athens International Master's Programme for Neurosciences*" together with the Kapodistrian University of Athens, the NHRF, BRFAA, the Institutes Pasteur, and the Fleming Institute.

Co-corganizer of the course «*Cellular and Molecular Neurosciences»* of the Athens International Master's Programme in Neurosciences.

Alternate Member of the Research Ethics Committee of the NCSR "Demokritos"

Supervisor of the PhD dissertations of the Graduate students: Paschalina Pallaki, Christos Karoussiotis, Jenny Crespa (until 10/2021) and Alexandra Symeonof.

Supervisor of the BSc theses of the Undergraduate students: Georgia Trasani, Department of Biology, Kapodistrian University of Athens.

Supervision of the MSc students H. Tsakogioannis , C. Kyriakopoulou and Maritina Zerva of the Athens International Master's Program in Neurosciences, Kapodistrian University of Athens

Member of the Advisory Committee in the Department of Biology of the Kapodistrian University in Athens for the PhD students P. Pallaki, S. Koutloglou C. Crespa J. and Karoussiotis and A. Symeonof.

Teaching in the Interdepartmental Master Course program of the Kapodistrian University of Athens, Department of Biochemistry and Molecular Biology "*Molecular Basis of Human Disease"* entitled "*G-Protein Coupled Receptors in Health and Disease",* (6 hours, 30 students).

Member of the Advisory Committee of the MSc students Isis Anzel-Koutrouli and Katerina Mouskouris

Co-supervisor of the MSc Thesis of the MSc Student candidate Foteini Tzoanou of the «Athens International Master's Programme in Neurosciences»

Teaching in the MSc program «Athens International Master's Programme in Neurosciences» on «*Signalling of Neurotransmitter Receptors*» of the Kapodistrian University of Athens (18 hours, 20 students)

Teaching in the MSc program of the IBE in collaboration with the University of Patras Chemistry Department Applied Biochemistry, Clinical Chemistry, Biotechnology and Evaluation of bioactive compounds of pharmacological importance- on "Cellular Signalling of membrane bound receptors-Molecular Pharmacology" (6 hrs, 16 students)

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) "The Biology of Stress in Health homeostasis", Medical School, National and Kapodistrian University of Athens
Teaching at the postgraduation (Master) course (4 hours, 20 students) "Biological Applcuations in Medicine", Medical School, National and Kapodistrian University of Athens
Teaching at the postgraduation (Master) course «Interdepartmental Program for Postgraduate Studies of IBE and the Department of Chemistry, University of Patras; Molecular Pharmacology, (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 (ΕΚΠΑ), Crete Neuroscience Master (Παν. Κρήτης), ΜΠΣ Νευροεκφυλιστικών νοσημάτων (ΑΠΘ), 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 Master 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 for the Institute of Biosciences & Applications

Z. Georgoussi

Member of the Infrasctucture OPENSCREEN-*GR "An Open–Access Research Infrastructure for Target–Based Screening Technologies for Human and Animal Health, Agriculture and the Environment*" funded by GSRI (Δράση Ενίσχυση των Υποδομών Έρευνας και Καινοτομίας, Επιχειρησιακό Πρόγραμμα «Ανταγωνιστικότητα, Επιχειρηματικότητα και Καινοτομία» ΕΣΠΑ 2014-2020)
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 scientific publications in 2021:

Z. Georgoussi: 4.41 (for 1 publication)
Citations for 2021 (excluding self-citations): 36
Total citations for 2016-2021 (excluding self-citations): 168
h-factor: 19 (Scopus), 21 (Google Scholar)

I. Sotriropoulos: 48.08 (for 7 publications)

Citations for 2021 (excluding self-citations): 267
Total citations for 2017-2021 (excluding self-citations): 1035
h-factor: 23 (Scopus), 24 (Google Scholar)

Current External Funding (outside IBA)

Programm EU–COST Action CA18133 entitled: *European Research Network on Signal Transduction (ERNEST)* funded by the EU with Z. Georgoussi as member of the National Representative of the Management Committee
Programm duration: 04/2019- 07/2023
Total funding: 164000 €
Laboratory Funding for 2021: 1506 €

Programme EU–COST Action CA18240 entitled *"ADHEsion GPCR Network: Research and Implementation Set the path for future Exploration" (Adher N' Rise),* Substitute National representative of the Management Committee.
Programme duration: 11/2019- 11/2023
Total funding: 120000 €
Laboratory Funding for 2021: 0 €

Research Activity: Insect Physiology and Ethology and Applications

Kostas Iatrou, Emeritus Scientist
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 preventing them from finding suitable hosts and transmitting infectious agents to them in the process of 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. Thus, 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. The combined activities should help minimize the spread of mosquito-borne infectious diseases to animal hosts including humans. This research aims at the reduction in the transmission of mosquito-borne infectious diseases to animal hosts including humans.

2021 Findings

In previous studies, we had used a cell-based 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 use of the specific platform, which relies on the expression of the co-receptor of the African malaria mosquito vector *Anopheles gambiae* in insect cells, in conjunction with small collections of volatile organic compounds (VOCs) of natural origin, resulted in the identification of 15 ORco antagonists acting as anosmic agents for multiple mosquito species that may vector pathogens causing dangerous infectious diseases to agricultural and domestic animals as well as humans. The experimental classification of the identified antagonists in orthosteric and allosteric classes allowed the design of a pharmacophore predicting the binding of orthosteric antagonists to an ORco-specific site capable of accommodating specific structural motifs of the confirmed antagonists (collaboration with Dr. Ada Thireou, Agricultural University of Athens). Following the necessary training with the 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 toward the *in silico* screening of a new collection of as yet uncharacterized natural VOCs for the presence of ORco ligands possessing orthosteric antagonist activities. The experimental validation of the identified hits is in progress.

During the same period, we have also completed the generation of a new series of expression vectors directing the *ex vivo* expression of N-terminally tagged ORco channels in insect cells. The new vectors permit the stable expression and easy isolation of large quantities of the tagged receptors by affinity chromatography and their processing to their authentic forms by digestion with specific proteases. The functional characterization of the new ORco expression vectors for the presence of the corresponding receptor subunits in insect cells is in progress. The ultimate goal for these studies is the employment of the new expression vectors toward 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).

Publications

Kythreoti, G, Sdralia, N, Tsitoura, P, Papachristos, P, Michaelakis, AP, Karras, V, Ruel, DM, Yakir, E, Bohbot, JD, Schulz, S, and Iatrou, K (2021). Volatile allosteric antagonists of mosquito odorant receptors inhibit human-host attraction. J Biol Chem. 2021 296:100172. doi: 10.1074/jbc.RA120.016557 (IF 5.157)

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", "BioMed Research International" και "Insects".

Reviewing of manuscripts in scientific journals

Reviewer of article submissions for "Insect Biochemistry and Molecular Biology", "BioMed Research International", "Scientific Reports", "Journal of Medical Microbiology", "Viruses", "Archives of Insect Biochemistry & Physiology", "Journal of Insect Physiology", "Agronomy", "Insect Science", "Insects".

Total Impact Factor for your original publications in 2021: 5.157

Citations for 2021 (without self-citations): **206 (Scopus)**

Total citations 2016-2021 (without self-citations): **975 (Scopus)**

h-factor (from Scopus and Google scholar): **37 (Scopus), 45 (Google scholar)**

Current External Funding (outside IBA) to conduct scientific research, travels, transnational collaborations, etc. (separately for each supported program)

Organization that finances the programme: Inscent, Inc., USA

Programme title: *Identification of new insect olfactory and taste enhancers of natural or synthetic origin*

Programme duration: 2020-2023

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 for 2021: 0€
Funding of your Research Group by the programme for 2021: 0€

Organization that finances the programme: Hellenic Foundation for Research and Innovation (HFRI)
Programme title: *3D-ORco: The structure of ORco, the odorant receptor co-receptor of mosquitoes*
Programme duration: 2020-2023
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 for 2021: 90.000€ (to NHRF Special Accounts)
Funding of your Research Group by the programme for 2021: 20.000€ (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
Marina-Gemma Kelemeni, Collaborating Graduate Student (MSc) – *MSc obtained in 2021*
Eleni Kaplani, Collaborating Graduate Student (MSc) – *MSc obtained in 2021*
Konstantina Louka, Collaborating Graduate Student (MSc)
Anastasia Kypraiou, Collaborating Graduate Student (MSc)
Maria Dimozi, Collaborating Graduate Student (MSc)
Chrysanthi Andriani Economou, Summer Trainee – *Training completed*
Marialina Tsinidis, Research project – *Project 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 - 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 process of ageing and the development of age-related diseases, including 1. cancer progression, 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.

2021 Findings
Main goal of the Laboratory is the study of the role of the senescent cell in the manifestation of age-related diseases, including cancer. We showed that senescent human breast fibroblasts

express a catabolic phenotype, characterized by decreased collagen synthesis and overexpression of metalloproteases, and display changes in proteoglycan expression, such as syndecan 1 (SDC1) overexpression and decorin (DCN) underexpression. It is well established that all these alterations, when occurring in the breast stroma, are important risk factors for tumor development, indicating a key role of stromal cells' senescence in the progression of carcinogenesis. Furthermore, we studied an additional important stromal cell type in the same tissue, that is adipose-derived mesenchymal stem cells (AdMSCs). We showed that senescent AdMSCs display a significantly reduced capacity for osteogenic, adipogenic and chondrogenic differentiation (Figure 1A). In parallel, they display a pro-inflammatory and catabolic phenotype, SDC1 overexpression and DCN underexpression. These findings indicate that accumulation of different types of senescent breast stromal cells may contribute to the creation of a favorable microenvironment for the progression of carcinogenesis.

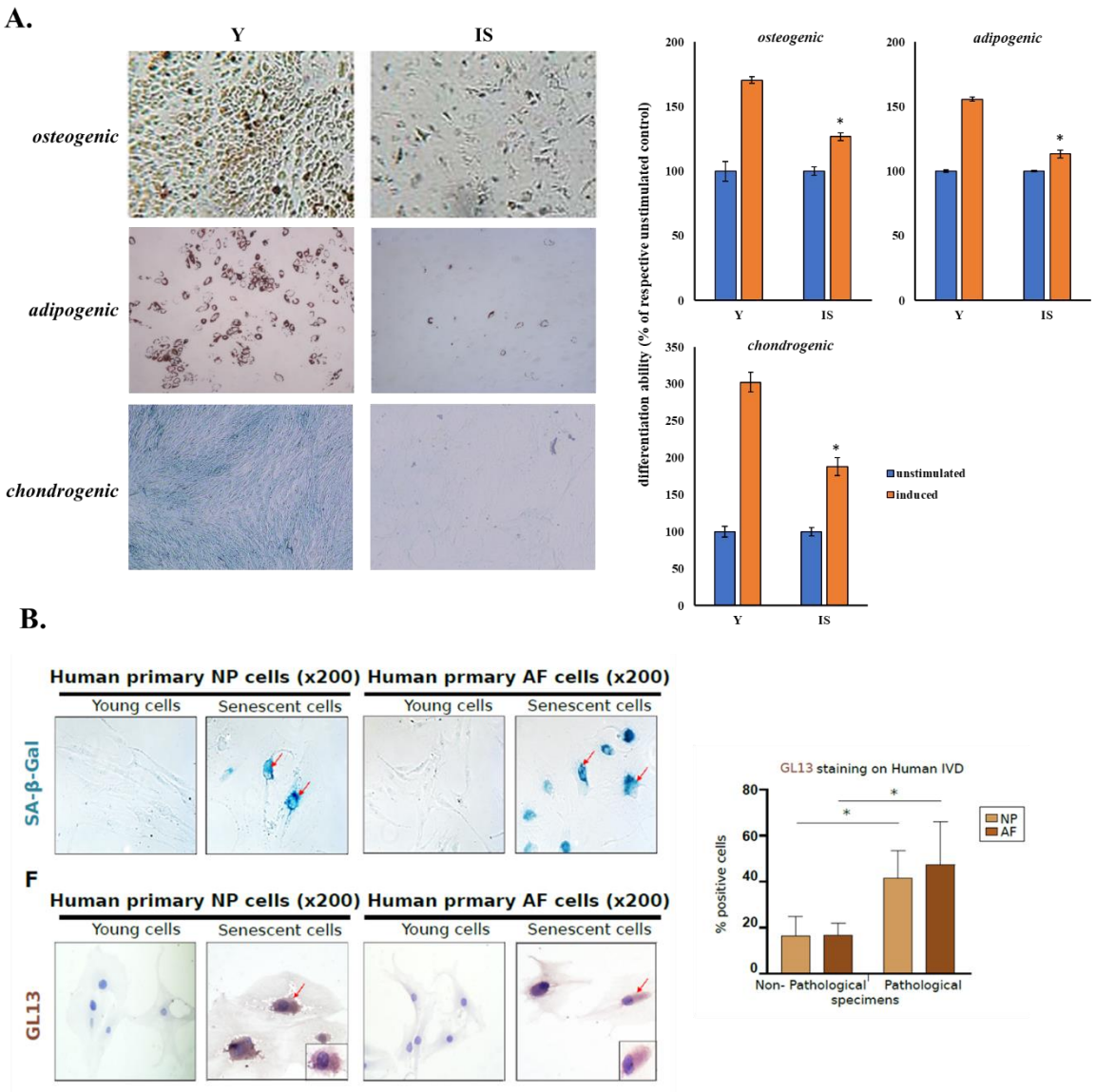


Figure 1: *A. Ionizing radiation-induced prematurely senescent AdMSCs show a reduced capacity for osteogenic, adipogenic and chondrogenic differentiation [Y: young cells, IS: ionizing radiation-induced senescent cells, Papadopoulou et al., IUBMB Life. 2022 Oct;74(10):969-981]. B. The presence of senescent cells in the nucleus pulposus and the annulus fibrosus of the intervertebral disc was confirmed with the classical SA-β-GAL staining and the new method relying on lipofuscin detection (GL13). In all cases, the percentage of senescent cells in pathological tissues was found to exceed 40% [NP: Nucleus pulposus, AF: Annulus fibrosus, Veroutis et al., Mech Ageing Dev. 2021 Oct;199:111564].*

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. Our laboratory has previously shown for the first time the presence of a significant number of senescent cells in degenerated discs, which are believed to contribute to tissue degeneration. We recently confirmed the presence of high percentages of senescent cells (greater than 40%) in human and rat tissues *in vivo*, using a novel detection method of senescent cells based on the localization of lipofuscin, an important senescence marker (Figure 1B). In addition, 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, compared to the plasma and a vascularized tissue (the skin), known compounds (zoledronic acid and doxorubicin) show a delayed, prolonged and at low concentrations accumulation in the periphery of the disc (annulus fibrosus) of rabbits. In contrast, they were not detected in the center of the disc (the nucleus pulposus).

We studied the effect of UVB irradiation on human dermal fibroblasts and found that high UVB doses are cytotoxic. Furthermore, we showed that activation and co-operation of the JNKs and ATM-p53 pathways are indispensable for cytoprotection.

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

Publications

Papastathopoulos A, Lougiakis N, Kostakis IK, Marakos P, Pouli N, Pratsinis H, Kletsas D. (2021). New bioactive 5-arylcarboximidamidopyrazolo[3,4-c]pyridines: Synthesis, cytotoxic activity, mechanistic investigation and structure-activity relationships. Eur J Med Chem. 2021 Jun 5;218:113387. (IF: 7.088)

Mavrogonatou E, Papadopoulou A, Fotopoulou A, Tsimelis S, Bassiony H, Yiacoumettis AM, Panagiotou PN, Pratsinis H, Kletsas D. (2021). Down-regulation of the proteoglycan decorin fills in the tumor-promoting phenotype of ionizing radiation-induced senescent human breast stromal fibroblasts. Cancers (Basel). 2021 Apr 20;13(8):1987. (IF: 6.575)

Veroutis D, Kouroumalis A, Lagopati N, Polyzou A, Chamilos C, Papadodima S, Evangelou K, Gorgoulis VG, Kletsas D. (2021). Evaluation of senescent cells in intervertebral discs by lipofuscin staining. Mech Ageing Dev. 2021 Oct;199:111564. (IF: 5.498)

Sklirou AD, Angelopoulou MT, Argyropoulou A, Chaita E, Boka VI, Cheimonidi C, Niforou K, Mavrogonatou E, Pratsinis H, Kalpoutzakis E, Aligiannis N, Kletsas D*, Trougakos IP*, Skaltsounis AL*. (2021). Phytochemical study and in vitro screening focusing on the anti-aging features of various plants of the Greek flora. Antioxidants (Basel). 2021 Jul 28;10(8):1206. (IF: 7.675)

Mavrogonatou E, Kouroumalis A, Papadopoulou A, Pratsinis H, Kletsas D. (2021). Cell-based therapies for the regeneration of the intervertebral disc: promises and challenges. Acta Orthopaedica Et Traumatologica Hellenica. 2021. 72, 21-29. (IF: -)

Articles in Press

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: 3.205)

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: 10.002)

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)

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)

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)

Kloukos D, Mavrogonatou E, Kletsas D, Makras P, Koukos G, Stavropoulos A, Katsaros C. (2021). 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)

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. IUBMB Life. 2022 Oct;74(10):969-981. (IF: 4.709)

Piperigkou Z, Koutsandreas A, Franchi M, Zolota V, Kletsas D, Passi A, Karamanos NK. ESR2 drives mesenchymal-to-epithelial transition in triple-negative breast cancer and tumorigenesis *in vivo*. Front Oncol. Mol and Cell Oncol. 2022 Jun 3;12:917633. (IF: 5.738)

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

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

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

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

Madbouly EA, Lashine E-SM, Al-Karmalawy AA, Sebaiy MM, Pratsinis H, Kletsas D, Metwally K. 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 in press (IF: 3.591)

Mavrogonatou E, Angelopoulou M, Rizou SV, Pratsinis H, Gorgoulis VG, Kletsas D. 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)

Scientific book editions

Al Naqbi, S.R., H. Pratsinis, D. Kletsas, A.E. Athanasiou, and T. Eliades, Biological Properties of Aligners in “Orthodontic Aligner Treatment, A Review of Materials, Clinical Management, and

Evidence" (T. Eliades, and A.E. Athanasiou, eds.) Georg Thieme Verlag, Stuttgart-Feuerbach, 2021. pp. 170-176.

International Conferences

Mavrogonatou E, Angelopoulou M, Rizou S, Pratsinis H, Gorgoulis VG, Kletsas D. (2022). UVB-mediated cytotoxicity in skin fibroblasts. 9th International Conference on Oxidative Stress in Skin Biology and Medicine, September 9-12, 2021, Virtual

Almpani C, Santorinaiou A, Kikidou L, Grammatikaki S, Livaniou E, Kletsas D, Pratsinis H. Responses of human skin fibroblasts to thymosinic peptides related to wound repair. 9th International Conference on Oxidative Stress in Skin Biology and Medicine, September 9-12, 2021, Virtual

Kouroumalis A, Christophoridis C, Kletsas D. Accumulation and biological role of zolendronate in rabbit intervertebral discs. 12th International Conference on Instrumental Methods of Analysis-Modern Trends and Applications, September 20-23, 2021, Virtual

Kletsas D. UVB-mediated cytotoxicity and premature senescence in skin fibroblasts. Joint EWMA & Journées Cicatrisations, October 26-27, 2021, Paris, France, Virtual

National Conferences

Papadopoulou A, Kanioura A, Petrou PS, Argitis P, Kakabakos S, Kletsas D. Reacquisition of a spindle cell shape does not lead to the restoration of a youthful state in senescent human skin fibroblasts. 3rd Session of webinars of the Hellenic Society of Biochemistry & Molecular Biology: Mechanisms of Ageing, April 8, 2021, Virtual

Kletsas D. Cell therapies for the intervertebral disc. 77th Conference of the Hellenic Society of Surgery, Orthopedics and Traumatology, October 6-9, 2021, Athens

Kletsas D. Cellular senescence and cancer. 5th Annual Meeting on Cancer Biology and New Molecules in Cancer Therapy, November 25-27, 2021, Athens

Mavrogonatou E, Angelopoulou M, Pratsinis H, Rizou S, Gorgoulis VG, Kletsas D. Activation of the ATM-p53 axis is indispensable for the cytoprotection of UVB-exposed dermal fibroblasts. 71st Congress of the Hellenic Society of Biochemistry and Molecular Biology, November, 26-28, 2021, Athens

Mavrogonatou E, Papadopoulou A, Fotopoulou A, Tsimelis S, Bassiony H, Yiacoumettis AM, Panagiotou PN, Pratsinis H, Kletsas D. The tumor-promoting phenotype of ionizing radiation-induced senescenthuman breast stromal fibroblasts is complemented by the down-regulation of the proteoglycan decorin. 71st Congress of the Hellenic Society of Biochemistry and Molecular Biology, November, 26-28, 2021, Athens

Pratsinis H, Sklirou AD, Angelopoulou MT, Argyropoulou A, Chaita E, Boka VI, Cheimonidi C, Niforou K, Mavrogonatou E, Kalpoutzakis E, Aligiannis N, Skaltsounis A-L, Trougakos IP, Kletsas D. High-throughput screening of Hellenic plant extracts for the identification of bioactive natural products with probable anti-ageing properties. 71st Congress of the Hellenic Society of Biochemistry and Molecular Biology, November, 26-28, 2021, Athens

Papatsirou M, Katsaraki K, Kontos CK, Kletsas D, Scorilas A. Unraveling the intricacy of the breast cancer transcriptome: novel circular RNAs of the PRMT1 gene display a wide range of splicing events. 71st Congress of the Hellenic Society of Biochemistry and Molecular Biology, November, 26-28, 2021, Athens

Beta RAA, Arsenopoulou ZV, Samiotaki M, Dalkidis D, Kletsas D, Panayotou G, Balatsos NAA. Time-of-day interacting partners of poly(A)-specific ribonuclease in mouse liver. 71st Congress of the Hellenic Society of Biochemistry and Molecular Biology, November, 26-28, 2021, Athens

Manou D, Karagiorgou Z, Fountas P, Kletsas D, Moustakas A, Karamanos NK, Theocharis AD. Serglycin cooperates with cytokines to orchestrate LN-18 glioblastoma cells and fibroblasts behavior. 71st Congress of the Hellenic Society of Biochemistry and Molecular Biology, November, 26-28, 2021, Athens

Temponeras I, Stamatakis G, Samiotaki M, Pratsinis H, Panayotou G, Stratikos E. An ERAP2 inhibitor induces cell-surface presentation of many new and potentially antigenic peptides by cancer cells. 71st Congress of the Hellenic Society of Biochemistry and Molecular Biology, November, 26-28, 2021, Athens

Theochari I, Ilic T, Nikolic I, Dobricic V, Savic S, Papahatjis D, Tenchiu A, Pratsinis H, Xenakis A, Papadimitriou V, Pletsa V. Oil-in-water microemulsions as carriers of compounds of pharmaceutical interest-Dermal applications. 71st Congress of the Hellenic Society of Biochemistry and Molecular Biology, November, 26-28, 2021, Athens

Other Scientific Activities

Participation in Greek and international scientific bodies and organizations

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

Member of the Council and of the Fellowships Committee 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)

Co-ordinator of the Committee for the selection of General Director of the Hellenic Pasteur Institute (D. Kletsas)

Member of the Evaluation Committee for GRAMMER European Spine Journal Award (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” και “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” (E. Mavrogonatou)

Organization of scientific conferences or participation in conference organizing committees

Organization of the 3rd Session of webinars of the Hellenic Society of Biochemistry & Molecular Biology: Mechanisms of ageing, April 8, 2021 (D. Kletsas)

President of the Organizing Committee of the 8th Young Scientific Forum of the Hellenic Society of Biochemistry & Molecular Biology, November 25, 2021, NCSR “Demokritos”, Athens (H. Pratsinis)

Reviewing of manuscripts in scientific journals

European Spine Journal (3), Mechanisms of Ageing and Development (2), Biogerontology (3), Oxidative Medicine and Cellular Longevity, Matrix Biology, Experimental Gerontology (2), Journal of Investigative Dermatology, Matrix Biology Plus, Ageing Research Reviews, FEBS Journal (2), Aging Cell, European Journal of Orthodontics, Journal of Cellular and Molecular Medicine, Experimental Dermatology, Scientific Reports, Antioxidants (D. Kletsas)

Arabian Journal of Chemistry (3), Cancers, Cells, Cosmetics (3), European Journal of Pharmacology (3), FEBS Journal, Genes & Diseases, International Journal of Molecular Sciences, Journal of Xenobiotics, Life, Molecules (4), Pharmaceutics (2), South African Journal of Botany (H. Pratsinis)

European Spine Journal, International Journal of Molecular Sciences (5), American Journal of Orthodontics & Dentofacial Orthopedics (8), Cancers (7), Antioxidants (3), Biomedicines (2), Diagnostics (2), Journal of Personalized Medicine (2) Plants (2), Applied Biosciences and Bioengineering, Enzyme and Microbial Technology, Frontiers in Microbiology (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)

Responsible for the Organization of the Lab Seminar for the training of Secondary Education Biology Teachers in collaboration with the European Learning Laboratory for the Life Sciences (ELLS) of the European Molecular Biology Laboratory (EMBL) (11-12/9/2021) (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 Marina-Gemma Kelemeni, Eleni Kaplani, Konstantina Louka, Anastasia Kypraiou and Maria Dimozi (D. Kletsas)

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

Supervision of the summer trainee Chrysanthi Andriani Economou (E. Mavrogonatou)

Supervision of the research project of Marialina Tsinidis (E. Mavrogonatou)

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

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

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

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

"Cell senescence and tissue homeostasis", Post-graduate Master's Degree in Cosmetology, Department of Pharmacy of the University of Athens, 10 students (D. Kletsas)

"Cell senescence: Molecular mechanisms and role in tissue homeostasis", Harokopio University, 2 hours, 15 students (D. Kletsas)

Post-graduate Master's Degree "Applied Biomechanics and Biomaterials in Orthopaedics", 1 hour, 20 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, 2 hours, 20 students (H. Pratsinis)

Participation in the Inter-Institutional Joint Post-Graduate Programme (JPGP) in "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" between the Institute of Biosciences and Applications and the University of Patras, 6 hours, 8 students (D. Kletsas, H. Pratsinis and E. Mavrogonatou)

Participation in the Lab Seminar for the training of Secondary Education Biology Teachers in collaboration with the European Learning Laboratory for the Life Sciences (ELLS) of the European Molecular Biology Laboratory (EMBL) (11-12/9/2021) (D. Kletsas, H. Pratsinis and E. Mavrogonatou)

Member of examination committees for PhD, MSc and BSc theses
Marina-Gemma Kelemeni concluded her MSc thesis entitled "Study of the effect of ionizing radiation on the paracrine interactions of breast cancer and stromal cells" 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". The thesis was unanimously accepted and awarded the degree "Excellent" (Scientific Supervisor D. Kletsas)

Eleni Kaplani concluded her MSc thesis entitled "Study of estrogen receptors' expression in young and senescent intervertebral disc cells" in the framework of the Master's Degree Programme of the Medical School of the University of Athens "Molecular and Applied Physiology". The thesis was unanimously accepted and awarded the degree "Excellent" (Scientific Supervisor D. Kletsas)

Dimitra Manou concluded her PhD thesis entitled "The role of serglycin in malignancies" in the Department of Chemistry, University of Patras. The thesis was unanimously accepted and awarded the degree "Excellent" (D. Kletsas and H. Pratsinis, members of the seven-member committee)

Polyxeni Lazaridou concluded her MSc thesis entitled "Optimization of lavender ethereal oil recovery method. Annual variation of production in Kozani" in the framework of the Master's Degree Programme of the Department of Chemistry, University of Ioannina "Agronutrition and Environment" (H. Pratsinis, member of the seven-member committee)

Other Activities in IBA and in NCSR "Demokritos"
D. Kletsas:
Director of IBA & Member 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 Competitions of ELKE, NCSR "Demokritos" (proclamations 015/2020-2876, 015/2020-3662 and 015/2021-660), evaluation of candidates for temporary staff positions (project 12259) 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 (along with V. Labropoulou and M. Sagnou) of the organizing committee for the online presentations of the deliverables of the IBA programme Sanitura
Member of the Committee for the receipt of deliverables for the projects E-12384 and E-12388
Substitute member of the Committee for the receipt of contracts for the supply of laboratory consumables in the framework of the implementation of Sub-project 3 of the OPENSCREEN-GR Action
Substitute member of the three-member Committee regarding the process of opinion formulation of Researchers for the evaluation of the Director of IBA at the end of his term
Substitute member of the five-member Committee of Researchers for the evaluation of the candidates for the selection of Director of NCSR "D"

Impact Factors
D. Kletsas (for 4 out of 5 publications): 26.836
H. Pratsinis (for 3 out of 4 publications): 21.338
E. Mavrogonatou (for 2 out of 3 publications): 14.250

Citations 2021 (without self-citations)
D. Kletsas: 914
H. Pratsinis: 291
E. Mavrogonatou: 201

Total Citations 2016-2021 (without self-citations)
D. Kletsas: 3742
H. Pratsinis: 1090
E. Mavrogonatou: 654

h-factor
D. Kletsas: 49 (Scopus), 55 (Google Scholar)
H. Pratsinis: 33 (Scopus), 36 (Google Scholar)
E. Mavrogonatou: 20 (Scopus), 22 (Google Scholar)

Current External Funding
Project entitled "Study of the accumulation of anti-cancer compounds in intervertebral disc tissues and their effect on cellular aging (MIS 5047829)", co-financed by Greece and the European Union (European Social Fund-ESF) through the Operational Programme "Human Resources Development, Education and Lifelong Learning 2014-2020"
Scientific Supervisor: Dr. D. Kletsas

Duration: 2020-2021
Total programme funding (for the entire duration of the programme): 41.541,50 €
Funding of the lab for 2021: 21.541 €

Project entitled “Development of innovative cosmeceuticals based on the greek flora (CosmAGE)” (T2ΕΔΚ-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 2021: 0 €

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)” (T2ΕΔΚ-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 2021: 80.000,00 €

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: 2021-2022
Total programme funding (for the entire duration of the programme): 7.136,49 €
Funding of the lab for 2021: 7.136,49 €

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: 2021-2022
Total programme funding (for the entire duration of the programme): 25.000,00 €
Funding of the lab for 2021: 0 €

Current External IBA Funding
Project entitled “SANITURA (TARGET IDENTIFICATION AND DEVELOPMENT OF NOVEL APPROACHES FOR HEALTH AND ENVIRONMENTAL APPLICATIONS)”, funded by the General Secretariat for Research and Innovation (Action for the Strategic Development on the Research and Technological Sectors, Operational Programme “Competitiveness, Entrepreneurship and Innovation”, NSRF 2014-2020)
Scientific Supervisor: Dr. D. Kletsas
Duration: 2017-2021

Total programme funding (for the entire duration of the programme): 740.000,00 €
Funding for 2021: 0 €

Project entitled “OPENSCREEN-GR: A Greek Research Infrastructure for visualizing and monitoring fundamental biological processes, funded by the General Secretariat for Research and Innovation (Action “Reinforcement of the Research and Innovation Infrastructure”, Operational Programme “Competitiveness, Entrepreneurship and Innovation”, NSRF 2014-2020)
Scientific Supervisor: Dr. D. Kletsas
Duration: 2017-2021
Total programme funding (for the entire duration of the programme): 899.600,00 €
Funding for 2021: 215.500,00 €

Project entitled “BIOIMAGING-GR: A Greek Research Infastructure for Visualizing and Monitoring Fundamental Biological Processes”, funded by the General Secretariat for Research and Innovation (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: 2017-2021
Total programme funding (for the entire duration of the programme): 211.250,00 €
Funding for 2021: 51.250,00 €

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 2021: 1.300,00 €

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 2021: 0 €

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 2021: 480.000,00 €

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: 2020-2022
Total programme funding (for the entire duration of the programme): 2.000.000,00 €
Funding for 2021: 1.333.992,00 €

Research Group: Nuclear Proteins and Chromatin Function

Research Staff
Thomae Sourlingas, Senior Researcher B' Grade
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.

2021 Findings

Cancer and Histones:

Histone deacetylase inhibitors (HDACIs) are used as tools for the investigation of epigenetic regulation of chromatin and they can be used alone, or in combination with other anticancer agents, in therapeutic regimens. For these reasons, we studied three histone H3 epigenetic modifications (acetylation, trimethylation and dimethylation) and three histone H1 subtypes (H1.0, H1.3 and H1.5) in the absence and presence of the HDACI, sodium butyrate, in three leukemic cell lines (K562, NB4, Molt4) as compared to normal lymphocytes. Of importance are our findings showing that in the presence of sodium butyrate histone H3 acetylation and trimethylation, 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, 8 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, 21 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.

Research Group: Cell & Matrix Biochemistry/Pathobiology

Research Staff
Angeliki Chroni, Research Director
Athina Tzinia, Research Director
Paraskevi Kitsiou, Senior Researcher
Garyfalia Drossopoulou, Senior Researcher
Christina Gkolfinopoulou, Postdoctoral Fellow
Archontia Kaminari, Postdoctoral Fellow
Maria Karanikou, Postdoctoral Fellow
Anastasia Georgia Dedemadi, PhD student
Christina Mountaki, PhD student
Achillea Papagiannis, PhD student
Asimina Micha, MSc student
Lydia Voulgari, Diploma student
Lida krikoni, collaborating scientist
Effie Valanti, collaborating scientist
Nikolaos Giannakas, Technician

Research Interests

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

   A) Analysis of the molecular mechanisms underlyning the role of apoE4, the major risk factor for Alzheimer's disease, in the disease pathogenesis.

   B) Pursuing therapeutic strategies aiming at the correction of the pathogenic properties of apoE4 in Alzheimer's disease.

   C) Study of cell protection and survival mechanisms in age-related diseases like Alzheimer's Disease and type II Diabetes.

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

   A) Understanding 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

3.Diabetes Mellitus and Diabetic Nephropathy

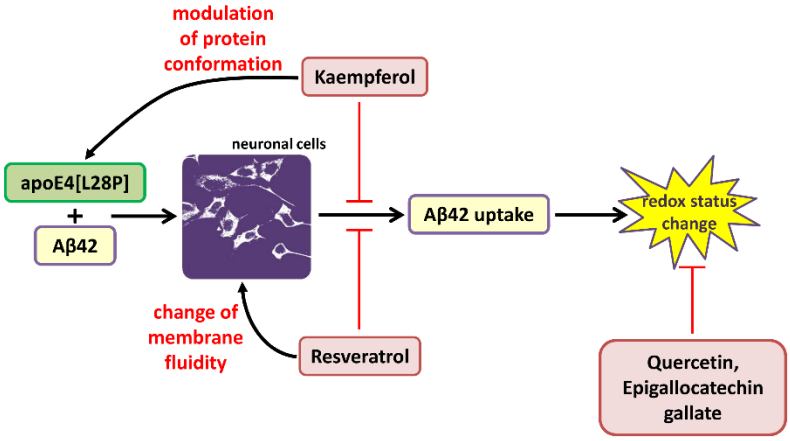
A) Study of pancreatic β-cell survival mechanisms in diabetic conditions:
i) Cross talk between nephrin and survival signaling pathways in pancreatic insulin producing beta cells ii) Study of the effect of liraglutide (a human GLP-1 analogue) on islet β-cell survival signaling in db/db lepr−/− type 2 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.

2021 Findings

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

A) We investigated the molecular mechanisms by which the naturally occurring polyphenols quercetin, resveratrol, kaempferol and epigallocatechin gallate prevent the increase in oxidative stress in neuronal cells induced by Aβ42 uptake in the presence of the pathogenic forms of apoE4 apoE4[L28P] and apoE4-165. Our analyses showed that resveratrol inhibited cellular uptake of Aβ42 via changes in cell membrane fluidity, while kaempferol inhibited cellular uptake of Aβ42 by apoE4[L28P], but not by apoE4-165, due to a modulating effect on secondary structure and stability of E4[L28P]. The action of quercetin and epigallocatechin gallate could be attributed to free radical-scavenging or other protective activity. Overall, we showed for the first time that natural compounds could modify the structure of apoE4 forms and ameliorate AD related pathogenic effects of apoE4 forms (Free Radic. Biol. Med. (2021) 171, 284-301).



B) To study common pathological mechanisms related to diabetes II and Alzheimer's disease the action of natural products and new synthetic biomolecules as therapeutic agents was evaluated. In particular, the prophylactic effect of two isatins was determined in terms of the cytotoxicity mediated by the Aβ peptide (collaboration with Drs. Sagnou and Pelekanou, IBE). Moreover,12 substances (derivatives of phenoxazines and MARK4 Kinase regulators) were tested for their toxicity in neuroblastoma cell lines by the MTT method and for their activity in regulating the activity of nodal proteins (AKT and GSK3b) in primary hippocampal cells by western analysis. Four of the above compounds were selected for further characterization (collaboration with Dr. Sarli).

2. Study of the molecular mechanisms of dyslipidemia and atherosclerosis

We applied high-throughput methods that monitor changes in apoA-I structure to screen chemical libraries in order to find new drugs that improve apoA-I/HDL structure and functions. Our analyses showed that already approved drugs can correct the defective structure and function of mutated apoA-I forms, such as apoA-I[L178P] that is associated with low HDL levels and early onset coronary disease, and may lead to new therapeutic approaches for dyslipidemias and increased cardiovascular risk.

3. Diabetes Mellitus and Diabetic Nephropathy

A) In mouse pancreatic β-cells (βTC-6), nephrin signaling promotes cell survival by inhibiting apoptosis. In islets of diabetic mice, decreased nephrin expression and increased β-cell apoptosis were observed. Nephrin expression was also reduced in isolated mouse islets incubated in the

presence of high glucose. This reduction is not accompanied by changes in the expression of other nephrin-associated proteins such as CD2AP, suggesting that nephrin downregulation may be an early and specific marker of β-cell glucotoxicity.
B) Diabetic nephropathy (DN) is a major chronic complication in diabetic subjects. The number of DN patients progressing to end-stage renal disease, requiring renal replacement therapy continues to increase. Therefore, there is an urgent need for a regenerative strategy. Treatment of isolated rat glomeruli with secreted condition media (CM) from human Amniotic Fluid Mesenchymal Stem/Stromal Cells (CM-AF-MSC) significantly decreased the high-glucose-mediated apoptosis and promoted glomerular survival, suggesting that this approach may provide a valuable tool for cell therapy applications regarding DN.

Peer-reviewed publications

1) Gkolfinopoulou C., Soukou F., Dafnis I., Kellici T. F., Sanoudou D., Mavromoustakos T., Stratikos E. and Chroni A. Structure-function analysis of naturally occurring apolipoprotein A-I L144R, A164S and L178P mutants provides insight on their role on HDL levels and cardiovascular risk. *Cell Mol Life Sci.* 78, 1523-1544 (2021) (IF: 9.261)
2) Mountaki C., Dafnis I., Panagopoulou E. A., Vasilakopoulou P. B., Karvelas M., Chiou A., Karathanos V. T. and Chroni A. Mechanistic insight into the capacity of natural polar phenolic compounds to abolish Alzheimer's disease-associated pathogenic effects of apoE4 forms. *Free Radic. Biol. Med.* 171, 284-301 (2021). (IF: 7.376)
3) Lagopati, N., Kotsinas, A., Veroutis, D., Evangelou, K., Papaspyropoulos, A., Arfanis, M., Falaras, P., Kitsiou, P.V., Pateras, I., Bergonzini, A., Frisan, T., Kyriazis, S., Tsoukleris, D.S., Tsilibary, E.-P.C.,Gazouli, M., Pavlatou, E.A., Gorgoulis, V.G. (2021). Biological Effect of Silver-modified Nanostructured Titanium Dioxide in Cancer. Cancer genomics & proteomics 18 (3), 425-439. (IF 3.280)

Articles in Press

1) Chroni A., Thymiakou E. and Kardassis D. Genetics and regulation of HDL metabolism. Biochim. Biophys. Acta Mol. Cell. Biol. Lipids doi: 10.1016/j.bbalip.2021.159060; Epub 2021 Oct 6. (IF: 4.698)
2) 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 doi: 10.1016/j.metabol.2021.154954; Epub 2021 Dec 4. (IF: 8.694)

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

Mountaki C., Dafnis I. and Chroni A. Natural polar phenols affect differently the structure of apoE4 forms and ameliorate apoE4 functions related to Alzheimer's disease pathogenesis. *Eur. Biophys J.* 50: S124 (2021)

Presentations at International conferences

1) Mountaki C., Dafnis I. and Chroni A. Natural polar phenols affect differently the structure of apoE4 forms and ameliorate apoE4 functions related to Alzheimer's disease pathogenesis. *13th European Biophysics Conference*, 24-28 July 2021, Vienna Austria
2) Mountaki C., Dafnis I., Panagopoulou E. A., Vasilakopoulou P. B., Karvelas M., Chiou A., Karathanos V. T. and Chroni A. Mechanistic insight into the capacity of natural polar phenolic compounds to abolish Alzheimer's disease-associated pathogenic effects of apoE4 forms. *First ESN-ISN School, entitled "From Neurodegeneration to Neural Carcinogenesis: Mechanisms and Common Biologies"*, 19-26 September 2021, Athens
3) Mountaki C., Dafnis I. and Chroni A. Natural polar phenols target the structure and functions of apoE4 forms related to Alzheimer's disease pathogenic processes. *10th*

International Conference of the Hellenic Crystallographic Association (HeCrA), 15-17 October 2021, Athens

Presentations at Greek conferences

1) Micha A., Mountaki C. and Chroni A. The role of apolipoprotein E and lipid transporter ABCA7 in the pathogenesis of Alzheimer disease. *71ο Annual Conference of the Hellenic Society for Biochemistry and Molecular Biology*, 26-28 November 2021, Athens
2) Dedemadi A. G., Gkolfinopoulou C., Nikoleri D., Nikoloudaki M., Sidiropoulos P., Bertsias G. and Chroni A. Effect of belimumab therapy on atheroprotective properties of HDL in systemic lupus erythematosus. *71ο Annual Conference of the Hellenic Society for Biochemistry and Molecular Biology, 26-28 November 2021, Athens*
3) Valanti E. K., Fotakis P., Dalakoura-Karagkouni K., Vafiadaki E., Chroni A., Kardassis D. Zannis V., and Sanoudou D. Reconstituted HDL-apoE3 promotes endothelial cell migration through ID1 and its downstream kinases ERK1/2, AKT and p38 MAPK. *9th Meeting of the working groups of the Hellenic Atherosclerosis Society*, **2-4 December 2021,** Athens (**1st oral presentation award)**
4) Tsouka A. N., Tellis C. C., Dafnis I., Gkolfinopoulou C., Chroni A. and Tselepis A. D. Interaction of PCSK9 with HDL lipoprotein. *9th Meeting of the working groups of the Hellenic Atherosclerosis Society*, 2-4 December 2021, Athens (3ος poster presentation award)

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) President of the Management Committee of Study Group of the Pathophysiology of Atherosclerosis, Hellenic Atherosclerosis Society, 2) Alternate Member of the General Assembly of the Hellenic Foundation for Research and Innovation

A. Tzinia: Member of the electoral committee for the election of an academic member at the Department of Biomedical Sciences, Univeristy of West Attica.

Participation in research panels of research proposals:

A. Χρόνη: 1) Reviewer of grant proposals under the scheme "IDEAS-Serbia Accelerating Innovation and Growth Entrepreneurship Project" funded by the Science Fund of the Republic of Serbia.

2) External evaluator of grant proposals under the scheme "Business partnerships with research and dissemination organizations in the Specialization Sectors of RIS3 of the Ionian Islands Region" funded by the Ionian Islands Region.

Review of Scientific publications:

A. Chroni: Bioscience Reports, Frontiers in Molecular Biosciences, Journal of Inflammation Research, Scientific Reports, International Journal of Molecular Sciences, Life Sciences, British Journal of Pharmacology, BBA-Molecular and Cell Biology of Lipids, Molecular Genetics and Genomic Medicine, ACS Chemical Neuroscience, Frontiers in Neurology

A. Tzinia: Cur Alz Res, Cellular Physiology and Biochemistry, Neural Regeneration Research

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

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

Other scientific activities not covered by the previous questions:
A. Chroni, Presentation about research career and activities in the event GLOBAL WOMEN'S BREAKFAST "Women in Science: Empowering Diversity in Science" organised by IUPAC and the Department of Chemistry of the University of Athens, 9 February 2021

Educational Activities
A. Chroni:
1. Member of the Inter-Departmental Committee and faculty in the joined MSc Programme "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" of the Department of Chemistry of the University of Patras and of the Institute of Biosciences and Applications of NCSR Demokritos
2. 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» (1 h - 9 students, Course: «Molecular & Cellualr Biology-Molecular Biotechnology»),
Title of lecture: «Methods for analysis and characterization of proteins, lipids and hydrocarbons» (2 h-9 students, Cource: « Biochemical Analysis- Clinical Biochemistry ».
3. Guest lecturer in graduate course "Clinical Chemistry", "Clinical Chemistry-Molecular Diagnostics" Graduate Program, Faculties of Biology, Chemistry and Nursing, University of Athens
Title of lecture: "Alzheimer's disease: a) diagnosis (clinical, laboratory, imaging), b) risk factors (genetic factors, age, sex, cardiovascular factors, traumatic injuries, depression, medications, etc.), c) latest data on the mechanisms of occurrence and progression of the disease and on treatment "(2 hours – 25 students)
4. Chair of PhD Advisory Committee of C. Mountaki and A. G. Dedemadi at the Department of Chemistry, University of Athens
5. MSc supervisor for A. Micha
6. Member of PhD Advisory Committee of E. Valanti at the School of Medicine, University of Athens and A. Papagianni at the School of Medicine, Aristotle University of Thessaloniki
7. Presentation entitled "Postgraduate studies in the Institute of Biosciences and Applications" at the 55th Summer School of NCSR "Demokritos", July 2021, (20 min, 450 students)
8. Presentation entitled "Cardiovascular disease: causes and therapeutic approaches" at the 55th Summer School of NCSR "Demokritos", July 2021, (30 min, 450 students)

G. Drossopoulou:
1. Guest Lecturer in the postgraduate 46pecialization 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 – 15 students). Lectures on "Biochemical Analysis – Clinical Biochemistry).
2. Guest lecturer in MSc postgraduate program "Molecular and Applied Physiology", Medical School, University of Athens «Regulation of Apoptosis in disease progression: Is it desirable or must be avoided?» October 2018 (3 hours lecture – 35 students)
3 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 – 30 students)

Other Activities at the Institute of Biosciences and Applications
A Chroni: 1) Person in charge for education issues in the Institute of Biosciences and Applications (IBA). Representative of IBA in the Education Committee of NCSR "Demokritos".
2) Member of Special Committee for the utilization of research findings, NCSR "Demokritos"

A. Tzinia: Member of the Scientific Board of IBA
G. Drossopoulou: Person in charge for the Histology Unit of the Institute of Biosciences and Applications (IBA).

Impact factor for all publications of 2021
A. Chroni: 16,637 (2 publications)
P. Kitsiou: 3,280 (1 publication)

Citations 2021 (without self-citations)
A. Chroni: 169 (Scopus)
A. Tzinia: 82 (Scopus)
P. Kitsiou: 31 (Scopus)
G. Drossopoulou: 63 (Scopus)

Total Citations 2016-2021 (without self-citations)
A. Chroni: 891 (Scopus)
A. Tzinia: 461 (Scopus**)**
P. Kitsiou: 177 (Scopus)
G. Drossopoulou: 409 (Scopus)

h-factor
A. Chroni: 23 (Scopus); 29 (Google Scholar)
A. Tzinia: 19 (Scopus); 21 (Google Scholar)
P. Kitsiou: 11 (Scopus, Google Scholar)
G. Drossopoulou: 14 (Scopus), 15 (Google Scholar)

Current External Funding
1) Project entitled "Complementary neuroprotective action of currant as a natural dietary supplement. Highlighting the mechanisms of action of currant using animal models of neurodegenerative diseases", funded under the call "RESEARCH-CREATE-INNOVATE" of the Ministry of Economy and Development of Greece/ NSRF 2014-2020 with Dr. A. Chroni as Principal Investigator for NCSR Demokritos.
Duration: 2018-2022
Total funding (lab): 188.000 €
Funding of the lab for 2021: 20.000€

2) Project entitled "New therapies aiming to improve the atheroprotective and immunomodulatory properties of HDL for the treatment of autoimmune and cardiovascular diseases", funded under the call "RESEARCH-CREATE-INNOVATE" of the Ministry of Economy and Development of Greece/ NSRF 2014-2020 with Dr. A. Chroni as Coordinator of the project.
Duration: 2020-2022
Total funding (lab): 250.000 €
Funding of the lab for 2020: 60.000€

3) Project entitled "The National Research Infrastructures on Integrated Structural Biology, Drug, Screening, Efforts and Drug Target Functional Characterization-INSPIRED", funded under the call "Reinforcement of the Research and Innovation Infrastructure" of the Ministry of Economy and Development of Greece/ NSRF 2014-2020 with Dr. G. Nounessis as Principal Investigator for NCSR Demokritos and Dr. A. Chroni as team member.
Duration: 2018-2022

Total funding (lab): 16.000 €
Funding of the lab for 2021: 6.000€

4) 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), with Dr E. Startikos as Scientific Supervisor for NCSR Demokritos and A. Chroni as Deputy Scientific Supervisor.
Duration: 2021-2024
Total funding (NCSR Demokritos): 486.035 €

5) Project entitled “Lifestyle and cardiovascular disease: From pathophysiological mechanisms to clinical practice- CARDIOLIFE”, funded by the Hellenic Foundation for Research & Innovation (ELIDEK) under the CALL “Science and Society” - “Research, Innovation and Dissemination Hubs” with Dr. A. Chroni as Principal Investigator for NCSR Demokritos.
Duration: 2021-2023
Total funding (lab): 2.800 €
Funding of the lab for 2021: 800€

6) Project entitled “Nephroprotective role of VitaminD3”, funded by AENORASIS SA
Principal Investigator: G. Drossopoulou
Duration: 2017-2022
Funding of the lab for 2021: 10.440€

Research Group: Molecular Carcinogenesis and Rare Disease Genetics-

Research Staff

Gerassimos Voutsinas, Research Director
Stefanos Smyrniotis, Post-graduate research collaborator
Labrina Bondi, Graduate student
Periklis Michailidis, Graduate student
Konstantina Panagopoulou, Undergraduate student
Aimilia Pateli, Undergraduate student
Anna Athanasouli, Undergraduate student
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

2021 Findings

From Proteomic Mapping to Invasion-Metastasis-Cascade Systemic Biomarkering and Targeted Drugging of Mutant BRAF-Dependent Human Cutaneous Melanomagenesis: Melanoma is classified among the most notoriously aggressive human cancers. Despite the recent progress, due to its propensity for metastasis and resistance to therapy, novel biomarkers and oncogenic molecular drivers need to be promptly identified for metastatic melanoma. Hence, by employing nano liquid chromatography-tandem mass spectrometry deep proteomics technology, advanced bioinformatics algorithms, immunofluorescence, western blotting, wound healing protocols, molecular modeling programs, and MTT assays, we comparatively examined the respective proteomic contents of WM115 primary (n=3955 proteins) and WM266-4 metastatic (n=6681 proteins) melanoma cells. It proved that WM115 and WM266-4 cells have engaged hybrid epithelial-to-mesenchymal transition/ mesenchymal-to-epithelial transition states, with TGF-β controlling their motility *in vitro*. They are characterized by different signatures of SOX-dependent neural crest-like stemness and distinct architectures of the cytoskeleton network. Multiple signaling pathways have already been activated from the primary melanoma stage, whereas HIF1α, the major hypoxia-inducible factor, can be exclusively observed in metastatic melanoma cells. Invasion-metastasis cascade-specific sub-routines of activated Caspase-3-triggered apoptosis and LC3B-II-dependent constitutive autophagy, were also unveiled. Importantly, WM115 and WM266-4 cells exhibited diverse drug response profiles, with epirubicin holding considerable promise as a beneficial drug for metastatic melanoma clinical management. It is the proteome navigation that enables systemic biomarkering and targeted drugging to open new therapeutic windows for advanced disease.

Publications

1. Giannopoulou A.F., A.D. Velentzas, A.K. Anagnostopoulos, A. Agalou, N.C. Papandreou, S.A. Katarachia, D.G. Koumoundourou, E.G. Konstantakou, V.I. Pantazopoulou, A. Delis, M.T. Michailidi, D. Valakos, D. Chatzopoulos, P. Syntichaki, V.A. Iconomidou, O.E. Tsitsilonis, I.S. Papassideri, G.E. Voutsinas, P. Hatzopoulos, D. Thanos, D. Beis, E. Anastasiadou, G.Th. Tsangaris and D.J. Stravopodis (2021) From Proteomic Mapping to Invasion-Metastasis-Cascade Systemic Biomarkering and Targeted Drugging of Mutant BRAF-Dependent Human Cutaneous Melanomagenesis, Cancers 13: 2024. (IF: 6.126)

Articles for 2022

Taouktsi E., E. Kyriakou, F. Borbolis, S. Smyrniotis, L. Bondi, S. Avgeris, E. Trigazis, S. Rigas, G.E. Voutsinas and P. Syntichaki (2022) Organismal and Cellular Stress Responses to Disruption of Mitochondrial LONP1 Protease, Cells 11(8), 1363. (IF: 6.600).

Other Scientific Activities

Reviewer of research articles for: FEBS-OPEN (2 articles), JPM (Journal of Personalized Medicine), OncoTargets and Therapy, Cancers, Scientific Reports.

Educational Activities

Stefanos Smyrniotis has completed his work in the Elidek-funded project “LonP1 protease in aging and cancer”.

Labrina Bondi has presented her Master Dissertation entitled "Study of LonP1 protease expression in aging and cancer" (October 2021), at the Department of Biology, National and Kapodistrian University of Athens, Greece.

Periklis Michailidis has started the experimental work for his Master Dissertation entitled “Crosstalk of signal transduction pathways after induction of dysfunction in cancer cell mitochondria and endoplasmic reticulum”, to be presented at the Department of Biology, National and Kapodistrian University of Athens, Greece. The work is in progress.

Konstantina Panagopoulou has started 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.

Practical laboratory internships of Aimilia Pateli and Anna Athanasouli 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", Thursday 12 April 2021 (number of attendants: 10 students, teaching hours: 2).

Lecture for Secondary Education Biology Teachers at the ELLSconnect Learning LAB 2020, co-organized by IBA and EMBO, 11-12 September 2021 (number of attendants: ? teachers, teaching hour: 30 minutes).

Teaching of the undergraduate course: “Introduction to Molecular Biology” (3 semesters), American College of Greece (Deree College), Agia Paraskevi Attikis, January - December 2021 (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 27, 2021, 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, 2021, Athens (number of attendants: 20 individuals, 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, Tuesday, November 23, 2021, Athens (number of students: 30, teaching hours: 2).

Participation in the review committee of Hebatullah Nader Abdel Monem's diploma thesis entitled "Detection of ASXL1, c-CBL, IDH1 and IDH2 Mutations in Egyptian Patients with Acute Myeloid Leukemia", for obtaining a Master's degree from the Zoology Dept, Faculty of Science, Cairo University, 2021.

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 (October 25, 2021 until December 31, 2021).

Deputy Director of IBA (January 1, 2021 until December 31, 2021).

Member of the Research Council of the Institute (ESI) (January 1, 2021 – December 31, 2021).

Member of the Research Committee of NCSR "Demokritos" (January 1, 2021 – December 31, 2021).

Member of 10 Evaluation Committees for recruitment of scientific collaborators at IBA (January 29, 2021; February 24, 2021; April 19, 2021; April 21, 2021; April 27, 2021; May 13, 2021; August 31, 2021; September 7, 2021; December 3, 2021; December 20, 2021).

Member of the Summary Tender Committee for Openscreen IBE Consumables (October 14, 2021).

Member of the Summary Public Tender Evaluation Committee for the IBA Anti-Doping Laboratory (June 5, 2021).

Member of the Evaluation Committee regarding the "Supply of metal oil storage tank and phase change materials for the Institute of Nuclear and Radiological Sciences and Technology, Energy and Safety (IPRETEA)/EKEFE "D" of the "PROMETHEUS" Act" (February 5, 2021).

Member of the Evaluation Committee for the Selection of a New Director at IBA, NCSR "Demokritos" (December 22, 2021).

Member of 7 Equipment Acceptance Committees for the Openscreen program (March 16, 2021; March 18, 2021; April 14, 2021; May 17, 2021; May 18, 2021; June 7, 2021; July 8, 2021).

Member of the Committee for accepting deliverables for project E-12384 entitled "Study of the accumulation of anticancer compounds in intervertebral disc tissues and their effect on cellular aging" (May 28, 2021).

Substitute Member of the External Partners Selection Committee for Project E-12515 (December 22, 2021).

Member of the Certification Committee for the Scientific Part of the Flagship Action Projects to Combat the SARS-CoV-2 virus (starting from March 17, 2021).

Impact factors (for 1 publication): 6.126

Number of citations for 2021 (without self-citations): 83

Number of citations 2017-2021 (without self-citations): 390

h-factor: 20

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
Dimitrios Kontogiannatos, Postdoctoral Fellow
Ioannis Nektarios Maraidonis, Diploma Student
Izabela Prifti, Diploma Student
Giorgios Souliotis, Summer Student
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.

2021 Findings

Virus-like particles (VLPs) for efficient delivery of dsRNA to insect pests.

An important observation was that fusion proteins of the capsid shell protein of cytoplasmic polyhedrosis virus with GFP could efficiently assemble into viral-like particles that are also fluorescent. Experiments were initiated for the uptake of the fluorescent VLPs by insect cell lines and by midgut tissue. The mechanism of uptake of VLPs will be investigated by knockdown and over-expression experiments as well as by co-staining with subcellular markers. In addition, VLPs will be constructed that consist of a fusion between the capsid shell protein and the spike protein which are expected to have increased cellular uptake.

Single cell transcriptomics and the categorization of hemocytes of silkworm larvae.

Hemocyte subgroups were identified by clustering approaches and differential expression analysis was used for the identification of biomarkers that are characteristic for the hemocyte subtypes. Granulocytes constitute the highest proportion (65%) of the hemocytes and could be further subdivided in several categories (proliferative, antimicrobial, phagocytic). Another broad category constitutes the oenocytoids (28%) that are characterized by prophenoloxidase expression which is involved in melanization. Of interest are two specialized cell types, lamellocytes (7%) and spherulocytes (1%) that express important effector molecules related to the immune response and tissue repair (collaboration with South China Agricultural University, Guangzhou, China).

Antiviral immune response in Lepidopteran insects

In insects, the ligand of the Toll receptor, Spätzle (SPZ1) is activated after proteolytic processing by hemolymph proteases and is responsible for the activation of intracellular signaling. Functional assays in permanent cell lines that express the mature form of C106 (or Bck1), the C-terminal part of the molecule, showed an increase in transcription of antimicrobial peptide genes (8-fold for Cecropin, and 3-fold for Lebocin and Attacin). Another interesting observation is that the mature form of SPZ1 triggers the localization of C106 to the nucleus of the cells. Finally, the precursor form of SPZ1 was found to undergo processing after infection with the virus Ac-YFP.

Publications

Swevers, L., Denecke, S., Vogelsang, K., Geibel, S., Vontas, J. (2021). Can the mammalian organoid technology be applied to the insect gut? Pest Manag. Sci. 77, 55-63. IF = 4.85

Vlogiannitis, S., Mavridis, K., Dermauw, W., Snoeck, S., Katsavou, E., Morou, E., Harizanis, P., Swevers, L., Hemingway, J., Feyereisen, R., Van Leeuwen, T., Vontas, J. (2021). Reduced proinsecticide activation by cytochrome P450 confers coumaphos resistance in the major bee parasite *Varroa destructor*. Proc. Natl. Acad. Sci. USA 118:e2020380118. IF = 11.205

Feng, M., Kolliopoulou, A., Zhou, Y., Fei, S., Xia, J., Swevers, L., Sun, J. (2021). The piRNA response to BmNPV infection in the silkworm fat body and midgut. Insect Science 28, 662–679. IF = 3.262

Feng, M., Xia, J., Fei, S., Peng, R., Wang, X., Zhou, Y., Wang, P., Swevers, L., Sun, J. (2021) Identification of Silkworm Hemocyte Subsets and Analysis of Their Response to Baculovirus Infection Based on Single-Cell RNA Sequencing. Front. Immunol. 12, 645359. IF = 7.561

Feng, M., Fei, S., Xia, J., Zhang, M., Wu, H., Swevers, L., Sun, J. (2021). Global Metabolic Profiling of Baculovirus Infection in Silkworm Hemolymph Shows the Importance of Amino-Acid Metabolism. Viruses 13, 841. IF = 5.048

Swevers, L., Kontogiannatos, D., Kolliopoulou, A., Ren, F., Feng, M., Sun, J. (2021). Mechanisms of Cell Entry by dsRNA Viruses: Insights for Efficient Delivery of dsRNA and Tools for Improved RNAi-Based Pest Control. Front. Physiol. 12:749387. IF = 4.566

Kontogiannatos, D., Swevers, L., Kourti, A. (2021). Assessment of Sesamia nonagrioides (Lepidoptera: Noctuidae) EcR and USP Genes as Targets for Exogenous Non-Persistent RNAi. Diversity 13, 677. IF = 2.88

Articles in Press

Jiang, L., Yu, X.-Q., and Swevers, L. (2022). Editorial: Novel Insights Into Insect Antiviral Immunity. Front. Immunol. 12:740989. IF = 7.561

Samantsidis, G.-R., Denecke, S., Swevers, L., Skavdis, G., Geibel, S., and Vontas, J. (2022). Identification of Helicoverpa armigera promoters for biotechnological applications. Insect Biochem. Mol. Biol. 142, 103725. IF = 4.35

Feng, M., Swevers, L., and 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 = 7.561

De Schutter, K., Verbeke, I., Kontogiannatos, D., Dubruel, P., Swevers, L., Van Damme, E.J.M., and Smagghe, G. (2022). Use of cell cultures *in vitro* to assess the uptake of long dsRNA in plant cells. In Vitro Cellular & Developmental Biology – Plant. doi.org/10.1007/s11627-022-10260-1. IF = 2.252

Ren, F., Yan, J., Kontogiannatos, D., Wang, X. Li, J**.,** Swevers, L., and 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 = 6.953

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

Kontogiannatos, D., Kolliopoulou, A., and Swevers, L. (2021). The "Trojan Horse" approach for successful RNA interference in insects. In: "*RNAi for Plant Improvement and Protection*" (B. Mezzetti, J. Sweet, L. Burgos, eds.), pp 25-39. CAB International 2021.

Editing of scientific books

Jiang, L., Yu, X.-Q., Swevers, L., eds. (2022). Novel Insights into Insect Antiviral Immunity. Lausanne: Frontiers Media SA. doi: 10.3389/978-2-88974-410-7

Presentations at Greek 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

L Swevers: Member of the Editorial Board of the scientific journals: «Archives of Insect Biochemistry and Physiology» and «Journal of Insect Science». Guest Associate Editor in «Frontiers in Immunology»: Comparative Immunology.

Participation in committees for the evaluation of research proposals

L Swevers: Member of the committee of experts of the Funds of Scientific Research FWO-Vlaanderen (Belgium) «Bio2» (Functional Biology) for the evaluation of research proposals.
L Swevers: Expert for the funding agency «Agence Nationale de la Recherche (ANR)» (one proposal) (France) (L. Swevers).

Reviewing of manuscripts in scientific journals

L Swevers: Reviewer of scientific articles for the journals: «Archives of Insect Biochemistry and Physiology» (5x), «Biochimica et Biophysica Acta – Gene Regulatory Mechanisms», «BMC Genomics» (2x), «Current Opinion in Biotechnology», «Developmental and Comparative Immunology», «Frontiers in Agronomy», «Frontiers in Plant Sciences» (3x), «General and Comparative Endocrinology», «Gene», «Insect Biochemistry and Molecular Biology» (3x), «Insect Science» (5x), «Insects», «iScience», «Journal of Pesticide Science» (3x), «Journal of Experimental Biology», «Journal of General Virology», «Journal of Insect Physiology» (5x), «Journal of Insect Science», «Microbial Ecology», «Molecular Immunology», «Nature Ecology & Evolution», «Pesticide Biochemistry and Physiology» (2x), «PLoS ONE», «Pest Management Science» (7x), «Scientific Reports» (2x), «Science of the Total Environment», «Virus Research».

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, 8 students)
- V Labropoulou: Molecular and Cellular Biology – Molecular Biotechnology: lecture with title «The Baculovirus Expression System» (4 hours, 8 students)

Outside IBA:

L Swevers:

Lecture of 30 min with title: "CRISPR-Cas-based Genome Editing and Gene Therapy" at the Summer School of NCSR "Demokritos".

Participation in the program "Training course for Secondary School Biology Teachers" at NCSR "Demokritos", organized by EMBL and OPENSCREEN-GR. Lecture of one hour with title: "Genome Editing Techniques and Applications".

V Labropoulou:

Presentation of the thesis of the Diploma student Ioannis Nektarios Maraidonis (A.M. 1113201600144) 12 Oct 2021. Subject "Study of the viral infections in the silkworm and the immune response". University of Athens, Department of Biology, supervising professor Skarlatos Dedos.

Other Activities in IBA and in NCSR "Demokritos"

V Labropoulou:

Member of the scientific board of IBA

Team member of the Light Microscopy unit of IB-A

Committee member for the opinion of the research personnel for the evaluation of the Director of the Center at the end of his term

Committee member for the opinion of the research personnel for the evaluation of the candidates for the position of Director of NCSR "Demokritos"

Committee member for the opinion of the research personnel for the evaluation of the candidates for the position of Director of IBA

Member of the evalution committee for the recruitment of a scientific associate at INN

Total Impact Factor for your original publications in 2021

L Swevers: 39.372 (for 7 publications)

Citations for 2021 (without self-citations):

L Swevers: 389

V Labropoulou: 53

Total citations 2016-2021 (without self-citations):

L Swevers: 1744

V Labropoulou: 250

h-factor (from Scopus and Google scholar):

L Swevers: Scopus: 34, Google Scholar: 39

V Labropoulou: Scopus: 14, Google Scholar: 17

Current External Funding (outside IBA) to conduct scientific research, travels, transnational collaborations, etc.

Organization that finances the programme: FWO – Vlaanderen G093119N (Belgium)
Programme title: "Characterization of extracellular RNA-signals and their role in antiviral immunity in insects"
Programme duration: 1/2019-12/2022
Total programme funding : 700.800 €
Research groups participating in the programme: 3
Scientific Supervisor: J. Vanden Broeck
Funding for 2021: 0 €
Funding of your Research Group by the programme for 2021: 0 €

Organization that finances the programme: Hellenic Foundation for Research and Innovation (H.F.R.I.) under the "First Call for H.F.R.I. Research Projects to support Faculty members and Researchers and the procurement of high-cost research equipment grant"
Programme title: "Viral-like particles for increased RNAi delivery in insects" (VLP-RNAi, #785)
Programme duration: 2/2020-2/2023
Total programme funding : 152.000 €
Research groups participating in the programme: 2
Scientific Supervisor: L. Swevers
Funding for 2021: 45778 €
Funding of your Research Group by the programme for 2021: 45778 €

Other scientific activities not covered by the previous questions

V Labropoulou
Substitute member for the selection of candidates at the Assistant Professor level for the Department of BIO-MEDICAL SCIENCES of the UNIVERSITY OF WESTERN ATTICA with the Knowledge subject "Veterinary Medicine-Detection of molecular markers of parasites and well-being of animal models" (September 2021).

Research Group: Chemical Ecology and Natural Products

Research Staff
Maria Konstantopoulou, Research Director (from 26/4/2021)
Dimitris Raptopoulos, Graduate Research Associate (PhD)
Eleni Koutsoumpeli, Postdoctoral Fellow
Neoklis Manikas, PhD candidate
Petri-Christina Betsi, Graduate Research Associate (MSc)
Ioanna Dasenanki, Graduate Research Associate (MSc)
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.

2021 Findings

Within the framework of the programs OLEFINE (OLEaginous yeast platforms for FINE chemicals) and PHERA (Pheromones for Row crop Applications) HORIZON 2020: i) the production of insect sex pheromones using methods biotechnological (yeast fermentation) was continued and up-scaled and ii) the verification that yeast-produced pheromones are homologous to the chemically synthesised ones was repeated on the new batches of yeast-produced pheromones to verify that the new up-scaled production process does not interfere with the qualitative characteristics of the pheromones. The study of the electrophysiological response (electro-antennography EAG and electro-antennography system connected to the gas chromatograph GC-EAD) of the antennae of male moths to pheromone blends produced by yeast fermentation was carried out. In addition, bioassays on male insects in a wind tunnel were performed and monitored using a camera recording system. The analysis of their behavior

is done through a specialized software (behavioral tracking). To control the activity of biopheromones, field experiments were carried out in three regions in Greece (northern and central) where it was verified that yeast-produced pheromones are homologous to chemically synthesized pheromones ones. In particular, we performed monitoring experiments and trap-shut-down experiments using a flowable polymeric matrix in which the sex pheromone was formulated. For pheromone application a UAV was employed (Figure 1). We continued the research on the optimization of slow release systems for semiochemicals through their inclusion in non-toxic, biodegradable and environmentally friendly polymers and biopolymers endowed with special characteristics aiming at protecting the labile semiochemicals from ultraviolet radiation. We measured the release rate of biopheromones formulated in the flowable polymer (aged naturally under field conditions) using Solid Phase Micro Extraction (SPME) (Figure 1).

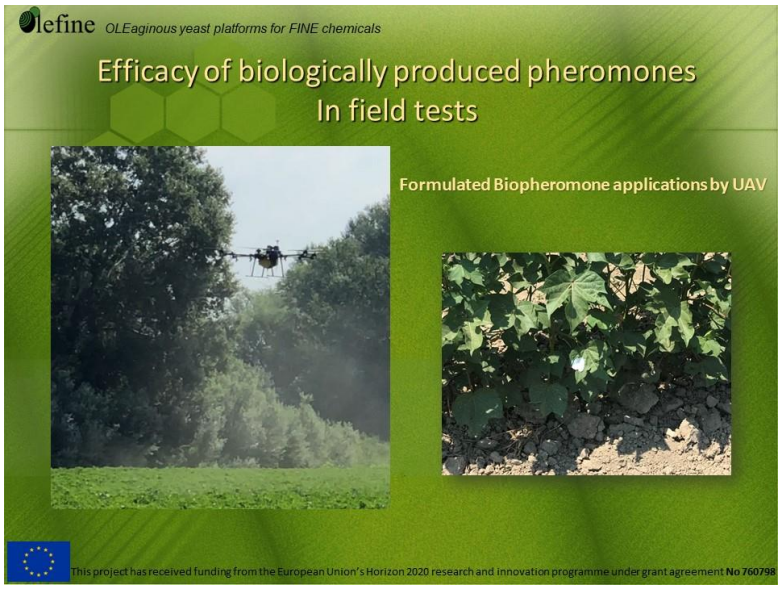


Figure 1

The effort for identification of infochemicals and other bioactive metabolites of natural origin (Biological Control Agents, BCAs) for their use as "smart" insecticides was continued. We tested the effect of secondary metabolites of *Pistacia lentiscus* and the entomopathogenic strain SMU-21 of *Mucor hiemalis* on the viability of *Lobesia botrana* larvae. Fruit extracts of *P. lentiscus* obtained by multi-step fractionation were obtained and it was shown that the most potent fraction was the hexanoic one (PLFHe). This was further analysed using column chromatography. Out of four fractions totally collected and tested for biological activity, only the second fraction induced significant mortality on *L. botrana* larvae equal to 75% of the initial fraction. Using 1H NMR the compound responsible for the observed mortality was identified as triglyceride and using Fatty Acid Methyl Ester Analysis (FAME technique) the constituting fatty acids were identified.

We continued the study of the cytostatic / cytotoxic action as well as the antioxidant action of plant extracts and their fractions from the collection of extracts, which has been generated and is maintained in the laboratory, in collaboration with the Laboratory of Cell Proliferation and Aging of IBA.

The study of psycho-physiological approach of olfactory stimuli of the odor bouquet of plants grown in therapeutic gardens was continued in collaboration with the Medical School of Athens and the Agricultural University of Athens.

In the framework of an MSc internship between our Laboratory and the Plant Sciences Group/ Biosystematics Group of the University of Wageningen a 5 months ERASMUS scholarship was awarded for the study of semiochemicals involved in the chemical communication of Lepidopterous species.

We maintain insect colonies of crop pests of great economic importance (*Helicoverpa armigera*, *Ostrinia nubilalis*, *Lobesia botrana*, *Tuta absoluta Plutella xylostella* and *Plodia interpunctella*). They serve in electrophysiological, behavioral and toxicity experiments.

Publications

Petkevicius Karolis, Koutsoumpeli Eleni, Betsi Petri Christina, Ding Bao-Jian, Kildegaard Kanchana Rueksomtawin, Jensen Hilbert, Mezo Nora, Mazziotta Andrea, Gabrielsson Anders, Sinkwitz Christina, Lorantfy Bettina, Holkenbrink Carina, Löfstedt Christer, Raptopoulos Dimitris, Konstantopoulou Maria, Borodina Irina, 2021. Biotechnological production of the European corn borer sex pheromone in the yeast *Yarrowia lipolytica. Biotechnology Journal* 2100004. (IF: 4.677)

Chrysargyris Antonios, Xylia Panayiota, Koutsoumpeli Eleni, Fytrou Anastasia Maria Konstantopoulou, Nikolaos Tzortzakis, 2021 Organic Cultivation and Deficit Irrigation Practices to Improve Chemical and Biological Activity of *Mentha spicata* Plants. *Agronomy* 11, 599. (IF: 3.417)

Publications accepted

Dasenaki, I.; Betsi, P.-C.; Raptopoulos, D.; Konstantopoulou, M. Insecticidal Effect of *Pistacia lentiscus* (Anacardiaceae) Metabolites against *Lobesia botrana* (Lepidoptera: Tortricidae). Agronomy (IF: 3.417).

Presentations at International Conferences

Petkevicius K., Koutsoumpeli E., Betsi P.Ch., Ding B.J., Kildegaard K.R., Jensen H., Mezo N., Mazziotta A., Gabrielsson A., Sinkwitz Chr., Lorantfy B., Holkenbrink C., Löfstedt Chr., Raptopoulos D., Konstantopoulou M., Borodina I. 2021. Biotechnological Production of the European Corn Borer Sex Pheromone in the Yeast Yarrowia Lipolytica. Annual virtual meeting of AICHe. Abstract 634630.

Other Scientific Activities

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

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

President of the Union of Greek Researcher

Member of the Gender Equality Committee of NCSR “D”

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

Member of organizing committee of XII European Entomological Congress 2023 held in Crete

Topic Editor of 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"

Evaluator of research proposals funded from French National Research Agency (ANR).

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.

Other activities for the Institute of Biosciences & Applications

Member of the Scientific Advisory Board (ESI) of the Institute

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

President of the Scientific Advisory Board (ESI) of the Institute (06/2019-06/2020) and member (07/2020- now).

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

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

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

Total Impact Factor for your original publications in 2021: 8,094 (for 2 publications)

Citations for 2021 (without self-citations): 93
Total citations 2017-2021 (without self-citations): 368
h-factor: 15 (Scopus), 19 (Google Scholar)

Current External Funding

Project entitled *Oleaginous yeast platforms for Fine chemicals* (Horizon 2020, Call: H2020-NMBP-2016-2017/H2020-NMBP-BIO-2017, GRANT AGREEMENT 760798) funded by EU, and Scientific responsible Dr. M. Konstantopoulou.

Duration: 1/1/2018 – 31/12/2021

Total program funding: 441.311 €

Laboratory Funding for2021: 64.235 €

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 2021: 20.000 €

Research Group: Chronobiology

Research Staff

Anastasia Prombona, Senior Researcher
Angeliki Galeou, Postdoctoral Fellow (IKY fellowship)
Danae Farmaki, PhD student
Chrysanthi Stefanatou, Diploma student (completed)
Ioanna Gerodimou, Trainee
Despina Simitsopoulou, Trainee
Tsigaras Marios, Trainee

Research Interests

The research interests of our laboratory aim to explore gene expression regulation and 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 focus on gene expression analysis and regulation of *P. vulgaris* circadian clock genes. The role of the circadian clock in plant defense mechanisms following infection with pathogenic bacteria (*Pseudomonas syringae*) is additionally investigated.

Interaction of the mammalian circadian clock with pathological disorders/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 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. In addition, our studies explore the role of histone modifications in the promoters of clock genes.

2021 Findings

The circadian clock of *P. vulgaris*

In the pathosystem *P. vulgaris* cultivar Red kidney - *Pseudomonas syringae* pathovar *phaseolicola* we have investigated the gene expression of two groups of enzymes that are involved in the oxidative burst and the production of reactive oxygen species (ROS), as the first line of plant defence against invading bacteria. The family of the nine respiratory burst oxidase homologs of *P. vulgaris* (PvRBOHs) and the French bean peroxidase 1 (FBP1) were studied. Our results showed that the oxidative defense of *P. vulgaris* relies on the morning-specific rhythmic activity of FBP1 and on acute and sequentially non-rhythmic response of rhythmic and non-rhythmic oxidases. This work was performed by Dr. A. Galeou (IKY fellowship) and by the Diploma student of the Agricultural University of Athens C. Stefanatou (work accepted for publication in Physiological and Molecular Plant Pathology).

Interaction of the circadian clock with pathological conditions

Our efforts are aimed to achieve recession of carcinogenic properties of cancer cell lines by treatment with circadian clock modulators. During this year we have concentrated on modulators of the activity of the cryptochromes. Our results showed that under specific conditions, the cell cycle is arrested, but with no significant changes in apoptosis levels. The mechanisms are under investigation. This work constitutes part of the PhD work of D. Farmaki.

Articles in Press

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

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 (IF: 2.576).

Presentations at International conferences

A. Galeou, C. Stefanatou and A. Prombona (2021). Circadian clock and pathogen-triggered immunity in *Phaseolus vulgaris*, Plant Biology Europe PBE 2021, Jointly organized by FESPB and epso, 28 June to 01 July, Turin, Italy, Poster no.- 513 –

Presentations at Greek conferences

D. Farmaki, D. Stravopodis, A. Prombona (2021). Exploring the effects of pharmacological modulation of the circadian clock on the oncogenic properties of cancer cell lines 71st HSBMB Congress, 26-28 November NCSR 'Demokritos', Athens, Greece, Poster no.6

A. Galeou, C. Stefanatou and A. Prombona (2021). Interaction between the Circadian Clock and Pathogen-Triggered Immunity in *Phaseolus vulgaris* 71st HSBMB Congress, 26-28 November NCSR 'Demokritos', Athens, Greece, Poster no.43

Total Impact Factor for your original publications in 2021

Citations for 2021 (without self-citations): 36
Total citations 2016-2021 (without self-citations): 157
h-factor (from Scopus and Google scholar): 9

Education

Supervision of the PhD candidate D. Farmaki
Supervision of the Diploma student C. Stefanatou

Other activities in IB-A

Person in charge for the collection and safe removal of chemical waste.

Impact Factor for the 2021 publications: -

Citations for the year 2021 (without self citations): 36

Citations for the years 2016-2021 (without self citations): 157

h-index: 9

Current External Funding (outside IBA) to conduct scientific research, travels, transnational collaborations, etc. (separately for each supported program)

Organization that finances the programme: IKY

Programme title: “Reinforcement of Postdoctoral Researchers - 2nd Cycle” (MIS-5033021), co-financed by Greece and the European Union (European Social Fund- ESF) through the Operational Program «Human Resources Development, Education and LifelongLearning» in the context of the project implemented by the State Scholarships Foundation (IKY). Scholarship contract number: 2019-050-0503-18278
Project title: *The circadian clock in the defence and the phytoprotection of Phaseolus vulgaris during infection by Pseudomonas*
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: A. Prombona
Funding for 2021: 13.200,0
Funding of your Research Group by the programme for 2021: 13.200,0

Research Group: Microbial Molecular Genetics

Research Staff
Vicky Sophianopoulou, Research Director
Christos Gournas, Researcher
Ada Biratsi, Post-Graduate Fellow (PhD candidate)
Amalia Megarioti, Post-Graduate Fellow (PhD candidate)
Spiros Gerostathis, Post Graduate (MA candidate)
Alexandros Valianatos, Post-Graduate Student (Master Thesis completed)
Tatiana Zakopoulou, Undergraduate Student (Diploma Thesis)
Spiros Gaitanos, Undergraduate Student (Diploma Thesis completed)
Georgia-Despina Ifanti, Undergraduate Student (Diploma Thesis)
Vassilis Perpiniadis (Diploma Thesis)

Research interests
Our group is primarily interested in the function, regulation and organization of the fungal plasma membrane (PM). The plasma membrane, as the boundary between the cell and its environment, is a platform for numerous functions. A major efford is to understand how the PM coordinates these diverse processes and the mechanisms underlay them, while maintaining its barrier function.
Our work is targeted to understanding how specific compartments/domains of the PM regulate their structure/function to regulate the activity and /or trafficking of nutrient transporters, persistence of fungal cells, critical stress responses and how these processes are related to 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*). Our models of choice are two genetically tractable model organisms: the non-pathogenic filamentous fungus *Aspergillus nidulans* and the budding yeast *Saccharomyces cerevisiae*. These fungi, for which state-of-the-art genetic tools are available, have been extensively used for the discovery of numerous biological processes and the characterization of their underlying molecular mechanisms.

Long-term objectives: identification of new pharmaceutical targets and future development of highly-targeted antifungals/vaccines.
In parallel, our group is interested in elucidate the molecular mechanisms underlie detoxification of toxic amino acid analogues. L-Azetidine-2-Carboxylic Acid (AZC) is a proline toxic analogue, produced by the flowering plant *Convallaria majalis* (valley lily), certain species of the genus *Polygonatum* and beets (*Beta vulgaris*). In nature, AZC has a protective role for the plants that produce it, and at the same time is a toxic substance for a multitude of organisms, including various bacteria, fungi and mammals. Our studies targeted to understanding the molecular mechanisms underlie catabolism and detoxification of toxic substances by soil fungi.

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

2021 findings

In *Biratsi et al., 2021* we characterized a widespread mechanism for AZC resistance in microorganisms. Our work showed that *A. nidulans* resists AZC toxicity and utilizes it as a nitrogen source via GABA catabolism and the action of the AzhA hydrolase, a member of the

HAD superfamily of detoxifying enzymes, which is highly conserved in bacteria and fungi, and in many pathogens. This detoxification process is further assisted by the NgnA acetyltransferase, which acetylates and detoxifies L-AZC.

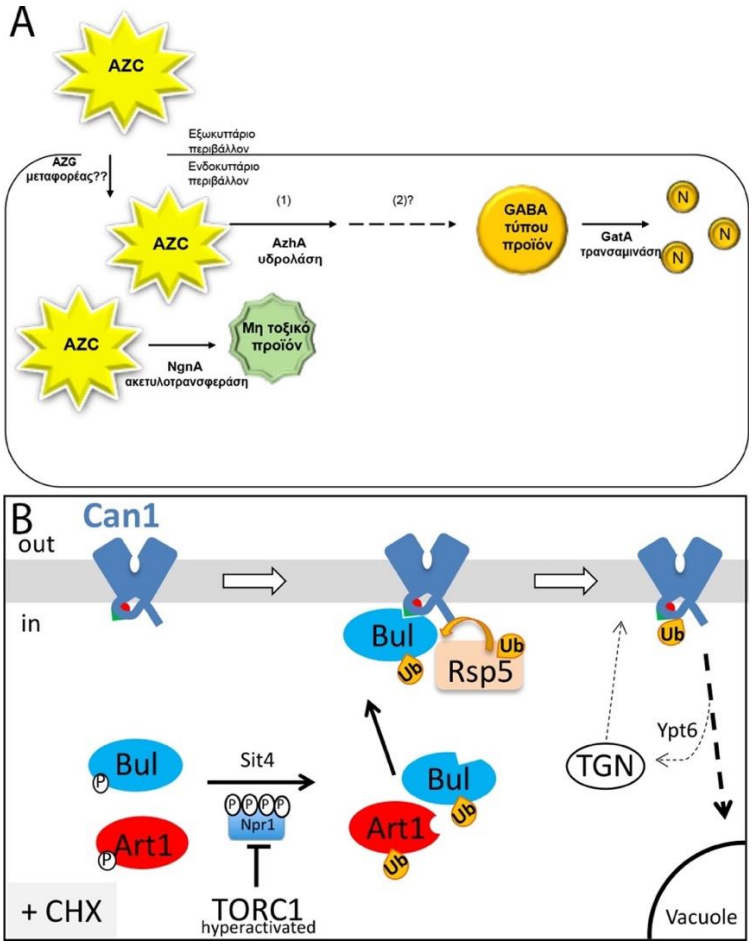
In *Athanasopoulos et al., 2021* we developed a new microscopy-based method, which allows the quantification of the growth rate of the hyphae of filamentous fungi, using an open-source software.

In *Megarioti et al., 2021,* we characterized the mechanism of degradation of the Can1 permease of yeast upon cycloheximide-induced hyperactivation of the TORC1 signalling pathway. Upon cycloheximide treatment, Can1 is sorted to the vacuole via ubiquitin-dependent endocytosis that requires the Rsp5 ubiquitin ligase. Recruitment of Rsp5 to the transporter is independent of Can1 conformation, requires the Bul1/2 α-arrestins, and a specific region at the N-terminal tail of Can1.

In the context of the PhD thesis of A. Megarioti, it was found that eisosomes in quiescent yeasts stabilize the FLPs ubiquinone reductases. FLPs are essential for the long-term survival of quiescent cells, and seem to protect these cells from lipid peroxidation in the presence of polyunsaturated fatty acids, in parallel with the glutathione peroxidases.

In the context of the Master Thesis of A. Vallianatos, it was found that the PstB flavodoxin-like protein (FLP) of *A. nidulans* is not an eisosome (MCC)-resident protein. Following this work, we have identified *in silico* the FspA and FspB proteins of *A. nidulans*, homologues of the human quinone reductase Fsp1, a glutathione-independent ferroptosis suppressor. The subcellular distribution and the role(s) of FspA, B in protection from quinone-mediated oxidative stress and ferroptosis, as well as in promotion of virulence of quiescent conidia, are under investigation.

In the context of the Diploma Thesis of S. Gaitanos it was found that SurG and AnNce102 eisosome (MCC)-resident tetraspan proteins of *A. nidulans* are targeted to the vacuole for degradation during eisosome disassembly, induced either genetically or upon sphingolipid depletion that is known to induce TORC2. The underlying mechanism differs from that of other fungal transmembrane proteins reported to date, is independent of the carbon source, differs in quiescent conidia and the developing hyphae and is a TORC2 inhibition promoting endocytosis. This novel mechanism is under investigation.



A. Schematic representation of the model for the assimilation and detoxification of the toxic proline analog L-azetidine-2-carboxylic acid (L-AZC) in Aspergillus nidulans. L-AZC is taken up by cells via yet unidentified transporter(s). In the cytoplasm, it is hydrolyzed by AzhA hydrolase to a product resembling γ-aminobutyrate (GABA), and assimilated as a nitrogen source by GABA deaminase. In parallel, L-AZC is acetylated and rendered non-toxic by NgnA acetyltransferase. B. Model for endocytosis of the yeast Can1 arginine transporter upon addition of cycloheximide (CHX). Cycloheximide increases the concentration of free amino acids and hyperactivates the TORC1 signaling pathway. TOR kinase phosphorylates and inactivates the Npr1 kinase, leading to dephosphorylation and activation of the α-arrestins Bul1/2 and Art1. In the absence of arginine, Can1 does not expose the Art1 recognition sequence (red semicycle) and is only recognized by Bul1/2 in a different sequence (green triangle). Bul1/2 recruit Rsp5, which ubiquitinylates Can1, causing its endocytosis and targeting to the vacuole for degradation.

Publications in peer-reviewed journals

Biratsi, A., Athanasopoulos, A., Kouvelis, V.N., Gournas, C., Sophianopoulou, V. (2021). A highly conserved mechanism for the detoxification and assimilation of the toxic phytoproduct L-azetidine-2-carboxylic acid in Aspergillus nidulans. *Sci. Rep. 11*, 7391, doi:10.1038/s41598-021-86622-3 (IF = 4.996)

Athanasopoulos, A., Biratsi, A., Gournas, C., Sophianopoulou, V. (2021). Quantitative Analysis of Aspergillus nidulans Growth Rate using Live Microscopy and Open-Source Software. *J. Vis. Exp.*, e62778, doi:10.3791/62778 (IF = 1.4)

Megarioti, A.H., Primo, C., Kapetanakis, G.C., Athanasopoulos, A., Sophianopoulou, V., André, B., Gournas, C. (2021). The Bul1/2 Alpha-Arrestins Promote Ubiquitylation and Endocytosis of the Can1 Permease upon Cycloheximide-Induced TORC1-Hyperactivation. *Int. J. Mol. Sci.*, *22*, 10208, doi:10.3390/ijms221910208 (IF = 6.208)

Kapetanakis, G.C., Gournas, C., Prévost, M., Georis, I., André, B. (2021). Overlapping Roles of Yeast Transporters Aqr1, Qdr2, and Qdr3 in Amino Acid Excretion and Cross-Feeding of Lactic Acid Bacteria. *Front. Microbiol., 12, 1-12,* doi:10.3389/fmicb.2021.752742. (IF = 6.064)

Presentations at International conferences

A. Biratsi, A. Athanasopoulos, C. Gournas, V. Sophianopoulou. A double mechanism for the detoxification and assimilation of the toxic phytoproduct L-azetidine-2-carboxylic acid in Aspergillus nidulans. 71st Conference of the Panhellenic Society for Biochemistry and Molecular Biology, November 26-28, 2021, NCSRD, Athens, Greece (Oral presentation).

Poster presentations :

A.H. Megarioti, T. Zakopoulou, A. Athanasopoulos, B. André, V. Sophianopoulou, & C. Gournas. Eisosome membrane domains are essential for the long-term survival of Quiescent yeasts. 15th International Congress on Yeasts (ICY) and the 30th International Conference on Yeast Genetics and Molecular Biology. August 23-27, 2021. Vienna, Austria.

A.H. Megarioti, T. Zakopoulou, A. Athanasopoulos, B. André, V. Sophianopoulou, & C. Gournas. Eisosome membrane domains are essential for the long-term survival of Quiescent yeasts. 71st Conference of the Panhellenic Society for Biochemistry and Molecular Biology, November 26-28, NCSRD, Athens, Greece.

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

Patents granted in 2021

Patent number WO/2021/219558. Yeast strains for reducing contamination by lactic acid bacteria. Inventors: Bruno André, Christos Gournas.

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, & 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)].

Member of the Advisory Committee & supervisor for the Master thesis of A. Vallianatos, Biology Department, University of Athens (Grade: Excellent) (V. Sophianopoulou)

Member of the Advisory Committee & supervisor for the Dipoma thesis of S. Gaitanos, Biology Department, University of Athens (Grade: Excellent) (V. Sophianopoulou)

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 & supervisor for the Dipoma thesis of T. Zakopoulou, Chemistry Department, University of Athens (V. Sophianopoulou)

Member of the Advisory Committee & supervisor for the Dipoma thesis of G. Ifanti, Biology Department, University of Athens (C. Gournas)

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

Member of the examining committee for the assessment of the doctoral thesis of Georgia Papadaki, entitled "Mechanisms of subcellular Membrane trafficking", Department of Biology, University of Athens (C. Gournas).

Member of the examining committee for the assessment of the doctoral thesis of Athanasia Vassiliki Kourkoulou, entitled "Structure-function relationships in transmembrane transporters", Department of Biology, University of Athens (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 (2018-2021) (V. Sophianopoulou)

Member of the 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” (2018-2021) (V. Sophianopoulou)

Deputy member of the Electoral Body for the tenure of Associate Professor, University of West Attica, School of Health and Welfare Sciences, Department / Institute of Biomedical Sciences, with the subject “Microbiology & Virology” (V. Sophianopoulou)

Deputy member of the Electoral Body for the tenure of Assistant Professor, of the School of Plant Sciences, Agricultural University of Athens, with the subject "Microbiology - Biotechnology of Microorganisms" (V. Sophianopoulou)

Deputy member of the Electoral Body for the tenure of Assistant Professor, of the School of Health Sciences, University of Thessaly, with the subject "Molecular Genetics - Polymorphisms and gene expression in humans, animals and microorganisms" (V. Sophianopoulou)

Deputy member of the Evaluation Committee for the tenure of Assistant Professor, of the School of Health Sciences, University of Thessaly, with the subject "Molecular Genetics - Polymorphisms and gene expression in humans, animals and microorganisms" (V. Sophianopoulou)

Deputy member of the Evaluation Committees for the promotion as Director of Researcher of a Research B of IB-A with the subject “Chemical Ecology & Biotechnology” (V. Sophianopoulou)

Depute member of the Executive Committee for the evaluation of candidates for the election of the Director of IB-A (V. Sophianopoulou)

Reviewing of manuscripts in scientific journals
Biomolecules MDPI, JoF (Journal of Fungi) MDPI (V. Sophianopoulou)

FEMS letters, Oxford Academic; Biology of the Cell, Wiley (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 as Editorial Board member 2 articles of Scientific Reports (V. Sophianopoulou)

Organization of scientific conferences or participation in conference organizing committee
Member of the Organizational/Scientific comitte of the 71st congress of the Hellenic Society of Biochemistry and Molecular Biology, 26-28 November 2021, NCSRD, Athens, Greece (C. Gournas)

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

Presentation at an event of the Panhellenic Union of Bioscientists (PEB) aiming at the assessment the effects of the implementation of the restrictive measures due to coronavirus in the academic field. 14/03/2021 via YouTube, PEB (A. Biratsi).

Seminar for graduate students, within the framework of the Inter-Institutional Inter-Departmental Graduate Program of the Institute of Molecular Biology-Biotechnology and the Institute of Life Sciences of the University Research Center of the University of Ioannina entitled "Molecular-Cellular Biology and Biotechnology". (C. Gournas).

Participation in teaching courses and other 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 (7 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).

Teaching undergraduate students, in the context of the course "Molecular Microbiology", Biology Department of Ahens University (C. Gournas, 2 hours).

Other activities at the IBA and the NCSR “D”
Lecture at the 56th Summer School of NCSR “D” entitled “Confocal Microscope Images & Machine Learning based Super Resolution (A. Panagiotpoulou, A. Athanasopoulos, C. Gournas, V. Sophianopoulou, E. Charou).

Total Impact Factor for original publications in 2021
18.668 (4 publications)

Citation 2021 (without self-citations)
V. Sophianopoulou: 108
C. Gournas: 135

Total citations 2017-2021 (without self-citations)
V. Sophianopoulou: 425
C. Gournas: 504

h-factor
V. Sophianopoulou: 20
C. Gournas: 14 (Scopus), 15 (Google Scholar)

Current external funding
Grant entitled *Plasma membrane organization in quiescence,* by the Fondation Santé - Biomedical Research Grants.
Scientific coordinator: C. Gournas.
Duration: 02/2019 - 10/2021
Total funding for the laboratory: 50.000 €
Funding of the laboratory during 2021: 14.988,37 €

Grant entitled *Study of the role of eisosomal proteins in the quiescent state of fungi,* funded by the ministry of finance and development (Support in researchers, emphasizing on new Researchers, 2nd cycle).
Scientific coordinator, C. Gournas; Academic advisor, V. Sophianopoulou.
Duration: 04/2020-01/2022
Total funding for the laboratory: 45.500 €
Funding of the laboratory during: 21.470,56 €

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.

2021 Findings

Industrial wastewaters are recognized as a valuable resource, however, their disposal without proper treatment can result in environmental deterioration. The associated environmental/operational cost of wastewater treatment necessitates upgrade of applied processes towards the goals of sustainability and mitigation of climate change. The implementation of cyanobacteria-based processes can contribute to these goals via resources recovery, production of high-value products, carbon fixation and green-energy production. The present study evaluates the cyanobacterium Synechococcus elongatus PCC 7942 (S7942) as a biological component for novel and sustainable alternatives to typical biological nutrient removal processes. Valuable results regarding cultivation temperature boundaries, applied disinfection techniques and analytical methods, as well as regarding relations between

parameters expressing S7942 biomass concentration are presented. The results show that at typical industrial wastewater temperatures, S7942 efficiently grew and removed nitrates from treated snack-industry's wastewater. Moreover, in cultures with treated and relatively saline dairy wastewater, its growth rate slightly decreased, but nevertheless nitrates removal rate remained efficiently high. A comparison between typical denitrification processes and the proposed nutrient removal process indicated that a S7942-based system may constitute an alternative or a supplementary to denitrification process. Thus, Synechococcus elongates PCC 7942 proved to be a potent candidate towards sustainable industrial wastewater treatment applications.

Publications

Samiotis, G., Stamatakis, K., Amanatidou, E (2021). Assessment of *Synechococcus elongatus* PCC 7942 as an option for sustainable wastewater treatment. Water Science and Technology 84: 1438-1451 (IF 1.915)

Articles in Press

1. 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)

2. 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)

Presentations at International conferences

1. K. N. Panagiotaki, A. Papavasiliou, K. Stamatakis, Z. Sideratou (2021), Enhanced antimicrobial activity of N-sulfopropylated hyperbranched polyethyleneimine and its effect on photosynthesis, Advanced Nano Materials Conference 2021(ANM2021), 22 – 24 July 2021, Aveiro, Portugal.

2. G. Samiotis, S.A. Theofanidis, K. Stamatakis, E. Amanatidou Cultivation of cyanobacterium Synechococcus elongatus PCC 7942 in wastewater substrate - A challenge to be addressed (2021)
8th International Conference on Sustainable Solid Waste Management SESSION XXIV: Recovery of materials from wastewater & sludge - Sludge Management Conference on Sustainable Solid Waste Management 23-26 June Thessaloniki Greece.

Presentations at Greek conferences

1. P.-I. Broussos, E. Amanatidou, K. Stamatakis (2021) The effect of high temperature on the intracellular sucrose accumulation of the cyanobacterial strains Synechococcus elongatus PCC 7942 and Synechocystis sp. PCC 671471st Conference of the Hellenic Society of Biochemistry and Molecular Biology, NCSR "Demokritos",26–28/11/2021

2. A. Yiakoumidaki Voyiatzi, E. Amanatidou, A. Melis, K. Stamatakis (2021) Study on photosynthesis of recombinant cyanobacteria lacking phycocyanin. 71st Conference of the Hellenic Society of Biochemistry and Molecular Biology, NCSR "Demokritos",26–28/11/2021

Total Impact Factor for your original publications in 2021: 1.915

Citations for 2021 (without self-citations): 76 (Scopus), 89 (Google Scholar)
Total citations 2016-2021 (without self-citations): 299 (Scopus) 373 (Google Scholar):
h-factor (from Scopus and Google scholar): 14 (Scopus) 16 (Google Scholar)

Current External Funding (outside IBA) to conduct scientific research, travels, transnational collaborations, etc.

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: 10000 €
Funding for 2021:
Funding of your Research Group by the programme for 2021:

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.

2021 Findings

During this year, the genomic compositional rule largely known as 'Chargaffs 2nd parity rule' (asserting equimolarity between Adenine-Thymine and Guanine-Cytosine in any of the two DNA strands) is studied in association with Noether's theorem, linking symmetries with conservation laws in physics. In the case of the genome, the strict physical and mathematical prerequisites of Noether's theorem do not hold. However, we conclude that a metaphor can be established with Noether's theorem, as inter-strand symmetry concerning DNA functionality engenders specific features in genome composition. Inversely, when inter-strand symmetry does not hold, the corresponding quantitative relations fail to appear. This association is also considered from the point of view of the existence of emergent laws and properties in evolutionary genomics.

Publications 2021

S. Papageorgiou, Disappearance of temporal collinearity in vertebrates and its eventual reappearance. Biology (2021), 10, 1018. [I.F. = 5.08]

S. Papageorgiou, Physical laws shape up Hox gene collinearity. Journal of Developmental Biology (2021), 9, 17. [I.F. = 2.75]

Articles accepted for publication 2022

Y. Almirantis, A. Provata & W.Li. Noether's Theorem as a Metaphor for Chargaff's 2nd Parity Rule in Genomics. Journal of Molecular Evolution (2022) https://doi.org/10.1007/s00239-022-10062-4

W. Li, Y. Almirantis & A. Provata. Revisiting the neutral dynamics derived limiting guanine-cytosine content using human de novo point mutation data. *Meta Gene* 31 (2022) 100994

Other Scientific activities

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

Teaching

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

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

Impact Factor: 7.83

Citations 2021 (without self- citations): 74

Total Citations 2017-2021 (without self-citations): 331

h-factor: 16 (Scopus)

Research Group: Designed Bioactive Molecules Laboratory

Research Staff

Athanasios Papakyriakou, Senior Researcher
Anastasia Mpakali, Postdoctoral Fellow
Lykourgos Chiniadis, PhD Student
Alexandros Athanasoulis, PhD Student
Evangelos Tsoukas, MSc Student
Luca Landini, Erasmus+ Graduate Student
Maria-Angeliki Siountri, Undergraduate Student
Soultana Kechagia, Undergraduate Student

Research Interests

Design and synthesis of inhibitors for the M1 family of zinc aminopeptidases and structure-based discovery of allosteric inhibitors of the insulin-regulated aminopeptidase (IRAP) in collaboration with Prof. E. Stratikos (National and Kapodistrian University of Athens).

Crystallographic study of a Ru(III)-based antimetastatic agent (NAMI-A) with model proteins to decipher the selectivity of Ru(III)-based drugs as a function of their ligands.

Structure-based design and structure-activity relationships of β-adrenoreceptor ligands in collaboration with Prof. Barbata Richichi (University of Florence, Italy).

Study of the structure and molecular dynamics acetylcholine receptors in complex with toxins (Collaboration with Dr. Petros Giastas, Agricultural University of Athens).

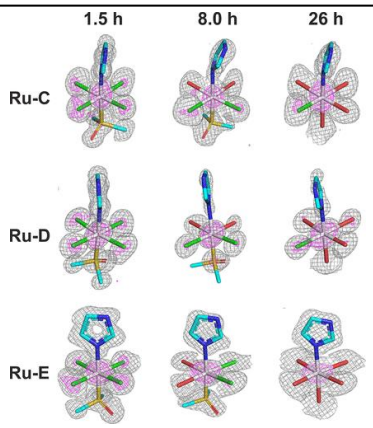
Study of the stabilization mechanism of PIN1 enzyme via phosphorylation from JNK kinase in collaboration with Prof. Salvatore Papa (University of Leeds, UK).

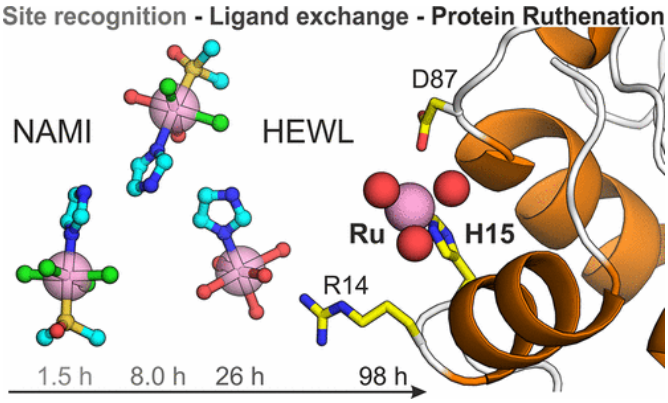
Biophysical study of an LMTK3 kinase inhibitor with α-/β-tubulin dimers using biophysical and computational methods (collaboration with Prof. G. Giamas, University of Sussex, UK).

Structure-based discovery of allosteric inhibitors of phosphatase enzyme through virtual screening of small-molecule compounds (collaboration with Dr. D. Kletsas).

2021 Findings

Dr. Lykourgos Chiniadis has defended his thesis successfully. Title: “Crystallographic study of bioactive ruthenium complexes with model proteins”, Agricultural University of Athens, 12 Nov. 2021 with Prof. E. Eliopoulos, Prof. K. Bethanis and Dr. A. Papakyriakou. The second article of Lykourgos Chiniadis as a first author has been published in the ACS journal *Inorganic Chemistry*.





Project "ALLINIRAP" has been completed successfully with the discovery of an allosteric inhibitor of IRAP, which also blocks hydrolysis of the natural substrate oxytocin (article published in the journal Pharmaceuticals, 2021)

The has been a good progress in the synthesis of M1 zinc aminopeptidase inhibitors based on the β-amino-α-hydroxy acid scaffold of bestatin by the PhD student Alexandros Athanasoulis, which were important to complete a series of inhibitors for publication of the results at a high impact journal. The next inhibitors will target mainly ERAP2, as well as APN and APA aminopeptidases.

Structural characterization of the complex ERAP1/ERAP2 has been completed using computational methods, considering that Dr. A. Mpakali has not succeeded to co-express the dimeric complex. A publication with the computational results obtained has been accepted for publication at Frontiers in Immunology (2022).

The collaborating studies with Prof. S. Papa and Prof. G. Giamas, with two publications in the journals Hepatology and Molecular Cancer, respectively, have been completed (Lepore A. et al. *Hepatology 2021 and* Cilibrasi C, et al. *Mol Cancer 2021*). Another collaboration with Prof. B. Richichi and the Erasmus student L. Landini has been fruitful in the discovery of several β-adrenoreceptor ligands, so a publication is currently under preparation.

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

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: 7.6]

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: 5.0]

Presentations at International Conferences

A. Athanasoulis, E. Stratikos, A. Papakyriakou (2021) *Design and synthesis of peptidomimetic inhibitors for the M1 family of zinc aminopeptidases.* 56th International Conference on Medicinal Chemistry, RICT 2021, July 7–9, 2021, Virtual Event.

A. Mpakali, E. Stratikos, A. Papakyriakou (2021) *Investigation of the heterodimerization between endoplasmic reticulum aminopeptidases ERAP1/ERAP2.* 56th International Conference on Medicinal Chemistry, RICT 2021, July 7–9, 2021, Virtual Event.

A. Athanasoulis, I. Mavridis, I. Temponeras, E. Stratikos, A. Papakyriakou, D. Vourloumis (2021) *Design and synthesis of peptidomimetic inhibitors for the M1 family of zinc aminopeptidases.* Athens Conference on Advances in Chemistry, ACAC 2020, March 10–14 2021, National and Kapodistrian University of Athens, Athens Greece.

G. Mavridis, A. Mpakali, A. Athanassoulis, A. Lelis, D. Georgiadis, A. Papakyriakou and E. Stratikos (2021) *Examination of potential interaction between Endoplasmic Reticulum Aminopeptidase 1 (ERAP1) and Major Histocompatibility Complex I (MHC I).* Athens Conference on Advances in Chemistry, ACAC 2020, March 10–14 2021, National and Kapodistrian University of Athens, Athens Greece.

A. Athanasoulis, I. Mavridis, I. Temponeras, D. Vourloumis, E. Stratikos, A. Papakyriakou (2021) *Design, synthesis and biochemical evaluation of α-hydroxy-β-amino-acid based inhibitors for the M1 family of zinc aminopeptidases.* Athens Summer School on Organic Synthesis 2021 and International Young Investigator Symposium on Organic Synthesis. August 25–27, 2021, Department of Chemistry, National and Kapodistrian University of Athens, Greece.

Presentations at Greek conferences

A. Papakyriakou (2021) *The drug development roadmap: from bench to clinic*. EMBL–IBA seminar, September 12, 2021, Athens, Greece

A. Papakyriakou (2021) *Computational study of protein dynamics and free energy calculations in drug design*. ELIXIR-GR, May 20, 2021, University of Patras, Greece.

Other Scientific Activities

Member of the Organizing Committee of the *10th International Conference of the Hellenic Crystallographic Association*, held in 15–17 October 2021 at NCSR "Demokritos".

Member of the Evaluation Panel of the Hellenic Foundation for Research & Innovation (ELIDEK).

Evaluator and rapporteur of the Latvian Council of Science for basic and applied research (Health, Nov. 2021).

Journal referee in *Molecules, International Journal of Molecular Sciences, Biomedicines, Nutrients, Pharmaceuticals* και *Marine Drugs* (MDPI), καθώς και στα *Frontiers in Immunology* και *Frontiers in Chemistry* (Frontiers).

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

Participation in teaching courses and other educational activities

Interdepartmental Program for Postgraduate Studies of IBE and the Department of Chemistry, University of Patras; Molecular Pharmacology, 2nd semester 2021 (8 hours), Courses: "*Drugs acting on receptors», «Drugs acting on enzymes», και «The adrenergic nervous system – structure-activity relationships of agonists and antagonists»*

Other Activities in IBA and in NSCR "Demokritos"

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

Total Impact Factor for your original publications in 2021: **64.4**
Citations for 2021 (excluding self- citations): 177 (Scopus)
Total Citations 2016-2021 (excluding self-citations): 896 (Scopus)
h-factor: 22 (Scopus), 25 (Google scholar)

Current External Funding (outside IBA) to conduct scientific research, travels, transnational collaborations, etc. (separately for each supported program)

Research grant *ARIA "Atomic Resolution Insight into the Antigen processing machinery"*, funded by from the Hellenic Foundation for Research & Innovation (HFRI).
Coordinator: A. Papakyriakou
Duration: 11/10/2018 – 10/4/2022
Total Program Funding: 180.000€
Funding of the lab for 2021: 60.000€

Research grant to support doctoral students (ΕΔΒΜ) from the Greek Ministry of Development & Investments, *ALLINIRAP* "Allosteric Inhibitors of Insulin-Regulated-Aminopeptidase"
Academic Supervisor: E. Stratikos
Academic co-supervisor: A. Papakyriakou
Duration: 6/4/2020 – 5/7/2021
Total Program Funding: 41.000€
Funding of the lab for 2021: 9.000€

Research Group: Structural Studies of Biomolecules and Pharmaceuticals with NMR

Research Staff
Maria Pelecanou, Research Director
Marina Sagnou, Researcher
Angeliki Panagiotopoulou, **Functional Scientist B**
Barbara Mavroidi, Postdoctoral Fellow
Dimitris Matiadis, Postdoctoral Fellow
Eleftherios Halevas, Postdoctoral Fellow
Michalis Kaplanis, Postdoctoral Fellow
Georgia Athanasopoulou, Postgraduate student, NKUA
Elina Kostaloupi, Undergardutae student – summer internship- University of Patras
Panayota Pantiora, Scientific collaborator

Research Interests

Development (design, synthesis, structural/biochemical characterization, biological evaluation) of new compounds/agents of pharmacological interest for the diagnosis and/or treatment of diseases as well as for biotechnological and nanotechnological applications. Our main fields of research are Alzheimer's disease and cancer, and our tools are NMR and CD spectroscopies for structural 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 evaluation 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, crocine, chrysin, quercetin, sideritis etc.), as well as their complexes (with copper, palladium, platinum, gallium, zinc, silver, etc) with dual activity from the metal and the pharmacophore. 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 suitable ligands, designed for targeted action for diagnosis with SPECT and/or treatment of widespread diseases, in collaboration with INRASTES. Within the same framework, gallium complexes for targeted diagnosis of malignant tumours with PET.

Photochemically active molecules as photosensitisers in photodynamic therapy of cancer and 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 to study the degree of purity of organic compounds, antibiotics, hormones etc., as well as methods of metabolomics NMR analysis for the characterization/ classification of oils, wines, natural extracts, beverages etc.

2021 Findings

The use of natural products and known pharmacophoric structures in the preparation of novel bioactive compounds continued successfully during 2021 through the fruitful contribution of the postodoctoral fellows D. Matiadis (organic synthesis), E. Halevas (complexation, crystalization, encapsulation) and B. Mavroidi (chemical analysis, biological evaluation) producing interesting results. Characteristic examples include • complexes of flavonoids, pyrazoline derivatives, and tetramic acid with Cu(II), Zn(II), Ag(I) and Cd(II) with cytostatic, antimicrobial and antioxidant activity • curcumin complexes with Ga(III) as photosensitizers in cancer photodynamic therapy • curcumin derivatives as mosquito larvicides, anti-trypanosomal agents and as neprilysin inducers • novel dendrimeric hyperbranched nanocarriers with encapsulated artemisinin and remdesivir.

Within the framework of Industrial Scholariships (B. Mavroidi) of the Stavros Niarchos Foundation and in collaboration with the company PharmaGnose SA, the photoprotecting capacity of bioactive natural products from the Greek flora against skin cell lines is in progress, for cosmetic and medical applications.

In continuation of the study of benzothiazole and benzimidazole complexes with radioactive cyclopentadienyl ^{99m}Tc and stable cyclopentadienyl Re, which exhibit remarkable blood brain barrier penetration and properties which make them ideal for the diagnosis (^{99m}Tc) and therapy (Re) of CNS diseases, the evaluation of their anticancer activity against brain cancer cells was completed with very exciting results (IC_{50} value of the order of 1 μM against U-251 MG glioblastoma cell lines, superior to the clinically used chemotherapeutic temozolomide), while the evaluation of their activity against metastatic brain cancer from breast, ovaries, lung, continues. In the area of Alzheimer's disease (AD), in vivo experiments on the 4-month administration of the Re complexes in transgenic 5xFAD mice, recognized AD models, have been completed and the analysis of the data on brain protein expression levels is in progress.

Taking advantage of the IB-A infrastructure, our activity is also expanding to new areas through collaborations, with characteristic examples the:
Confocal microscopy study on the staining of systemic light-chain amyloidosis for diagnostic applications (collaboration with Prof. I. Andreadou, School of Pharmacy, NKUA & Ass. Prof. Efstathios Kastritis, Medical School, NKUA)
CD studies on the aggregation of light chain amyloid proteins responsible for systemic amyloidosis (collaboration with Prof. I. Andreadou, School of Pharmacy, NKUA)
Study on the effect of pesticides on native and cultivated plants of the Greek nature applying metabolomic NMR techniques (collaboration with Assis. Prof. K. Aliferis, AUA)
Assessment of the purity of organic compounds, antibiotics, hormones with the quantitative NMR (qNMR) technique accredited by the Hellenic Accreditation System (collaboration with Dr. E. Kakoulidis, Chemical Metrology Lab, General Chemical State Laboratory)
Confocal microscopy study of porphirinoid and cyclodextrin nanomaterials for photodynamic therapy (collaboration with Dr. K. Yannakopoulou).

Publications

Halevas, E., Mitrakas, A., Mavroidi, B., Athanasiou, D., Gkika, P., Antoniou, K., Samaras, G., Lialiaris, E., Hatzidimitriou, A., Pantazaki, A., Koukourakis, M., Sagnou, M., Pelecanou, M., Lialiaris, T. (2021). Structurally characterized copper-chrysin complexes display genotoxic and cytotoxic activity in human cells. Inorg. Chim. Acta. 515, 120062. (IF: 2.44)

Matiadis, D., Karagiaouri, M., Mavroidi, B., Nowak, K.E., Katsipis, G., Pelecanou, M., Pantazaki, A., Sagnou, M. (2021). Synthesis and antimicrobial evaluation of a pyrazoline-pyridine silver(I) complex: DNA-interaction and anti-biofilm activity. BioMetals, 34, 67-85. (IF: 2.134)

Halevas, E., Hatzidimitriou, A., Mavroidi, B., Sagnou, M., Pelecanou, M., Matiadis, D. (2021). Synthesis and structural characterization of (E)-4-[(2-hydroxy-3-methoxybenzylidene)amino]butanoic acid and its novel Cu(II) complex. MolBank, 1, 1179, 1-24. (IF: 0.54)

Halevas, E., Mavroidi, B., Pelecanou, M., Hatzidimitriou, A.G. (2021). Structurally characterized zinc complexes of flavonoids chrysin and quercetin with antioxidant potential. Inorg. Chim. Acta. 523, 120407. (IF: 2.44)

Halevas, E., Arvanitidou, M., Mavroidi, B., Hatzidimitriou, A.G., Politopoulos, K., Alexandratou, E., Pelecanou, M., Sagnou, M. (2021). A novel curcumin gallium complex as photosensitizer in photodynamic therapy: Synthesis, structural and physicochemical characterization, photophysical properties and in vitro studies against breast cancer cells. J. Mol. Struct. 1240, 130485. (IF: 2.011)

Halevas, E., Mavroidi, B., Kokotidou, Ch., Mitraki, A., Pelecanou, M., Sagnou, M., (2021). Advanced bis-MPA hyperbranched dendritic nanocarriers of artemisinin with anticancer potential, J. Nanopart. Res. 23, 135. (IF: 2.132)

Matiadis, D., Stefanou, V., Tsironis, D., Panagiotopoulou, A., Igglesi-Markopoulou, O., Markopoulos, J. (2021). Synthesis and preliminary biological evaluation of antibacterial and antifungal 5-arylidene tetramic acid-cadmium(II) complexes. Arch. Pharm. 1-11, 2100305. (IF: 3.751)

Papasavva, A., Shegani, A., Kiritsis, C., Roupa, I., Ischyropoulou, M., Makrypidi, K., Pilatis, I., Loudos, G., Pelecanou, M., Papadopoulos, M., Pirmettis, I. (2021). Comparative study of a series of $^{99m}Tc(CO)_3$ mannosylated dextran derivatives for sentinel lymph node detection. Molecules, 16, 4797 (IF: 4.411)

Shegani, A., Ischyropoulou, M., Roupa, I., Kiritsis, C., Makrypidi, K., Papasavva, A., Raptopoulou, C., Psycharis, V. , Hennkens, H. H., Pelecanou, M., Papadopoulos, M., Pirmettis, I. (2021). Synthesis and evaluation of new mixed "2 + 1" Re, ^{99m}Tc and ^{186}Re tricarbonyl dithiocarbamate complexes with different monodentate ligands. Bioorg. Med. Chem. 47, 116373 (IF: 3.073)

Lazopoulos, A., Triantis, C., Shegani, A., Papasavva, A., Raptopoulou, C.P., Psycharis, V., Chiotellis, A., Pelecanou, M., Pirmettis, I., Papadopoulos, M.S. (2021). Effective Labeling of Amine Pharmacophores through the Employment of 2,3-Pyrazinedicarboxylic Anhydride and the Generation of fac-$[M(CO)_3(PyA)P]$ and cis-trans-$[M(CO)_2(PyA)P_2]$ Complexes (PyA = Pyrazine-2-carboxylate, P = Phosphine, M = Re, ^{99m}Tc). Inorg. Chem. 23, 17509-17516 (IF: 5.165)

Matiadis, D., Liggri, P.G.V., Kritsi, E., Tzioumaki, N., Zoumpoulakis, P., Papachristos, D.P., Balatsos, G., Sagnou, M., Michaelakis, A. (2021). Curcumin derivatives as potential mosquito larvicidal agents against two mosquito vectors, culex pipiens and aedes albopictus. Int. J. Mol. Sci. 16, 8915. (IF: 5.923)

Matiadis, D., Ng, S.-T., Chen, E.H.-L., Nigianni, G., Vidali, V.P., Canko, A., Chen, R.P.-Y., Sagnou, M. (2021). Synthesis and biological evaluation of hydroxylated monocarbonyl curcumin derivatives as potential inducers of neprilysin activity. Biomedicines, 8, 955 (IF: 6.081)

Matiadis, D., Nowak, K.E., Alexandratou, E., Hatzidimitriou, A., Sagnou, M., Papadakis, R. (2021). Synthesis and (fluoro)solvatochromism of two 3-styryl-2-pyrazoline derivatives bearing benzoic acid moiety: A spectral, crystallographic and computational study. J. Mol. Liq. 331, 11573 (IF: 6.165)

Matiadis, D., Saporiti, T., Aguilera, E., Robert, X., Guillon, C., Cabrera, N., Pérez-Montfort, R., Sagnou, M., Alvarez, G. (2021). Pyrazol(in)e derivatives of curcumin analogs as a new class of anti-Trypanosoma cruzi agents. Future Med. Chem. 8, 701-714 (IF: 3.808)

Articles in Press

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 $\{Ni_2Ln\}$ (Ln^{III} = Dy, Ho) and $\{Ni_2Y\}$ 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)

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)

International Conference Participation

E. Halevas, M. Kaplanis, B. Mavroidi, A. Hatzidimitriou, G. Litsardakis, M. Pelecanou (2021). Bis-MPA nanocarriers with Zn(II)-morin load with anticancer potential. 18th International Conference on Nanosciences & Nanotechnologies (NN21), July 6-9, 2021, Thessaloniki, Greece

P. G. V. Liggri, D. Matiadis, E. Kritsi, N. Tzioumaki, P. Zoumpoulakis, D. P. Papachristos, G Balatsos, M. Sagnou, A. Michaelakis. (2021) Curcumin derivatives as potential mosquito larvicidal agents against two mosquito vectors, Culex pipiens and Aedes albopictus. 10th International Conference of the Hellenic Crystallographic Association (HeCrA), 15-17 October 2021, Athens, Greece.

D. Dermitzaki, A. Panagiotopoulou, C. Raptopoulou, V. Psycharis. (2021) 3d/4f chiral complexes: The case of $\{Cu_8Ln_4\}$ (Ln^{III} = Dy, Ho) clusters. 10th International Conference of the Hellenic Crystallographic Association (HeCrA), 15-17 October 2021, Athens, Greece

P. Kallimanis, P. Magiatis, T. Tsiaka, P. Zoumpoulakis, A. Panagiotopoulou, I. Chinou. (2021) Quantitative and qualitative evaluation of 60 Labiatae species, growing in Greece, regarding the content of selected abietane-type diterpenes using ^{1}H-qNMR. 69th International Congress and Annual Meeting of the GA, September 5–8, 2021, Bonn, Germany

National Conference Participation

B. Mavroidi, E. Thoma, A. Argyropoulou, A-L Skaltsounis, M. Pelecanou (2021). Greek Medicinal Plants for Photoprotection. 71st Annual Conference of the Hellenic Society of Biochemistry and Molecular Biology (HSBMB), November 26-28, 2021, Athens, Greece

B. Mavroidi, M. Sagnou, A. Shegani, M. Paravatou-Petsotas, I. Pirmettis, M. Papadopoulos, M. Pelecanou (2021). Development of 99mTc/Re 2-phenylbenzothiazole agents against breast cancer. 18th Hellenic Symposium on Medicinal Chemistry, February 25 – 27, 2021

D. Matiadis, B. Mavroidi, H. Pratsinis, D. Kletsas, M. Pelecanou, M. Sagnou (2021). Novel pyrazoline-bearing curcuminoid derivatives: synthesis and evaluation of their potential anticancer activity. 18th Hellenic Symposium on Medicinal Chemistry, February 25 – 27, 2021

P. Pantiora, D. Matiadis, B. Mavroidi, F. Perperopoulou, M. Sagnou, M. Pelecanou, N. Labrou (2021). Inhibition activity of curcumin derivatives against the glutathione s-transferase enzyme. Hellenic Society for Biochemistry and Molecular Biology (HSBMB), January – June, 2021

Patents granted in 2021

A European Patent application was granted (EP3755383, 22-7-21) “TRICARBONYL COMPLEXES OF
TRANSITION METALS WITH BENZO-HETEROCYCLIC DERIVATIVES OF THE CYCLOPENTADIENYL ANION” M. Pelecanou (IB-A), M. Sagnou (IB-A), M. Papadopoulos (INRASTES), I. C. Pirmettis (INRASTES), (IB-A) and A. Shegani (INRASTERS).

Other Scientific Activities

Academic Editor for the Special Issue "Novel Approaches for Asymmetric Synthesis", Symmetry, MDPI – M. Sagnou

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

Teaching and Educational activities

Inside IBA: Lectures in the Bi-Institutional Program of Graduate Studies, a collaboration of the Chemistry Department of the University of Patras with IBA of the NCSR “Demokritos” entitled «Applied Biochemistry: Clinical Chemistry, Biotechnology, Validation of Pharmaceutical Drugs». Molecular Pharmacology – Special topics (A’ semester) – Structure and function of mucleic acids – DNA structure/DNA targeting drugs/RNA structure/RNA targeting drugs/ nucleic acid targeting drugs/ molecular biology and genetic engineering) (B’ Semester). – 9 students (M. Sagnou)

Other Activities for the Institute of Biosciences & Applications

M Pelecanou:
Co-responsible (with M. Vlassi) for the operation of the circular dichroism spectrometer (CD) at IB-A. (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, Head Dr. K. Yannakopoulou)

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 of the CD spectropolarimeter and the 250 MHz and 500 MHz NMR spectrometers and Provision of Specialized Scientific Services
Responsible for the Blood Bank of NCSR "Demokritos"

Maria Pelecanou
Total Impact Factor for publication in 2021: 24.346
Citations in 2021 (without selfcitations): 165 (Scopus)
Total citations during 2016-2021 (without selfcitations): 557 (Scopus)
h-factor (Scopus): 23

Marina Sagnou
Total Impact Factor for publication in 2021: 31.234
Citations in 2021 (without selfcitations): 127 (Scopus)
Total citations during 2016-2021 (without selfcitations): 407 (Scopus)
h-factor (Scopus): 17

Angeliki Panagiotopoulou
Total Impact Factor for publication in 2021: 3.751
Citations in 2021 (without selfcitations): 37 (Scopus)
Total citations during 2016-2021 (without selfcitations): 35 (Scopus)
h-factor (Scopus): 8

Other Activities that are not mentioned in above questions

Evaluation of the competence of the NMR laboratory, suitability of the qNMR method used and of the equipment involved, including its state of calibration and maintenance for accreditation from ESYD (A. Panagiotopoulou).

Participation in proficiency testing schemes and interlaboratory comparisons of the High Resolution NMR laboratory NCSR “Demokritos” (A. Panagiotopoulou).

Current External Funding (outside IBA) to conduct scientific research, travels, transnational collaborations, etc. (separately for each supported program)

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 2021: 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 2021: 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”, School of Medicine & Department of Pharmacy, NKUA
Total Program Funding: 250.000 $
Funding for the lab: The project was approved in December 2021 and funding has started during 2022

Project entitled: The effect of the new curcumin derivative C66 on cardiomyopathy caused by doxorubicin, funded Icelandic Cancer Society- Science Fund.
Responsible for IB-A: M. Sagnou
Duration: 1 year, 2021-2022
Collaborating teams: NCSR “Demokritos”, Faculty of Medicine (University of Iceland)
Total Program Funding: ISK 10 million
Funding of the lab for 2021: 3.800 €

Research Group: Protein Structure and Molecular Modeling

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

Research Interests

Protein folding

Sequence/structure relationships of amino-acid repeats / Role in protein-protein interactions

Molecular dynamics of proteins

Molecular dynamics simulations & development of related tools

Kinases

Protein interactions

Intrinsically disordered proteins

Structure & dynamics of enzymes as potential therapeutic targets

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

2021 Findings

With the aim to elucidate sequence-structure-function relationships of proteins (kinases in particular), in 2021:

1) We continued and extended *in silico* structural studies of the tyrosine kinase Tyk2, which plays a pivotal role in signal transduction and autoimmune diseases and of its protective P1104A variant (see also *Lesgidou et al, Bioinformatics 2018*) that is however, linked to cancer. The aim of these studies is to elucidate the effects of the Pro1104 to Ala substitution on the structure and dynamics of Tyk2 towards an in depth understanding of the atomic-details of its function. More specifically, in 2021 we performed comparative analyses of several long, microsecond-scale (up to 4 μs) MD trajectories of pre-phosphorylation forms of the wtTyk2 and P1104A catalytic domains (KD) that we had previously obtained using the National HPC facility-ARIS @GRNET (project ID: *KIN_IMMUNMD_II;* pr008030). Based on these analyses, some of the existing MD trajectories were extended to longer time-scales, whereas additional MD experiments were designed for new KD forms as well as for longer fragments of both proteins. Due to lack of known crystal structures for these Tyk2 forms, construction of initial 3D-models was required prior to the MD simulations. The additional long MD simulations were performed also on the ARIS system @GRNET under a new project (ID: *KIN_IMMUNMD_III)* that was submitted to GRNET in January 2021 in the framework of the "*10th Call for ARIS Project Access* "and was approved in March 2021. This project (pr010026) received computing resources of 1.900.000,0 core-hours for 12 months. Comparative analyses (such as those shown in Figure 1) of the new MD trajectories as well as additional analyses of previously obtained MD data, are in progress.

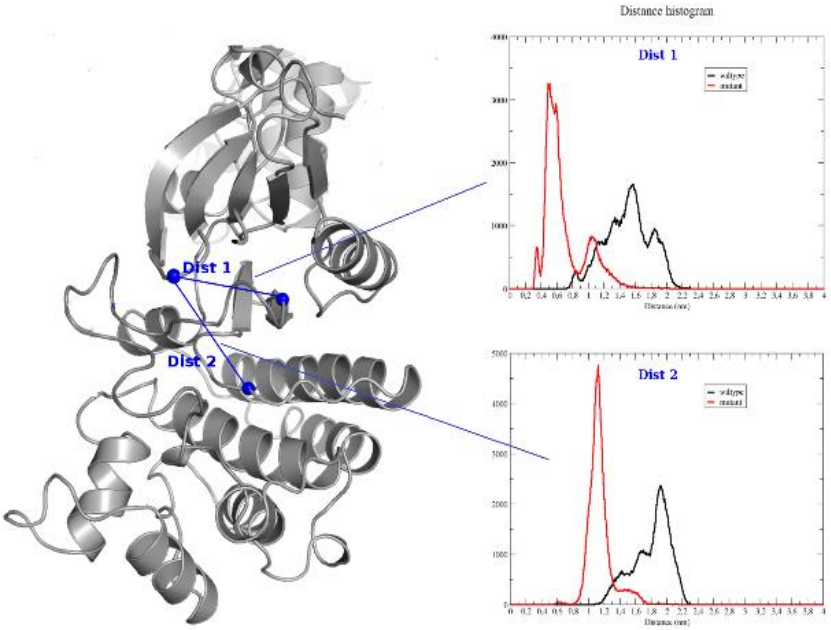


Figure 1*. Comparative analyses of long MD trajectories of wtTyk2 and P1104A, such as those shown in this Figure (up to 4 μs), contribute not only to elucidate the effects of the Pro1104 to Ala substitution on the structure and dynamics of the kinase domain of Tyk2, but also to shed light on structure-dynamics-function relationships of the wild type protein itself.*

2) Regarding the SRPK1 kinase that we have also studied in the past (see *Sellis et al BBA-General Subjects 2012*; *Vlassi et al Data in Brief 2019*), MD simulations of its KD in complex with peptides from a human protein linked to carcinogenesis were extended to much longer time-scales (up to 1 μs). Direct association of these two proteins have been observed experimentally (biochemically) by our collaborators (T. Giannakouros' group, Aristotle University of Thessaloniki) and the aim of the *in silico* structural study is to elucidate the atomic details of this particular SRPK1 protein interaction. The MD simulations used previously constructed 3D-models, as initial conformations, and were performed using local computing resources; namely, a 64-core server. Various analyses of the long MD trajectories as well as comparative analyses, are in progress.

In parallel, and in the framework of the INSPIRED project (see *Funding* section), in 2021 we collaborated with the Institute of Applied Biosciences, CERTH, Thessaloniki (M. Koutroumani; States Fellowship Foundation-IKY fellowship recipient) on the spliceosome protein, SF3B1. More specifically, we predicted *in silico* the structural and functional consequences of an amino-acid change corresponding to a *SF3B1* gene mutation related to chronic lymphocytic leukemia.

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

Presentations in Scientific Conferences

N. Lesgidou and M. Vlassi (2021) Understanding the conformational differences between Tyk2 kinase and a protective variant against autoimmune diseases through microsecond-scale molecular dynamics simulations. **Virtual Congress of the Hellenic Society of Biochemistry & Molecular Biology / Chemical, Structural Biology & Disease Treatment session**, 3 March 2021. Book of abstracts P 39. (eposter/short talk).

N. Lesgidou, Metaxia Vlassi (2021) Using large-scale molecular dynamics simulations to elucidate sequence-structure-function relationships of a tyrosine kinase, **10th International Conference of the Hellenic Crystallographic Association (HeCrA), NCSR "Demokritos",** Athens, Greece, 15-17 October 2021. Book of abstracts, Pg 89-90.

Other Scientific Activities

Ad hoc reviewer of the International scientific journal, *Cancers* (MDPI) (one article)

Ad hoc reviewer of the International scientific journal, *Cells* (MDPI) (one article)

Member of the Scientific Committee of the *10th International Conference of the Hellenic Crystallographic Association (HeCrA), NCSR "Demokritos", Athens, Greece, 15-17 October 2021*

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 ad hoc appointment committees of NCSR "Demokritos" for two positions (1 post-doctoral and 1 temporary personnel) in the framework of a research grant: HORIZON 2020/Marie Skłodowska-Curie Innovative Training Networks (IIT).

Member of the European Network INSTRUCT-ERIC (INSTRUCT: An integrated Structural Biology Infrastructure for Europe)

Member of the related National Research Infrastructure project: "INSTRUCT-EL, an initiative of Greek Researchers related to Structural Biology". The related RI project "***INSPIRED:*** *The National RIs on Integrated Structural Biology, Drug Screening efforts and Drug-target functional characterization"* is funded by the GSRT (funding approved: June2018. 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 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 at IB-A & NCSR "D"

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

Member of various committees of NCSR “D”

Citations 2021 (excluding self-citations): 34

Total citations 2017-2021 (excluding self-citations): 148

h-factor: 14

Funding-Projects

“INSPIRED: The National Research Infrastructures on Integrated Structural Biology, Drug Screening Efforts and Drug Target Functional Characterization”, implemented under the Action “Reinforcement of the Research and Innovation Infrastructure”, funded by the Operational Programme "Competitiveness, Entrepreneurship and Innovation" (NSRF 2014-2020) and co-financed by Greece and the European Union (European Regional Development Fund) (Role of M. Vlassi: member of the group of Scientists of 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 2021 for the group: 19.079,22€€

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 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 2021: 1.500.000,0 core-hours

CENTRAL PROJECTS
IBA

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

SANITURA

The project TARGET IDENTIFICATION AND DEVELOPMENT OF NOVEL APPROACHES FOR HEALTH AND ENVIRONMENTAL APPLICATIONS (acronym: SANITURA, MIS 5002514) coordinated by the Director of IBA, was concluded in April 2021. It was part of the Action for the Strategic Development on the Research and Technological Sectors, funded by the Operational Programme "Competitiveness, Entrepreneurship and Innovation" (NSRF 2014-2020) and co-financed by Greece and the European Union (European Regional Development Fund). Aim of the project was the support of IBA research activities falling into the National Research and Innovation Strategies (RIS), such as the delineation of disease mechanisms, the identification of biomarkers and novel treatment targets, the development of preclinical disease models, the discovery of bioactive molecules and natural products for pharmaceutical and cosmetic applications, and the design of technologies for suppressing the environmental footprint of the agro-food sector. The project started in 2017, and was implemented with the active participation of almost all permanent IBA researchers, whose effort summed up in approximately 138 person-months. Twenty-three external collaborators at PhD and MSc levels were also recruited providing in total 274 person-months. The total budget for the project was 740,000 €, 98.9% of which was consumed in the period 2017-2021. 60% of the budget was used for external collaborators' salaries, 11% for consumables, 6% for purchasing new equipment, and 23% for other expenditures and overheads withheld by the Dept. of Research Special Accounts, NCSR "Demokritos". Thirty-four (34) publications in international peer-reviewed journals were produced with support from SANITURA, as well as, twenty (20) communications in international and national conferences.

OPENSCREEN-GR

IBA coordinates the project AN OPEN-ACCESS RESEARCH INFRASTRUCTURE OF CHEMICAL BIOLOGY AND TARGET-BASED SCREENING TECHNOLOGIES FOR HUMAN AND ANIMAL HEALTH, AGRICULTURE AND THE ENVIRONMENT (acronym: OPENSCREEN-GR, MIS 5002691), which is implemented under the Action "Reinforcement of the Research and Innovation Infrastructure", funded by the Operational Programme "Competitiveness, Entrepreneurship and Innovation" (NSRF 2014-2020) and co-financed by Greece and the European Union (European Regional Development Fund). Coordinator of the project is the Director of IBA. OPENSCREEN-GR aims at the consolidation of a national infrastructure for medium to large-scale molecular target-based screening of existing libraries of synthetic small molecules, but also natural products. This infrastructure will provide the necessary equipment, as well as, trained personnel for implementing a vast array of bioactivity assessment methodologies. Beyond the identification of novel bioactive compounds, OPENSCREEN-GR can proceed to their characterization, through studies of their biological effects and of the underlying molecular mechanisms, making use of a variety of model systems both *in vitro* and *in vivo*. These studies can also be combined with bioinformatics tools (*in silico*) for modeling the interactions of the bioactive compounds with their cellular targets, as well as, for analyzing structure-activity relationships (SAR). Apart from IBA, six other research and academic institutions are members of OPENSCREEN-GR: Aristotle University of Thessaloniki, Democritus University of Thrace, University of Ioannina, National Hellenic Research Foundation, Biomedical Research Foundation of the Academy of Athens, and Agricultural University of Athens.
OPENSCREEN-GR as a whole project was concluded at the end of 2021, while the part delivered by IBA was finished in November 2021. The total budget for IBA within the project was

899,600€, from which 336,760€ were consumed for equipment (Figure 1) and 325,880€ for external collaborators' salaries. The remaining budget was used for consumables, small equipment and other expenditure, including overheads. Finally, 97.7% of the initial budget was disbursed. Eight IBA's researchers participated in the project, providing in total approximately 30 research person-months, while fifteen external collaborators were also recruited, delivering in total 192 research person-months. OPENSCREEN-GR supported sixteen (16) publications by IBA researchers in international peer-reviewed journals up to now.
Moreover, the national infrastructure OPENSCREEN-GR is connected to the corresponding European Research Infrastructure Consortium (ERIC) EU-OPENSCREEN, through the participation in the European project EU-OPENSCREEN-DRIVE, which is currently in progress.

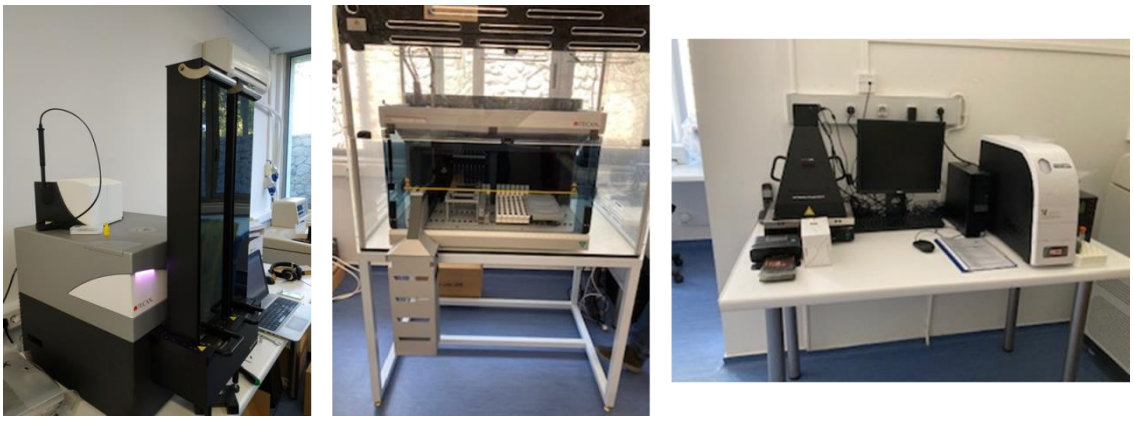


Figure 1: *Parts of the laboratory equipment of the Research Infrastructure OPENSCREEN-GR in IBA*

BIOIMAGING-GR

IBA is one of the eleven partners of the project A GREEK RESEARCH INFASTRUCTURE FOR VISUALIZING AND MONITORING FUNDAMENTAL BIOLOGICAL PROCESSES (acronym: BIOIMAGING-GR, MIS 5002755), which is implemented under the Action "Reinforcement of the Research and Innovation Infrastructure", funded by the Operational Programme "Competitiveness, Entrepreneurship and Innovation" (NSRF 2014-2020) and co-financed by Greece and the European Union (European Regional Development Fund), and is coordinated by the Foundation for Research and Technology-Hellas (FORTH). Regarding IBA's part of the project, it aims at the optimal function of the Imaging Unit, consisting mainly in an inverted confocal / multiphoton microscope and two UV / visible microscopes (one upright and one inverted). Hence, this Unit is expected to contribute in the development of research collaborations for the *in vitro* identification and imaging of biomolecules, facilitating the study and delineation of biological mechanisms, cellular functions, biochemical pathways, as well as, the development of novel small molecules capable for selective interactions with the above molecular and cellular systems. Head of the IBA's part of the project is the Director of the Institute, while the scientific team comprises 14 more IBA researchers and two external collaborators, the Imaging Unit operator and a specialist in stem cell research (expert in flow cytometry and imaging techniques). BIOIMAGING-GR -GR as a whole project was concluded at the end of 2021, while the part delivered by IBA was finished in November 2021. The total budget for IBA within the project was 211,250€, from which 80,700€ were consumed for

external collaborators' salaries, and the rest for consumables, equipment upgrading and other expenditure, including overheads. Finally, 90% of the initial budget was disbursed. BIOIMAGING-GR supported ten publications by IBA researchers in international peer-reviewed journals, as well as, three communications in international and national conferences up to now.

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 2021, the flagship national initiative entitled CREATION OF A NATIONAL RESEARCH NETWORK IN THE VALUE CHAIN OF "HONEY" (acronym: THE ROUTES OF BEE) was continued. 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 is coordinated by the Aristotle University of Thessaloniki. Ten more partners are involved, including IBA, which participates 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 €.

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 2021

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. Contacts were made with foreign anti-doping laboratories accredited by WADA for cooperation in the transfer of knowledge and training as well as for the purchase of a new LIMS (Laboratory Information Management System). At the same time, the hire two

new scientific staff members, with a one-year contract with the possibility of renewal, increasing the number of scientific staff members to ten, was proceeded.

Two new LC-HRMS analytical instruments (Orbitrap Plus) were installed following an international tender. Two international tenders were launched for the supply of two new GC-MS/MS analytical instruments (qqq) and one new GC-IRMS. A tender was launched for the supply of a new HPLC. Validation of the analytical methods continued with the aim of re-accreditation of the Laboratory by WADA in the field of doping control of athletes.

A tender for the supply of reference materials and consumables of worth €60,000 was continued.

The research activities continued within the framework of a research program funded by WADA, while a new funded research program was approved following a collaboration proposal of the Laboratory and the Institute of Nanoscience and Nanotechnology (INN) of the NCSR "Demokritos".

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

A new alarm system was installed while the CCTV system restarted after appropriate maintenance and expansion of the existing system.

The quantities of the Laboratory's consumables were recorded and lists of reference materials and consumables/materials were prepared for the start of an international tender for their purchase in the amount of approximately €400,000.

At the same time, the staff of DCLA continued the research activity, which led to three publications in international scientific journals.

Original publications

Wagener F, Guddat S, Gorgens C, Angelis YS, Petrou M, Lagojda A, Kuhne D, Thevis M. (2021). Investigation into the elimination profiles and metabolite ratios of micro-dosed selective androgen receptor modulator LGD-4033 for doping control purposes. Anal Bianal Chem. doi.org/10.1007/s00216-021-03740-7 (IF: 4.29).

Kiousi P, Fragkaki AG, Kioukia-Fougia N, Angelis YS (2021). Liquid chromatography-mass spectrometry behavior of Girard's T derivatives of oxosteroid intact phase II metabolites for doping control purposes. Drug Test Anal. doi: 10.1002/dta.3056 (IF: 3.23).

Sakellariou P, Kiousi P, Fragkaki AG, Lyris E, Petrou M, Georgakopoulos C, Angelis YS. (2021). Alternative markers for methylnortestosterone misuse in human urine. Drug Test Anal. doi:10.1002/dta.2887 (IF: 3.23).

HUMAN TISSUE BANK

Personnel
Helen Vavouraki Senior Researcher, Scientific Responsible
Yiannis Ninios, Ph.D, Research Collaborator
Lydia Panagopoulou, MSc, Research Collaborator
Eleutherios Kosmidis, MSc, Scientific Collaborator

Laboratory Description – Research Interests

A) Development activity

The main objective of Human Tissue Bank (HTB) is the collection of various human tissues, their processing and the production of grafts to be used in Regenerative Medicine and Reconstructive Surgery.

It is one of the first legislated laboratories of NCSR "DEMOKRITOS", recently licensed as a Tissue and Cell Bank by the Ministry of Health (Greek Government Gazette 768, 26.02.2021) after thorough preparation and submission of all necessary documents.

Member of the European Association of Tissue Banks, it is the only bank of its kind in Greece, applying its "knowhow" in the processing of a great variety of human tissues. It has gradually developed the necessary expertise in each procedure (procurement, tissue processing, irradiation sterilization and disposal of tissue grafts) involved in the Tissue Banking. All the above activities comply with the European Directives 23/2004, 17/2006 and 86/2006 concerning human tissues and cells, as they were implemented in Greece by the 26/2008 Law, as well as, to the recommendations of International Atomic Energy Agency (IAEA).

In over 46 years of continuous operation, HTB has delivered more than 54.000 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.

Funded by a NSRF Research Project, we have developed a new, specially designed bone graft to accompany a patented surgical tool in Neurosurgery. The innovative human bone graft we have produced from living donors, will replace the synthetic grafts which were in use before.

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.

Our research activities are therefore based on collaborations with universities and healthcare institutions, in order to promote Public Health by launching improved products, publishing original papers and participating in doctorate degrees (Ph.D. theses)

2021 Findings

Despite all problems entrained by the SARS-CoV-2 pandemic, HTB managed to collect adequate tissues from collaborating hospitals. More precisely, we have processed femur heads from 132 living donors and we have produced and delivered 848 bone grafts to be used in Dentistry and Orthopedic Surgery. Meanwhile, we have processed 17 cranium grafts from Neurosurgery Depts.

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

On line Attendance /Participation in Congresses/Fairs

71^{o} Congress of Hellenic Society of Biochemistry and Molecular Biology.
January 2021

Conference EUandU, Organized by European Commission Delegation in Greece under the title: *"Science and Innovation in our Life",*
January 2021

Conference of Health Tech Hub Styria (HTH Styria), in the field of Medical Technology and Biotechnology, in collaboration with Enterprise Europe Network.
January 2021

Participation in the Webinar "Digital Health and Intellectual Property"

Laboratory of Applied Research Exploitation, Archimidis Center and ECB

"Research and Innovation in Greece – Public Conference. "

Dianeosis, March 2021

"Tech Transfer: From Research to Market"

Uni Fund /Onassis Foundation, May 2021

Other Scientific Activities

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

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

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

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

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

Research Proposals Assessor

Other Activities at the NCSR "DEMOKRITOS"

Quality Manager of the Lab, according the **ISO 9001/2015**

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

Establishment of a spin-off company of NCSR "DEMOKRITOS" by the name "Ygeia Innovations" for the exploitation of the Lab expertise in the field of Human Tissue Grafts.

Educational activities

Joint MSc Program «Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products», April 2021: Course: Tissue Banking-Development, Production and Quality Control of Tissue grafts

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

Citations 2021 (without self- citations):10

Total Citations 2016-2021 (without self- citations): 156

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

Current External Financing

NSRF Project:

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

Duration: June 2018 – October 2021

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

Research Supervisor: H. Vavouraki

Overall funding: 188.800 €

Funding for 2021: 49.747,61 €

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. Currently, the aim of the Animal House is the supply of small laboratory animals to be used in experimentation in basic science, in the development of therapeutic regimes and new technologies, as well as in educational purposes. Today, the Animal House functions in compliance with the national and international standards and covers the most recent demands for research conducted on animal models.

The function of 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. Finally, The Scientific and Administrative Head of the Animal House is an alternate member of the National Committee for the well-being of Laboratory Animals.

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 2021 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 (wild type and transgenic AD 5xFAD and TgMMP-9)

5. Rats, strain WISTAR ALBINO

6. Rabbits, strain New Zealand ALBINO

7. Colonies of aged mice and rats are also available

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: A. Tzinia, 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 member of the National Committee for the wellbeing of laboratory animals.

During 2021

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

Seven (7) new protocols for animal experimentation have been approved.

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

A new system of telemetry for the surveillance of the environment of the Animal house has been established.

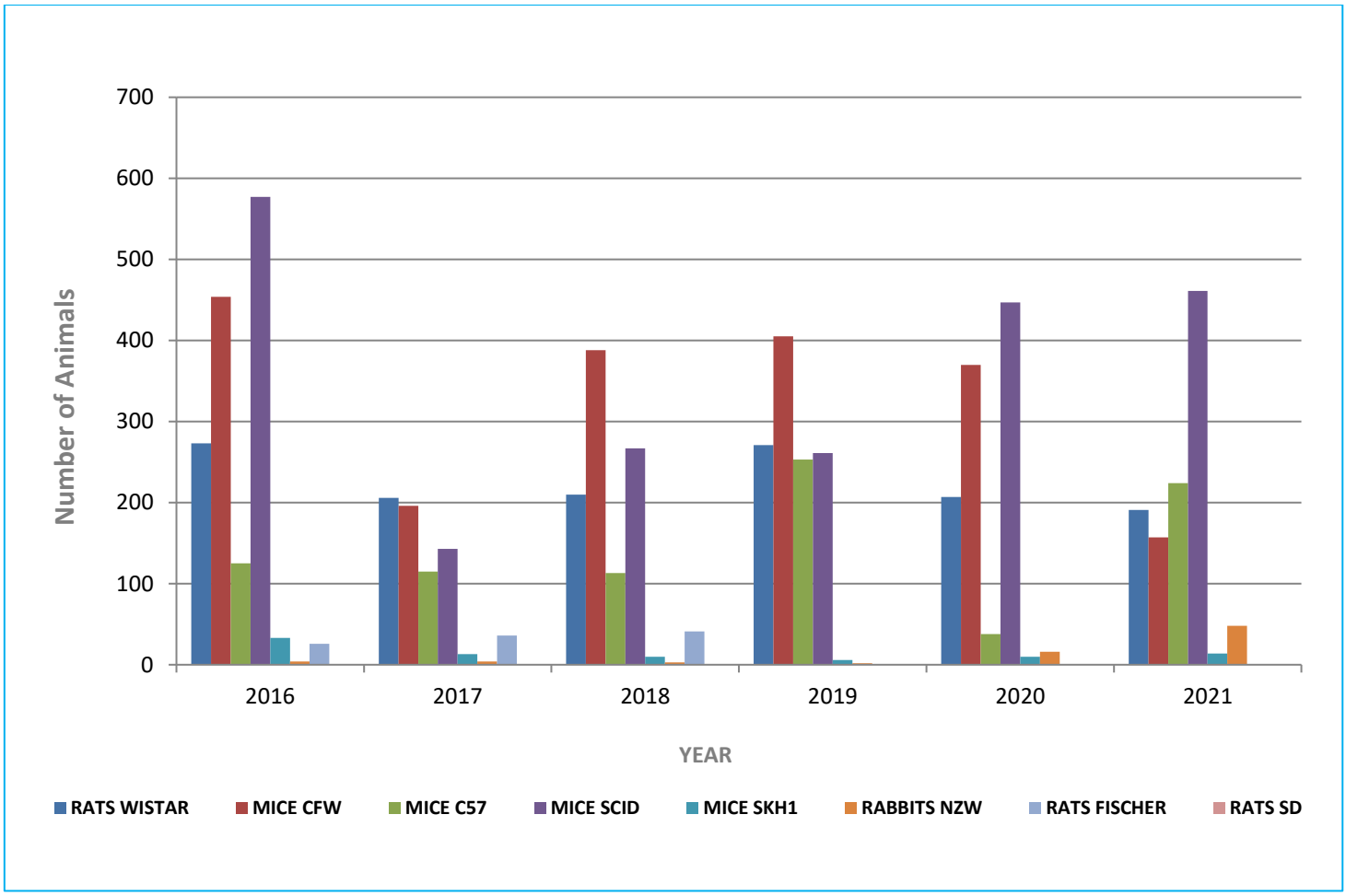
A new colony for the reproduction of New Zealand rabbits has been established.

The personnel of the Animal House followed several educational seminars.

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

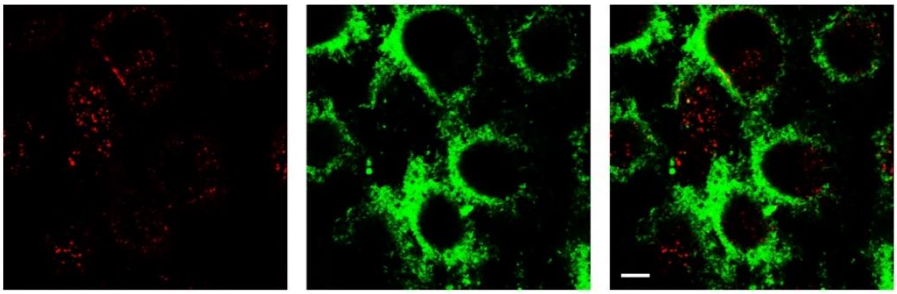
STATISTICS

DISPOSAL OF LABORATORY ANIMALS 2016 - 2021



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 2021
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 2021 the light microscopy unit recorded 300 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.

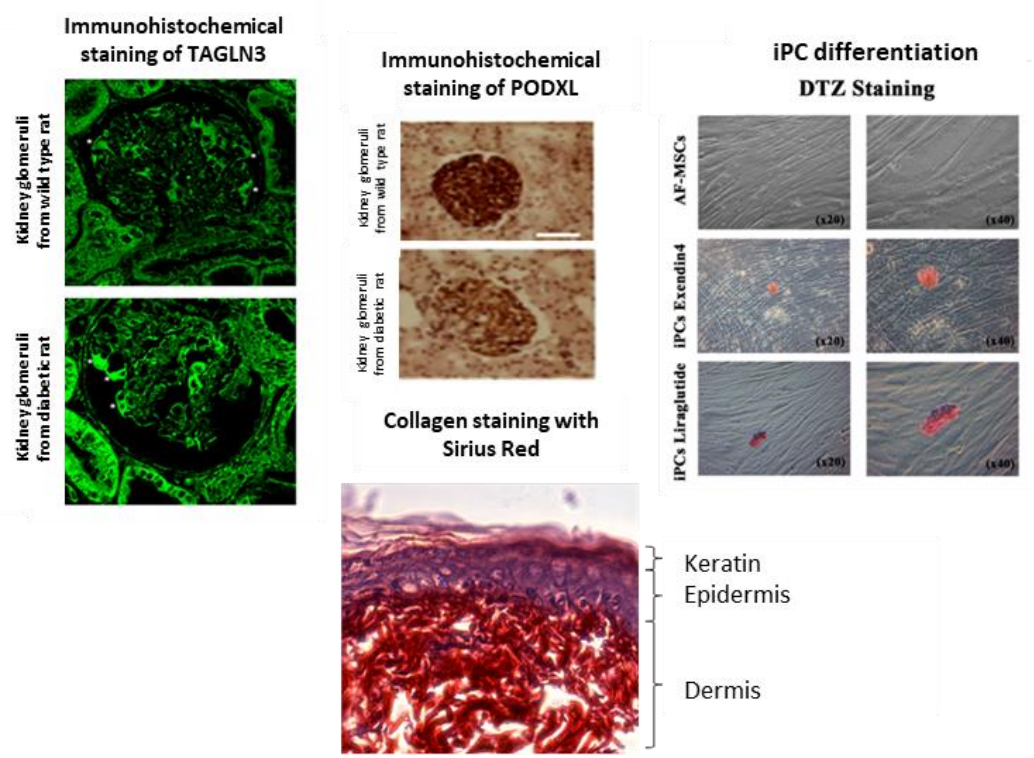
The HU supports the scientific work of several research groups and focuses on the investigation and phenotypic analysis at the tissue level of human and animal model specimens that are related to several pathologies, many of which derive from the Experimental Animal Facility of IBA.

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.

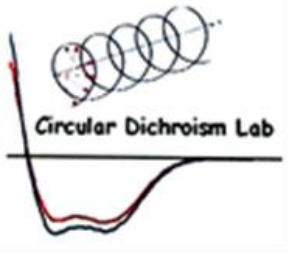
During 2020 IBA HU, participated in research protocols regading the following:

Mode of action of TAGLN3 in the survival of glomerular podocytes.
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



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

Achievements - Progress in 2021

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 2021, as in previous years, the CD Lab has supported research projects of at least 12 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 National Tehnical University of Athens (Chemical Engineering Dept), the Universities of Patras and Thessaloniki (Biology and Chemistry Depts, respectively), and the NHRF (Institute of Biology, Pharmaceutical Chemistry and Biotechnology). Income from the provision of services is solely used to cover the operation and repair needs of the spectrophotometer.

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

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

Personnel
Paraskevi Kitsiou, Senior Researcher (Admin)
Athina Tzinia, Senior Researcher
Garyfallia Drossopoulou, Senior Researcher

Laboratory Description – Research Objectives

The laboratory of Cell & Matrix Pathobiology focus on isolation, culture and characterization of stem cells from different tissues of various organisms aiming at their use in therapeutic applications in the frame of regenerative Medicine. The laboratory successfully isolates and characterizes human umbilical cord, human umbilical cord blood (UCB) stem cells and stem cells from other sources (skin and fat tissue). The mesegchymal 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 A. Charonis and Dr P. Politis {Research, Biomedical Research Foundation Academy of Athens (BRFAA), as well as: Dr Pedro: Dr Pedro Escada, Dr José Pratas-Vital (Hospital de Egas Moniz, Centro Hospitalar de Lisboa, Ocidental, Lisbon, Portugal), Dr. Ch. Gogo (EKPA, Attikon Hospital, B' Neurosurgical Clinic).

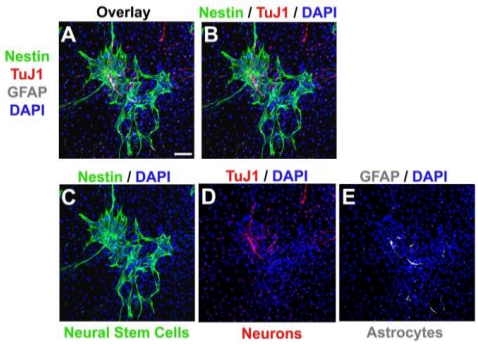


Figure: Culture of OECs results to enriched population of neural stem cells (NSC), as it appears from the use of appropriate indicators. These cells maintain the ability of proliferation and renewal.

Progress achieved

During 2021, the laboratory focus on the isolation and culture of mesegchymal stem cells isolated from mouse fat tissue. Characterization of the above-mentioned cells was achieved by the use of flow cytometry.

Funding

The research activities of the laboratory of Cell & Matrix Pathobiology are founded by the company Biophylaxis, Hellas A.E., which is a pioneering family bank of cryopreservation of stem cells from umbilical cord blood and other tissues of the human body.

LABORATORY OF CELL-BASED ASSAY SYSTEMS AND BIOACTIVE COMPOUNDS

Personnel

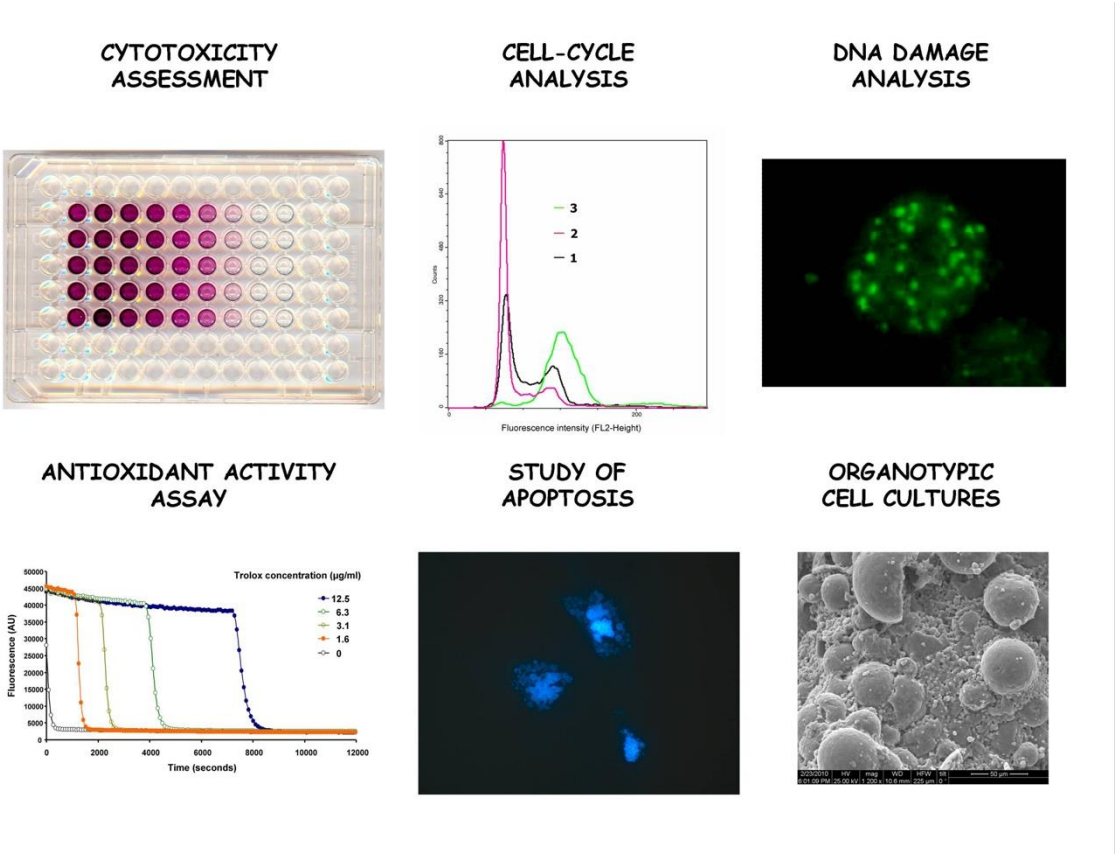
Dimitris Kletsas, Research Director
Harris Pratsinis, Senior Researcher
Eleni Mavrogonatou, Researcher
Adamantia Papadopoulou, Post-doctoral Fellow

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.

2021 Findings

During 2021, a new contract was signed between the service lab and the company UNI-PHARMA SA for the study of compounds with putative senolytic or senomorphic activity. Moreover, a collaboration was initiated 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 particular, factors eluted during the ageing of aligners produced by three-dimensional printers are being studied in cell-based assay systems.



EDUCATIONAL ACTIVITIES

EDUCATION

The Institute of Biosciences and Applications has continued the successful implementation of a variety of educational programs and activities in 2021, 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 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 2021, 17 postdoctoral researchers were trained at IBA, while, 30 PhD students and 19 MSc students carried out their research projects at the Institute under the supervision of IBA researchers. In 2021, 4 students completed their Master's theses successfully. Moreover, 10 undergraduate students from Greek Universities performed their final year project at IBA, 2 of which completed their project successfully. Additionally, 18 undergraduate students undertook research practice in IBA laboratories.

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

Lecture entitled "Molecular mechanisms of carcinogenesis and pharmaceutical inhibition of selected therapeutic cellular targets" in the framework of the Post-Graduate Specialization Diploma "Drug development: Research, commercialization and accessibility" (**Dr. G. Voutsinas**, Medical School, University of Athens)

Lecture entitled "Molecular mechanisms of carcinogenesis and pharmaceutical inhibition of selected therapeutic cellular targets" in the framework of the Post-Graduate Specialization Diploma "Applications of Biology in Medicine" (**Dr. G. Voutsinas**, Department of Biology and Medical School, University of Athens)

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" (Dr. 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" (**Dr. 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" (**Dr. Z. Georgoussi**, Department of Biology, University of Athens)

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

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

Teaching at different postgraduation (Master) courses (2-3 hours/pre course/ 20-25 students) 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), Master of Hleath Sciences (Univ. of Minho, Portugal) (**Dr. I. Sotiropoulos**).

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

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

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

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

Lecture entitled "Cell types for the regeneration of the intervertebral disc" in the framework of the postgraduate course "Applied Biomechanics in Orthopaedics" (Dr. D. Kletsas)

Lecture entitled "Regenerative medicine in intervertebral discs" in the frame work of the postgraduate course "Stem cells and regenerative medicine" (Dr. D. Kletsas, 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" and laboratorty visits (**Dr. D. Kletsas, Dr. H. Pratsinis** and **Dr. E. Mavrogonatou**, Department of Biology, University of Athens)

Lecture entitled "Cell systems in the research of carcinogenesis" in the framework the Postgraduate Master's Degree "Neoplastic Disease in Humans: Diagnosis, Modern Treatment and Research" (**Dr. H. Pratsinis,** Medical School, University of Athens)

Lecture entitled "Cell Cycle: Checkpoints and Consequences for Normal Cellular Function when Cell Cycle Progress Dysfunctions" in the framework of the course "Cell cultures – Tissue cultures" within the postgraduate programme "Application of Biology in Medicine" (**Dr. Th. Sourlingas**, Department of Biology & Medical School, University of Athens)

Lecture entitled "Alzheimer' s Disease: a) diagnosis (clinical, laboratory, imaging), b) risk factors (genetics, age, sex, cardiovascular, trauma, depression, drugs etc), c) recent data for the mechanisms of disease initiation and progress and therapeutic strategies)" in the framework the Postgraduate Master's Degree "Clinical Biochemistry-Molecular diagnosis" (**Dr. A. Chroni**, Department of Chemistry, University of Athens)

Lecture entitled "Regulation of Apoptosis in disease progression: Is it desirable or must be avoided?" in the framework of the graduate course "Molecular and Applied Physiology" (**Dr. G. Drossopoulou,** Medical School, University of Athens)

Lecture entitled "Metabolic Syndromes – Diabetes Mellitus and its complications" in the framework of the graduate course "Clinical Biochemistry – Molecular Diagnostics" (**Dr. G. Drossopoulou**, Department of Biology, University of Athens)

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

Teaching in the framework of the postgraduate program “Bioinformatics”, the course “Introduction to Computational Biology” (**Dr. I. Almyrantis**, Department of Biology, University of Athens)

Teaching in the framework of the postgraduate program “Clinical Biochemistry-Molecular Diagnostics”, the course “Introduction to Computational Biology” (**Dr. I. Almyrantis**, Departments of Biology, Chemistry and Nursing, University of Athens)

Lectures on “Principles of X-Ray Crystallography: Applications in Structural Biology” within the course “Current biochemical and biophysical analytical methods” in the framework of the postgraduate program entitled “Clinical Biochemistry – Molecular Diagnosis” (**Dr. M. Vlassi,** Department of Biology, Chemistry & Nursing, University of Athens)

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

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

Moreover, in July 2021, within the framework of the 56th NCSR “Demokritos” Summer School, IBA reserchers delivered a series of lectures on various frontier subjects of biological interest (see list below).

In 2021 8 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”* **(Dr. G. Drossopoulou)**
- Lecture entitled “*Chemical ecology: Applications of bioactive secondary metabolites of natural origin”* **(Dr. M. Konstantopoulou)**
- Lecture entitled*“The drug development roadmap. From bench to clinic”* **(Dr. M. Sagnou)**
- Lecture entitled *“Methods for the analysis and study of proteins, lipids and carbohydrates”* **(Dr. A. Chroni)**

Advanced Biochemistry
- Lecture entitled *“Protein Structure – Experimental & Theoretic approaches”* **(Dr. M. Vlassi)**
- Lecture entitled *“Signalling of* G protein-coupled receptors, trimeric G proteins, cAMP pathway, protein kinase A” **(Dr. Z. Georgoussi)**
- Lecture entitled “*Trascription factors (CREB, CREM, NF-kB, AP-1, STAT), identification methods for transcription factors activation”* **(Dr. G. Drossopoulou)**
- Lecture entitled “*Ca2+signaling*” (**Dr. E. Mavrogonatou**)
- Lecture entitled *«MAP kinases (ERK1,2, JNKs, p38).»* **(Dr. D. Kletsas)**
- Lecture entitled *“Signaling pathways of main cytokines and developmental factors IL-1, TNF-α, TGF-β (SMAD proteins), PDGF, EGF, FGF”* **(Dr. H. Pratisnis)**
- Lecture entitled *“Extracellular matrix interaction with cells”* **(Dr. H. Pratsinis)**
- Lecture entitled “*Lateral compartmentalization and function of plasma membrane: eisosomes and transmembrane transporters*” (**Dr. V. Sophianopoulou & Dr. C. Gournas**)

Molecular Pharmacology – Immunology

- Lecture entitled *"Opioid analgesics [morphine, morphine derivatives, analgesic receptor theory, agonists and antagonists, encephalines and endorphins, receptor mechanisms (μ, κ, δ and σ receptors"* **(Dr. Z. Georgoussi**)
- Lecture entitled *"Pharmaceutical activity on the receptors (the role of the receptor, neurotransmitters and hormones, receptors, signal transduction, receptor structural rearrangements, agonists and antagonists design, representative agonists, reverse antagonists, desensitization and sensitization, toleranceand addiction, cellular receptors, types and subtypes of receptors)"* **(Dr. Z. Georgoussi & Dr. Papakyriakou)**
- Lecture entitled *"Pharmaceutical activity on enzymes (binding interactions, competitive and non-competative inhibitors, allosteric inhibitors, the catalytic role of enzymes, enzyme regulation, isoenzymes, pharmaceutical applications of inhibitors (antimicrobial, antiviral and human enzyme inhibitors)"* **(Dr. Papakyriakou & Dr. M. Sagnou)**
- Lecture entitled "Structure and function of nucleic acids (DNA structure, anti-DNA drugs, RNA, anti-RNA drugs, drugs derived from nucleic acid structural motifs, molecular biology and genetic engineering)" **(Dr. Papakyriakou & Dr. M. Sagnou)**
- Lecture entitled "*The adrenergic neuronal system (the adrenergic system, adrenergic receptors, adrenergic transducers, catecholamine biosynthesis and metabolism, neurotransmission, drugtargets, adrenergic binding area, structure-activity-relationships, agonists, antagonists of adrenergic receptors, other drugs affecting adrenergic transduction"* **(Dr. A. Papakyriakou)**
- Lecture entitled *"The RNAi as a defence mechanism against insect viruses"* **(Dr. L. Swevers & Dr. B. Labropoulou**)

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

Furthermore, in 2021 the IBA researcher **Dr. Z. Georgoussi** participated for another year in the joined MSc Programme **"Athens International Master's Programme in Neurosciences"**
In 2021 IBA, in collaboration with the European Learning Laboratory for the Life Sciences (ELLS) of the European Molecular Biology Laboratory (EMBL) and the OPENSCREEN-GR network, organized a Laboratory Seminar (Workshop) for Secondary School Biology teachers (11-12/9/2021). The Seminar was attended by 20 teachers from various schools of Attica and other regions of Greece. The aim of the Workshop was to support the continuing education of Secondary School Biology teachers. Participants had the opportunity to gain theoretical know-how and hands-on expertise on current topics in biochemistry and molecular biology, such as gene expression, gene modification, bioinformatics, personalized medicine, confocal microscopy, drug design and identification of bioactive compounds, bioethics. In particular, visits were made to confocal microscopy, cell cultures and high-throuput screening facilities and the following lectures were given:
"Gene expression across cells, tissues, species", Dr. Irene Papatheodorou, EMBL
"Confocal microscopy (principles of optical and confocal microscopy)", Dr. Alexandros Athanassopoulos, IBA, NCSR Demokritos

“Biomedical Sciences in the era of Big Data. Challenges and Perspectives.”, Dr. Christoforos Nikolaou, BSRC Alexander Fleming
“Precision Medicine”, Dr. Makis Voutsinas, IBA, NCSR Demokritos
“Genome editing techniques and applications”, Dr. Luc Swevers, IBA, NCSR Demokritos
”The ethics of genetic engineering in humans after CrisprCas9”, Dr. Takis Vidalis, National Bioethics Committee
“EU-OPENSCREEN and its connection to the international scientific community” , Kathy Skopelitou, EU-OPENSCREEN-DRIVE
“Natural products: From traditional remedies to contemporary therapeutics”, Dr. Marina Sagnou, IBA, NCSR Demokritos
“The drug development roadmap. From bench to clinic”, Drs. Thanos Papakyriakou & Marina Sagnou, IBA, NCSR Demokritos
“Cell-based high-throughput screening of bioactive compounds”, Dr. Harris Pratsinis, IBA, NCSR Demokritos
“Photosynthesis and green energy”, Dr. Kostas Stamatakis, IBA, NCSR Demokritos
“Real time-PCR and its application for the detection of viral infections”, Dr. Eleni Mavrogonatou, IBA, NCSR Demokritos

COMPLETION OF MASTER THESES IN 2021

POSTGRADUATE STUDENT	TITLE OF MSc THESIS	IBA SUPERVISOR	UNIVERSITY
Labrina Bondi	*Study of LonP1 protease expression in aging and cancer*	G. Voutsinas	Dept. Biology, University of Athens
Marine-Gemma Kelemeni	*Effect of ionizing radiation on the paracrine interactions between cancer and stroma breast cells*	D. Kletsas	Dept. Chemistry, University of Patras
Eleni Kaplani	*Expression of estrogen receptors in young and senescent intervertebral disc cells*	D. Kletsas	Dept. Biology, University of Athens
Alexandros Vallianatos	*Lateral compartmentalization of plasma membrane of Aspergillus nidulans*	V. Sophianopoulou	Dept. Biology, University of Athens

COMPLETION/AWARD OF DOCTORAL THESES IN 2021

PhD STUDENT	TITLE OF DOCTORAL THESIS	IBA SUPERVISOR	UNIVERSITY
Lykourgos Chiniadis	*Crystallographic study of bioactive Ruthenium complexes with model proteins*	A. Papakyriakou	Department of Biotechnology, Agricultural University of Athens

IBA LECTURES' CONTRIBUTION TO THE 2021 SUMMER SCHOOL

DATE	SPEAKER	TITLE
12/7/2021	**Dr. D. Kletsas**	The multiple roles of cell senescence in tissue homeostasis
12/7/2021	**Dr. A. Chroni**	Cardiovascular disease: Causes and therapeutic approaches
12/7/2021	**Dr. L. Swevers**	Genome editing and gene therapy by CRISPR-Cas technology
12/7/2021	**Dr. H. Pratsinis**	In vitro studies of natural and synthetic bioactive products
12/7/2021	**Dr. M. Sagnou**	The drug development roadmap: from bench to clinic. Curcumin: from traditional medical wisdom to modern therapeutic applications
12/7/2021	**Dr. I. Sotiropoulos**	Chronic stress, depression and Alzheimer's disease: the triangle of oblivion

2021 IBA'S GRADUATE STUDENTS SEMINARS

DATE	SPEAKER	TITLE
9/6/2021	**Christina Mountaki**	Effect of polar phenolic molecules on apoE functions related to the pathogenesis of Alzheimer's disease
16/6/2021	**Lykourgos Chiniadis**	Crystallographic study of bioactive Ruthenium complexes with model proteins
16/6/2021	**Alexandros Athanasoulis**	Design and synthesis of inhibitors for the M1 family of zinc aminopeptidases
23/6/2021	**Asimina Fotopoulou**	Effect of UV radiation on skin homeostasis
23/6/2021	**Amalia Megarioti**	The organization of the fungal plasma membrane in the quiescent state.
30/6/2021	**Efstathios Tsimelis**	Anabolic copmpounds and cellular senescence
30/6/2021	**Anastasia-Georgia Dedemadi**	Study of high density lipoprotein (HDL) composition and function in pathological conditions
7/7/2021	**Ada Biratsi**	Study of the genes responsible for the detoxification and assimilation of L-azetidine-2-carboxylic acid in *Aspergillus nidulans*
7/7/2021	**Nastazia Lesgidou**	Analysis of structure and dynamics of disease-associated proteins by molecular dynamics simulations
16/7/2021	**Panayiotis Broussos**	Studies on cyanobacterial Hydrogen production
21/7/2021	**Christos Caroussiotis**	Alternative pathways of k-opioid receptor: Autophagy and the role in synapses
21/7/2021	**Aikaterini Vogiatzi-Giakoumidaki**	Studies on photosynthesis of cyanobacteria able to produce terpene

2021 INVITED SPEAKERS SEMINARS

DATE	SPEAKER	TITLE
8/4/2021	**Prof. Marco Demaria** European Research Institute for the Biology of Aging (ERIBA), University Medical Centre Groningen (UMCG).	Heterogeneity in senescence: from mechanisms to interventions.
8/4/2021	**K. Lenhard Rudolph, M.D.** Leibniz Institute on Aging – Fritz Lipmann Institute (FLI)	Inflammation and mitochondrial metabolism in stem cell and organism aging.
16/12/2021	**Dr. Lefteris Michailidis** School of Medicine, Emory University, USA.	Modeling hepatitis B virus in hepatocyte systems and humanized mice.
22/12/2021	**Prof. Grigoris Amoutzias** School of Sciences, University of Thessaly.	The evolutionary history of Coronaviruses provides insights for the COVID-19 pandemic and the future evolutionary paths of SARS-CoV-2.
22/12/2021	**Prof. Martin Götte** Münster University Hospital, Germany	Role of Cell Surface Heparan Sulfate Proteoglycans in Cancer and Inflammation

COLLECTIVE DATA

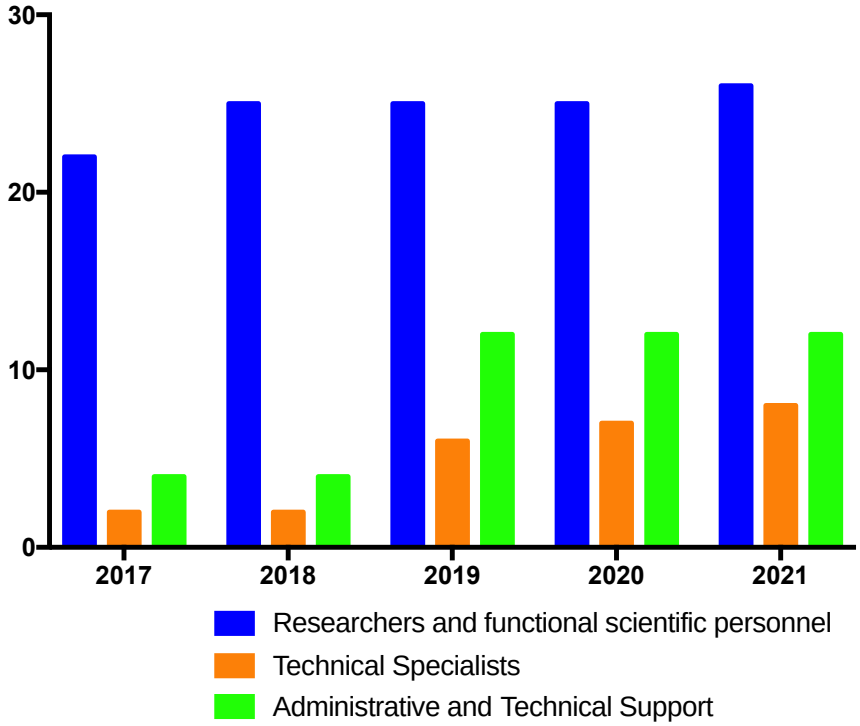
SUMMARIZED DATA ON THE PRODUCTIVITY OF SCIENTIFIC PROGRAMMES

	PROGRAMME			
	A	**B**	**C**	**INSTITUTE**
Researchers & functional scientific personnel	11	7	6	25[α]
Technical Specialists	2	1	-	8[b]
Collaborating & Emeritus Scientists	2	1	0	3
Postdoctoral Fellows	9	4	5	19[c]
PhD candidates	15	6	3	24
MSc students	11	5	2	18
Graduate Research Associates	7	3	1	13[d]
Undergraduate and other training students	13	10	4	27
Administrative and Technical Support	-	-	-	12
Total Personnel	**71**	**37**	**15**	**144**
Publications in Peer-Reviewed Journals	**19**	**14**	**22**	**58[e]**
Cumulative Impact Factor in Peer-Reviewed Journals	**111.63**	**66.681**	**122.304**	**311.398[f]**
Proceedings in Conferences	**7**	**1**	**-**	**8**
Total Publications	**26**	**15**	**22**	**66**
Citations	**1868**	**890**	**577**	**3464[f]**
International Patents	**-**	**1**	**1**	**2**
Greek Patents	**-**	**-**	**-**	
Presentations in International Conferences	**11**	**8**	**9**	**28**
Presentations in International Conferences	**17**	**6**	**8**	**31**
Total Number of Presentations in Conferences	**28**	**14**	**17**	**59**

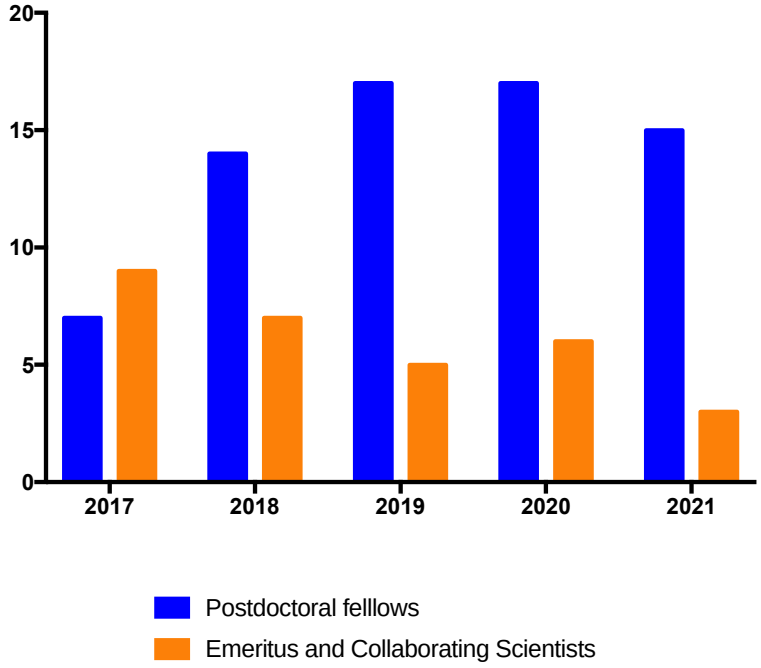
[α] *One Scientist of the Human Tissue Bank included*
[b] *5 Technical Specialists of the Laboratory for Doping Control and Metabolic Studies included*
[c] *1 Graduate Research Associate of the Human Tissue Bank included*
[d] *2 Graduate Research Associates of the Human Tissue Bank included*
[e] *3 publications of the Laboratory for Doping Control and Metabolic Studies included*
[f] *Citations of the Human Tissue Bank and of the Laboratory for Doping Control and Metabolic Studies included*

CHANGES IN IBA STAFF DURING 2017-2021

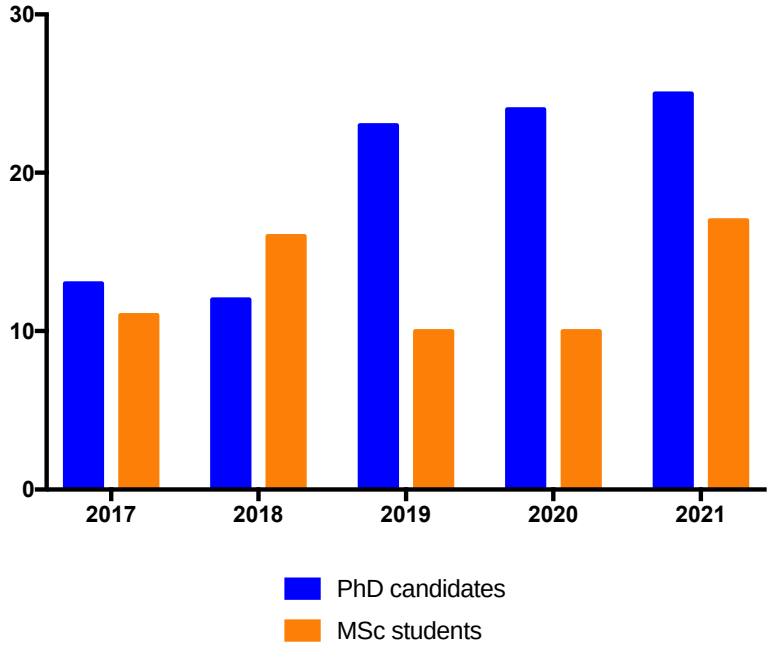
Tenured Staff



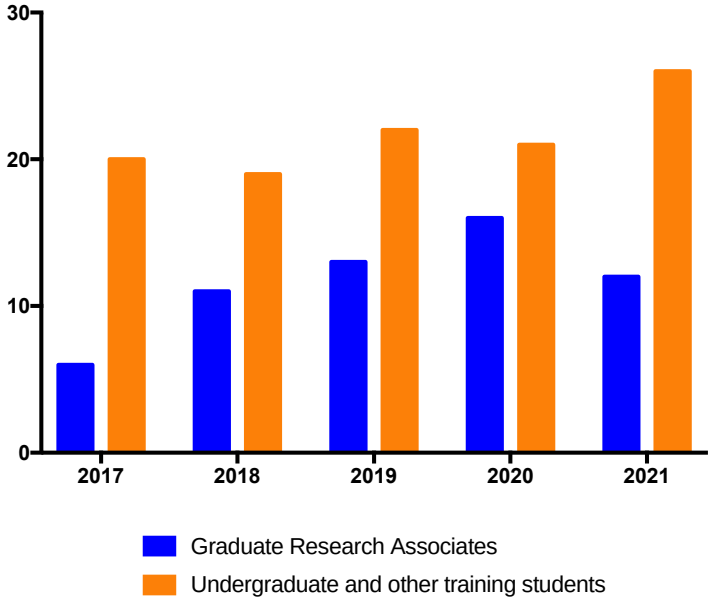
Postdoctoral fellows/ Emeritus & Collaborating Scientists



PhD candidates / MSc students

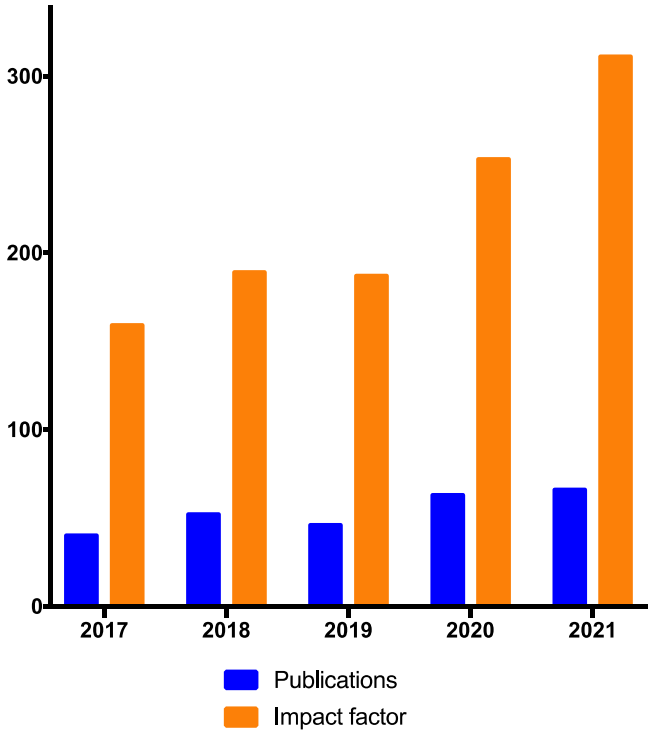


Undergratuate & other training students

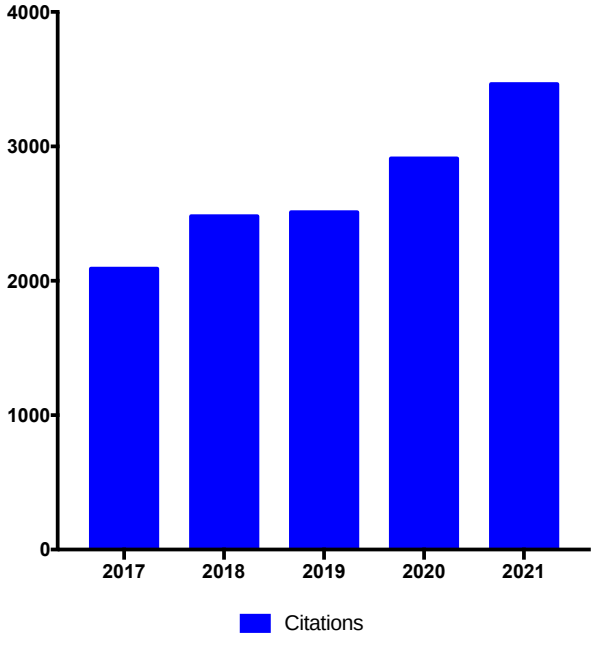


QUALITATIVE AND QUANTITATIVE DATA ON IBA PUBLICATIONS DURING 2017 – 2021

Publications in peer-reviewed Journals / Cumulative impact factor



Citations



EXTERNAL IBA FUNDING DURING 2017 – 2021