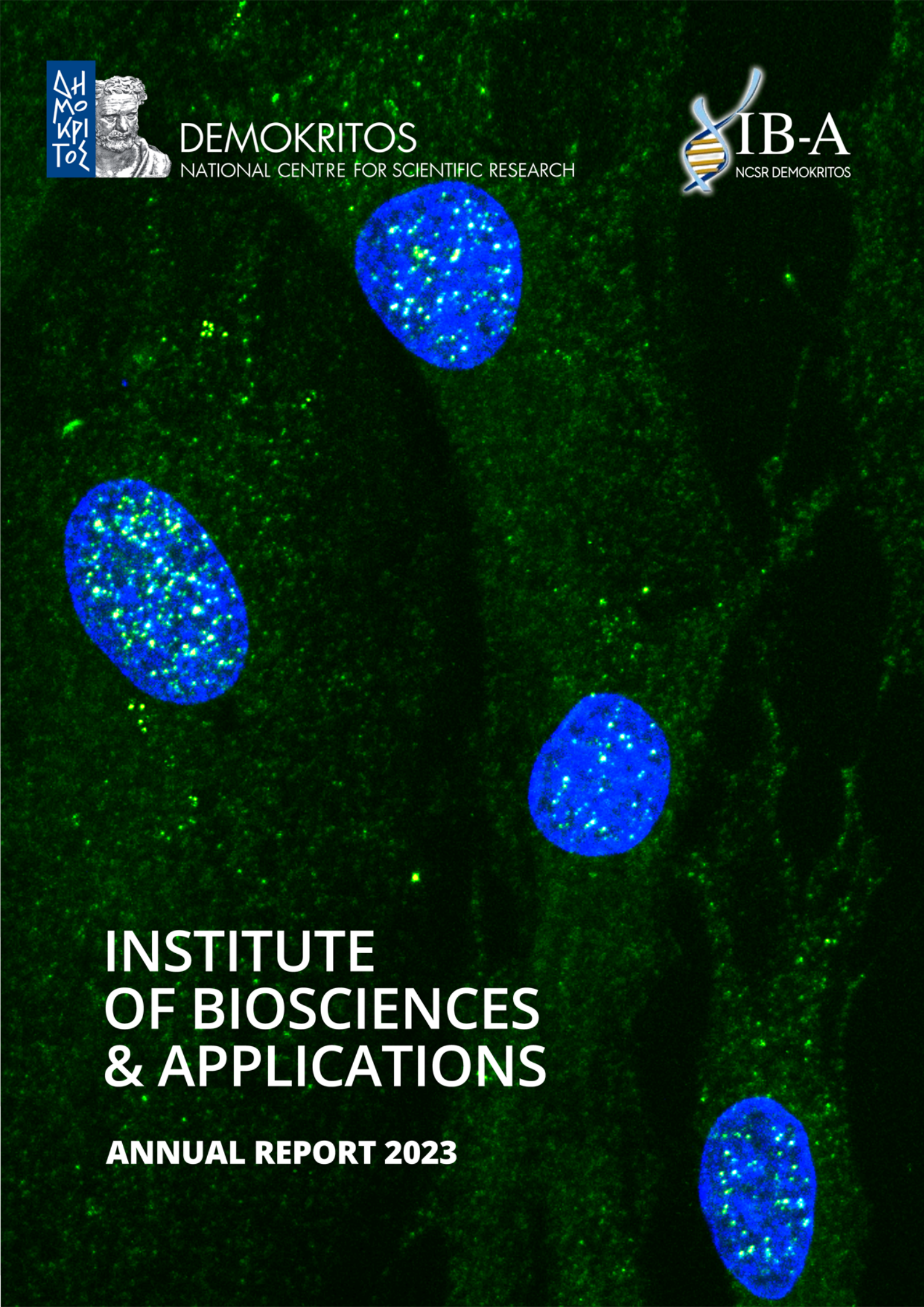
DEMOKRITOS
NATIONAL CENTRE FOR SCIENTIFIC RESEARCH
IB-A
NCSR DEMOKRITOS
INSTITUTE
OF BIOSCIENCES
& APPLICATIONS
ANNUAL REPORT 2023

NATIONAL CENTRE FOR SCIENTIFIC RESEARCH

"DEMOKRITOS"

INSTITUTE OF BIOSCIENCES & APPLICATIONS

ANNUAL REPORT 2023

AGIA PARASKEVI

NOVEMBER 2024

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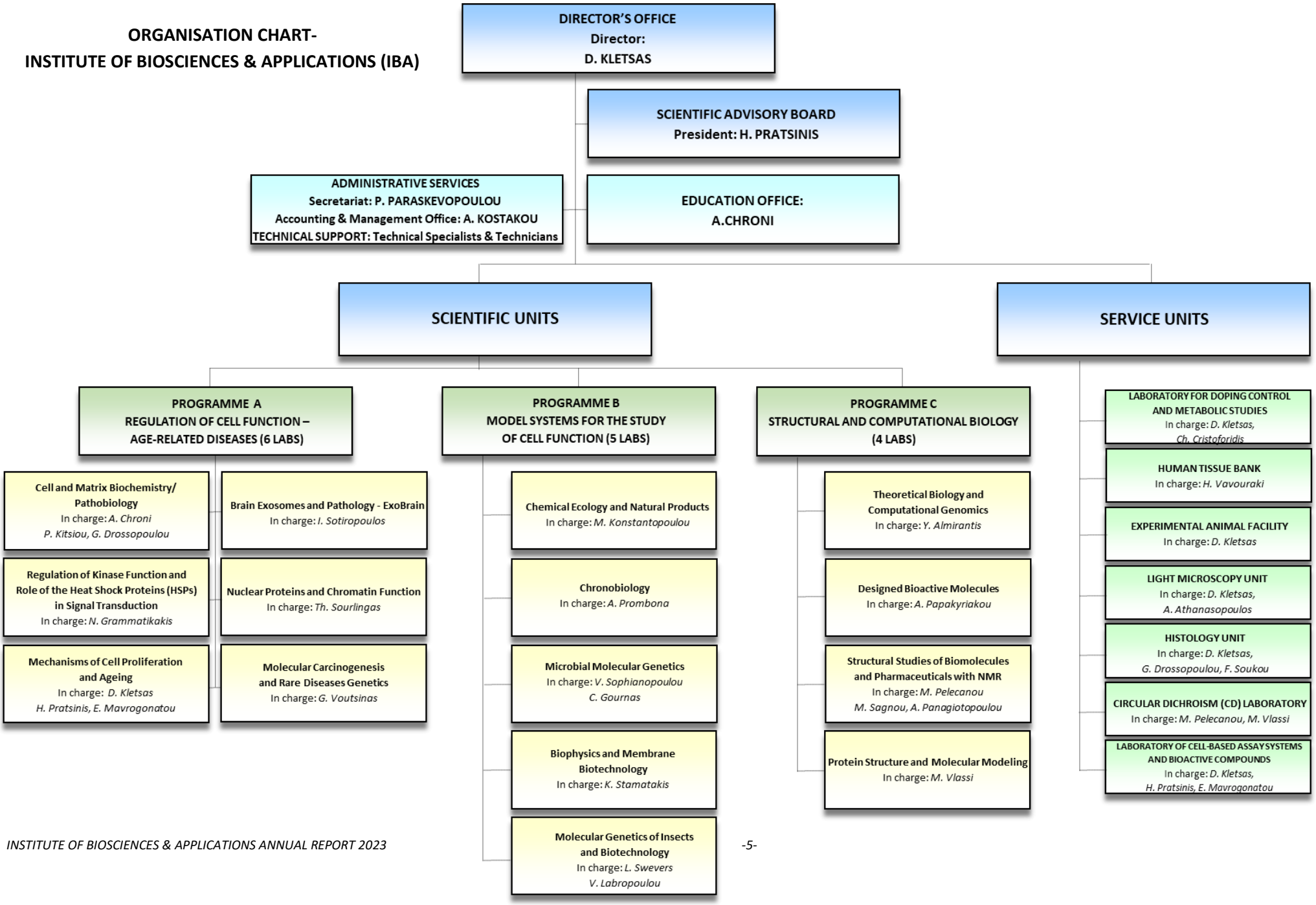
ORGANISATION CHART-
INSTITUTE OF BIOSCIENCES & APPLICATIONS (IBA)



IBA PERSONNEL

DIRECTOR

Kletsas Dimitris	Dr. Biologist

SCIENTIFIC STAFF

Research Directors

Almirantis Yannis	Dr. Theoretical Biologist
Chroni Angeliki	Dr. Chemist
Kletsas Dimitris	Dr. Biologist
Konstantopoulou Maria	Dr. Biologist
Labropoulou Vassiliki	Dr. Biochemist
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
Papakyriakou Athanasios	Dr. Chemist
Pratsinis Harris	Dr. Chemist
Prombona Anastasia	Dr. Molecular Plant Biologist
Sagnou Marina	Dr. Biologist/Chemist
Sourlingas Thomae	Dr. Biologist
Vavouraki Helen	Dr. Pharmacist

Researchers

Gournas Christos	Dr. Biologist
Mavrogonatou Eleni	Dr. Biologist
Sotiropoulos Ioannis	Dr. Biologist

Functional Scientific Personnel

Panagiotopoulou Angeliki	Dr. Biochemist

TECHNICAL SPECIALISTS

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

ADMINISTRATIVE & TECHNICAL SUPPORT

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

EMERITUS & COLLABORATING SCIENTISTS

Scientists	**IBA Researcher**
Georgoussi Zafiroula-Iro (Dr. Biochemist) – *Collaborating*	Sotiropoulos I.
Iatrou Kostas (Dr. Biochemist & Molecular Biologist) – *Emeritus*	Sotiropoulos I.
Papageorgiou Spyros (Dr. Physicist) – *Collaborating*	Almirantis Y.
Sekeri Kalliope (Dr. Biochemist) – *Collaborating*	Sourlingas Th.

POSTDOCTORAL FELLOWS

Fellow	**IBA Researcher**
Dioli Chrysoula	Sotiropoulos I.
Georgiadou Dafni	Chroni A.
Karoussiotis Christos	Georgoussi Z.
Kolliopoulou Anna	Swevers L.
Kouroumalis Anastasios	Kletsas D.
Kythreoti Georgia	Iatrou K.
Mavroidi Barbara	Pelecanou M.
Ninios Ioannis	Vavouraki E.
Papadopoulou Adamantia	Kletsas D.
Valanti Eftaxia-Konstantina	Chroni A.

GRADUATE RESEARCH ASSOCIATES

Research Associate	**IBA Researcher**
Balouri Aggeliki (MSc)	Sotiropoulos I.
Betsi Petri-Christina (MSc)	Konstantopoulou M.
Christoforidis Christoforos (PhD)	Kletsas D.
Goula Olga (BSc)	Kletsas D.
Katsaitis Filippos (MSc)	Sotiropoulos I.
Klamarias Lykourgos (Veterinarian)	Kletsas D.
Kosmidis Eleutherios (MSc)	Vavouraki H.
Makrygianni Emilia (MSc)	Kletsas D.
Mamoucha Stavroula (PhD)	Prombona A.
Matiadis Dimitris (PhD)	Sagnou M.
Raptopoulos Dimitris (PhD)	Konstantopoulou M.

Sahou Adelaida (MSc)	Panagiotopoulou A.
Sakellariou Panagiotis (PhD)	Kletsas D.
Sotiropoulou Nefeli-Sofia (MSc)	Konstantopoulou M.
Tsiagkas Giannis (MSc)	Almirantis Y.
Voudommatis-Stergiou Charalampos (MSc)	Vavouraki H.

PhD CANDIDATES AND MSc STUDENTS

PhD candidate (University)	**Supervisor in IBA**
Angelopoulou Maria (NKUA) – *Completed*	Kletsas D.
Athanasoulis Alexandros (NKUA)	Papakyriakou A.
Broussos Panayiotis (AUA)	Stamatakis K.
Dedemadi Anastasia-Georgia (NKUA)	Chroni A.
Farmaki Danae (NKUA)	Prombona A.
Fotopoulou Asimina (Univ. of Patras)	Kletsas D.
Liakou Eleni (Univ. of Patras) – *Completed*	Kletsas D.
Lesgidou Nastazia (DUT) – *Completed*	Vlassi M.
Manikas Neoklis (AUA)	Konstantopoulou M.
Megalokonomou Anastasia (Univ. of Crete)	Sotiropoulos I.
Megarioti Amalia (NKUA) – *Completed*	Gournas C.
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**
Anagnostou Theofano (Univ. Of Patras)	Kletsas D.
Christogianni Mariam (NKUA)	Kletsas D.
Dinopoulou Melina (Aix-Marseille Univeristy)	Sotiropoulos I.
Gerontidi Dimitra (NKUA)	Sotiropoulos I.
Gerostathis Spyros (Univ. of Patras) – *Completed*	Sophianopoulou V.
Gratsia Eirini (Univ. of Crete)	Sotiropoulos I.
Karanikou Maria (Univ. of West. Macedonia) – *Completed*	Pratsinis H.
Karava Alexandra (NKUA)	Sotiropoulos I.
Karnava Sofia (NKUA)	Kletsas D.
Kavellari Marina (Univ. of Patras) – *Completed*	Kletsas D.
Kavvoura Dafni-Alexandra (NKUA) – *Completed*	Pratsinis H.
Kokkovou Vassiliki (NKUA)	Sotiropoulos I.
Kostaki Anna-Maria (NKUA)	Sagnou M.
Kypraiou Anastasia (Univ. of Patras) – *Completed*	Kletsas D.
Lymperopoulos Dimitris – *Completed*	Chroni A.
Papadimitriou Georgia-Zeta (NKUA)	Sotiropoulos I.
Souma Maria (NKUA)	Pratsinis H.
Tsoukas Evangelos (Univ. of Patras)	Papakyriakou A.

UNDERGRATUATE & OTHER TRAINING STUDENTS

Student (University)	**Supervisor in IBA**
Abatzopoulos Marios (Deree College)	Drossopoulou G.
Anastasiou Stella (AUA)	Papakyriakou A.
Charisis Angelos (AUA)	Voutsinas G.

Georgiou Eirini (NKUA) – *Completed*	Chroni A.
Karakike Margarita (AUA)	Sourlingas T.
Katsirma Irini (AUA)	Sourlingas T.
Kavvadia Vassiliki (NKUA) – *Completed*	Mavrogonatou E.
Kotsikou Zoe (NKUA)	Sotiropoulos I.
Koulouris Dimitris (NKUA)	Gournas C.
Lygoni Despoina (Univ. of Patras)	Sotiropoulos I.
Makatsoris Christos (NKUA)	Sotiropoulos I.
Manakou Vassiliki (Kenyon College Ohio)	Sagnou M.
Moutselos Andreas (Doukas School of International Baccalaureate)	Sagnou M.
Panagopoulou Konstantina (NKUA)	Voutsinas G.
Pappa Athina (Univ. of Patras)	Sotiropoulos I.
Paraskevas Sotirios (NKUA)	Sotiropoulos I.
Pedi Elisabeth (AUA)	Sophianopoulou V.
Siaka Alexandra (AUA)	Sophianopoulou V.
Serfioti Eva-Eleni (Univ. of Crete)	Sotiropoulos I.
Simopoulos Georgios (NKUA)	Chroni A.
Skourti Kalliopi (AUA)	Sotiropoulos I.
Timotheatou Stella (Univ. of Ioannina)	Sagnou M.
Trasani Georgia (NKUA)	Georgoussi Z.
Tsamadia Eleni (NKUA)	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. The IBA focuses its research and developmental activities in various areas of life sciences and especially in the study of cellular function, with an emphasis on ageing and age-related diseases, on biotechnology and the environment, as well as on structural and computational biology. In addition, the Institute houses a considerable number of laboratories, some of them unique in Greece, that support the research efforts and provide advanced technological research services to the Public and Private Sectors, and the Society, in general.

Within 2023, there was a significant upgrading of Institute's research and developmental work, as shown by the significant increase of the quality of IBA researchers' publications. For this achievement I would like to congratulate the scientific, technical and administrative staff of the Institute. I would like to thank the Vice Director G. Voutsinas and the members of the Scientific Council (ESI) of the IBA H. Pratsinis (President), M. Konstantopoulou, A. Papakyriakou, L. Swevers and G. Voutsinas (Members), and A. Kostakou (Representative of the administrative and technical personnel) for the orderly function of the Institute, as well as the Responsible of the Educational Committee A. Chroni and the Deputy M. Sagnou for the upgrading of the education within IBA.

During 2023 the implementation of central IBA projects OPENSCREEN-GR, BIOIMAGING and INSPIRED, as well as of the European project EU-OPENSCREEN-DRIVE has continued. The new Biosafety Laboratory of IBA has been finalized with the financial support for the European Investment Bank. The Doping Control Laboratory of Athens (DCLA), of the Institute was granted the "Candidate Doping Control Laboratory" status from the World Anti-Doping Agency (WADA). This decision reflects that WADA recognizes the systematic efforts and investments that have been made in recent years to obtain its accreditation from the Agency. The implementation of these projects, as well as of the other funded projects that have been recruited by the Institute members have attracted a large number of young scientists and have further strengthened the research and development effort of the IBA.

This year, our colleague Z. Georgoussi has been retired. The Institute is thanking her for her work and her contribution for the upgrading the IBA. Within 2023 V. Labropoulou was promoted to Research Director (Grade A') and M. Sagnou to Senior Researcher, as merited. Congratulation to both colleagues!

During 2023, 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". In addition, the "IBA Summer Camp for Lyceum Students", enabling participating students to work in the laboratories of the Institute and to perform small research projects, was organized for the fifth time, with a 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.

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

Dimitris Kletsas
IBA Director
November 2024

PROGRAMME A

“REGULATION OF CELL FUNCTION – AGE-RELATED DISEASES”

Research Group: Biochemistry and Pathobiology of Cells and Matrix

Research Staff
Angeliki Chroni, Research Director
Paraskevi Kitsiou, Senior Researcher
Garyfalia Drossopoulou, Senior Researcher
Dafni Georgiadou, Postdoctoral Fellow
Eftaxia-Konstantina Valanti, Postdoctoral Fellow
Anastasia Georgia Dedemadi, PhD student
Dimitris Lymperopoulos, MSc student (defended)
Eirini Georgiou, Diploma student (defended)
George Simopoulos, Diploma student
Marios Abatzopoulos, Summer student

Research Interests

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

2. ***Molecular mechanisms of Alzheimer's disease***
   - Elucidation of the molecular mechanisms underlying the role of apoE4, the major risk factor for Alzheimer's disease, amyloid peptide beta (Aβ), tau protein, neuroinflammation and cholesterol homeostasis in disease pathogenesis.
   - Examination of the neuroprotective activity of natural products.

3. Diabetes Mellitus and Diabetic Nephropathy

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

Research findings during 2023

Dyslipidemia, atherosclerosis and cardiovascular disease

HDL has important atheroprotective functions that are mediated by its composition, while disturbances in HDL functions are associated with cardiovascular morbidity. In a prospective study of 199 consecutive patients who were admitted with acute ischemic stroke we examined whether changes in HDL functions and composition are associated with ischemic stroke severity and outcome. Cholesterol efflux capacity (CEC), phospholipid levels, lecithin:cholesterol acyl transferase (LCAT)-phospholipase activity, paraoxonase-1 (PON1)-arylesterase activity and serum amyloid A1 (SAA1) content of HDL were measured. We showed that changes in CEC, phospholipid levels and LCAT-phospholipase activity of HDL were lower and SAA1 content of HDL was higher in patients with severe stroke. Patients who were dependent at discharge had lower CEC, PON1-

arylesterase activity, phospholipid content and LCAT-phospholipase activity of HDL and higher HDL-SAA1 content. In patients who died during hospitalization, phospholipids, LCAT-phospholipase and PON1-arylesterase activities of HDL were lower. Overall, changes in CEC and composition of HDL appear to be associated with the severity and outcome of acute ischemic stroke and could represent biomarkers that may inform risk stratification and management strategies in these patients (Papagiannis et al, *Clin. Chim. Acta* 540, 117229 (2023)).

Alzheimer's Disease

Alzheimer's disease (AD) is associated with oxidative stress in brain. Corinthian currant, a low glycemic index dried fruit, and its components display pleiotropic neuroprotective effects in AD. We evaluated the effect of a Corinthian currant paste-supplemented diet (CurD), provided to 1-month-old 5xFAD mice for 1, 3, and 6 months, on the levels of oxidation markers in serum and the brain of mice as compared to a control diet (ConD). Administration of CurD for up to 3 months increased the activity of antioxidant enzyme paraoxonase 1 (PON1) and decreased oxidized species levels in serum and brain of male and female mice compared to ConD (Figure 1A). Longer-term administration of CurD did not, however, affect PON1 activity and oxidized species levels. Overall, our findings suggest that dietary Corinthian currant administration in the AD mouse model 5xFAD reduces the oxidative stress in the circulation and the brain at the early stages of the disease. However, during later stages of the disease, when AD pathology has significantly impacted the brain, no beneficial effects are observed.

Diabetes Mellitus and Diabetic Nephropathy Diabetes Mellitus and Diabetic Nephropathy

A) Liraglutide, a long lasting human GLP-1 analogue, is used for the treatment of type 2 diabetes, since it improves glucose metabolism. The type 2 diabetes mouse model (db/db lepr-/-) was used to study the effects of liraglutide in beta-cell apoptosis which characterizes type 2 diabetes. It is observed a decreased in islet size and increased expression of activated caspase-3 in islet beta-cells of diabetic mice compared to control animals (db/db lepr+/-). Treatment of diabetic animals (db/db lepr-/-) with liraglutide, for two weeks, resulted in re-establishment of islet size and a significant decrease in activated caspase-3. These results demonstrate that liraglutide protects from and/or inhibits glucotoxicity-induced beta-cell apoptosis (Figure 1B).

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

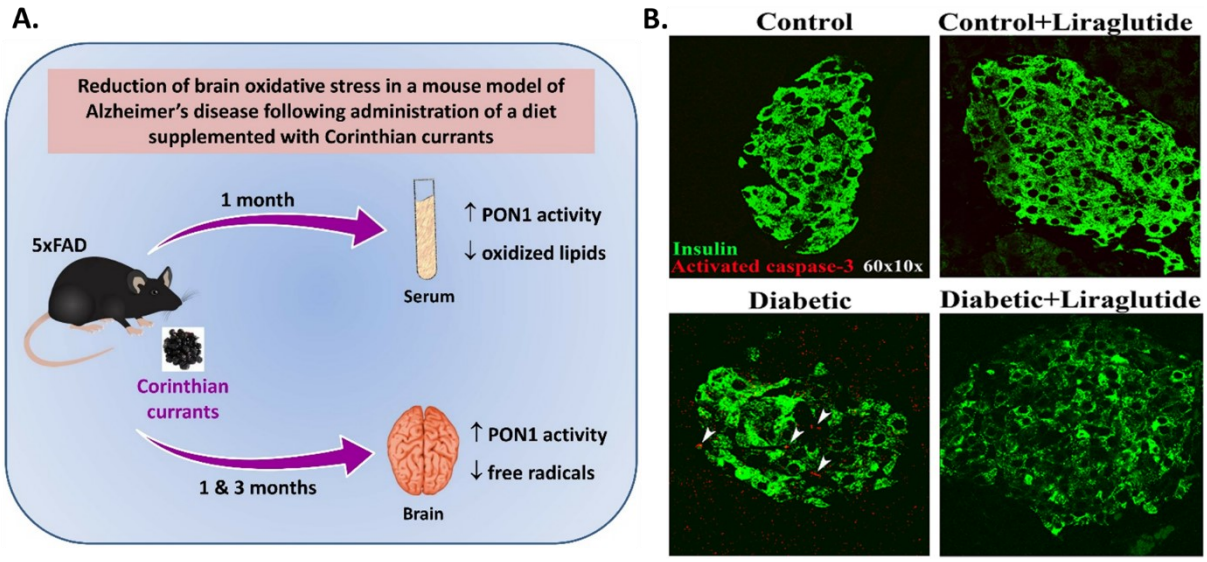


Figure 1: *A. Corinthian currants enhance the antioxidant status in serum and brain of 5xFAD mouse model of Alzheimer's Disease. B. Effect of liraglutide in islet beta-cell survival in diabetic mice (db/db lepr-/-).* Dual immunofluorescence in sections of formalin-fixed paraffin-embedded murine pancreata from diabetic mice revealed the *presence of activated caspase-3 (red, white arrows) in islet beta-cells (green) compared to control healthy animals. Activated caspase-3 was not detected in control animals (db/db lepr+/-) or diabetic animals treated with liraglutide. Treatment of diabetic animals with liraglutide resulted in inhibition of islet beta-cell apoptosis.*

Publications

Loch R. A., Wang H., Perálvarez-Marín A., Berger P., Nielsen H., Chroni A. and Luo J. Cross interactions between Apolipoprotein E and amyloid proteins in neurodegenerative diseases. *Comput. Struct. Biotechnol. J.* 21, 1189-1204 (2023). (IF 5.8)

Papagiannis A., Gkolfinopoulou C., Tziomalos K., Dedemadi A. G., Polychronopoulos G., Milonas D., Savopoulos C., Hatzitolios A. I. and Chroni A. HDL cholesterol efflux capacity and phospholipid content are associated with the severity of acute ischemic stroke and predict its outcome. *Clin. Chim. Acta* 540, 117229 (2023). (IF 5.0)

Chernyaeva L., Ratti G., Teirilä L., Fudo S., Rankka U., Pelkonen A., Korhonen P., Leskinen K., Keskitalo S., Salokas K., Gkolfinopoulou C., Crompton K.E., Javanainen M., Happonen L., Varjosalo M., Malm T., Leinonen V., Chroni A., Saavalainen P., Meri S., Kajander T., Wollman A.J., Nissilä E., Haapasalo K. Reduced binding of apoE4 to complement factor H promotes amyloid-β oligomerization and neuroinflammation. *EMBO Rep.*, e56467 (2023). (IF 7.6)

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

Gkolfinopoulou C, Bourtsala A., Georgiadou D., Dedemadi A. G. and Chroni A. Identification of small molecules as potential correctors for defective apolipoprotein A-I structure and function. *Eur. Biophys. J.* 52 (Suppl 1): S74 (2023).

Presentations at International conferences

Gkolfinopoulou C., Bourtsala A., Georgiadou D., Dedemadi A. G. and Chroni A. Identification of small molecules as potential correctors for defective apolipoprotein A-I structure and function. *14th European Biophysics Conference*, 29 July – 4 August 2023, Stockholm, Sweden

Barkas G., Trohatou O. (equal contribution), Critselis E., Charonis A., Roubelakis M. and Drossopoulou G. Secreted condition media from induce insulin-producing cells ameliorate podocyte injury in isolated diabetic rat glomeruli. 35th Annual Meeting of the European Renal Cell Study Group (ERCSG) March 30th-April 1st 2023, Netherlands

Presentations at Greek conferences

Dafnis I., Fanarioti E., Georgiou E., Dedemadi A. G., Karvelas M., Karathanos V. T., Tzinia A., Dermon C. R. and Chroni A. Time-dependent effects of currant (*Vitis vinifera*) consumption on neuroinflammation and oxidative stress in the 5xFAD mouse model of Alzheimer's Disease. *30th Meeting of the Hellenic Society for* Neuroscience, 24-26 November 2023, Athens

Gkolfinopoulou C., Bourtsala A., Georgiadou D., Dedemadi A. G. and Chroni A. Small-molecule Structure Correctors Target Abnormal Apolipoprotein A-I Structure and Function Related to Cardiovascular Risk. *73rd Annual Conference of the Hellenic Society for Biochemistry and Molecular Biology*, 1-3 December 2023, Athens

Dedemadi A. G., Gkolfinopoulou C. και and Chroni A. Activation of the antioxidant enzyme paraoxonase 1 (PON1) by existing drugs. *10th Meeting of the working groups of the Hellenic Atherosclerosis Society*, 1-2 December 2023, Athens

Sevdali E., Neofotistou Themeli E., Chanis T., Thymiakou E., Dedemadi A. G., Valanti E., Georgiadou D., Kardassis D., Chroni A. and Sidiropoulos P. Differential effects of HDL modulating agents in arthritis and HDL properties in mouse models of experimental arthritis. *10th Meeting of the working groups of the Hellenic Atherosclerosis Society*, 1-2 December 2023, Athens

Trohatou O., Charonis A., Roubelakis M., Iatrou C. and Drossopoulou G. Liraglutide ameliorates glucose-induced podocyte injury by activating the nephrin-signalling survival pathway. 49th Panhellenic Medical Conference 11th-13th May 2023, Athens

Other Scientific Activities

Participation in Greek and international scientific bodies and organizations

Chairman of the Management Committee of Working Group on the “Study of Pathophysiology of Atherosclerosis” of the Hellenic Atherosclerosis Society (A. Chroni)

Alternate Member of the General Assembly of the Hellenic Foundation for Research and Innovation (A. Chroni)

Member of WG1 of COST Action CA21153 (AtheroNET) (A. Chroni)

Member of WG2 of COST Action CA22169 (EU-METAHEART) (A. Chroni)

Participation in editorial boards of scientific journals

Editorial board member, Atherosclerosis Plus, Elsevier (A. Chroni)

Editorial board member, Biomolecules, MDPI (A. Chroni)

Associate editor, Frontiers in Cardiovascular Medicine - Lipids in Cardiovascular Disease (A. Chroni)

Topic editor for Frontiers in Cardiovascular Medicine: Rising Stars 2023 (A. Chroni)

Organization of scientific conferences or participation in conference organizing committees

Organization of a Round Table on "Pathophysiology of Atherosclerosis", 10th *Meeting of the working groups of the Hellenic Atherosclerosis Society*, 1 December 2023, Athens (A. Chroni)

Member of the Organizing Committee of the Annual Summer School at the NCSR "Demokritos" (A. Chroni)

Participation in peer review panels for research proposals

Grant evaluator for Swiss National Science Foundation (A. Chroni)

Grant evaluator for Science Fund of the Republic of Serbia (A. Chroni)

Independent Expert for the evaluation of applications for H.F.R.I scholarships for PhD Candidates (A. Chroni)

Reviewing of manuscripts in scientific journals
Arteriosclerosis, Thrombosis, & Vascular Biology, Circulation, Circulation Research, Journal of the American Heart Association, Frontiers in Cardiovascular Medicine, Atherosclerosis, Atherosclerosis Plus, Clinica Chimica Acta, Biomolecules, Cells, International Journal of Molecular Sciences, Future Neurology, Pharmaceutics, Pharmaceuticals, Pharmacology and Therapeutics, ACS Omega, Cellular and Molecular Life Sciences, MedComm, Journal of Atherosclerosis Prevention and Treatment, Frontiers in Nutrition, Stroke and Vascular Neurology, Protein Science (A. Chroni)

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

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

Other lectures or presentations of scientific content
"Analysis of structure-function relationship of apolipoproteins for the understanding of molecular mechanisms of human diseases", Inspired-RIs Conference, 13-15 March 2023, Athens (A. Chroni)

"Links between atherosclerosis, dementia and Alzheimer's disease: cholesterol, apolipoproteins, inflammation", 10th *Meeting of the working groups of the Hellenic Atherosclerosis Society*, 1 December 2023, Athens (A. Chroni)

Participation in teaching courses and other educational activities
A. Chroni:
Member of the Inter-Departmental Committee and Faculty in the joined MSc Programme "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" of the Department of Chemistry of the University of Patras and of the Institute of Biosciences and Applications of NCSR Demokritos.

Member of the Candidates Evaluation Committee for the joined MSc Programme "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" of the Department of Chemistry of the University of Patras and of the Institute of Biosciences and Applications of NCSR Demokritos.

Lecturer in the joined MSc Programme "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" of the Department of Chemistry of the University of Patras and of the Institute of Biosciences and Applications of NCSR Demokritos:
a) Title of lecture: «Cardiovascual disease and current therapeutic approaches» (2 h - 12 students), Course: "Molecular & Cellular Biology-Molecular Biotechnology"
b) Title of lecture: "Methods for analysis and characterization of proteins, lipids and hydrocarbons" (2 h -12 students), Course: "Biochemical Analysis- Clinical Biochemistry"

Guest lecturer in graduate course "Clinical Chemistry", "Clinical Biochemistry-Molecular Diagnostics" Graduate Program, Faculties of Biology, Chemistry and Nursing, University of Athens: Title of lecture: "Alzheimer's disease: a) diagnosis (clinical, laboratory, imaging), b) risk factors (genetic factors, age, sex, cardiovascular factors, traumatic injuries, depression, medications, etc.), c) latest data on the mechanisms of occurrence and progression of the disease and on treatment" (2 hours - 25 students).

Chair of PhD Advisory Committee of A. G. Dedemadi at the Department of Chemistry, University of Athens.

MSc supervisor for D. Lymperopoulos, “Clinical Biochemistry-Molecular Diagnostics” Graduate Program, University of Athens.

Participation in the three-member Examination Committee for the evaluation of thesis of D. Lymperopoulos for obtaining a MSc in Clinical Biochemistry-Molecular Diagnostics from the University of Athens. D. Lymperopoulos defended his MSc thesis at the University of Athens (December 2023). Title of thesis: "Effect of polyphenolic-rich Corinthian Currant extract on the expression and activity of the antioxidant enzyme paraoxonase 1 (PON1): relation to Alzheimer’s disease".

Diploma thesis supervision for undergraduate students E. Georgiou and G. Simopoulos of the Chemistry Department, University of Athens.

Eirini Georgiou presented her Diploma thesis at the Department of Chemistry of the University of Athens (October 2023). Title of thesis: " Study of the activity of the antioxidant enzyme paraoxonase 1 (PON1) in the brain of mouse model of Alzheimer's disease 5xFAD in relation to the age of mice and diet with Corinthian currants".

Member of PhD Advisory Committee of C. Mahalia at the Chemistry Department, University of Athens and A. Papagianni at the School of Medicine, Aristotle University of Thessaloniki.

Presentation entitled “Research activities and educational opportunities at the Institute of Biosciences and Applications”, 57th Summer School of NCSR “Demokritos”, 14 July 2023, (20 min - 450 students)

Presentation entitled “Dyslipidemia: the great enemy of the heart and blood vessels”, 57th Summer School of NCSR “Demokritos”, 14 July 2023, (30 min - 450 students)

Supervisor of a laboratory exercise for high school students (Topic: Biochemistry laboratory techniques for the study of proteins), Summer Scientific Workshops for high school students organized by the IBA of the NCSR "Demokritos", 3-7 July 2023.

P. Kitsiou and G. Drossopoulou:
Summer Camp, IBA (26 June – 7 July 2023). Study of the effect of induced cell-stress on the survival of cell culture systems

G. Drossopoulou:
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 2023 (3 hours lecture - 30 students)

Guest lecturer in MSc postgraduate course Clinical Biochemistry – Molecular Diagnostics, Unit: Physiology Chapters, Department of Biology, National and Kapodistrian University of Athens, “Metabolic Syndromes – Diebetes Mellitus and its complications”. (3 hours - 18 students)

Guest Lecturer in the postgraduate specialisation programme (MSc) “Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products”, Department of Chemistry, University of Patras and Institute of Biosciences and Applications (IBA), NCSR Demokritos. (4 hours - 13 students, Lectures on “Biochemical Analysis – Clinical Biochemistry).

Other Activities in IBA and in NCSR “Demokritos”
Person in charge for education issues in the IBA. Member of the Education Coordinating Council of the NCSR “Demokritos”. (A. Chroni)

Member of the Research Committee of the NCSR “Demokritos” (A. Chroni)

Coordinator of the Histology unit of IBA (G. Drossopoulou)

Other scientific activities

Evaluation of abstracts for the annual conference of the Working Groups of the Hellenic Atherosclerosis Society (A. Chroni)

Member of the Evaluation Committee for the recruitment or promotion of Researchers or University Teaching/Research Staff: NCSR "Demokritos", University of Ioannina (A. Chroni)

Issues of gender equality in academia: Thirteen interviews with women academics. The Vima of Social Sciences, Scientific Journal of University Publications of Thessaly, 21 (7), pp 167-169 (2023) (A. Chroni)

Total Impact Factor for original publications in 2023

A. Chroni: 18.4 (for 3 publications)

Citations for 2023 (without self-citations)

A. Chroni: 154 (Scopus)
P. Kitsiou: 44 (Scopus)
G. Drossopoulou: 69 (Scopus)

Total citations 2019-2023 (without self-citations)

A. Chroni: 795 (Scopus)
P. Kitsiou: 192 (Scopus)
G. Drossopoulou: 432 (Scopus)

h-index

A. Chroni: 28 (Scopus), 32 (Google Scholar)
P. Kitsiou: 12 (Scopus, Google Scholar)
G. Drossopoulou: 15 (Scopus, Google Scholar)

Current External Funding

Programme entitled *New therapies aiming to improve the atheroprotective and immunomodulatory properties of HDL for the treatment of autoimmune and cardiovascular diseases* funded by the Ministry of Economy and Development of Greece/ NSRF 2014-2020, Action "RESEARCH-CREATE-INNOVATE" with A. Chroni as Scientific Supervisor
Programme duration: 2020-2023
Total lab funding (for the entire duration of the programme): 250.000 €
Funding of the lab for 2023: 47.000 €

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

Programme 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 E. Stratikos as Scientific Supervisor for NCSR Demokritos and A. Chroni as Deputy Scientific Supervisor
Programme duration: 2021-2024
Total funding for NCSR Demokritos (for the entire duration of the programme): 486.035 €
Total lab funding (for the entire duration of the programme): 30.000 €

Funding of the lab for 2023: 10.000 €

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

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
Christophoros Christophoridis, Postdoctoral Fellow
Anastasios Kouroumalis, Postdoctoral Fellow
Eleni Liakou, PhD Student – *PhD obtained in 2023*
Maria Angelopoulou, PhD Student – *PhD obtained in 2023*
Asimina Fotopoulou, PhD Student
Efstathios Tsimelis, PhD Student
Anastasia Kypraiou, Graduate Student (MSc) – *MSc obtained in 2023*
Marina Kavellari, Graduate Student (MSc) – *MSc obtained in 2023*
Dafni-Alexandra Kavvoura, Graduate Student (MSc) – *MSc obtained in 2023*
Maria Karanikou, Graduate Student (MSc) – *MSc obtained in 2023*
Mariam Christogianni, Graduate Student (MSc)
Theofano Anagnostou, Graduate Student (MSc)
Maria Souma, Graduate Student (MSc)
Vassiliki Kavvadia, Undergraduate Student (BSc) – *BSc obtained in 2023*

Research Interests
The Laboratory is focusing on the investigation of the mechanisms of ageing and longevity. Cellular senescence - as a result of successive duplications *in vitro* - and premature senescence - as a response of the cells to exogenous stresses (such as γ or UV irradiation, oxidative stress, cytokines, etc.) - are investigated, while the structural and functional alterations 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) and the senescence-associated alterations in extracellular matrix components, in the development of important age-related diseases, including 1. cancer progression, 2. intervertebral disc degeneration and manifestation of low back pain and 3. inherent skin ageing, as well as photo-ageing. 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 to the development of cell replacement therapies. Finally, we investigate natural products and new synthetic compounds with putative anti-cancer, anti-ageing/anti-oxidant, photo-protective and wound healing properties, as well as their mode of action.

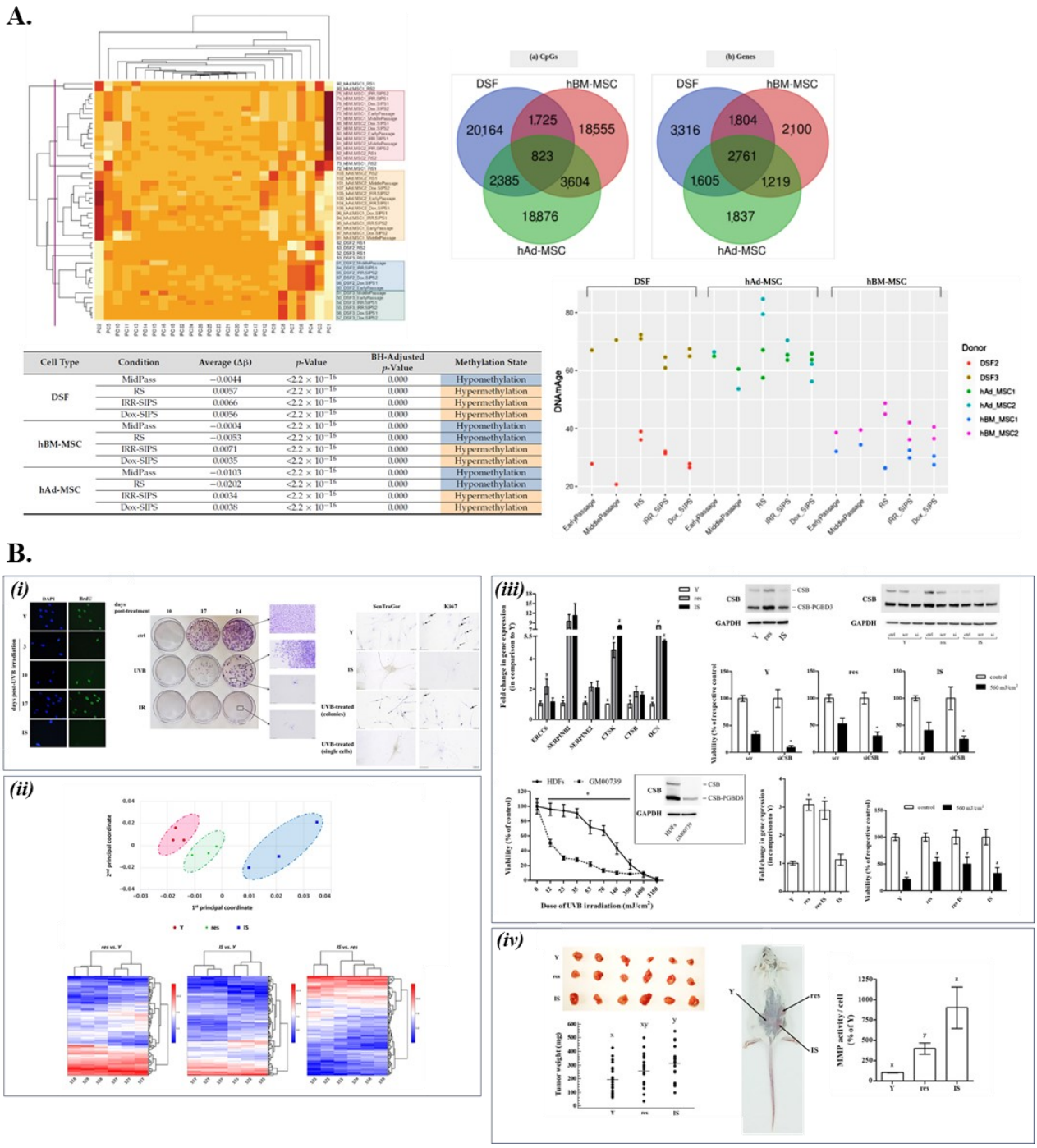
2023 Findings
Main goal of the Laboratory is the study of the role of the senescent cell in the manifestation of age-related diseases. Cellular senescence can be induced by different stimuli and thus the question whether various types of senescent cells are identical remains. We studied three types

of human cells (dermal fibroblasts, as well as bone marrow- and adipose-derived mesenchymal cells), driven to senescence after serial sub-culturing, exposure to ionizing radiation or treatment with doxorubicin. A whole genome methylation analysis was performed and revealed different epigenetic signatures, dependent on the cell type and the senescence-inducing stimulus (Figure 1A). Furthermore, enrichment in pathways linked to degenerative/neurological pathologies and to changes in extracellular matrix organization was shown that may be related to specific senescence-associated effects on tissue homeostasis.

UVB irradiation is a main contributor to skin photo-ageing, as well as to dermal cells' senescence. We demonstrated for the first time the existence of a resistant to UVB-induced senescence subpopulation among dermal fibroblasts (Figure 1B). After RNA-seq analysis and functional experiments we showed that these cells constitute a distinct subpopulation in-between young and senescent cells. In addition, we provided evidence on the role of the DNA damage response in conferring resistance to this population and specifically the overexpression of Cockane Syndrome group B (CSB) protein. Finally, we showed that resistant cells remain normal, but still affect tissue homeostasis and promote carcinogenesis.

Low back pain constitutes one of the most important chronic age-related diseases, in the manifestation of which intervertebral disc degeneration is a critical parameter. Given the lack of vascularization in the intervertebral disc, we aimed to investigate whether improvement of the physiology of this tissue using pharmaceutical approaches is plausible. In the past we have shown that zoledronic acid, traditionally used to treat osteoporosis, compared to a vascularized tissue (the skin), shows a delayed, prolonged and at low concentrations accumulation in the periphery of the disc (annulus fibrosus) of rabbits, while it is not detected in the center of the disc (the nucleus pulposus). During 2023 we showed that after administration of the anticancer drug doxorubicin, a similar kinetics of its accumulation is followed, indicating that the phenomenon is independent of the administered substances' chemical composition. These findings are important for the design of therapeutic approaches against low back pain. Finally, the role of young and senescent mesenchymal stem cells in the regeneration of degenerated discs was studied. We showed that senescent cells express an inflammatory and catabolic phenotype, which may exacerbate intervertebral disc degeneration in a rabbit model.

Finally, we continued our research on the investigation of novel synthetic compounds and natural products from the Greek flora with anti-cancer, anti-ageing, anti-oxidant and cosmetic applications. A particularly positive effect was found using *Ceratonia silica* and *Rosa canina* extracts obtained by both classical extraction methods or by using natural deep eutectic solvents (NADES).



Cell Type	Condition	Average (Δβ)	*p*-Value	BH-Adjusted *p*-Value	Methylation State
DSF	MidPass	−0.0044	$<2.2 \times 10^{-16}$	0.000	Hypomethylation
	RS	0.0057	$<2.2 \times 10^{-16}$	0.000	Hypermethylation
	IRR-SIPS	0.0066	$<2.2 \times 10^{-16}$	0.000	Hypermethylation
	Dox-SIPS	0.0056	$<2.2 \times 10^{-16}$	0.000	Hypermethylation
hBM-MSC	MidPass	−0.0004	$<2.2 \times 10^{-16}$	0.000	Hypomethylation
	RS	−0.0053	$<2.2 \times 10^{-16}$	0.000	Hypomethylation
	IRR-SIPS	0.0071	$<2.2 \times 10^{-16}$	0.000	Hypermethylation
	Dox-SIPS	0.0035	$<2.2 \times 10^{-16}$	0.000	Hypermethylation
hAd-MSC	MidPass	−0.0103	$<2.2 \times 10^{-16}$	0.000	Hypomethylation
	RS	−0.0202	$<2.2 \times 10^{-16}$	0.000	Hypomethylation
	IRR-SIPS	0.0034	$<2.2 \times 10^{-16}$	0.000	Hypermethylation
	Dox-SIPS	0.0038	$<2.2 \times 10^{-16}$	0.000	Hypermethylation

Figure 1: A. *Cellular senescence is characterized by heterogeneity at the epigenetic level. Epigenetic profile is cell type- and senescence-inducing stimulus-dependent and the only epigenetic signature that exceeds cell type specificity is that of replicative senescence [Kwiatkowska et al., Cells. 2023 Mar 17;12(6):927].* ***B.*** *Repetitive exposure to non-cytotoxic UVB irradiation doses reveals the existence of a resistant to UVB-induced senescence subpopulation of human dermal fibroblasts. (i) A subset of UVB-irradiated human dermal fibroblasts regains its proliferative capacity after an initial arrest. (ii) Resistant to UVB-induced senescence cells constitute a distinct population in-between young and senescent cells, as shown after RNA-seq analysis. (iii) CSB protein overexpression plays an important role in UVB resistance. (iv) Resistant to UVB-induced senescence cells remain normal, but affect tissue homeostasis and cancer promotion [Fotopoulou et al., Aging Cell. 2024 Dec 19:e14422].*

Publications

Mourkioti I, Polyzou A, Veroutis D, Theocharous G, Lagopati N, Gentile E, Stravokefalou V, Thanos DF, Havaki S, Kletsas D, Panaretakis T, Logothetis CJ, Stellas D, Petty R, Blandino G, Papaspyropoulos A, Gorgoulis VG. (2023). A GATA2-CDC6 axis modulates androgen receptor

blockade-induced senescence in prostate cancer. J Exp Clin Cancer Res. 2023 Jul 29;42(1):187. (IF: 11.400)

Lougiakis N, Sakalis N, Georgiou M, Marakos P, Pouli N, Skaltsounis AL, Mavrogonatou E, Pratsinis H, Kletsas D. (2023). Synthesis, cytotoxic activity evaluation and mechanistic investigation of novel 3,7-diarylsubstituted 6-azaindoles. Eur J Med Chem. 2023 Dec 5:261:115804. (IF: 6.000)

Kwiatkowska KM, Mavrogonatou E, Papadopoulou A, Sala C, Calzari L, Gentilini D, Bacalini MG, Dall'Olio D, Castellani G, Ravaioli F, Franceschi C, Garagnani P, Pirazzini C, Kletsas D. (2023). Heterogeneity of cellular senescence: cell type-specific and senescence stimulus-dependent epigenetic alterations. Cells. 2023 Mar 17;12(6):927. (IF: 5.100)

Kavvoura DA, Stefanakis MK, Kletsas D, Katerinopoulos HE, Pratsinis H. (2023). Biological activities of *Ceratonia siliqua* pod and seed extracts: a comparative analysis of two Cretan cultivars. Int J Mol Sci. 2023 Jul 28;24(15):12104. (IF: 4.900)

Mavrogonatou E, Papadopoulou A, Pratsinis H, Kletsas D. (2023). Senescence-associated alterations in the extracellular matrix: deciphering their role in the regulation of cellular function. Am J Physiol Cell Physiol. 2023 Sep 1;325(3):C633-C647. (IF: 5.000)

Koutela A, Loudos G, Rouchota M, Kletsas D, Karameris A, Vilaras G, Zografos GC, Grypari IM, Dougenis D, Papalois AE. (2023). A novel experimental rat model for the *in vivo* assessment of myocardial ischemia based on single photon emission computed tomography. In Vivo. 2023 Mar-Apr;37(2):649-654. (IF: 1.800)

Articles in Press

Angelopoulou A, Theocharous G, Valakos D, Polyzou A, Magkouta S, Myrianthopoulos V, Nisotakis T, Thanos D-F, Pantazaki A, Kletsas D, Bartek J, Petty R, Thanos D, McCrimmon RJ, Papaspyropoulos A, Gorgoulis VG. (2024). Loss of the tumor suppressor LKB1/STK11 uncovers a leptin-mediated sensitivity mechanisms to mitochondrial uncouplers for targeted cancer therapy. Molecular Cancer. 2024 (in press). (IF: 27.700)

Parisi L, Mavrogonatou E, Sculean A, Kletsas D, Degen M. (2024). Reviewing the benefits and clinical outcomes of oral fibroblasts over mesenchymal stem cells for repairing periodontal defects during or after orthodontic tooth movement. Periodontology 2000 2024 (in press). (IF: 17.500)

Fotopoulou A, Angelopoulou MT, Pratsinis H, Mavrogonatou E, Kletsas D. (2024). A subset of human dermal fibroblasts overexpressing Cockayne syndrome group B protein resist UVB radiation-mediated premature senescence. Aging Cell 2024, in press. (IF: 8.000)

Fotopoulou T, Papadopoulou A, Tzani A, Mamais M, Mavrogonatou E, Pratsinis H, Koufaki M, Kletsas D, Calogeropoulou T. (2024). Design and synthesis of novel antioxidant 2-substituted-5,7,8-Trimethyl-1,4-Benzoxazine hybrids: effects on young and senescent fibroblasts. Antioxidants 2024, 13(7), 798. (IF: 6.000)

Mavrogonatou E, Kletsas D. (2024). Plant-derived senotherapeutics for the prevention and treatment of intervertebral disc degeneration and aging. Metabolites. 2024 Feb 28;14(3):146. (IF: 3.400)

Koutela A, Loudos G, Rouchota M, Kletsas D, Karameris A, Vilaras G, Zografos GC, Myoteri D, Dougenis D, Papalois AE. (2024). Mesenchymal stem cell transplantation has a regenerative effect in ischemic myocardium: an experimental rat model evaluated by SPECT-CT assessment. Diagnostics (Basel). 2024 Feb 12;14(4):401. (IF: 3.000)

Karamanidou T, Krommydas K, Karanikou M, Tsamos D, Michalakis K, Kletsas D, Tsouknidas A, Pratsinis H. (2024). Biological activities of citrus-derived extracellular vesicles on human cells: the role of preservation. Curr Issues Mol Biol. 2024 Jun 11;46(6):5812-5824. (IF: 2.800)

Angelis YS, Sakellariou P, Fragkaki AG, Karnava S, Goula O, Kiousi P, Kioukia-Fougia N, Georgakopoulos C, Loui S, Chlapana F, Kletsas D. (2024). New long-standing metabolites of 17α-methyltestosterone are detected in HepG2 cell *in vitro* metabolic model and in human urine. Drug Test Anal. 2024 Jun;16(6):604-615. (IF: 2.600)

International conferences

Lemus Ringele GB, Argyropoulou A, Fotopoulou A, Gumeni S, Gkogkou E, Stavropoulos G, Angeli K, Pratsinis H, Kletsas D, Beis D, Trougakos IP, Kalpoutzakis E, Halabalaki M. Phytochemical and bioactivity profile of plants from the Greek flora towards the development of cosmeceuticals. 71st International Congress and Annual Meeting of the Society for Medicinal Plant and Natural Product Research (GA), July 2-5, 2023, Dublin, Ireland

Gumeni S, Fotopoulou A, Agalou A, Lemus Ringele GB, Manola MS, Stavropoulos G, Karamanou K, Evangelakou Z, Theodoridi A, Angeli K, Gianniou DD, Louka XP, Gkogkou SE, Mavrogonatou E, Argyropoulou A, Pratsinis H, Halabalaki M, Beis D, Kletsas D, Trougakos IP. Determination of the anti-aging and skin-protective potential of Greek plants. 71st International Congress and Annual Meeting of the Society for Medicinal Plant and Natural Product Research (GA), July 2-5, 2023, Dublin, Ireland

Mavrogonatou E, Angelopoulou MT, Rizou SV, Pratsinis H, Gorgoulis VG, Kletsas D. Activation of a JNKs/ATM-p53 loop is required for the cytoprotection of UVB-exposed dermal fibroblasts. The 47th FEBS Congress, July 8-12, 2023, Tours, France

Theodoridi A, Tsiasioti E, Tsata V, Agalou A, Argyropoulou A, Papachristodoulou A, Halabalaki M, Skaltsounis A-L, Gumeni S, Trougakos IP, Stavropoulos G, Angeli K, Fotopoulou A, Pratsinis H, Kletsas D, Beis D. Identification of novel bioactive compounds from Greek plants, using *in vivo* zebrafish phenotypic assays. 12th European Zebrafish Meeting (EZM2023), July 9-13, 2023, Krakow, Poland

Kavvoura D-A, Bekiaris G, Tagkouli D, Amerikanou C, Stefanakis MK, Valsamidou E, Kletsas D, Katerinopoulos HE, Kalogeropoulos N, Pratsinis H, Kaliora AC. FT-IR fingerprint and bioactivities of Ceratonia siliqua fruit of Cretan origin. 4th International Conference on Food Bioactives & Health, September 18-21, 2023, Prague, Czech Republic

National conferences

Sakalis N, Georgiou M, Mavrogonatou E, Pratsinis H, Kletsas D, Marakos P, Pouli N, Lougiakis N. Design, synthesis and cytotoxic activity evaluation of new 3,7-diarylsubstituted-6-azaindoles. 19th Panhellenic Symposium of Medicinal Chemistry, March 9-11, 2023, Patras

Lampiri P, Pousias A, Mavrogonatou E, Pratsinis H, Kletsas D, Marakos P, Pouli N, Lougiakis N. Design and synthesis of novel pyrrolo[2,3-c]pyridines with potent antiproliferative activity. 19th Panhellenic Symposium of Medicinal Chemistry, March 9-11, 2023, Patras

Mavrogonatou E, Kwiatkowska KM, Papadopoulou A, Garagnani P, Pirazzini C, Franceschi C, Kletsas D. Cell type-specific and senescence stimulus-dependent epigenetic signatures support heterogeneity in cellular senescence. 73rd Congress of the Hellenic Society of Biochemistry and Molecular Biology, December 1-3, 2023, Athens

Fotopoulou A, Angelopoulou M, Pratsinis H, Mavrogonatou E, Kletsas D. Molecular and functional characterization of a subset of human skin fibroblasts that resist UVB-mediated premature senescence. 73rd Congress of the Hellenic Society of Biochemistry and Molecular Biology, December 1-3, 2023, Athens

Kavvoura DA, Stefanakis MK, Kletsas D, Katerinopoulos HE, Pratsinis H. Biological activities of *Ceratonia siliqua* pod and seed extracts towards skin cell protection. 73rd Congress of the Hellenic Society of Biochemistry and Molecular Biology, December 1-3, 2023, Athens

Fotopoulou A, Gumeni S, Agalou A, Lemus Ringele GB, Papadopoulou A, Manola MS, Karamanou K, Stavropoulos G, Evangelakou Z, Theodoridi A, Angeli K, Gianniou DD, Louka XP, Gkogkou E, Mavrogonatou E, Argyropoulou A, Pratsinis H, Skaltsounis AL, Halabalaki M, Beis D, Trougakos IP, Kletsas D. A high-throughput screening of Greek plants for the discovery of novel compounds with anti-ageing and skin-protective properties. 73rd Congress of the Hellenic Society of Biochemistry and Molecular Biology, December 1-3, 2023, Athens

Fotopoulou T, Papadopoulou A, Tzani A, Pratsinis H, Koufaki M, Kletsas D, Calogeropoulou T. Design and synthesis of novel 2-substituted-5,7,8-Trimethyl-1,4-Benzoxazine hybrids against ageing. 73rd Congress of the Hellenic Society of Biochemistry and Molecular Biology, December 1-3, 2023, Athens

Other Scientific Activities

Participation in Greek and international scientific bodies and organizations

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

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

Coordinator of the National Research Infrastructure OPENSCREEN-GR (D. Kletsas)

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

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

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

Participation in editorial boards of scientific journals

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

Guest Editor in the Special Issue "Antioxidants as Anti-Aging Interventions" for the Journal Antioxidants (with M. Kapetanou and A. Mladenovic) (D. Kletsas)

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

Reviewer board member of the Journal “Frontiers in Bioscience-Landmark” (H. Pratsinis)

Reviewer board member of the Journal “International Journal of Molecular Sciences” (E. Mavrogonatou)

Review Editor for Craniofacial Biology and Dental Research του περιοδικού “Frontiers in Physiology” (E. Mavrogonatou)

Reviewing of manuscripts in scientific journals

Nature Aging, Aging Cell, Mechanisms of Ageing and Development, J. Gerontology: Biological Sciences, Cell Proliferation, Cancer Communications, Wound Repair and Regeneration, Molecular Biology Reports, European Spine Journal (4), Antioxidants (2) (D. Kletsas)

Antioxidants (6), Chemistry & Biodiversity, Biomedicines, Current Issues in Molecular Biology, European Journal of Pharmacology, Frontiers in Bioscience-Landmark (2), Geriatrics & Gerontology International, International Journal of Molecular Sciences (3), Molecular Biology Reports (4), Stem Cells International (H. Pratsinis)

International Journal of Molecular Sciences (9), American Journal of Orthodontics & Dentofacial Orthopedics (5), Nutrients (4), Cancers (3), Biomolecules, Antioxidants (4), Biomedicines (4), Pharmaceutics (2), Progress in Orthodontics, Genes, Scientia Pharmaceutica, Frontiers in Physiology (15), Frontiers in Public Health (E. Mavrogonatou)

Awards and distinctions

Prize to Asimina Fotopoulou, Maria Angelopoulou, Harris Pratsinis, Eleni Mavrogonatou and Dimitris Kletsas for the poster presentation entitled "Molecular and functional characterization of a subset of human skin fibroblasts that resist UVB-mediated premature senescence" in the 73rd Congress of the Hellenic Society of Biochemistry and Molecular Biology, December 1-3, 2023, Athens

Educational Activities

Member of the special interinstitutional committee and lecturer in the Joint Post-Graduate Programme (JPGP) in "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" of the Department of Chemistry of the University of Patras and of the Institute of Biosciences and Applications of NCSR "Demokritos" (D. Kletsas)

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

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

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

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

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

"*In vitro* studies of natural and synthetic bioactive products", 58th NCSR "Demokritos" Summer School, 1 hour, 100 students (H. Pratsinis)

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

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

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

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

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

"Cell systems in the research of carcinogenesis", Post-graduate Master's Degree "Neoplastic Disease in Humans: Diagnosis, Modern Treatment and Research", Medical School of the University of Athens, 1 hour, 25 students (H. Pratsinis)

"Tissue imaging applications", Post-graduate Master's Degree "Musculoskeletal Oncology: Diagnosis-Therapy-Research", Medical School of the University of Athens, 1,5 hours, 25 students (H. Pratsinis)

Participation in the Inter-Institutional Joint Post-Graduate Programme (JPGP) in "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" between the Institute of Biosciences and Applications and the University of Patras, 6 hours, 12 students (D. Kletsas, H. Pratsinis and E. Mavrogonatou)

Participation in the Fund Drive event organized by the Athens College-Psychico College to support the Educational Office of NCSR "Demokritos" in Science Communication, May 6 Μαΐου, 2023 (E. Mavrogonatou)

Member of examination committees for PhD, MSc and BSc theses
Maria Angelopoulou concluded her PhD thesis entitled "Study of the anti-oxidant and photo-protective action of natural products" in the Department of Pharmacy, University of Athens. The thesis was unanimously accepted and awarded the degree "Excellent" (Scientific Supervisor D. Kletsas)

Eleni Liakou concluded her PhD thesis entitled "Study of paracrine interactions between stromal and breast cancer cells. The role of cellular senescence" in the Department of Chemistry, University of Patras. The thesis was unanimously accepted and awarded the degree "Excellent" (Scientific Supervisor D. Kletsas, Member of the seven-member examination committee H. Pratsinis)

Anastasia Kypraiou concluded her MSc thesis entitled "Study of interleukin 6 expression in normal (young and senescent) and cancer cells" in the framework of 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". The thesis was unanimously accepted and awarded the degree "Excellent" (Scientific Supervisor D. Kletsas, Member of the three-member examination committee E. Mavrogonatou)

Marina Kavellari concluded her MSc thesis entitled "Study of interleukin 8 expression in senescent and cancer cells as a biomarker of inflammatory response" in the framework of 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". The thesis was unanimously accepted and awarded the degree "Excellent" (Scientific Supervisor D. Kletsas)

Dafni-Alexandra Kavvoura concluded her MSc thesis entitled "Biological activities of *Ceratonia siliqua* pod and seed extracts on human skin cells: comparative analysis of two Cretan cultivars" in the framework of the Master's Degree Programme "Cosmetology-Dermatopharmacology" in the Department of Pharmacy, University of Athens. The thesis was unanimously accepted and awarded the degree "Excellent" (Scientific Supervisor H. Pratsinis)

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

Vassiliki Kavvadia concluded her thesis entitled "Response of adipose-derived mesenchymal stem cells towards high osmolality" for the acquisition of her BSc diploma in the Department of Biology, University of Athens. The thesis was unanimously accepted and awarded the degree "Excellent" (Scientific Supervisor E. Mavrogonatou)

Other Activities in IBA and in NCSR "Demokritos"

D. Kletsas:

Director of IBA & Member of the Board of NCSR "Demokritos"
Vice-President of the Board of NCSR "Demokritos"
Member of the Committee for Research Exploitation in NCSR "Demokritos"
Scientific and Administrative Responsible of the Experimental Animal Facility
Administrative Responsible of the Laboratory for Doping Control and Metabolic Studies
Scientific and Administrative Responsible of the Light Microscopy Unit and the Histology Unit

H. Pratsinis:

President of the Scientific Board of IBA
Responsible for the conducted tours in the Institute of Biosciences and Applications of NCSR "Demokritos"
Member of the Committee for the monitoring of the renovation procedure of the central building of IBA
Member of the Evaluation Committees for the evaluation of candidates for temporary staff positions (projects 11499, 12584 and 12609 of ELKE, NCSR "Demokritos")
Member of the Committee for the accomplishment of an open electronic competition for deliverables' supply in the framework of the implementation of project 12499 of ELKE, NCSR "Demokritos"

E. Mavrogonatou:

Organization of the teaching and examination schedule of the course "Molecular & Cellular Biology-Molecular Biotechnology" course in the framework of the Inter-Institutional Joint Post-Graduate Programme between the Institute of Biosciences and Applications and the University of Patras "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" (Spring semester)
Member of the three-member evaluation committee for the evaluation of candidates for temporary staff positions in the framework of the implementation of projects E-11499, E-12584 and E-12609
Member of the Committee for the accomplishment of an open electronic competition for deliverables' supply in the framework of the implementation of project E-12499

Total Impact Factor for original publications in 2023

D. Kletsas (for 6 publications): 34.200
H. Pratsinis (for 3 publications): 15.900
E. Mavrogonatou (for 3 publications): 16.100

Citations 2023 (without self-citations)

D. Kletsas: 804
H. Pratsinis: 324
E. Mavrogonatou: 221

Total Citations 2019-2023 (without self-citations)

D. Kletsas: 4095
H. Pratsinis: 1383
E. Mavrogonatou: 931

h-index

D. Kletsas: 54 (Scopus), 61 (Google Scholar)
H. Pratsinis: 35 (Scopus), 40 (Google Scholar)
E. Mavrogonatou: 22 (Scopus), 24 (Google Scholar)

Current External Funding

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 lab (for the entire duration of the programme): 229.999,99 €
Funding of the lab for 2023: 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 lab (for the entire duration of the programme): 200.000,00 €
Funding of the lab for 2023: 0 €.

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

Project entitled “In vitro assessment of combinations of known senotherapeutics for their potential application in the prevention and/or treatment of intrinsic and ultraviolet radiation-induced skin ageing”, financed by UNI-PHARMA Pharmaceutical Laboratories S.A.
Scientific Supervisor: Dr. D. Kletsas
Duration: 2021-2023
Total programme funding for the lab (for the entire duration of the programme): 25.000,00 €
Funding of the lab for 2023: 8.400,00 €.

Project entitled “Rational Identification and Evaluation of Antifungals Targeting Quiescent Cells”, financed by the Hellenic Foundation for Research and Innovation (HFRI)
Scientific Supervisor: Dr. V. Sophianopoulou
Duration: 2024-2025
Total programme funding for the lab (for the entire duration of the programme): 58.000,00 €
Funding of the lab for 2023: 0 €.

Current External IBA Funding

Project entitled “Ensuring long-term sustainability of excellence in chemical biology within Europe and beyond (EU-OPENSCREEN-DRIVE)”, funded by the European Union (Action “Reinforcement of the Research and Innovation Infrastructure”, Operational Programme "Competitiveness, Entrepreneurship and Innovation", NSRF 2014-2020)
Scientific Supervisor in IBA: Dr. D. Kletsas
Duration: 2019-2023
Total programme funding (for the entire duration of the programme): 16.875,00 €
Funding for 2023: 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 2023: 278.754,08 €.

Project entitled “Upgrading of the Analytical Equipment of the Laboratory for Doping Control”, funded by the General Secretariat for Research and Innovation
Scientific Supervisor: Dr. D. Kletsas
Duration: 2019-2022
Total programme funding (for the entire duration of the programme): 2.000.000,00 €
Funding for 2023: 0 €.

Research Group: Laboratory of Brain Exosomes and Pathology - ExoBrain

Research Staff
Ioannis Sotiropoulos, Researcher
Zafiroula-Iro Georgoussi, Research Director (retired)
Kostas Iatrou, Emeritus Research Director
Chrysoula Dioli, Postdoctoral researcher
Christos Karoussiotis, Postdoctoral researcher (PhD student until March 2023)
Georgia Kythreoti, Postdoctoral researcher
Alexandra Symeonof, PhD student
Anastasia Vamvaka-Iakovou, PhD student
Anastasia Megalokonomou, PhD student
Nikoletta Karabetsou, Research Assistant
Aggeliki Balouri, Research Assistant
Filippos Katsaitis, Research assistant
Zeta-Georgia Papadimitriou, Master student
Dimitra Gerontidi, Master student
Eirini Gratsia, Master student
Eirini Portokali, Master student
Alexandra Karava, Master student
Vasso Kokkovou, Master student
Melina Dinopoulou, Master student
Eva-Eleni Serfioti, Undergraduate student
Eleni Tsamadia Undergraduate student
Kalliopi Skourti, Undergraduate student
Zoe Kotsikou, Undergraduate student
Athina Pappa, Undergraduate student
Georgia Trasani, Undergraduate student
Despoina Lygoni, Undergraduate student
Sotirios Paraskevas, Undergraduate student
Christos Makatsoris, Undergraduate student

Research Interests
The research work of Dr Sotiropoulos and his team focuses on the study of different clinically-relevant risk factors in the onset and progression of Alzheimer's disease (AD) and their relationship with brain exosomes. Specifically, Dr. Sotiropoulos' research focuses on:
1. elucidating the etiopathological mechanisms of AD and depression with a particular focus on chronic stress and Tau protein as key regulators of neuroplasticity and neuropathology,

2. testing novel therapeutic strategies, targets and compounds (e.g. antisense oligonucleotides (ASOs), cannabidiol) against AD and stress-induced depression,

3. clarifying the dual role of brain extracellular vesicles (EVs) and brain exosomes as mediators/transporters of AD brain pathology as well as brain biomarkers in peripheral blood.

The research activities of Dr Z. Georgoussi are focusing on the elucidation of the mechanisms governing G protein-coupled receptors (GPCRs) signaling using as model the δ, μ and κ-opioid receptors involved in neurotransmission, neuronal plasticity and emotional behaviors such as stress, anxiety, and depression.
More specifically, Dr Z. Georgoussi's research *objectives are focused on:*

1. The elucidation of novel signaling pathways and analysis of genes, transcription factors and proteins implicated in autophagy, plasticity, neuronal differentiation upon administration of opioids.
2. The pharmacological characterization of new bioactive compounds for opioid or other GPCRs in order to identify "*smart drugs*", or food supplements to combat diseases of the CNS, stress and cognition from natural products of the Greek flora.

Dr. K. Iatrou's research activities are focusing on the study of the olfactory functions of insects. Genomic, pharmacological, behavioral and computational methodologies are employed with the goal of identifying volatile compounds of natural origin capable of inhibiting the function of the obligatory olfactory receptor co-receptor ORco, whose presence is required for the functionality of all insect odor receptors. The ultimate aim is to achieve an effective and environmentally safe interference with the capacity of hematophagous insects to detect their animal or human hosts in their environment and thus reduce the rate of infectious disease transmission to them

Research Progress in 2023

Dr Ioannis Sotiropoulos

Our research findings were published in 2 scientific papers describing: a) the link between chronic stress, depression and AD and b) the development of a new method for isolating brain exosomes. *Novel stress-induced molecular mechanisms in AD:* Given the important role of inflammation and microglial cells in the establishment of AD brain pathology, we used transgenic mice with selective deletion of glucocorticoid receptors in neuronal or glial brain cells. Behavioral as well as molecular findings supported the distinct contribution of both cell types to stress-induced memory loss and depression-like behavior as well as the induction of Tau hyperphosphorylation and its accumulation.

Exosomes and chronic stress: In light of the current technical limitations and problems in the existing methods of isolating exosomes from brain tissue, our research group developed and tested a new method of isolating exosomes from the brain based on their spontaneous release =and avoiding any mechanical or biochemical isolation of brain cells. Based on advanced analytical platforms for exosome analysis, we demonstrated that our method produced purer and exosome-enriched small EV yield of intact and function brain exosomes while we shoed for the first time exposure to chronic, psychological stress induces the release of brain exosomes.

Dr Zafiroula Georgoussi

Autophagy: A novel signaling mechanism of opioid receptors: Given that the dynorphin/κ-opioid receptor (κ-OR) system plays a key role in modulating anxiety and stress related behaviors we identified a novel signaling pathway via which κ-OR induces the autophagic machinery resulting in synaptosomal changes in hippocampus under stress stimuli (Figure 1C). In this repsect, mice administrated with the κ-OR antagonist Aticaprant (Phase III clinical trials) produced an anxiolytic and antidepressant effect, reversed stress-induced impairments in long-term memory, and restored the stress-induced autophagy with concomitant alterations of hippocampal synaptic proteins.

Pharmacological characterization of bioactive compounds in cell-based throughput platforms: Under the program "NUTRIMED" in collaboration with IBA, UOA and INTERMED S.A, we identified that natural extracts from Greek medicinal plants selectively bind to the κ-OR and the 5-HT1A serotonin receptors using cell-based assays.

Development of neuronal networks on graphene microelectrode nanostructures: In collaboration with Dr Dimitrakis, INN NCSR "D", we developed neuronal cells on graphene nanoribbon interconnects aiming in the design of functional biosensors.

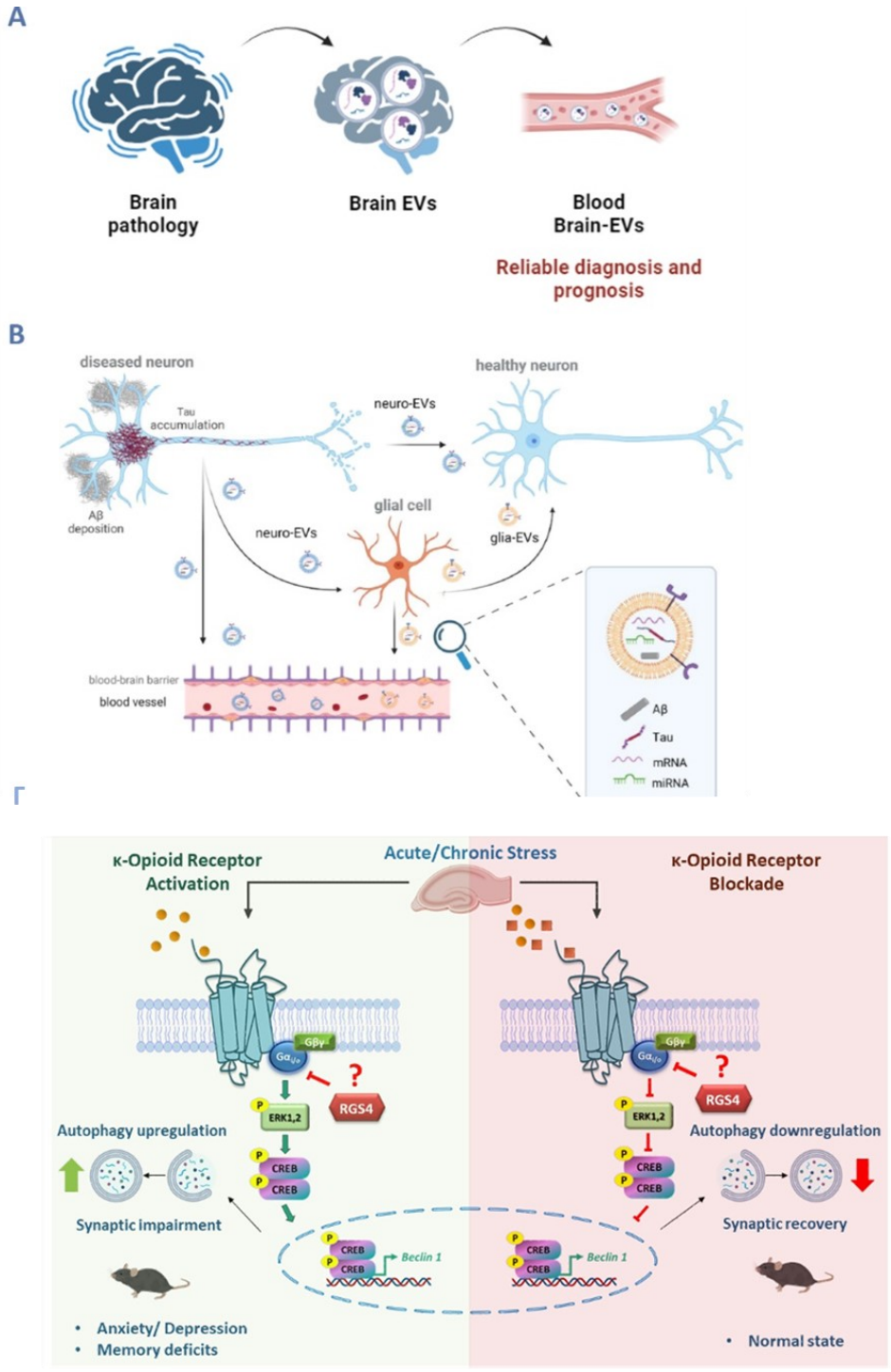


Figure 1: A*. Illustration of the use of small extracellular vesicles (EVs) e.g. exosomes produced by brain cells to monitor brain pathology in peripheral blood.* ***B****. The role of extracellular vesicles (e.g. exosomes) in the spread of Alzheimer's disease pathology between different cells & regions of the brain, and their localization in peripheral blood as potential biomarkers of brain pathology – note that exosomes carry different types of biological material (e.g. e.g. proteins (tau), mRNA, miRNA etc.) from the brain cells of origin such as neurons and glial cells.* ***C****. Schematic representation of a putative signaling pathway via which κ-opioid receptor activation by agonist or acute stress triggers the autophagic machinery resulting in synaptic alterations in hippocampus.*

Dr. Kostas Iatrou

Previous *in silico* screening of collections of small molecules of natural origin with a pharmacophore (collaboration with Drs Trias Thireou, Athens Agricultural University and Spyros Zographos, NHRF) resulted in the identification of putative antagonists of the evolutionarily conserved olfactory receptor co-receptor ORco, which might act as spatial inhibitors of the odor detection machinery in mosquitoes. This year, we undertook the functional testing of randomly selected ORco antagonist candidates using ex vivo and in vivo assays. Our assays confirmed the value of the specific pharmacophore as detection tool for novel volatile ORco antagonists. These induce spatial anosmia on mosquitoes, which are rendered incapable of locating their hosts for blood-feeding.

Publications

Gomes P.A. , Bodo C. , Nogueras-Ortiz C. , Samiotaki5 M. , Chen M., Soares-Cunha C., Silva J.M., Coimbra B. , Stamatakis G. , Santos L. , Panayotou G. , Tzouanou F. , Waites C.L. , Gatsogiannis C. , Sousa N., Kapogiannis D. , Costa-Silva3 B., & Sotiropoulos I. (2023). A novel isolation method for spontaneously released extracellular vesicles from brain tissue and its implications for stress-driven brain pathology, Cell Comm Sign 21:35 (IF: 8.2)

Articles in Press

Clarissa Waites, Qing Yu, Fang Du, Irla Belli, Patrícia Gomes, Ioannis Sotiropoulos, (2023) 'Glucocorticoid stress hormones stimulate vesicle-free Tau secretion and spreading in the brain' Res Sq [Preprint].

Hodes GE, Bangasser D, Sotiropoulos I, Kokras N, Dalla C. "Sex Differences in Stress Response: Classical Mechanisms and Beyond". Curr Neuropharmacol. 2024;22(3):475-494.

Basso M, Gori A, Nardella C, Palviainen M, Holcar M, Sotiropoulos I, Bobis-Wozowicz S, D'Agostino VG, Casarotto E, Ciani Y, Suetsugu S, Gualerzi A, Martin-Jaular L, Boselli D, Kashkanova A, Parisse P, Lippens L, Pagliuca M, Blessing M, Frigerio R, Fourniols T, Meliciano A, Fietta A, Fioretti PV, Soroczyńska K, Picciolini S, Salviano-Silva A, Bergese P, Zocco D, Chiari M, Jenster G, Waldron L, Milosavljevic A, Nolan J, Monopoli MP, Witwer KW, Bussolati B, Di Vizio D, Falcon Perez J, Lenassi M, Cretich M, Demichelis F. "International Society for Extracellular Vesicles Workshop. QuantitatEVs: multiscale analyses, from bulk to single extracellular vesicle" J Extracell Biol. 2024 Jan;3(1):e137.

Wang HL, Siow R, Schmauck-Medina T, Zhang J, Sandset PM, Filshie C, Lund , Partridge L, Bergersen LH, Juel Rasmussen L, Palikaras K, Sotiropoulos I, Storm-Mathisen J, Rubinsztein DC, Spillantini MG, De Zeeuw CI, Watne LO, Vyhnalek M, Veverova K, Liang KX, Tavernarakis N, Bohr VA, Yokote K, Saarela J, Nilsen H, Gonos ES, Scheibye-Knudsen M, Chen G, Kato H, Selbæk G, Fladby T, Nilsson P, Simonsen A, Aarsland D, Lautrup S, Ottersen OP, Cox LS, Fang EF. "NYO3 5th NO-Age/AD Meeting and the 1st Norway-UK Joint Meeting on Aging and Dementia: Recent Progress on the Mechanisms and Interventional Strategies" J Gerontol A Biol Sci Med Sci 2024 79(4):glae029.

Necla Birgül Iyison, Clauda Abboud, Dayana Abboud, Abdulrasheed O. Abdulrahman, Ana-Nicoleta Bondar, Julie Dam, Soner Dogan, Zafiroula Georgoussi, Jesús Giraldo, Anemari Horvat, Christos Karoussiotis, Meliha Karsak, Alba Paz-Castro, Miriam Scarpa, Hannes Schihada, Nicole Scholz, Bilge Güvenç Tuna, Jan Vacek, Nina Vardjan, (2023) ''Physiology of GPCRs in the Nervous System and the Contribution of Orphan GPCRs'' British Journal of Pharmacology.

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

Karoussiotis C., Sotiriou A., Polissidis A. V., Papavranoussi-Daponte D., Symeonof A., Nikoletopoulou V. and Georgoussi Z., *''The role of κ-opioid receptor-induced autophagy in stress-driven synaptic alterations''* 8th ERNEST meeting, Crete, Greece, May 2023.

Symeonof A., Karoussiotis C., Sotiropoulos I., Georgoussi Z., *"The effects of Aticaprant, a κ-opioid receptor antagonist, in stress-driven synaptic alterations.",* 8th ERNEST Meeting, Crete, Greece, May 2023.

Contribution to books (e.g. book chapters)

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

International conferences

I. Sotiropoulos

"The etiopathogenic role and biomarker potential of chronic stress on Alzheimer's disease brain pathology" Steroids and Nervous system 2024, Tori, Italy (February 2024) – Invited Speaker

"A novel method for spontaneous release of small EVs from human and mouse brain" ISEV symposium neuroEVs, Rome, Italy (December 2023) – Selected Speaker

"Chronis Stress and Exosomes as key players in progression and diagnosis of Alzheimer's disease" - Mediterranean Neuroscience Society conference 2023, Cartage, Tunisia (October 2023) – Symposium Organizer & Speaker

"Preclinical research & small EV: tasks and promises" European College of Neuropsychopharmacology (ECNP) 2023 meeting, Barcelona, Spain (October 2023) – Education committee speaker

"The Stressed brain: a gate along the pathway from depression to Alzheimer's disease"- 5th NO-AgingAD, Oslo, Norway (September 2023) – Invited Speaker

"RNA-binding proteins and Stress granules in brain plasticity and pathology" FENS Regional meeting 2023, Algarve, Portugal (May 2023) – Symposium Organizer & Speaker

"Persistent pain causes Tau-mediated hippocampal malfunction and memory deficits", 4th EuroTau 2023, Lile, France (April 2023) – Invited speaker

"Novel method of spontaneously-released extracellular vesicles isolation from mouse and human brain: implications for brain pathology" AD/PD 2023 conference, Gothenburg, Sweden, (April 2023) – Selected speaker

"A novel isolation method for spontaneously released extracellular vesicles from brain tissue and its implications for stress-driven brain pathology" – ISEV workshop QuantitatEVs, Trento, Italy (January 2023) – Selected Speaker

Chania C., Vamvaka-Iakovou A., Megalokonomou A., Efentakis P., Christodoulou A., Livadiotis A., Pavlidi P., Dalla C., Sotiropoulos I., Andreadou I. Investigating the effect of depression and cognitive disorders on myocardial ischemia/reperfusion injury: the influence of the gender. XXV Conference of Young SIF Pharmacologists 2023, Urbino (PU), Italy, 5-8 September, 2023 (oral presentation).

Guerreiro, S. R., Vamvaka Iakovou, A., Guimaraes, M. R., Silva, J. M., Dioli, C., Gomes, P., Megalokonomou, A., Campos Marques, C., Cunha, A. M., Almeida, A., Sousa, N., Leite Almeida, H., Sotiropoulos, I. A novel role of Tau protein in chronic pain-driven hippocampal pathology &

memory deficits. AD/PD 2023 International Conference on Alzheimer's and Parkinson's Diseases and related neurological disorders, Gothenburg, Sweden, March 28th - April 1st 2023 (poster presentation).

Vamvaka-Iakovou A., Guerreiro S. R., Guimaraes M. R., Silva J. M., Dioli C., Gomes P., Megalokonomou A., Marques C. C., Cunha A. M., Almeida A., Sousa N., Almeida H. L., Sotiropoulos I. ´´A novel role of Tau protein in chronic pain-driven hippocampal pathology & memory deficits´´- AD/PD 2023 International Conference on Alzheimer´s and Parkinson´s Diseases and related neurological disorders, Sweden 2023 (poster presentation)

Chania C., Vamvaka-Iakovou A., Megalokonomou A., Efentakis P., Christodoulou A., Livadiotis A., Pavlidi P., Dalla C., Sotiropoulos I., Andreadou I. ´´Investigating the effect of depression and cognitive disorders on myocardial ischemia/reperfusion injury: the influence of the gender. ´´ XXV Conference of Young SIF Pharmacologists, Italy 2023 (oral presentation)

Z. Georgoussi

Karoussiotis C., Sotiriou A., Polissidis A. V., Papavranoussi-Daponte D., Symeonof A., Nikoletopoulou V. and Georgoussi Z., ''The role of κ-opioid receptor-induced autophagy in stress-driven synaptic alterations'' 8th ERNEST meeting, Crete, Greece, May 2023 (oral presentation)

Symeonof A., Karoussiotis C., Sotiropoulos I., Georgoussi Z., "The effects of Aticaprant, a κ-opioid receptor antagonist, in stress-driven synaptic alterations.", 8th ERNEST Meeting, Crete, Greece, May 2023 (poster presentation)

K. Iatrou

T. Thireou, G. Kythreoti P.G.V Liggri, A. Michaelakis, D.P. Papachristos, K.E. Tsitsanou, S.E. Zographos, K. Iatrou (2023). Structural determinants of ORco ligands antagonizing odorant receptor function for mosquito vector control. XII European Congress of Entomology (ECE2023), October 16-20, 2023, Heraklion, Crete, Greece.

T. Thireou, G. Kythreoti, P.G.V Liggri, A. Michaelakis, D.P. Papachristos, K.E. Tsitsanou, S.E. Zographos, K. Iatrou (2023). Combining a pharmacophore and an artificial intelligence approach to predict ORco ligands antagonizing mosquito odorant receptor function. 30th Annual Meeting, Hellenic Society for Neurosciences, November 24-26, 2023, Athens, Greece (poster presentation)

National conferences

I. Sotiropoulos

Megalokonomou A., Campos-Marques C., Godinho B., Watts J., Samiotaki M., Panayotou G., Papadimitriou G., Vamvaka-Iakovou A., Barros-Santos B., Skourti K., Katsaitis F., Silva J., Sotiropoulos I. A novel RNA-targeted therapeutic approach against Tau-driven neuronal pathology in Alzheimer's disease brain pathology. 73rd National Conference of Hellenic Society of Biochemistry and Molecular Biology (HSBMB), Athens, Greece, 1-3 December 2023 (poster presentation).

Vamvaka-Iakovou A., Silva J., Gomes P., Campos-Marques C., Samiotaki M., Panayotou G., Megalokonomou A., Brakatselos Ch., Katsaitis F., Skourti K., Papadimitriou G., Barros-Santos B., Antoniou K., Sotiropoulos I. Unravelling cannabidiol´s therapeutic potential in stress and Alzheimer´s disease brain pathologies. 73rd National Conference of Hellenic Society of Biochemistry and Molecular Biology (HSBMB), Athens, Greece, 1-3 December 2023 (oral presentation).

Kotsikou Z., Gratsia E., Ntinou N., Megalokonomou A., Dioli C., Sotiropoulos I. The role of glucocorticoid receptor signaling in stress-induced disruption of dentate gyrus plasticity in Tau pathology. 73rd National Conference of Hellenic Society of Biochemistry and Molecular Biology (HSBMB), Athens, Greece, 1-3 December 2023 (poster presentation).

Megalokonomou A., Campos-Marques C., Godinho B., Watts J., Samiotaki M., Panayotou G., Papadimitriou G., Vamvaka-Iakovou A., Barros-Santos B., Skourti K., Katsaitis F., Silva J., Sotiropoulos I. A novel RNA-targeted therapeutic approach against Tau-driven neuronal pathology in Alzheimer's disease brain pathology. 10th Young Scientists Day of National Conference of Hellenic Society of Biochemistry and Molecular Biology (HSBMB), Athens, Greece, 30 November 2023 (poster presentation).

Vamvaka-Iakovou A., Silva J., Gomes P., Campos-Marques C., Samiotaki M., Panayotou G., Megalokonomou A., Brakatselos Ch., Katsaitis F., Skourti K., Papadimitriou G., Barros-Santos B., Antoniou K., Sotiropoulos I. Unravelling cannabidiol´s therapeutic potential in stress and Alzheimer´s disease brain pathologies. 10th Young Scientists Day of National Conference of Hellenic Society of Biochemistry and Molecular Biology (HSBMB), Athens, Greece, 30 November 2023 (poster presentation).

Megalokonomou A., Campos-Marques C., Godinho B., Watts J., Samiotaki M., Panayotou G., Papadimitriou G., Vamvaka-Iakovou A., Nóbrega-Martins R., Skourti K., Katsaitis F., Silva J., Sotiropoulos I. Antisense oligonucleotide (ASOs) therapeutic approach against Tau-driven neuronal pathology in Alzheimer's disease brain pathology. 30th Meeting of the Hellenic Society for Neuroscience (HSfN), NCSR Demokritos, Athens, Greece, 24-26 November 2023 (poster presentation).

Dioli C., Silva J., Gomes P., Vamvaka-Iakovou A., Megalokonomou A., Marques C., Samiotaki M., Stamatakis G., Panagiotou G., Benecke A., Kokras N., Dalla Ch., Faucon-Biguet N., Meloni R., Sousa N., Tronche F., Vyas Sh., Sotiropoulos I. Dissecting the cell-specific contribution in the precipitating role of chronic stress on Tau pathology. 30th Meeting of the Hellenic Society for Neuroscience (HSfN), NCSR Demokritos, Athens, Greece, 24-26 November 2023 (poster presentation).

Vamvaka-Iakovou A., Silva J., Gomes P., Campos-Marques C., Samiotaki M., Panayotou G., Megalokonomou A., Brakatselos Ch., Katsaitis F., Skourti K., Papadimitriou G., Nóbrega-Martins R., Antoniou K., Sotiropoulos I. Monitoring the potential therapeutic role of cannabidiol against Stress and Alzheimer's disease brain pathologies. 30th Meeting of the Hellenic Society for Neuroscience (HSfN), NCSR Demokritos, Athens, Greece, 24-26 November 2023 (oral presentation).

Gratsia E., Kotsikou Z., Ntinou N., Megalokonomou A., Dioli C., Sotiropoulos I. Chronic stress disrupts dentate gyrus plasticity in Tau pathology affecting complex neuron-microglia interplay. 30th Meeting of the Hellenic Society for Neuroscience (HSfN), NCSR Demokritos, Athens, Greece, 24-26 November 2023 (poster presentation).

Brakatselos C, Ntoulas G., Asprogerakas M. Z., Tsarna O., Vamvaka-Iakovou A., Nakas G., Delis A., Silva J., Delis F., Oliveira J. F., Sotiropoulos I., Polissidis A.V., Antoniou K. ´´Cannabidiol restores ketamine-induced schizophrenia-like symptomatology by multi-level action on the underlying neurobiological substrate´´- 30th Meeting of the Hellenic Society for Neuroscience (HSfN), Greece 2023 (oral presentation)

Mouatsou C., Karali K., Vamvaka-Iakovou A., Silva J.M. , Gomes P., Gravanis A., Sotiropoulos I., Charalampopoulos I. ´´Investigating the neurogenic effects of BNN237 in a mouse model of stress´´- 30th Meeting of the Hellenic Society for Neuroscience (HSfN), Greece 2023 (poster presentation)

Z. Georgoussi

Karoussiotis C., Symeonof A., Polissidis A.V., Vamvaka-Iakovou A., Megalokonomou A., Sotiropoulos I., Papavranoussi-Daponte D., Tsamadia E., Georgoussi Z. Effects of κ-opioid receptor in stress-driven synaptic alterations due to autophagy induction. 30th Meeting of the Hellenic Society for Neuroscience (HSfN), NCSR Demokritos, Athens, Greece, 24-26 November 2023 (oral presentation).

Symeonof A., Vamvaka-Iakovou A., Megalokonomou A., Karoussiotis Ch., Sotiropoulos I., Georgousi Z. The effects of Aticaprant, a κ-opioid receptor antagonist, in stress-induced deficits in mood and cognition. 73rd National Conference of Hellenic Society of Biochemistry and Molecular Biology (HSBMB), Athens, Greece, 1-3 December 2023 (poster presentation)

Symeonof A., Vamvaka-Iakovou A., Megalokonomou A., Karoussiotis Ch., Sotiropoulos I., Georgousi Z. The effects of Aticaprant, a κ-opioid receptor antagonist, in stress-induced deficits in mood and cognition. 30th Meeting of the Hellenic Society for Neuroscience (HSfN), NCSR Demokritos, Athens, Greece, 24-26 November 2023 (poster presentation).

K. Iatrou

T. Thireou, G. Kythreoti, K.E. Tsitsanou, S.E. Zographos, K. Iatrou (2023). Generating a two-step *in silico* screening protocol to predict ORco ligands antagonizing mosquito odorant receptor function. 11th Conference of the Hellenic Crystallographic Association, October 20-22, 2023, Larissa, Greece.

Other Scientific Activities

I. Sotiropoulos

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

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

Z. Georgoussi

President of the organizing Committee of the 8th ERNEST meeting of the European Cooperation in Science and Technology, COST-CA18133 "European Research Network on Signal Transduction (ERNEST)" *"GPCR structure and function: The present and perspectives for the future",* in the Orthodox Academy of Crete, Kolymbari, Crete 3-7 May 2023.

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

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

Member of the Administrative and Educational board of the "Athens International Master's Programme in Neurosciences".

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

Member of the evaluation committee for the MSc Students of the "Athens International Master's Programme in Neurosciences".

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

Member of the Research Consortium "Normolife Network" responsible for the identification of novel opioid compounds to alleviate pain.

Participation in editorial boards of scientific journal publications

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

Guest Editor of special issue "Molecular and cellular mechanisms of Tauopathy" of scientific journal Neuroscience IBRO-Official Journal (I. Sotiropoulos)

Review Editor of scientific journal Frontiers in Neuroscience (I. Sotiropoulos)

Associate Editor Experimental Pharmacology and Drug Discovery (Frontiers in Pharmacology) (Z. Georgoussi)

Member, Editorial Boards for "Sericologia", "Insect Biochemistry and Molecular Biology", “Archives of Insect Biochemistry and Physiology”, “BioMed Research International" και "Insects" (K. Iatrou)

Organization of scientific conferences or participation in organizing committees of conferences
Member of the organizing Committee of the 30th Conference of the Hellenic Society of Neurosciences (HSNF) 24-26 November 2023, NCSR “Demokritos” (I. Sotiropoulos)

President and co-organizer with Dr K. Iatrou of the 8th ERNEST meeting of the European Research Network on Signal Transduction (ERNEST COST-CA18133), “GPCR structure and function: The present and perspectives for the future”, in the Orthodox Academy of Crete, Kolymbari Crete, May 3-7 2023 (Z. Georgoussi)

Member of the organizing Committee of the 30th Conference of the Hellenic Society of Neurosciences (HSNF) 24-26 November 2023, NCSR “Demokritos” (Z. Georgoussi)

Member of the organizing Committee of the 3d hybrid Conference of the Ethical Committee of NCSR “Demokritos” “Contemporary Ethics and Law Issues in Biological Sciences and Medicine”, 29 November 2023 (Z. Georgoussi)

Co-organizer (with Z. Georgoussi), 8th Conference of the European Research Network on Signal Transduction (ERNEST8, COST No. CA18133) “GPCR structure and function: The present and perspectives for the future,” Orthodox Academy of Crete, Kolymbari, Chania, Crete, Greece, May 3-7, 2023 (K. Iatrou)

Member of the Scientific Committee and co-organizer of the scientific session on “Ecology and Behavior,” XII European Congress of Entomology (ECE2023), Heraklion, Crete, Greece, October 16-20, 2023 (K. Iatrou)

Reviewer of funding and evaluation applications
Reviewer of research proposals for the AAIC (Alzheimer’s Association International) and France Alzheimer (I. Sotiropoulos)

Cyprus Research Promotion Foundation (RPF) (Z. Georgoussi)

Operational Programme Competitiveness, Entrepreneurship and Innovation (EPAnEK) (Z. Georgoussi)

Hellenic General Secretary for Research and Technology (GSRT) (Z. Georgoussi)

State Scholarship Foundation (IKY) (Z. Georgoussi)

Reviewer in scientific Journals
EMBO Journal, Molecular Psychiatry, Aging Cell, Journal of Alzheimer’s Disease, Molecular Neurodegeneration, Neurobiology of Aging, Frontiers in Neuroscience, Neurobiology of Disease, European Neuropsychopharmacology, Neuropharmacology, European Journal of Neuroscience (I. Sotiropoulos)

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

Insect Biochemistry and Molecular Biology, Archives of Insect Biochemistry & Physiology, Insect Science, Insects, Computational and Structural Biotechnology Journal, The Open Biotechnology Journal, Entomologia Generalis, Pesticide Biochemistry and Physiology, and Pest Management Science (K. Iatrou)

Scientific achievements and prizes

Christos Karoussiotis defensed his doctoral thesis entitled "Novel mechanisms regulating κ-opioid receptor signaling" with Honors in the National Kapodistrian University of Athens, Department of Biology (January 2023).

Christos Karoussiotis and Alexandra Symeonof were funded by the EU to participate and present their work in the COST-Action meeting ERNEST8 (Kolymbari, Crete).

Alexandra Symeonof was co-financed by Greece and the European Union (European Social Fund-ESF) through the Operational Programme "Human Resources Development, Education and Lifelong Learning" in the context of the Act "Enhancing Human Resources Research Potential by undertaking a Doctoral Research" Sub-action.

Alexandra Symeonof was financed by IKY Scholarship Programme for PhD candidates in the Greek Universities for the implementation of her doctoral thesis.

Anastasia Megalokonomou received the Best Poster Award for her work entitled "A novel RNA-targeted therapeutic approach against Tau-driven neuronal pathology in Alzheimer's disease brain pathology" - 10th Young Scientists Day of National Conference of Hellenic Society of Biochemistry and Molecular Biology (HSBMB), Eugenides Foundation, Athens, Greece (November 2023).

Teaching and other educational activities

inside IBA:

Organization and teaching of a series of theoretical and practical courses (training protocol) at the breeding facility of the Institute of Biosciences and Applications (IBA) (I. Sotiropoulos)

outside IBA:

I. Sotiropoulos

Teaching in the master's program *"The Science of Stress and Health Promotion"* (14 hours, 16 students), Medical School, National and Kapodistrian University of Athens (NKUA).

Teaching in the master's program *"Applications of Biology in Medicine"* (4 hours, 20 students), Medical School, NKUA.

Teaching in the master's program *"Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products"* (joint program of IBA & Department of Chemistry, University of Patras) (2 hours, 16 students).

Teaching in various master's programs (2-3 hours per program, 20-25 students) at universities in Greece and abroad, including *Athens Neuroscience Master (NKUA), Crete Neuroscience Master (University of Crete), MSc in Neurodegenerative Diseases (Aristotle University of Thessaloniki), Brain Aging & Pathology Master Program (University of Coimbra, Portugal).*

Supervisor of PhD theses of Miss Anastasia Vamvaka Iakovou and Miss Anastasia Megalokonomou.

Supervisor and/or co-supervisor of master's theses of students Zeta Papadimitriou, Dimitra Gerontidi, Katerina Tsirtsaki, Nikolina Ntinou, Fotini Tzouanou, and Laurentia Grigoriadou (Departments of Medicine and Biology, NKUA, and Department of Medicine, Aristotle University of Thessaloniki).

Z. Georgoussi:

Member of the Administrative and Educational board of the "Athens International Master's Programme in Neurosciences".

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

Member of the evaluation committee for the MSc Students of the "Athens International Master's Programme in Neurosciences".

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

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

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

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

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

Teaching in the National Kapodistrian University of Athens (NKUA) Master Program "Athens International Master's Programme in Neurosciences" on "*Neurotransmitters, G protein coupled receptor signaling from the membrane to the nucleus*" (20 hours)

Teaching in the NKUA Master Program "Molecular basis of Human Diseases" on "*G Protein Coupled Receptors in Health, Disease and Drug Development*", Inter-departmental Master Program NKUA (4 hours)

Seminars in the Inter-constitutional and Inter-departmental Master Program in collaboration of the IBA of NCSR "D" and University of Patra's in "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Medicinal Products" on "*Cellular Signaling of Transmembrane Receptors- Molecular Pharmacology"* (6 hours)

Oral presentation of C. Karoussiotis entitled "The *κ-opioid receptor-induced autophagy is implicated in stress-driven synaptic alterations*" in the session 2, "*Progress and Challenges in GPCR signaling in health and disease*" on the 8th ERNEST meeting, Orthodox Academy of Crete, Greece, May 2023.

Other Activities in the Institute of Biosciences & Applications

Substitute Member of the Protocol Evaluation Committee (PEC) of the Animal Breeding Facility of the Institute of Biosciences & Applications at the National Centre for Scientific Research "Demokritos" (I. Sotiropoulos)

Member of the Research Infrastructure OPENSREEN-GR "An Open–Access Research Infrastructure for Target–Based Screening Technologies for Human and Animal Health, Agriculture, and the Environment" funded by the General Secretariat for Research and Technology (Action for Enhancing Research and Innovation Infrastructures, Operational Program "Competitiveness, Entrepreneurship, and Innovation" NSRF 2014-2020) (Z. Georgoussi)

Responsible for the operation of Beckman Coulter OPTIMA-MAX & L8-8OM ultracentrifuges and the Speed Vac (Z. Georgoussi)

Total Impact Factor for original publications in 2023

I. Sotiropoulos: 8.2 (for 1 publication)
Z. Georgoussi: 7.3 (for 1 publication)

Citations for 2023 (without self-citations)
I. Sotiropoulos: 244
Z. Georgoussi: 52
K. Iatrou: 153

Citations for 2019-2023 (without self-citations)
I. Sotiropoulos: 1394
Z. Georgoussi: 226
K. Iatrou: 1212

h-index
I. Sotiropoulos: 25 (Scopus), 27 (Google Scholar)
Z. Georgoussi: 20 (Scopus), 23 (Google Scholar)
K. Iatrou: 39 (Scopus), 48 (Google Scholar)

Current External Funding
Research Personnel Funding Program – ELIDEK 2023 (Coordinator: I. Sotiropoulos)
Program Duration:11/2023-10/2025
Funding: €209,000
Laboratory Funding for 2023: €0

Programme NIH R1 Grant Subcontract Program (USA) (Coordinator: I. Sotiropoulos)
Program Duration: 09/2023-08/2025
Funding: €260,000
Laboratory Funding for 2023: €0

Programme *"Brain Precision - Neurodegenerative Diseases Network"* Program (Coordinator: I. Sotiropoulos)
Program Duration: 06/2023-05/2026
Funding: €80,000
Laboratory Funding for 2023: €0

Programme EU–COST Action CA18133 entitled *European Research Network on Signal Transduction (ERNEST)* funded by the EU–COST Action, with Dr. Z. Georgoussi as Member and National Representative of the Management Committee.
Duration: 04/2019- 03/2023
Total Funding :164000 €
Funding for 2023: 5500

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

Programme *"Co-actions Science and Innovation in Hellenic Republic Region of Attica (ESPA 2014-2020), code ATTP4-0339288, code of action MIS 5185062 and title "Food supplements with anxiolytic and antidepressive effect from Greek medicinal plants"* Program Duration: 04/08/2022-08/2024 (Coordinator: Z. Georgoussi).
Total Funding: €400,000
Laboratory Funding for 2023: €62,000

Programme *"OPIAUTO-NEUD" Program - "Opioid-induced autophagy, neuronal plasticity, and stress-related behavioral disorders"* funded from the Hellenic Foundation of Research and Innovation (HFRI) (Coordinator: Z. Georgoussi).
Program Duration: 2024-2025
Total Funding: €388,010
Total Funding for the Entire Program: €219,940
Laboratory Funding for 2023: €0

Identification of New Insect Olfactory and Taste Enhancers of Natural or Synthetic Origin Program funded by Inscent, Inc., USA (Scientific Supervisor: K. Iatrou).
Program Duration: 2017-2023
Total Funding for the Entire Program: €40,000
Laboratory Funding for 2023: €0

Programme *3D-ORco Program: The Structure of ORco, the Odorant Receptor Co-receptor of Mosquitoes* funded by the Hellenic Foundation for Research and Innovation (ELIDEK) (Scientific Supervisor: S. Zografos-EIE, Participant from NCSR "Demokritos": K. Iatrou).
Program Duration: 2020-2023
Total Funding for the Entire Program: €180,000
Laboratory Funding from the Program: €90,000 (from EIE)
Laboratory Funding for 2023: €20,000 (from EIE)

Programme *Organization of the 8th and Final ERNEST (European Research Network on Signal Transduction) Meeting funded by COST Action, European Commission*, and Private Donations (Scientific Supervisor: K. Iatrou, Participant: Z. Georgoussi).
Program Duration: 2023
Total Funding for the Entire Program: €17,000 (€10,000 COST + €7,000 Donations)
Laboratory Funding for 2023: €17,000

Research Group: Nuclear Proteins and Chromatin Function

Research Staff
Thomae Sourlingas, Senior Researcher
Irini Katsirma, Undergratuate Student
Margarita Karakike, Undergratuate Student
Kalliope Sekeri, Research Collaborator, Retired Research Director

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).

2023 Findings
Histone deacetylase inhibitors (HDACIs) are used as tools for the investigation of epigenetic regulation of chromatin and they can be used alone, or in combination with other anticancer agents, in therapeutic regimens. For these reasons, we studied three histone H3 epigenetic modifications (acetylation, trimethylation and dimethylation) and three histone H1 subtypes (H1.0, H1.3 and H1.5) in the absence and presence of the HDACI, sodium butyrate, in three leukemic cell lines (K562, NB4, Molt4) as compared to normal lymphocytes. Important findings were that in the presence of sodium butyrate we have increased levels of histone H3 acetylation and trimethylation but no changes in the levels of H3 dimethylation, which is associated with closed, inactive chromatin. 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 (as is histone H3 dimethylation which was also found to remain unaffected in the presence of this drug). 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.

Publications

Xydous, M., Chrysanthou-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., Sourlingas, T. G. (2023). Alterations in the levels of an H1 DNA linker histone subtype in peripheral blood leukocytes from schizophrenia patients are linked with this disorder. J. of Biol. Res. (Greece). 30 (1).

Educational Activities

Inside IBA:

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

Outside IBA:

"Cell Cycle: Checkpoints and Consequences for Normal Cellular Function when Cell Cycle Progression Dysfunctions" within the framework of the course "Ageing and Age-Related Diseases" of the Graduate Masters' Program: Applications of Biology in Medicine, Dept. of Biology and Medical School of the University of Athens (3 hours, 19 students).

Other activities in the Institute of Biosciences and Applications

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

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

Other scientific activities

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

Scientific collaborations:

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

Total Impact Factor for publications in 2023: 2.0 (for 1 publication)

Citations 2023 (without self-citations): 20

Total citations 2019-2023 (without self-citations): 106

h-index: 11 (Scopus), 15 (Google scholar)

Research Group: Molecular Carcinogenesis and Rare Disease Genetics

Research Staff

Gerassimos Voutsinas, Research Director
Konstantina Panagopoulou, Undergraduate student
Angelos Charisis, 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

2023 Findings

Mitochondrial p38 Mitogen-Activated Protein Kinase: Insights into Its Regulation of and Role in LONP1-Deficient Nematodes: p38 Mitogen-Activated Protein Kinase (MAPK) cascades are central regulators of numerous physiological cellular processes, including stress response signaling. In C. elegans, mitochondrial dysfunction activates a PMK-3/p38 MAPK signaling pathway (MAPKmt), but its functional role remains elusive. Here, we demonstrate the induction of MAPKmt in worms deficient in the lonp-1 gene, which encodes the worm ortholog of mammalian mitochondrial LonP1. This induction is subjected to negative regulation by the ATFS-1 transcription factor through the CREB-binding protein (CBP) ortholog CBP-3, indicating an interplay between both activated MAPKmt and mitochondrial Unfolded Protein Response (UPRmt) surveillance pathways. Our results also reveal a genetic interaction in lonp-1 mutants between PMK-3 kinase and the ZIP-2 transcription factor. ZIP-2 has an established role in innate immunity but can also modulate the lifespan by maintaining mitochondrial homeostasis during ageing. We show that in lonp-1 animals, ZIP-2 is activated in a PMK-3-dependent manner but does not confer increased survival to pathogenic bacteria. However, deletion of zip-2 or pmk-3 shortens the lifespan of lonp-1 mutants, suggesting a possible crosstalk under conditions of mitochondrial perturbation that influences the ageing process. Furthermore, loss of pmk-3 specifically diminished the extreme heat tolerance of lonp-1 worms, highlighting the crucial role of PMK-3 in the heat shock response upon mitochondrial LONP-1 inactivation.

Microtubule Dynamics Deregulation Induces Apoptosis in Human Urothelial Bladder Cancer Cells via a p53-Independent Pathway: Bladder cancer (BLCA) is the sixth most common type of cancer and has a dismal prognosis if diagnosed late. To identify treatment options for BLCA, we systematically evaluated data from the Broad Institute DepMap project. We found that urothelial BLCA cell lines are among the most sensitive to microtubule assembly inhibition by paclitaxel treatment. Strikingly, we revealed that the top dependencies in BLCA cell lines include genes encoding proteins involved in microtubule assembly. This highlights the importance of microtubule network dynamics as a major vulnerability in human BLCA. In cancers such as ovarian and breast, where paclitaxel is the gold standard of care, resistance to paclitaxel treatment has been linked to p53-inactivating mutations. To study the response of BLCA to microtubule assembly inhibition and its mechanistic link with the mutational status of the p53 protein, we treated a collection of BLCA cell lines with a dose range of paclitaxel and performed a detailed characterization of the response. We discovered that BLCA cell lines are significantly sensitive to low concentrations of paclitaxel, independently of their p53 status. Paclitaxel induced a G2/M cell cycle arrest and growth inhibition, followed by robust activation of apoptosis. Most importantly, we revealed that paclitaxel triggered a robust DNA-damage response and apoptosis program without activating the p53 pathway. Integration of transcriptomics, epigenetic, and dependency data demonstrated that the response of BLCA to paclitaxel is independent of p53 mutational

signatures but strongly depends on the expression of DNA repair genes. Our work highlights urothelial BLCA as an exceptional candidate for paclitaxel treatment. It paves the way for the rational use of a combination of paclitaxel and DNA repair inhibitors as an effective, novel therapeutic strategy.

Publications

Taouktsi E., E. Kyriakou, E. Voulgaraki, D. Verganelakis, S. Krokou, S. Rigas, G.E. Voutsinas, P. Syntichaki (2023) Mitochondrial p38 Mitogen-Activated Protein Kinase: Insights into Its Regulation of and Role in LONP1-Deficient Nematodes, Int J Mol Sci 24:17209. (IF: 5.6)

Drosos Y., E.G. Konstantakou, A.-S. Bassogianni, K.-S. Nikolakopoulos, D.G. Koumoundourou, S.P. Markaki, O.E. Tsitsilonis, G.E. Voutsinas, D. Valakos, E. Anastasiadou, D. Thanos, A.D. Velentzas and D.J. Stravopodis (2023) Microtubule Dynamics Deregulation Induces Apoptosis in Human Urothelial Bladder Cancer Cells via a p53-Independent Pathway, Cancers 15:3730. (IF: 5.2)

International conferences

Y. Drosos, E.G. Konstantakou, A.-S. Bassogianni, A.D. Velentzas, K.-S. Nikolakopoulos, O.E. Tsitsilonis, G.E. Voutsinas, E. Anastasiadou, D. Thanos, D.J. Stravopodis (2023). Microtubule Dynamics Deregulation Induces Apoptosis and Autophagy in Human Urothelial Bladder Cancer Cells via a p53-independent Pathway. The 3rd International Electronic Conference on Cancers: New Targets for Cancer Therapies (IECC 2023), 16–30 Mar 2023, Presentation number: sciforum-071194.

Other Scientific Activities

Reviewer of 1 research article for Histology and Histopathology.

Educational Activities

Inside IBA:

Lecture entitled "Molecular mechanisms of carcinogenesis and pharmacological inhibition of selected cellular targets for therapy", Common Post-Graduate Program "Applied Biochemistry" of the Dept of Chemistry, University of Patras, and the Institute of BioSciences and Applications, NCSR "Demokritos", April 18, 2022 (number of attendants: 12 students, teaching hours: 2).

Theoretical and laboratory training of high-school students on Molecular Diagnosis in Tuberous Sclerosis Complex patients, Summer Camp in Biology, IBA, NCSR “Demokritos”, Monday 26 June – Friday 7 July 2023 (number of attendants: 8, teaching days: 10).

Outside IBA:

Teaching of the undergraduate course: “Introduction to Molecular Biology” (3 semesters), American College of Greece (Deree College), Agia Paraskevi Attikis, January - December 2023 (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 18, 2023, Athens (number of attendants: 40 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 5, 2023, Athens (number of attendants: 20 students, teaching hours: 3).

Lecture entitled “Rare Diseases”, Post-Graduate Program "Applications of Biology in Medicine", Departments of Biology and Medicine, National and Kapodistrian University of Athens, June 13, 2023, Athens (number of attendants: 20 students, teaching hours: 3).

Two lectures entitled "Signaling pathways involved in cell immortalization - Wnt, Hippo, p53" and "Signaling pathways evading tumor suppressor messages pRB, p53, APC, BRCA1-2, PTEN, WT1-WT2, NF1-NF2", Post-Graduate Program "Neoplastic Disease in Man", Department of Medicine, National and Kapodistrian University of Athens, November 10, 2023, Athens (number of students: 27, teaching hours: 2).

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

In charge of 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".

Deputy Director of IBA (January 1, 2023 – December 31, 2023).

Member of the Research Council of the Institute (ESI) (January 1, 2023 – December 31, 2023).

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

Member of the Evaluation Committee for the promotion of an IBA Researcher to A-level Researcher, IBA, NCSR "Demokritos" (July 27, 2023).

Member of 3 Evaluation Committees for recruitment of scientific collaborators at NCSR "Demokritos" [Projects E-11499 (March 16, 2023), E-12609 (September 6, 2023), E-12578 (December 11, 2023)].

Member of an ad-hoc Committee for Research Exploitation of PLANTEX technology (June 30, 2023 – October 16, 2023).

Committee member for Receipt of Consumables for the project E12499 (November 9, 2023).

Total Impact Factor for original publications in 2023: 10.800 (for 2 publications)

Number of citations for 2023 (without self-citations): 97

Number of citations 2019-2023 (without self-citations): 466

h-index: 23

PROGRAMME B

"MODEL SYSTEMS FOR THE STUDY OF CELL FUNCTION"

Research Group: Chemical Ecology and Natural Products

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

Research Interests
Chemical ecology focuses on the isolation and identification of biologically active compounds involved in insect chemical communication and plant–insect interactions, such as pheromones and plant-derived volatile compounds. These compounds have potential applications in integrated pest management programs.

Isolation and identification of secondary metabolites, primarily of plant origin, that influence insect physiology and/or behavior (behavior-modifying agents, infochemicals). Laboratory and field evaluations are conducted to assess the bioactivity of the isolated metabolites, alongside studies on their mode of action. Additionally, chemical synthesis of semiochemicals (infochemicals) is carried out.

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.

2023 Findings
Within the framework of the PHERA (Pheromones for Row crop Applications) HORIZON 2020 program (Figure 1), the following were completed: i) Certification of Biopheromone Homology: The biopheromones produced were certified to be homologous to their chemically synthesized counterparts. This confirms the consistency and accuracy of the biopheromone production process. Ii) Behavioral Bioassays: Behavioral assays were performed on male insects, utilizing a wind tunnel and a camera tracking system to monitor and assess their responses. This was a key step in determining the effectiveness of the biopheromones in affecting insect behavior. Iii) Field Activity Testing: Field experiments conducted across various regions of Greece demonstrated that the biopheromones exhibited the same activity as the chemically synthesized versions. These tests involved monitoring insect populations and applying the Mating Disruption method, where a biopolymer encapsulating the sex pheromone was distributed using UAVs (Unmanned Aerial Vehicle), and also using, new, biodegradable dispensers.

Research continued on developing advanced systems for the release of semiochemicals, focusing on encapsulating them in biodegradable, non-toxic polymers that provide increased protection

against ultraviolet radiation. A significant biological control experiment was conducted in olive groves to manage populations of Bactrocera oleae, a major pest in olive cultivation.

Figure 1

The identification of infochemicals and other naturally occurring bioactive metabolites (referred to as Biological Control Agents, BCAs) have been key areas as they are being investigated for their potential use as "smart" insecticides, offering a more sustainable and environmentally friendly alternative to traditional chemical pesticides and helping to promote sustainable crop management practices. In this respect the effect of secondary metabolites of plants and microorganisms was studied. In particular secondary metabolites of one train of the fungus Mucor hiemalis (SMU-21), was examined on the viability of insect larvae that attack crops of great economic importance such as *Lobesia botrana* (the grapevine moth, a pest of grapevines), *Halyomorpha halys* and *Plutella xylostella* (*Flagship Action*). By exploring the properties and potential applications of these naturally occurring metabolites, the program contributes to the development of novel, eco-friendly solutions for pest control, with the goal of reducing reliance on harmful chemical pesticides and promoting biodiversity in agricultural ecosystems.

Within the framework of the FEAST project, challenges and opportunities at the local community level related to the transformation of practices and habits towards healthy and sustainable dietary behavior are being studied. Additionally, Living Labs were created, and priorities for local dietary behavior were mapped.

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

Within the framework of the Opti new - AromaQ project under the Excellence Hubs (Bridge Programmes) initiative, Dr. Antonis Chrysargyris (Cyprus University of Technology) visited the Laboratory of Chemical Ecology and Natural Products for two weeks. Joint experiments were conducted to test the activity of essential oils from aromatic and medicinal plants of Cyprus on

Lobesia botrana. Additionally, efforts continued to identify the properties of medicinal and aromatic plants and improve the quality, nutritional value, and storage capacity of fresh and dried products to support the competitiveness of SMEs.

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

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

Publications

Koutsoumpeli, E., Manassakis, G., Betsi, P.Ch. Raptopoulos, D. Konstantopoulou, M. 2023. Sex pheromone autodetection by *Lobesia botrana* females (Lepidoptera: Tortricidae). Crop Protection (accepted for publication). (IF=2.5).

International conferences

Raptopoulos D, Betsi PC and Konstantopoulou M. 2023. Biologically produced pheromones control *Helicoverpa armigera* and *Plutella xylostella*. XII European Congress of Entomology 16-20 October, Crete, Greece. Abstract: 602-603.

Other Scientific Activities

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

President of the Union of Greek Researcher

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

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

Topic Editor του Open Access Journal Insects

Review Editor for Chemical Ecology in Frontiers in Ecology and Evolution

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

Educational Activities

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

Participation in the Program of Postgraduate Studies: “Modern Trends in Agricultural Pharmacology” of the Agricultural University of Athens.

Invited Speaker in Erasmeios Ellinogermaniki Sxoli in the context of Professional Orientation: "Education and the professional future in the face of the challenges of the 21st century: Artificial Intelligence, Climate Change, Inequalities ", 19/2/2023.

Other activities in IBA

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

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

Researcher and Specialist Functional Scientist representative in NCSR "Demokritos" Board of Directors (till June 2023).

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

Total Impact Factor for original publications in 2023: 2. 5 (for 1 publication)

Citations for 2023 (without self-citations): 114

Total citations 2019-2023 (without self-citations): 523

h-index: 20 (Scopus), 22 (Google Scholar)

Current External Funding

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 2023: 20.000 €

Project entitled *Food systems that support transitions to hEalthy And Sustainable dieTs* (Horizon Europe) funded by EU, and Scientific responsible Dr. M. Konstantopoulou.
Duration: 01/07/2022-30/06/2027
Total program funding: 74.312,50 €
Laboratory Funding for 2023: 26.009,38 €

Project entitled *Regions4Climate* (Horizon Europe) funded by EU, and Scientific responsible Dr. A. Sfetsos (INRASTES).
Duration: 01/01/2023-31/12/2027
Total program funding: 605.500 €
Laboratory Funding for 2023: included in the budget of the SR.

Project entitled *Flagship Action: Innovative solutions for the sustainable and environmentally friendly plant protection of Greek fruit and vegetables, in the future of the Europe*, with EU funding - NextGenerationEU within the framework of the National Recovery and Resilience Plan Greece 2.0 and Scientific responsible Prof. J. Vontas (AUA).
Duration: 01/05/2023-31/10/2025
Total program funding: 70.000 €
Laboratory Funding for 2023: 35.000 €

Project entitled *Opti new -AromaQ Identification of Medicinal/Aromatic Plants properties and improving quality, nutritive value and storability of fresh and dry products to support SME competitiveness*, funded from The Research and Innovation Foundation Programmes for Research, Technological Development and Innovation, CYPRUS and Scientific responsible Dr. M. Konstantopoulou.
Duration: 01/04/2022-31/08/2024
Total program funding: 8.000 €
Laboratory Funding for 2023: 6.400 €

Project entitled *Nutritional supplements with anti-anxiety and anti-depressant properties from Greek pharmaceutical plants*, funded from Region of Attica, "Synergies Research and Innovation in Region of Attica" (ESPA 2014-2020) and Scientific responsible Dr Z. Georgoussi.

Duration: 04/08/2022-08/08/2024
Total program funding: 155.000 €
Laboratory Funding for 2023: included in the budget of the SR.

Research Group: Chronobiology

Research Staff
Anastasia Prombona, Senior Researcher
Danae Farmakis, PhD student
Angeliki Galeou, Postdoctoral Research Collaborator
Stavroula Mamoucha, Postdoctoral Research Collaborator

Research Interests
The research projects of our laboratory explore the 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 on the plant circadian clock focus on gene expression analysis and regulation of *P. vulgaris* clock and clock-controlled genes under physiological conditions and during infection of the plant with pathogenic bacteria (*Pseudomonas syringae* pathovar *phaseolicola*). We also explore the phytoprotection/prevention of infection by the use of bioactive compounds.

Interaction of the mammalian circadian clock with pathological conditions
We are interested in elucidating the molecular mechanisms involved in the interaction of the circadian clock and the cell cycle in cancer. The role of the transcription factor/oncoprotein c-MYC in the regulation of circadian clock genes and the effect of pharmacological treatment of cancer cell lines on cell cycle progression, apoptosis and autophagy are investigated. We also explore the regulation of gene expression by histone modifications at circadian promoters.

2023 Findings
Fighting plant and human bacterial infections by the use of plant extracts
The environmental impact of chemical products is growing in recent years steadily. In addition, chemical agents are used for fighting bacterial infections, despite the fact that bacteria can become resistant. Natural products, such as extracts from aromatic and medicinal plants, can establish new environmentally friendly fighting methods. Thus, we decided to examine the antimicrobial/biocidal effect of the essential oil (EO) from the leaves of the plant *Laurus nobilis* L. (laurel), against two strains of the bean (*Phaseolus vulgaris*) bacterial pathogen *Pseudomonas syringae* pv. phaseolicola and several human bacterial pathogens. Methods including the Well diffusion assay and the Disc diffusion assay were implemented. Our results showed that the EO of laurel is an effective bacteriostatic and biocidal agent. We report for the first time that the EO of laurel inhibits the growth of the phytopathogen *P. syringae* pv. phaseolicola, a finding that opens the way for further studies in the direction of phytoprotection. Moreover, the human pathogens *Micrococcus luteus, Escherichia coli, Staphylococcus aureus* and *Bacillus subtilis* were, differentially in each case, also growth-inhibited. This work was implemented by Dr. A. Galeou and Dr. S. Mamoucha.

Interaction of the circadian clock with pathological conditions
In this project a modulator of the circadian clock function is implemented with the aim to explore the potential of new clock-interacting agents as chemotherapeutic compounds in cancer cells. Towards this, we investigated in three pancreatic ductal adenocarcinoma (PDAC) cell lines, e.g. PANC-1, AsPC-1 and BxPC-3, the cytopathic effects of the compound TH301, which stabilizes the clock protein cryptochrome 2 (CRY2), whose levels are disturbed in cancer cells. Our results revealed that in the concentration of 40 μM (IC_{50}) TH301 induced an important cell growth inhibition. Flow Cytometry (FACS) analysis showed an arrest of cells at the G1-phase, which was accompanied by a corresponding decrease in the proportion of cells at the S-phase of the cell cycle. More importantly, the validation of the expression levels of proteins that critically control

cell cycle progression, elucidated a very important increase of the CDK inhibitor $p21^{CIP1/WAF1}$ (p21 protein), as well as of other cell cycle inhibitors, with simultaneous decrease of several cell-cycle activators (Figure 1). Ongoing experiments examine the apoptotic and autophagic effects of TH301 in these three cancer cell lines. This work is part of the PhD research work of D. Farmakis.

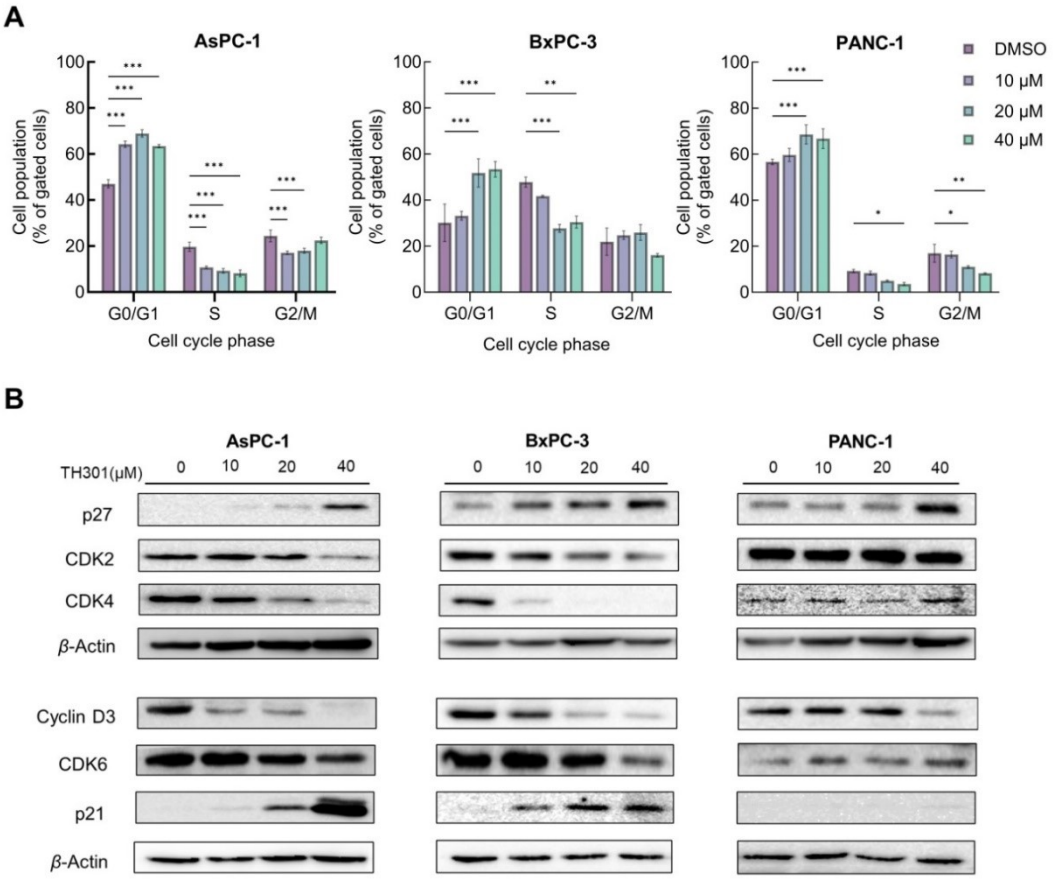


Figure 1: *TH301 causes cell cycle arrest at the G1-phase and important expression alterations of cell cycle control proteins.* ***A****. FACS analysis of PI-stained PDAC cells, treated for 24 h with increasing concentrations of TH301 (0, 10, 20 and 40 μM). Data are presented as Mean ± SD values (N = 3). Statistical significance in between control (0.1% DMSO) and TH301-treated cells (% of control) was defined with One-way ANOVA and comparisons at significance levels of 0.05 and below are delineated by asterisks (*: < 0.05; **: < 0.01; ***: < 0.001).* ***B****. Expression of main G1-phase-specific cell cycle regulators (Cyclin D3, CDK6, CDK4, CDK2, p21 and p27) of PDAC cells treated with TH301 (0, 10, 20 and 40 μM) for 24 h, as determined by Western blotting. β-Actin was used as the loading control (reference protein).*

Publications

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

Xydous, M., Chrysanthou-Piterou, M., Panagiotopoulou, C., Kloukina-Pantazidou, I., Havaki, S., Dedemadi, A.G., Kontaxakis, V.P., Kollias, C., Angelopoulos, E., Sekeri-Pataryas, K.E., Prombona, A., Sourlingas, T.G. (2023) Alterations in the levels of an H1 DNA linker histone subtype in peripheral blood leukocytes from schizophrenia patients are linked with this disorder. Journal of Biological Research (Greece) 30,1 (IF: 2.576)

Mamoucha, S., Prombona, A., Galeou, A. (2023) Evaluation of the antibacterial activity of essential oil of Laurus nobilis against *Pseudomonas syringae* pv. phaseolicola and potential biocidal action. Hellenic Plant Protection Journal 16(1), pp. 29-39 (IF: 1.4)

Tonis, E., Frousiou, E., Heliopoulos, N.S., Kagkoura, A., Stangel, C., Siamidis, D., Galeou, A., Prombona, A., Stamatakis, K., Boukos, N., Tagmatarchis, N., Vougioukalakis, G.C. (2023) VAR Fabric Modification: Inducing Antibacterial Properties, Altering Wettability/Water Repellence, and Understanding Reactivity at the Molecular Level. ACS Omega 8(47), pp. 44708-44716 (IF: 4.1)

Tonis, E., Frousiou, E., Heliopoulos, N.S., Kagkoura, A., Stangel, C., Canton-Vitoria R., Vasilakos, S., Siamidis, D., Galeou, A., Stamatakis K., Prombona, A., Boukos N., Tagmatarchis, N., Vougioukalakis G.C. (2023) Kevlar® and Nomex® modification via 2,4-dihydroxybenzophenone anchoring improves water repellency and induces antibacterial and UV protection properties. Materials Today Chemistry 33, 101695 (IF: 7.613)

Frousiou, E., Tonis, E., Rotas, G., Pantelia, A., Chalkidis, S.G., Heliopoulos, N. S., Kagkoura A., Siamidis, D., Galeou, A., Prombona, A., Stamatakis, K., Boukos, N., Vougioukalakis, G.C. (2023) Kevlar®, Nomex®, and VAR Modification by Small Organic Molecules Anchoring: Transfusing Antibacterial Properties and Improving Water Repellency. Molecules 28(14), 5465 (IF: 4.927)

National conferences

Mamoucha, S., Liapis, V., Prombona, A. (2023) Propolis as an antibacterial agent - Biotechnological Applications, 49th Annual Panhellenic Medical Conference, Hotel Divani Caravel, Athens, 11-13 May, oral presentation

Total Impact Factor for original publications for 2023: 23.35 (for 6 publications)

Citations for the year 2023 (without self citations): 26

Citations for the years 2019-2023 (without self citations): 148

h-index: 10 (Scopus and Google scholar)

Research Group: Microbial Molecular Genetics

Research Staff
Vicky Sophianopoulou, Research Director
Christos Gournas, Researcher
Amalia Megarioti, Postgraduate Fellow (*PhD obtained in 2023*)
Spiros Gerostathis, Postgraduate (*MSc obtained in 2023*)
Alexandra Siaka (Practical undergraduate)
Elisabeth Pedi (Practical undergraduate)

Research interests
Our group's fundamental research focuses on:

1. Function, regulation and organization of the fungal plasma membrane (PM). The plasma membrane, as the boundary between the cell and its environment, is a platform for numerous physiological processes. A major effort is to understand how the PM coordinates these diverse processes and the mechanisms that underlay them. Our studies aimed at identifying and/or characterizing the molecular mechanisms by which eisosomes, which are specific compartments of the fungal plasma membrane, regulate the homeostasis of the plasma membrane and the persistence of quiescent fungal cells, as well as how these processes are related to long-term survival and fungal pathogenicity (I. Vangelatos et al., 2010; C. Scazzocchio et al., 2011; A. Athanasopoulos et al., 2013, A. Athanasopoulos et al., 2015; Gournas et al, 2018; Athanasopoulos et al., 2019; Megarioti et al., 2023). In this context, we are currently investigating dicoumarol derivatives as novel antifungal leads (Peroulias, Pitsinos et al., 2024; unpublished results).

2. Nanoparticles as antifungal agents against quiescent fungal cells. Current research on novel antifungals is mainly focused on developing agents operating through a broad range of mechanisms, in an attempt to overcome the rapid development of fungal resistance to existing antifungal drugs, which operate via a narrow range of mechanisms targeting mainly growing cells. This includes the exploration of small molecules and polymeric compounds of either synthetic or natural origin. A subclass of such molecules is the so-called metallopolymers, macromolecules containing metals at different sites of their dendritic architecture, and another sub-class is the functionalized hyperbranched polyethyleneimine derivatives (PEIs). Our studies aimed at investigating the characteristics, the potential antifungal properties and the mechanisms underlying the function of both aforementioned sub-classes of macromolecules, against quiescent fungal cells, using the opportunistic pathogen *Aspergillus nidulans* as a model microorganism (Gerostathis et al., 2024).

Medium and long-term objectives: identification of new pharmaceutical targets and future development of highly-targeted quiescent cells' antifungals with enhanced safety profiles on humans.

3. Detoxification of toxic amino acid analogues. L-Azetidine-2-Carboxylic Acid (AZC) is a proline toxic analogue produced by certain plants to protect them from multitude predators, including various bacteria, fungi and mammals, since it is toxic for them. Our studies aimed at identifying and/or characterizing the molecular mechanisms underlying detoxification of toxic amino acid analogues from different microorganisms, including pathogenic fungi, using the opportunistic pathogenic fungus *Aspergillus nidulans* as a model system.

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

4. Regulation and structure/function analysis of amino acid transporters. Transporters are essential in nutrient and drug uptake, and involved in nutrition, signaling, neurotransmission &

cell communication. Transporter malfunction is linked with >50 human genetic diseases as well as with phenomena of drug or antibiotic resistance (Moore et al., 2023 and references therein) Understanding transporter function, specificity determination and trafficking to the plasma membrane is essential to understand transporter physiology.

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

2023 Findings

1. Eisosomes are induced in number and size in quiescent yeast cells, as has been shown for quiescent conidiospores of *A. nidulans* (Vangelatos et al., 2010, DOI: 10.1128/EC.00087-10), thus promoting their long-term viability. The protective role of eisosomes is related to the stabilization of the eisosome-hosted enzymes FLPs (Flavodoxin-like proteins) possessing ubiquinone oxidoreductase activity. In the absence of eisosomes or FLPs, quiescent yeast cells accumulate peroxidized phospholipids. Genetic data support that FLPs are essential for protecting quiescent cells from lipid peroxidation, while acting in parallel with glutathione peroxidases (GPXs). Strains that do not express FLPs and GPXs are driven to death by ferroptosis (*Megarioti et al., 2023*). Recent data in mammals show that the quinone reductase FSP1 prevents lipid peroxidation and ferroptosis (Doll et al., 2019). *In silico* approaches identified 2 orthologs of human FSP1 in *A. nidulans*, the FspA & B proteins, which are being studied for their biological role.

2. The antifungal properties of hyperbranched polymeric nanoparticles of polyethyleneimine (PEI) and two of their derivatives (QPEI, GPEI) were studied in *A. nidulans.* The results show that the aforementioned nanoparticles are initially localized in the plasma membrane and later accumulate within the interior of quiescent conidia and their derived germlings (hyphae). Low-toxicity nanoparticle concentrations, in the micromolar range and near the defined minimum inhibitory concentration (MIC), are capable of inhibiting the germination of quiescent conidiospores and gradually stopping apical hyphal germination. The same concentrations are sufficient to compromise the integrity of the fungal plasma membrane, while not being toxic to the human cell lines tested. These results suggest that PEI and its derivatives QPEI and GPEI have antifungal properties and are fungicidal for quiescent *A. nidulans* conidiospores *(Gerostathis et al., 2024)*.

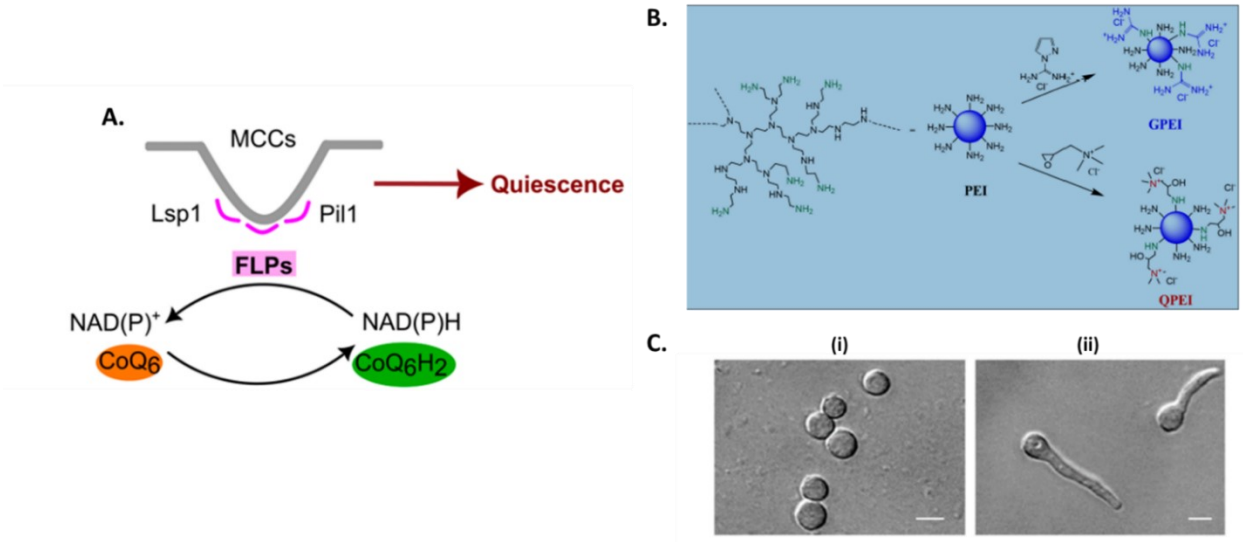


Figure: A. *Eisosomes host FLPs (Flavodoxin like proteins) which act as NAD(P)H ubiquinone oxidoreductases and protect quiescent cells from lipid peroxidation and ferroptosis. FLPs act in parallel with glutathione in yeast in ferroptosis protection.* ***B.*** *Schematic representation of the chemical structures and synthetic routes of polyethyleneimine (PEI), and its functionalized guanidinylated (GPEI), and quaternized polyethyleneimine (QPEI) derivatives.* ***C.*** *Growth inhibitory effects of polyethyleneimine (PEI) against quiescent fungal cells. Representative phase contrast microscopy images of Aspergillus nidulans conidia grown for 14 h (A) in the presence or (B) in the absence of 5 μg/mL PEI, at 25 °C. Scale bar: 5 μm.*

Publications

A.H. Megarioti, B. M. Esch, A. Athanasopoulos, D. Koulouris, M. Makridakis, V. Lygirou, M. Samiotaki, J. Zoidakis, V. Sophianopoulou, B. André, F. Fröhlich, Ch. Gournas (2023). Ferroptosis-protective membrane domains in quiescence. Cell Reports 42, 113561

Articles in Press

S. Gerostathis, A. Athanasopoulos, K. N. Panagiotaki, Z. Sideratou, D. Tsiourvas and V. Sophianopoulou (2024). *In vitro* subcellular localization and antifungal activity of functionalized hyperbranched polyethyleneimine derivatives against quiescent conidia and germlings of the opportunistic fungal pathogen Aspergillus nidulans. J. Biol. Regul. Homeost. Agents (JBRHA); 38(4): 2781–2794

Articles in Books and Conference Proceedings

Megarioti AH, Athanasopoulos A, Koulouris D, Esch BM, Makridakis M, Lygirou V, Samiotaki M, Zoidakis I, André B, Sophianopoulou V, Fröhlich F and Gournas C. Ferroptosis-protective membrane domains in Quiescence. EMBO Workshop Ferroptosis: when metabolism meets cell death.

International conferences

Megarioti AH, Athanasopoulos A, Koulouris D, Esch BM, Makridakis M, Lygirou V, Samiotaki M, Zoidakis I, André B, Sophianopoulou V, Fröhlich F and Gournas C. Ferroptosis-protective membrane domains in Quiescence. EMBO Workshop Ferroptosis: when metabolism meets cell death. 23-27 April 2023, Seeon, Germany

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)

Members of the Advisory Committee of the Biology Department, University of Athens, for the PhD thesis of A. Megarioti [V. Sophianopoulou, C. Gournas (supervisor)]. Completed with grade Excellent

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

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

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

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 (2018-2023) (V. Sophianopoulou)

Member of the Special Interdepartmental Committee of the Post-graduate Education Course (MSc) on "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" at the Department of Chemistry, University of Patras and Institute of Biosciences and Applications NCSR "D" (2018-2023) (V. Sophianopoulou)

Member of the Complaints and Objections Management Committee of the of the Post-graduate Education Course (MSc) on "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products" at the Department of Chemistry, University of Patras and Institute of Biosciences and Applications NCSR "D" (2023) (V. Sophianopoulou)

Regular member of the Electoral Body for the tenure of Assistant Professor in"Biology of pathogenic microorganisms and molecular transformation of cells in humans", University of West Attica, School of Health and Welfare Sciences (V. Sophianopoulou)

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

Deputy member of the Executive Body for the tenure of Assistant Professor in "Microbiology with emphasis on Biotechnology", School of Health Sciences, Department of Biochemistry & Biotechnology University of Thessaly (V. Sophianopoulou)

Deputy member of the Executive Body for the tenure of Associate Professor in "Microbiology, Molecular Microbe-Host Interactions", Biology Department, University of Crete (V. Sophianopoulou)

Deputy member of the Evaluation Committee for the tenure of Researcher A in IB-A (V. Sophianopoulou)

Invitation as a member of the Editorial Board of Methods and Protocols to participate with 2 more members as Quest Editor in a special issue on “Microbial Molecular Genetics” (V. Sophianopoulou).

Reviewing of manuscripts in scientific journals
Biomolecules (MDPI), Membranes (MDPI) (V. Sophianopoulou)

Handling the evaluation of 2 manuscripts submitted to Scientific Reports for publication, as Member of the Editorial Board (V. Sophianopoulou)

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)

Educational activities
Post-graduate Education Courses on:

Inside IBA
“Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products”, a Two - Years Graduate Course of the Interdisciplinary Department of Chemistry, University of Patras and the Institute of Biosciences & Applications, NCSR Demokritos (12 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).

Total Impact Factor for original publications for 2023: 7.5 (for 1 publication)

Citations for 2023 (without self-citations)
V. Sophianopoulou: 61

Total citations 2019-2023 (without self-citations)
V. Sophianopoulou: 411

h-index
V. Sophianopoulou: 19 (Scopus), 20 (ResearchGate)

Current external funding

Grant entitled “The organization of the fungal plasma membrane in the quiescent state”
Duration: 06/22-08/23
IKY PhD scholarship to A. Megarioti
Total funding: 15000 €
Funding for 2023: 8000 €

Project entitled “Rational Identification and Evaluation of Antifungals Targeting Quiescent Cells”, financed by the Hellenic Foundation for Research and Innovation (HFRI)
Principal Investigator (PI): V. Sophianopoulou
Research teams involved: Microbial Molecular Genetics Laboratory, Institute of Biosciences and Applications (IBA); Functional Nanomaterials of Organized Structure (FNOS) Laboratory, Institute of Nanoscience and Nanotechnology (INN); Natural Product Synthesis & Bioorganic Chemistry Laboratory Institute of Nanoscience and Nanotechnology (INN); Laboratory of Cell Proliferation and Ageing (LCPA), Institute of Biosciences and Applications (IBA)
Duration: 2024-2025
Total funding: 400.000 €
Funding of the lab for 2023: 0 €

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)

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.

2023 Findings
The surface modification of fabrics composed of Kevlar®, Nomex® or VAR has been extensively studied. Kevlar® and Nomex® are widely used aramid materials, while VAR is a technical fabric composed of 64% viscose, 24% para-aramid (Kevlar®), 10% polyamide and 2% antistatic fibers. Kevlar exhibits excellent mechanical properties, while cellulose is a natural linear polymer composed of repeating β-D-glucose units, with many applications in the materials industry. Here, we synthesized new, specially designed organic molecules that possess functional groups capable of anchoring to VAR fabrics and cellulose materials, thus altering their properties on demand. For this purpose, we used methyl-α-D-glucopyranose as a model compound, both for the optimization of the reaction conditions, before their application to the material and for the understanding and behavior of the material at the molecular level.

Both aramid and cellulose/viscose materials exhibit excellent mechanical properties that make them valuable in a wide range of applications. For the modification of Kevlar®, Nomex® and VAR studied here, we used small organic molecules 3-allyl-5,5-dimethylhydantoin (ADMH) and 3-(acrylamidopropyl)trimethylammonium chloride (APTAC), which were anchored to the materials under study through graft polymerization. In this way, excellent antibacterial properties were induced in the three studied fabrics. Their water repellency was also improved in most cases. Characterization studies were conducted to investigate the properties of the modified materials, using Raman and FTIR Spectroscopy, Scanning Electron Microscopy (SEM) and Thermogravimetric Analysis (TGA).

Aramid materials, such as Kevlar® and Nomex®, are aromatic polyamides exhibiting excellent chemical and mechanical properties. Because of their demanding applications, it is essential to enhance their water repellency, their endurance to UV radiation, as well as their antibacterial properties, while simultaneously preserving or even strengthening their durability. The present work describes the successful modification of aramid materials, in a way that improves the final product, by inducing the desired properties without significantly affecting the existing ones. The synthesis of a model compound simulating aramid materials is carried out followed by thorough studies, thus leading to a better understanding of the behavior of aramid materials at the molecular level, as well as to their optimal modification conditions. Subsequently, the attachment of 2,4-dihydroxybenzophenone to Kevlar® and Nomex® fabrics, using epichlorohydrin as the anchoring moiety, along with detailed characterization, via IR and Raman spectroscopies, thermogravimetric analysis, and SEM imaging, are implemented. The wettability of the modified materials is determined by the water contact angle test, to probe their hydrophilicity or hydrophobicity. The antibacterial protection of the modified aramid materials is determined qualitatively against the Gram-negative bacterium E. coli DH5α and quantitatively according to an in-situ method, using cyanobacterium *Synechococcus* sp. PCC7942. Moreover, the UV protection properties of the modified fabrics are studied by using the UV protection factor (UPF) and average UV-A and UV-B transmittance, while their ultimate strength is found well-preserved.

The multi-step modification process for the covalent transformation of Kevlar fabric and the incorporation of graphene oxide (GO) nanosheets was studied. Thermal and microscopic imaging techniques were used to step-by-step modify Kevlar and form the corresponding Kevlar-GO hybrid fabric.

The level of functionality of Kevlar can be controlled by its nitration time and the first reaction in the multiple organic transformation sequence, to obtain the hybrid fabric with GO content up to 30%. The most important result is that, the covalent transformation of Kevlar does not occur at the expense of the excellent mechanical properties of the fabric. Under optimal conditions, the Kevlar-GO hybrid fabric exhibits a 20% enhancement of its antimicrobial property. Specifically, when the Kevlar-GO hybrid fabric was exposed to the cyanobacterium *Synechococcus*, the growth of the bacteria was completely inhibited. Overall, the covalently modified fabric showed significant antibacterial behavior, excellent strength and stability under routine procedures. Due to its simplicity, the presented methodology not only promises to lead to a standard process to modify the *mer* units of Kevlar with a variety of chemicals and nanomaterials, but can also be extended to the modification and hybridization of other fabrics.

Publications

Tonis, E., Frousiou, E., Heliopoulos, N.S., Kagkoura, A., Stangel, C., Siamidis, D., Galeou, A., Prombona, A., Stamatakis, K., Boukos, N., Tagmatarchis, N., Vougioukalakis G.C. (2023) VAR Fabric Modification: Inducing Antibacterial Properties, Altering Wettability/Water Repellence, and Understanding Reactivity at the Molecular Level. ACS Omega, 8(47), 44708–44716 (IF 3.7)

Canton-Vitoria, R., Heliopoulos, N., Boukos, N., Vasilakos, S., Siamidis, D., Stamatakis, K., Tagmatarchis N. (2023) Covalently Modified Kevlar Fabric Incorporating Graphene Oxide with

Enhanced Antibacterial Properties and Preserved Strength. Chem. Eur. J, 29, e202301400 (1 of 7) (IF 3.9)

Tonis, E., Frousiou, E., Heliopoulos, N.S., Kagkoura, A., Stangel, C., Canton-Vitoria, R., Vasilakos, S., Siamidis, D., Galeou, A., Stamatakis, K., Prombona, A., Boukos, N., Tagmatarchis, N., Vougioukalakis G.C. (2023). Kevlar® and Nomex® modification via 2,4-dihydroxybenzophenone anchoring improves water repellency and induces antibacterial and UV protection properties. Materials Today Chemistry 33, 10169 (IF 6.7)

Frousiou, E., Tonis, E., Rotas, G., Pantelia, A., Chalkidis, S.G., Heliopoulos, N.S., Kagkoura, A., Siamidis, D., Galeou, A., Prombona, A., Stamatakis, K., Boukos, N., Tagmatarchis, N., Vougioukalakis G.C. (2023). Kevlar®, Nomex®, and VAR Modification by Small Organic Molecules Anchoring: Transfusing Antibacterial Properties and Improving Water Repellency. Molecules, 28, 5465 (IF 4.2)

Articles in press

Broussos, P.-I., Romanos, G.E., Stamatakis, K. (2024) H_2 production by the unicellular freshwater cyanobacterium *Synechococcus elongatus* PCC7942 PAMCOD strain. Inter. J. Hydrogen Energy 52, 1298–1303 (IF 8.1)

Broussos, P.-I., Romanos, G.E., Stamatakis, K. (2024) Salt and heat stress enhances hydrogen production in cyanobacteria. Photosynth Res (IF 2.9)

Canton-Vitoria, R., Kagkoura, A., Tonis, E., Heliopoulos, N., Galeou, A., Prombona, A., Stamatakis, K., Boukos, N., Siamidis, D., Vougioukalakis, G.C., Tagmatarchis, N. (2024) Covalent post-functionalization of kevlar with graphene oxide-melamine for UV-light protection and antibacterial properties. Materials Today Chemistry, 37, 102041 (IF 6.7)

Panagiotaki, N. K., Lyra, K-M., Papavasiliou, A., Stamatakis, K., Sideratou, Z. (2024) Synthesis of N-Sulfopropylated HyperbranchedPolyethyleneimine with Enhanced Biocompatibility andAntimicrobial Activity. ChemPlusChem, e202400454. (IF 3.0)

International conferences

Broussos P-I, Romanos GE, Stamatakis K. (2023) Enhanced Hydrogen production of *Synechococcus* sp PCC 7942 cells. "Photosynthesis and Hydrogen Energy Research for Sustainability –2023", 3-9 July, 2023 Istanbul, Turkey.

Broussos P-I, Stamatakis K (2023) Sucrose accumulation of cyanobacterial cells under stress conditions. "Photosynthesis and Hydrogen Energy Research for Sustainability –2023", 3-9 July, 2023 Istanbul, Turkey.

Other Scientific Activities

Organization of scientific conferences or participation in conference organizing committees

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

Total Impact Factor for original publications in 2023: 18.5 (for 4 publications)

Citations for 2023 (without self-citations): 96 (Scopus), 116 (Google Scholar)

Total citations 2019-2023 (without self-citations): 386 (Scopus), 485 (Google Scholar)

h-index: 15 (Scopus), 18 (Google Scholar)

Current External Funding

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

Research Group: Insect Molecular Genetics and Biotechnology

Research Staff
Luc Swevers, Research Director
Vasiliki Labropoulou, Senior Research Scientist
Anna Kolliopoulou, Postdoctoral Fellow
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.

2023 Findings

Viral-like particles for efficient dsRNA delivery to insect pests

Experiments were started to produce dsRNA-VLPs that are targeted to the agricultural pest *Helicoverpa armigera* (cotton bollworm). Two gene fragments corresponding to *Tubulin-α* and one gene fragment corresponding to *Trypsin-like protease* were amplified from cDNA of *Helicoverpa* larvae and cloned in the pLitmus-38i vector for production of dsRNA. At the same time, VLPs based on Cypovirus 1 (a Lepidoptera-specific virus) were produced by the baculovirus expression vector system and subsequently purified by ultracentrifugation (participation in the national action « Innovative solutions for sustainable and environmentally friendly protection of Greek fruit and vegetables, in the Europe of the future» (TAEDR-0535675)).

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

A reporter system for translation based on an "internal ribosomal entry site" (IRES) of the Cricket paralysis virus (CrPV) was constructed and characterized. The eIF4A translation factor was identified as an important modulator of translation initiation. It was found that Rocaglamide A (RocA), a natural product and eIF4A inhibitor, could stimulate IRES-dependent translation which could result in a strong enhancement of CrPV infection in lepidopteran cells. In future research, it will be investigated whether RocA can be used to enhance CrPV infection in insect larvae and can be applied as a biologically safe insecticide.

Differential gene expression in the brain of silkworm larvae during baculovirus infection: identification of factors that affect brain function.

Single nucleus RNA-seq was used to investigate the changes in cell-specific gene expression in the brain of silkworm (*Bombyx mori*) larvae following baculovirus (B. mori nucleopolyhedrovirus) infection (collaboration with South China Agricultural University). The class of genes that showed the greatest changes in expression corresponded to chemosensory proteins (CSPs) which are small secreted proteins with a flexible hydrophobic binding cavity. Silencing experiments have shown that CSP3 has a function in the regulation of "enhanced locomotory" behavior of the

larvae. Current experiments aim at the production of CSP proteins in bacteria for the screening of ligands that bind to the hydrophobic cavity – such ligands could be involved in the regulation of behavior of insect larvae and therefore could form the basis of a new strategy for pest control (collaboration with Thanos Papkyriakou, IBE, and Spyros Zographos, EIE).

Publications

Wu, H., Xia, J., Fei, S., Wang, Y., Zhang, M., Guo, Y., Li, X., Swevers, L., Sun, J., and Feng, M. (2023). BmCH25H, a vertebrate interferon-stimulated gene (ISG) homolog, inhibits BmNPV infection dependent on its hydroxylase activity in Bombyx mori. Insect Sci. 30, 321-337. (IF = 4.0)

Xia, J., Fei, S., Wu, H., Yang, Y., Yu, W., Zhang, M., Guo, Y., Swevers, L., Sun, J., and Feng, M. (2023). The piRNA pathway is required for nucleopolyhedrovirus replication in Lepidoptera. Insect Sci. 30**,** 1378-1392. (IF = 4.0)

Liang, Y., Wang, T., Yang, W., Chen, Z., Li, Q., Swevers, L., and Liu, J. (2023). Silencing of the immune gene BmPGRP-L4 in the midgut affects the growth of silkworm (Bombyx mori) larvae. Insect Mol. Biol. 32, 340-351. (IF = 2.6)

Santos, D., Feng, M., Kolliopoulou, A., Taning, C.N.T., Sun, J., and Swevers, L. (2023). What Are the Functional Roles of Piwi Proteins and piRNAs in Insects? Insects 14, 187. (IF = 3.0)

Ren, F., Yan, J., Wang, X., Xie, Y., Guo, N., Swevers, L., and Sun, J. (2023). Peptidoglycan recognition protein S5 of *Bombyx mori* facilitates the proliferation of *Bombyx mori* Cypovirus 1. J. Agric. Food Chem. 71, 6338-6347. (IF = 6.1)

Feng, M., Xia, J., Fei, S., Huang, Y., Lai, W., Swevers, L., and Sun J. (2023). Single-nucleus sequencing of fat body reveals distinct metabolic and immune response landscapes in silkworm larvae after *Bombyx mori* nucleopolyhedrovirus infection. J Immunol. 211, 140-153. (IF = 4.4)

Xue, Q., Swevers, L., and Taning, C.N.T. (2023). Plant and insect virus-like particles: Emerging nanoparticles for agricultural pest management. Pest Manag. Sci. 79, 2975-2991. (IF = 4.1)

Articles in Press

Xue, Q., Samakovli, D., Swevers, L., and Taning, C.N.T. (2024). Drosophila X virus-like particles as efficient dsRNA carriers for improved RNAi against the invasive species, *Drosophila suzukii*. J. Pest Sci. 97, 429-443. (IF = 4.8)

Xue, Q., Swevers, L., and Taning, C.N.T. (2024). Drosophila X virus-like particles as delivery carriers for improved oral insecticidal efficacy of scorpion Androctonus australis peptide against the invasive fruit fly, Drosophila suzukii. Insect Sci. Accepted Sep 8. (IF = 4.0)

Labropoulou, V., Wang, L., Magkrioti, C., Smagghe, G., and Swevers, L. (2024). Single domain von Willebrand factor type C “cytokines” and the regulation of the stress/immune response in insects. Arch. Insect Biochem. Physiol. 115, e22071. (IF = 2.2)

Xia, J., Fei, S., Huang, Y., Lai, W., Yu, Y., Liang, L., Wu, H., Swevers, L., Sun, J., and Feng, M. (2024). Single-nucleus sequencing of silkworm larval midgut reveals the immune escape strategy of BmNPV in the midgut during the late stage of infection. Insect Biochem. Mol. Biol. 164, 104043. (IF = 3.8)

Feng, M., Fei, S., Zou, J., Xia, J., Lai, W., Huang, Y., Swevers, L., and Sun, J. (2024). Single-Nucleus Sequencing of Silkworm Larval Brain Reveals the Key Role of Lysozyme in the Antiviral Immune Response in Brain Hemocytes. J Innate Immun. 16, 173-187. (IF = 5.3)

Yang, W., Lin, Y., He, Y., Li, Q., Chen, W., Lin, Q., Swevers, L., and Liu, J. (2024). BmPGPR-L4 is a negative regulator of the humoral immune response in the silkworm Bombyx mori. Arch. Insect Biochem. Physiol. 115, e22093. (IF = 2.2)

Xia, J., Peng, R., Fei, S., Awais, M.M., Lai, W., Huang, Y., Wu, H., Yu, Y., Liang, L., Swevers, L., Sun, J., and Feng, M. (2024). Systematic analysis of innate immune-related genes in the silkworm: Application to antiviral research. Insect Sci. Accepted Apr 3. (IF = 4.0)

Wang, L., Smagghe, G., Swevers, L., and Lu, Y. (2024). Metabolomics-based approaches in unraveling virus infections in insects: revealing unknown hidden interactions. Entomologia Generalis. Accepted April. (IF = 6.9)

International conferences

Kolliopoulou, A., Kontogiannatos, D., Xue, Q., Taning, C.N.T., De Schutter, K., Smagghe, G., Ren, F., Feng, M., Sun, J., and Swevers, L. (2023). Assessment of insect virus-like particles as nano-vehicles for efficient dsRNA delivery in insect tissues and cells. XII European Congress of Entomology, 16-20 October, Heraklion, Crete, Greece.

Christopoulou, V.M., Labropoulou, V., Taning, C.N.T., and Swevers, L. (2023). Development of a screening system for the identification of antiviral compounds that target the IRES of insect-specific dicistroviruses. XII European Congress of Entomology, 16-20 October, Heraklion, Crete, Greece.

Other scientific activities

Participation in editorial boards of scientific journals

Member of the Editorial Board of the scientific journals: "Archives of Insect Biochemistry and Physiology", "Journal of Insect Science", "Frontiers in Insect Science", "Frontiers in Plant Science", "Virus Research" and "Journal of Pest Science" (L. Swevers)

Reviewing of manuscripts in scientific journals

"Archives of Insect Biochemistry and Physiology" (5x), "BMC Biotechnology", "Cells", "Computational and Structural Biotechnology Journal", "Ecotoxicology and Environmental Safety", "Frontiers in Immunology", "Frontiers in Physiology", "Frontiers in Plant Science", "Gene", "Heliyon", "Insect Biochemistry and Molecular Biology" (7x), "International Journal of Biological Macromolecules" (5x), "International Journal of Molecular Sciences", "Insect Molecular Biology" (2x), "Insect Science" (4x), "Journal of Pest Science" (4x), "Journal of Insect Physiology", "Journal of Insect Science", "Nature Communications", "Pesticide Biochemistry and Physiology" (9x), "PLoS ONE" (2x), "Pest Management Science" (7x), "Virus Research", "Viruses" (3x), "Wellcome Open Research" (L. Swevers)

Participation in teaching courses and other educational activities

Inside IBA:

Participation in the Bi-Institutional Program of Graduate Studies of "Applied Biochemistry: Clinical Chemistry, Biotechnology, Validation of Pharmaceutical Drugs" (collaboration with the Chemistry Department of the University of Patras)

Molecular Pharmacology – Immunology: lectures with title: "Viral Immunology & Pharmacology" (focus on SARS-CoV-2 and COVID-19 (4 hours, 19 students) (L. Swevers)

Outside IBA:

Lecture of 30 min with title: "Virus infection of the insect brain and the modulation of larval behavior" at the Summer School of NCSR "Demokritos" (L. Swevers)

Member of the 7-member evaluation committee of PhD thesis of Thomas-Wolf Verdonckt with title "Virus-derived piRNAs in Lepidoptera and efficacy of RNAi in the pest species *Helicoverpa armigera*", K.U. Leuven, Faculty of Science, Department of Biology, Animal physiology and neurobiology division, Belgium. June 11th and July 3rd 2023 (L. Swevers)

Other Activities in IBA and in NCSR "Demokritos"
Member of the Scientific Board of the Institute (L. Swevers)
Biosafety Officer (Centre) (L. Swevers)

Total Impact Factor for original publications in 2023
L. Swevers: 28.2 (for 7 publications)

Citations for 2023 (without self-citations)
L. Swevers: 361
V. Labropoulou: 65

Total citations 2019-2023 (without self-citations)
L. Swevers: 1781
V. Labropoulou: 241

h-index
L Swevers: 39 (Scopus), 46 (Google Scholar)
V. Labropoulou: 14 (Scopus), 17 (Google Scholar)

Current External Funding
Project entitled: "Innovative solutions for sustainable and environmentally friendly protection of Greek fruit and vegetables, in the Europe of the future" (TAEDR-0535675) funded by "Flagship actions in interdisciplinary scientific areas with special interest in the connection with the productive sector", ID 16618, National Recovery and Resilience Plan (Greece 2.0) (Scientific Supervisor: John Vontas)
Research groups participating in the programme: Agricultural University of Athens, Hellenic Agricultural Organization - Demeter, Benaki Phytopathological Institute, Aristotle University of Thessaloniki, Demokritos University of Thrace, Foundation for Research and Technology - Hellas, Hellenic Mediterranean University. Subcontractor: NCSR "Demokritos" (Coordinator: AUA).
Programme duration: 2 years
Total programme funding (for the entire duration of the programme): 4.915.000,00 €
Funding for 2023: 1.230.000 €
Funding of the lab for 2023: 2.400 €

PROGRAMME C

“STRUCTURAL AND COMPUTATIONAL BIOLOGY”

Research Group: Theoretical Biology and Computational Genomics

Research Staff
Yannis Almirantis, Research Director
Spyros Papageorgiou, Emeritus Scientist
Giannis Tsiagkas, Collaborating 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.

2023 Findings
An iterative numerical procedure is formulated and explored, based on the digital structure of numbers, and despite its simplicity, unfolds a remarkable richness of patterns. This procedure, termed '*Iterative Digital Reversion*' (IDR), may be described as follows: ***Let N_0 be a natural number in its decimal form: N_0 = abc••• fgh. We subtract or add to N_0 its digital reverse $N_0^{(rev)}$ = hgf••• cba, provided that $N_0^{(rev)} < N_0$ or $N_0^{(rev)} \geq N_0$ respectively. Thus, we obtain N_1, and so on, for an unlimited number of steps***. *This description may be extended to any numeral system*. IDR presents features typical in the framework of the dynamics of complex systems: periodicities, the existence of 'attractors', ever-growing behavior, etc. Attractors (invariant IDR traps) often are pairs of integers, where the one is a 10-multiple of the other, which thus is a 'palintiple' with multiplicative factor 9. Less often, attractors consist of several integers. IDR can also lead to endless sequences of increasing physical numbers. Parallels may be drawn between IDR and procedures like Conway's Game of Life. The peculiar features of IDR depend on the well-known '1089 trick', generalized for any digital length and numeral system: the sequence of the steps: *(digital)*

reversion – subtraction – (digital) reversion – addition, usually leads to *only very few integers.* For consecutive digital lengths of the input numbers, the populations of integers that are the outcome of the above procedure had been shown to belong to the Fibonacci sequence, acting as bottlenecks contributing to the properties outlined herein.

Publications

Papageorgiou, S. (2023). Hox Gene Collinearity with Pulling Physical Forces Creates a Hox Gene Clustering in Embryos of Vertebrates and Invertebrates: Complete or Split Clusters. *Symmetry* 2024*, 16(5), 594-616*

Articles in press

Almirantis, Y., Provata A., Li, W. Range-limited Heaps' law for functional DNA words in the human genome. *Journal of Theoretical Biology. To appear.*

Other Publications 2023

Papageorgiou, S. (2023). The multiple roles of Temporal Collinearity in Hox gene clustering. Google Scholar Preprints: 2023111987.

Educational Activities

Outside IBA:

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. (Yiannis Almirantis)

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. (Yiannis Almirantis)

Total Impact Factor for original publications in 2023: 2.7 (for 1 publication, Spyros Papageorgiou)

Citations 2023 (without self- citations): 93 (Yannis Almirantis)

Total Citations 2019-2023 (without self-citations): 458 (Yannis Almirantis)

h-index: 17 (Scopus), 19 (Google scholar) (Yiannis Almirantis)

Research Group: Designed Biomolecules Research Lab

Research Staff
Athanasios Papakyriakou, Senior Researcher
Alexandros Athanasoulis, PhD student
Evangelos Tsoukas, MSc student
Stella Anastasiou, Undergraduate student

Research Interests
Design and synthesis of M1 zinc aminopeptidase inhibitors aiming to achieve selectivity towards ERAP2 and APN enzymes. Structure-based discovery of inhibitors of poly(ADP-ribose) polymerases, targeting the viral versus human PARP9, PARP14 and PARP15 from Chikungunya (CHK), Mayaro (MAY), Venezuelan equine encephalitis (VEEV) and the two severe acute respiratory syndrome (SARS1/2) viruses (collaboration with Prof. Georgios Spyroulias). Study of structure and dynamics of receptor of angiotensin 2 (ACE2) in complex with peptide substrate-analogues (collaboration with Dr. Petros Giastas). Discovery of allosteric inhibitors of phosphatases through virtual screening of small-molecule libraries, and computational investigation of potential senolytics through machine learning algorithms that are trained by a limited number of known senolytics (collaboration with Dr. Dimitris Kletsas and Dr. Anastasia Krithara). The latter was the study carried out by the undergraduate student Stella Anastasiou.

2023 Findings
Significant progress in the synthesis of aminopeptidase inhibitors by the PhD student Alexandros Athanasoulis considering we obtained a crystal structure of ERAP2 with a bound selective inhibitor. Based on the structure-activity relationships obtained, selected groups have been employed for the synthesis of compounds that target selectively aminopeptidases N and A (APN and APA). The results of these studies are expected to provide very interesting results that will be published after we investigate all possibilities for commercial exploitation of these inhibitors and after a patent application.

The graduate student Evangellos Tsoukas has presented his MSc thesis entitled “Study of the interaction and dynamics of transcription factors of the FOXO family with the tumor-suppressor protein p53”, who received the MSc diploma at the interdepartmental postgraduate program "Informatics for Life Sciences" of the department of Pharmacy and Medicine at the University of Patras (1/2/2023). The other two members of the committee comprised of Prof. G. Spyroulias and Prof. Zoi Lygerou (University of Patras).

The undergraduate student Soultana Kechagia has completed her internship with the presentation of her thesis entitled “Screening of potential allosteric inhibitors of the enzyme MKP7 (DUSP16) through computational study of small organic molecular libraries” at the Department of Biotechnology of the Agricultural University of Athens (9/1/2023).

The collaboration with Prof. Eleni Douni (Department of Biotechnology of the Agricultural University of Athens) on the discovery of small-molecules that target the NF-κB receptor (RANKL) that were based on computational virtual screening of small-molecular weight compound libraries was completed with the publication of the corresponding article.

The structural study of polymorphisms of the RNA elicase MDA5 (melanoma differentiation-associated 5) in collaboration with Prof. Elias Iliopoulos (Department of Biotechnology of the Agricultural University of Athens) and an article has been accepted for publication.

The collaboration with Prof. George Giamas has been successfully completed with the publication of an article describing the discovery and characterization of a new inhibitor for the LMTK3 kinase.

The collaboration with Prof. Barbara Richichi and the ERASMUS+ student Luca Landini has been completed with a publication of our joint work on the structure-activity relationships of novel beta-adrenergic receptors ligands at the European Journal of Medicinal Chemistry.

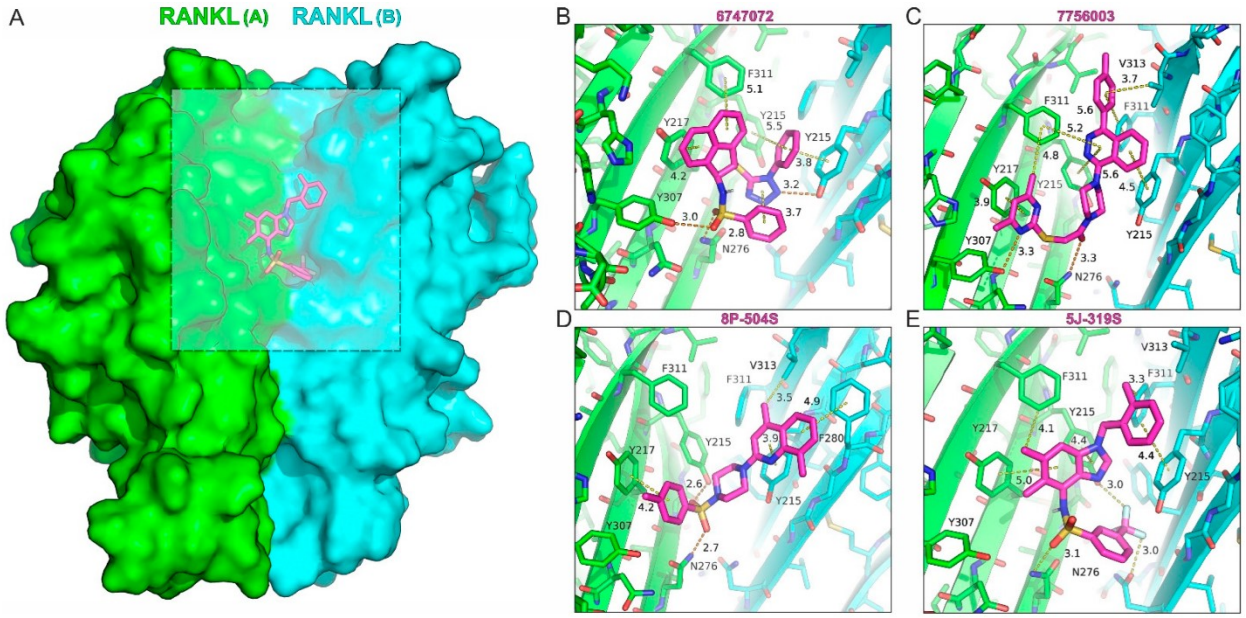
Publications

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

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

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

Rinotas V, Liepouri F, Ouzouni MD, Chalkidi N, Papaneophytou C, Lampropoulou M, Vidali VP, Kontopidis G, Couladouros E, Eliopoulos E, Papakyriakou A,* Douni E.* (2023) Structure-Based Discovery of Receptor Activator of Nuclear Factor-κB Ligand (RANKL)-Induced Osteoclastogenesis Inhibitors. International Journal of Molecular Sciences 24(14):11290 [IF: 6.2]



Other Scientific Activities

Member of the evaluation committee for the research proposals that were submitted at the Latvian Council of Science in the fields of Basic and Applied Research in Life Sciences (Oct-Dec 2023).

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

Member of the Organizing Scientific Committee of the 73rd Panhellenic Congress of the Hellenic Society of Biochemistry and Molecular Biology (HSBMB) at the Eugenides Foundation, Athens (1 – 3 December 2023)

Elected member of the Board – Treasurer of the Hellenic Crystallographic Association (HeCrA)

Member of the European Peptide Society (EPS) and of the Greek Chemists.

Educational activities

Interdepartmental Program for Postgraduate Studies of IBE and the Department of Chemistry, University of Patras; Molecular Pharmacology, 2nd semester 2023 (4 hours), Courses: "*Drugs acting on receptors", "Drugs acting on enzymes",* and *"The adrenergic nervous system – structure-activity relationships of agonists and antagonists"* for 12 students.

Other Activities in IBA and in NCSR "Demokritos"

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

Total Impact Factor for your original publications in 2023: 23.5 (for 4 publications)

Citations for 2023 (without self-citations from Scopus): 161

Total citations for 2019-2023 (without self-citations from Scopus): 910

h-index (from Scopus and Google scholar): 26 (Scopus), 31 (Google scholar)

Research Group: Structural Studies of Biomolecules and Pharmaceuticals with NMR

Research Staff
Maria Pelecanou, Research Director
Marina Sagnou, Senior Researcher
Angeliki Panagiotopoulou, **Functional Scientist B**
Barbara Mavroidi, Postdoctoral Fellow
Dimitris Matiadis, Postdoctoral Fellow
Adelaida Sahou, Graduate Fellow (MSc)
Anna-Maria Kostaki Graduate Fellow (MSc)
Vasiliki Manakou (Summer internship)
Stella Timotheatou (Summer internship)
Andreas Moutselos (Summer internship)

Research Interests
Development (design, synthesis, characterization, structural analysis, evaluation) of new compounds/agents of pharmacological interest for the diagnosis and/or treatment of diseases as well as for biotechnological and nano-technological applications. Our main fields of research are Alzheimer's disease (AD) and cancer, and our tools are NMR and CD spectroscopies for structural and molecular interaction studies, combined with methodologies of organic synthesis, complexation/labeling, encapsulation, and biological evaluation of the new compounds/agents in appropriate systems. Biological evaluation includes in vitro studies of interaction with biomolecules, biochemical/microscopic/cellular assays in cancer and primary neuronal 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, flavonoids etc), derivatives of these molecules with improved pharmacological properties, as well as their complexes (with copper, palladium, platinum, zinc, nickel, etc) with dual/combined activity from the pharmacophore-ligand and the metal. The compounds of interest are studied either free or encapsulated in nanostructures (nanoparticles, liposomes) for increased bioavailability and targeted transport and release.
- complexes of rhenium and radioactive technetium-99m, with appropriate ligands, designed for targeted action for diagnosis with SPECT and/or treatment of widespread diseases, in collaboration with INRASTES. Within the same framework, development of agents suitable for ^{18}F labeling labeling for PET imaging.
- photochemical active molecules as photosensitizers in the photodynamic treatment of cancer and as tracers of cellular processes.
- inhibitors of the aggregation of β-amyloid peptide (Aβ) of Alzheimer's disease to toxic oligomeric and polymeric forms. The effect of natural products and synthetic organic molecules, on the aggregation process of Aβ is studied mainly with Circular Dichroism (CD) but also through the reduction of its toxicity in primary neurons (rescue effect).
- application of quantitative NMR methods (q-NMR) in the study of the purity of organic compounds of antibiotics, aflatoxins, etc. (collaboration with the Laboratory of Chemical Metrology, General State Chemistry Laboratory) and metabolomic NMR methods in the study of the effect of pesticides on olive trees in Messinia for the qualitative and quantitative upgrading of olive oil production in Messinia (collaboration with Assistant Professor K. Aliferis, Agricultural University of Athens).

2023 Findings

The use of natural products and known pharmacophoric structures το to prepare novel bioactive compounds constitutes the major goal of our activities and continued successfully during 2023. Representative examples include • synthesis of novel pyrazolo-pyridines with affinity for amyloid plaques of AD • synthesis of isatin derivatives with multimodal activity against AD • development of novel dendrimeric hyperbranched nanocarriers with encapsulated remdesivir, a clinically used anti-COVID-19 drug, aiming at developing an inhalable suspension for clinical use • development of colloidal albumin as curcumin nanocarrier in collaboration with the National Hellenic Research Foundation • study of *Rosmarinus officinalis* extracts as aryl hydrocarbon receptor inhibitors in collaboration with the University of Athens.

Within the framework of Industrial Scholarships (B. Mavroidi) from the Stavros Niarchos Foundation and in collaboration with the company PharmaGnose SA, the photoprotecting capacity of various bioactive natural products from the Greek flora (pure compounds or extracts) against skin cell lines is studied for cosmetic and medical applications. In 2023, extracts from mountain tea (*Sideritis clandestina*, *Sideritis syriaca*, *Sideritis scardica*), olive leaves (*Olea europaea*), rose petals (*Rosa damascena*) and from the shrubby plant *Cistus creticus* were shown to have strong antioxidant and photoprotective activity against UV-A irradiation with extremely low, if any, cytotoxicity.

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

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

Publications

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

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

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

Halevas, E., Mavroidi, B., Pelecanou, M., Hatzidimitriou A.G. (2023). 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. (2023). Monocarbonyl curcumin derivatives as potent inhibitors against human glutathione transferase P1-1. Antioxidants, 12, 63 (IF: 6.0)

Articles in Press

Stouraitis, A., Sagnou, M., Mavroidi, B., Kiritsis C., Shegani, A., Raptopoulou, C., Psycharis, V., Methenitis, C., Pirmettis, I., Papadopoulos, M., Pelecanou, M. (2024). Mixed ligand Re and 99mTc tricarbonyl complexes bearing two important pharmacophores: 2-(4'-aminophenyl)benzothiazole and curcumin. Inorg. Chim. Acta. 571, 122172 (IF: 2.545)

Panagiotakis, S., Mavroidi, B., Athanasopoulos, A., Charalambidis, G., Coutsolelos, A.G., Pelecanou, M., Yannakopoulou, K. (2024). Amphiphilic Chlorin-β-cyclodextrin Conjugates in Photo-Triggered Drug Delivery: The Role of Aggregation. Chempluschem. 6, e202300743 (IF: 3.210)

Panagiotopoulou, A., Kyprianidou, P., Tsoukalas, C., Psycharis, V., Raptopoulou, C., Pirmettis, I., Papadopoulos, M., Pelecanou, M. (2024). New *fac*-$[Re(CO)_3(OO)(L)]$ and $[Re(CO)_2(OO)(L)_2]$ Complexes Bearing Two Natural Food Additives, Maltol and Kojic Acid, as OO Ligands. Crystals, 14(6), 515 (IF: 2.589)

Kallimanis, P., Magiatis, P., Panagiotopoulou, A., Ioannidis, K., Chinou, I. (2024). Extraction Optimization and Qualitative/Quantitative Determination of Bioactive Abietane-Type Diterpenes from Three Salvia Species (Common Sage, Greek Sage and Rosemary) by ^{1}H-qNMR. Molecules, 29(3), 625 (IF: 4.411)

Dermitzaki, D., Panagiotopoulou, A., Pissas, M., Psycharis, V., Raptopoulou, C.P. (2024). Chiral Heterometallic Cu_8Ln_4 Complexes with Enantiopure Schiff Base Ligands: Synthesis, Structural, Spectroscopic and Magnetic Studies. ChemPlusChem, e202400123 (IF: 3.210)

Bakalakou, V.-A., Mavroidi, B., Kalampaliki, A. D, Josselin, B., Bach; S., Skaltsounis, A.- L., Marakos, P., Pouli, N., Pelecanou, M., Myrianthopoulos, V., Ruchaud, S., Kostakis, I. (2024). The Pyrazolopyrazole Core as a Novel and Versatile Scaffold for Developing Dual DYRK1A-CLK1 Inhibitors Targeting Key Processes of Alzheimer's Disease Pathology. Eur. J. Med. Chem. in press (IF: 6.7)

Tsouri, S., Tselo, E., Premetis, G. E., Furlan, V., Pantiora, P. D., Mavroidi, B., Matiadis, D., Pelecanou, M., Papageorgiou, A. C., Bren, U., Sagnou, M., & Labrou, N. E. (2024). A Monocarbonyl Curcuminoid Derivative Inhibits the Activity of Human Glutathione Transferase A4-4 and Chemosensitizes Glioblastoma Cells to Temozolomide. Pharmaceuticals (Basel, Switzerland), 17(3), 365. (IF: 4.3)

International conferences

A. Shahu, V.S. Petrakis, T. Menidiati, A. Panagiotopoulou, P. Argitis, G. Pistolis (2023). Supramolecular synthesis and study of light-harvesting self-assembly consisting of functionalized BODIPY-dyes. Micro Nano 2023, 10th International Conference on Micro-Nanoelectronics, Nanotechnology and MEMS, September 2-5, 2023, Athens, Greece

K. Stamatis, A. Panagiotopoulou, V. Psycharis, C.P. Raptopoulou (2023). Zinc(II) complexes with chiral Schiff base ligands: Synthesis, characterization and DNA-interaction studies. 11th International Conference of the Hellenic Crystallographic Association (HeCrA), 20-22 October 2021, Larissa, Greece.

D. Dermitzaki, A. Panagiotopoulou, M. Pissas, V. Psycharis, C. P. Raptopoulou (2023). Chiral Complexes from Chiral Schiff Base Ligands: The case of $\{Cu_4Dy_2\}$ clusters. 2023 Joint CTMNM/NAGC Conference, 8-12 May 2023, Spetses, Greece.

A. Kokkali, A-M Kostaki, G. Athanassopoulou, A. Makri, M. Sagnou, V. P. Vidali , G. Kythreoti (2023) Natural Product Analogues as Antibacterial Agents: The Case of Cinnamaldehyde and Colupulone, 9th International Electronic Conference on Medicinal Chemistry, 1–30 November 2023, online symposium.

National conferences

P. Kallimanis, P. Magiatis, A. Panagiotopoulou, I. Chinou (2023). Extraction optimization of betulinic acid from *Rosmarinus officinalis* L. by ^{1}H-qNMR. 20th Panhellenic Pharmaceutical Congress, 16-17 December 2023, National Hellenic Research Foundation, Athens, Greece.

Patents granted in 2023

TRICARBONYL COMPLEXES OF TRANSITION METALS WITH BENZO-HETEROCYCLIC DERIVATIVES OF THE CYCLOPENTADIENYL ANION, M. Pelcanou, M. Sagnou, M. Papadopoulos, I. Pirmettis, B. Mavroidi, A. Seghani,

- USA (Appl. No US201917040117A, Publication No US11845763B2·19-12-2023)
- China (Appl. No CN201980020996A, Publication No CN111936173B·28-07-2023)
- India (Appl. No IN202017044136, Publication No IN464866. 01-11-2023)

Other Scientific Activities

Publication Reviewing activity

Letters in Drug Design & Discovery, Medicinal Chemistry, Bioorganic Medicinal Chemistry Letters, Pharmaceuticals, Molecules, Inorganics, Int J Mol Struct, Foods, Cancers, Antioxidants– M. Sagnou

Metals, Molecules, MDPI – A. Panagiotopoulou

Educational activities

Inside IBA

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

Participation in the Summer Scientific Workshops of the IBA for high school students, 26/06/2023-07/07/2023 (M. Sagnou, A. Panagiotopoulou, M. Pelecanou)

Participation in the NCSR “Demokritos” Summer School 2023: Presentation of the liquid sample NMR Spectroscopy Laboratory (Principles and Applications of NMR spectroscopy) (A. Panagiotopoulou)

Other activities in IBA

M. Pelecanou

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

M. Sagnou

- Deputy education responsible

A. Panagiotopoulou

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

Other Activities

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

Total Impact Factor for publications in 2023

Maria Pelecanou: 26.871 (for 5 publications)

Citations in 2023 (without selfcitations)

Maria Pelecanou: 219 (Scopus)
Marina Sagnou: 176 (Scopus)
Angeliki Panagiotopoulou: 35 (Scopus)

Total citations during 2019-2023 (without self-citations)

Maria Pelecanou: 808 (Scopus)
Marina Sagnou: 591 (Scopus)
Angeliki Panagiotopoulou: 139 (Scopus)

h-index (Scopus)

Maria Pelecanou: 27
Marina Sagnou: 21
Angeliki Panagiotopoulou: 8

Current External Funding

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

Project entitled: Novel 99mTc complexes as AL amyloidosis radiodiagnostic tracers (SPECT-AL), funded by Johnson & Johnson Innovation, QuickFire Challenge: Improving Detection of AL Amyloidosis (IDEA) s with Professor E. Kastritis (School of Medicine, NKUA) as scientific coordinator.

Responsible for IB-A: M. Pelecanou and M. Sagnou
Duration: 1 year, 2021-2022
Collaborating teams: NCSR "Demokritos" (IB-A and INRASTES), School of Medicine & Department of Pharmacy, NKUA
Total Program Funding: 250.000 $
Funding for the lab for 2022: 30.000 €

Project entitled: Qualitative and quantitative upgrading of olive oil production in Messinia area of Peloponnese through the development of a modern plant protection program against the disease "anthracnose" of olives, funded by Agricultural Development Program (RAP) 16.1-16.2.
Duration: 3 years 2022-2025
Collaborating teams: Dr. K. Aliferis AUA, NILEAS Agricultural Cooperative, GAIA EPICHEIREIN
Scientific Responsible: A. Panagiotopoulou
Total Program Funding: 144.933,52€
Total Funding of the lab for 2023: 6.961.50€

Research Group: Protein Structure and Molecular Modeling

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

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

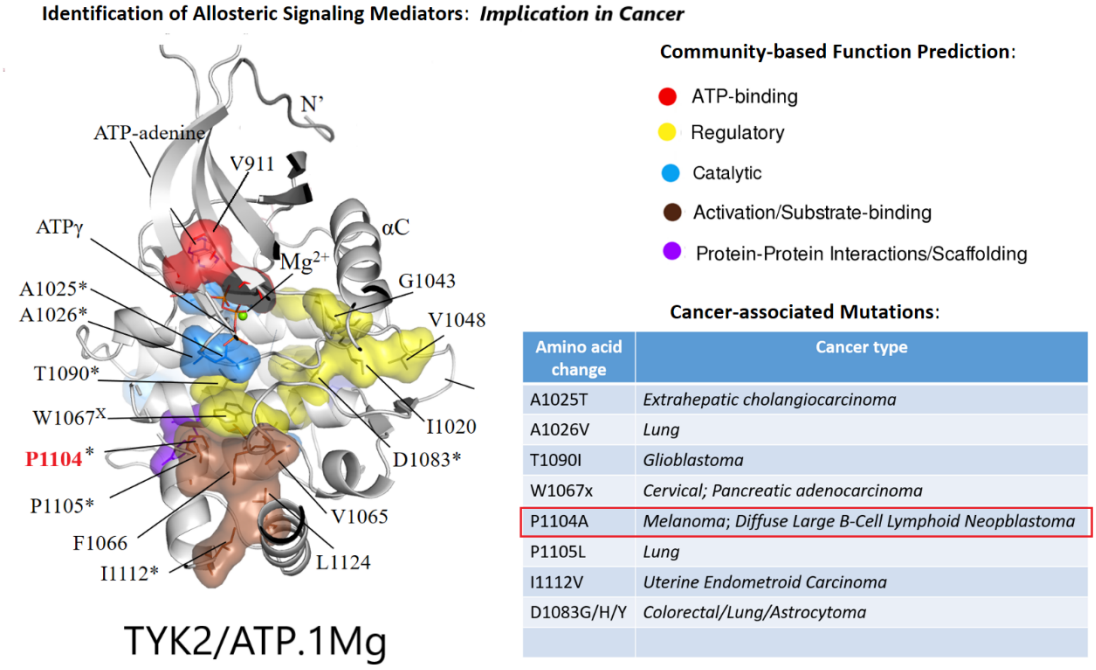
The approach we follow includes *in silico* techniques such as homology/comparative 3D-modeling and molecular dynamics (MD) simulations.

2023 Findings
With the aim of elucidating protein sequence/structure-function relationships, in 2023 we built on and expanded our previous in *silico* structural studies of the following protein kinases:

TYK2: We applied a protocol that we have developed in the past and is based on community-network analysis of MD trajectories, aiming at elucidating the dynamic architecture of a form of the kinase domain of wild type TYK2 (TYK2-KD) that corresponds to a critical step of the catalytic cycle of protein kinases. More specifically, we used community-network analysis of a long, microsecond-scale (3μs), all-atom MD simulation of TYK2-KD in the presence of ATP and one Mg^{2++} (ATP.1Mg), corresponding to activation. This long MD simulation was performed on the National HPC facility—ARIS, supported by computational time grants from the National Infrastructures for Research and Technology S.A. (GRNET) (project IDs: KIN_IMMUNMD_II and KIN_IMMUNMD_III). This type of analysis of the MD trajectory not only unraveled, for the first time, the dynamic profile of TYK2-KD during this critical step of its catalytic cycle but also allowed the identification of amino acids with pivotal role in the activation of this kinase. Corroborating our results, the majority of the identified amino acids correspond to cancer-associated mutations (Figure 1) as revealed by a search of a portal for Human Cancer Genomics (cBioPortal) (*see* ***Publication 1***). In addition, this approach allowed us to predict the functional role of key amino acids and to unravel the functional consequences of corresponding cancer-associated mutations. Interestingly, this type of analysis pointed to proline 1104 as one of key amino acids, in line with the disruptive role of its replacement by alanine (variant P1104A) that is also linked to protection against auto-immune diseases and that we have studied in the past (https://doi.org/10.1093/bioinformatics/bty556). This work was submitted and accepted for publication in ***Proteins: Structure, Function, Bioinformatics*** in 2023 (published **online** 10 Nov. 2023). For more details ***see Publication*** *at* ***https://doi.org/10.1002/prot.26631.***
Moreover, an application for additional computing resources to use ARIS was submitted to GRNET in 2023 in the framework of the "*14th Call for ARIS Project Access" (**approved: 30-3-2023**; see below for details: **Grant 2**).*

SRPK1: We performed a microsecond-scale all-atom MD simulation of the kinase domain of SRPK1 in the apo form aiming at a comparative study with long MD simulations (1.5 μs) in the presence of peptides from an interacting protein that we have performed in the previous years.

Community-network analyses of the MD trajectories, as applied to the TYK2-KD simulation, are currently in progress.



Amino acid change	Cancer type
A1025T	*Extrahepatic cholangiocarcinoma*
A1026V	*Lung*
T1090I	*Glioblastoma*
W1067x	*Cervical; Pancreatic adenocarcinoma*
P1104A	*Melanoma; Diffuse Large B-Cell Lymphoid Neopblastoma*
P1105L	*Lung*
I1112V	*Uterine Endometroid Carcinoma*
D1083G/H/Y	*Colorectal/Lung/Astrocytoma*

Figure 1. Identification of amino acids with pivotal role in TYK2 kinase activity; prediction of functional role; implications in cancer, *as predicted by community-network analysis of a 3 μs-long MD simulation of the wtTYK2 kinase domain at a critical step of the catalytic cycle. (**Left**): Mapping of key aa identified in this study on a MD snapshot depicted using surface-model illustration and colored according to predicted functional roles (**top Right**). Validating our results most of the identified aa correspond to cancer-associated mutations of the Tyk2 gene (denoted with Asterisks and 'x's, for missense or slice-site mutations, respectively). Interestingly, among these amino acids is proline 1104, replacement of which by alanine (P1104A) is related to several types of cancer (**bottom Right**) but at the same time has been found to confer protection against autoimmune diseases, in line with the notion that reduced TYK2 kinase activity is the mechanism for protection against autoimmune diseases, an idea that is also supported by our previous comparative work (see https://doi.org/10.1093/bioinformatics/bty556). More details on the current work can be found at https://doi.org/10.1002/prot.26631 (**Publication 1**)*

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

Publications

Lesgidou N, Vlassi M. (2023) Community analysis of large-scale molecular dynamics simulations elucidated dynamics-driven allostery in tyrosine kinase 2. *Proteins* 2023; 1-25. (*Published online: 10 November 2023*). (*In press for 2024: Proteins Volume 92, Issue 4, April 2024, Pages 474-498*).

National conferences

Lesgidou N, Vlassi M. (2023) Large Scale Molecular Dynamics Simulations Shed Light on Steps of the Catalytic Cycle of TYK2 Kinase: Implications in Diseases. *National Conference of the 73th HSBMB 2023, 1/3 Dec., Athens, Eugenides Foundation.* (Abstract in *Abstracts Book, page 164*).

Other Scientific Activities

Member of the ad hoc appointment committees (two committees) for a Researcher (one position, B or C grade) in the Institute of Chemical Biology of the Hellenic Research Foundation, Athens, Greece

Member of the National Research Infrastructure project: "*INSPIRED: The National RIs on Integrated Structural Biology, Drug Screening efforts and Drug-target functional characterization"* is funded by NSRF 2014-2020 and co-financed by Greece (GSRT) and the European Union (European Regional Development Fund) (funding approved: June 2018). Role of MV: member of the group of Scientists of the NCSR "Demokritos" node and responsible for the *in silico* structural studies of the node.

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

Educational Activities
Supervision of the PhD Thesis of N. Lesgidou (Democritus University of Thrace, Dept of Molecular Biology & Genetics) entitled: "Structural and dynamics studies of proteins related to diseases using molecular dynamics simulations" (completed in 2023: defense at the Democritus University of Thrace, Alexandroupolis, October 2023)

Lecturer in the framework of the following post-graduate (Masters) Programs:
1. "Clinical Biochemistry – Molecular Diagnosis" (Depts. of Biology/Chemistry/Nursing, National & Kapodistrian University of Athens). Lecture entitled: "Principles of X-Ray Crystallography: Applications in Structural Biology"
2. "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"
3. "Bioinformatics-Computational Biology" (Dept. of Biology, Kapodistrian University of Athens). Lecture entitled: "Protein Structure – Experimental & Theoretic approaches".

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

Total Impact Factor for publications in 2023: 3.2 (for 1 publication)

Citations 2023 (excluding self-citations): 40 (Scopus)

Total citations 2019-2023 (excluding self-citations): 186

h-factor: 17 (Scopus)

Funding-Projects
Computing Resources Grant 1 from GRNET entitled: *"Using microsecond-scale MD simulations to elucidate sequence -dynamics-function relationships of a tyrosine kinase linked to autoimmune diseases IV*". *Acronym/project ID:* KIN_IMMUNMD_IV in the framework of the *12th Call for Production Projects Accessing the supercomputer system ARIS* @ GRNET (P.I.: M. Vlassi). Proposal submitted: January 2022; Approved: March 2022 (pr012027). Duration: March 2022-March 2023. Total computing resources: 1.400.000,0 core-hours (for 2023: 350 core-hours).

Computing Resources Grant 2 from GRNET entitled: *"Microsecond-scale MD simulations of a kinase linked to autoimmune diseases and of a protective variant V*". *Acronym/project ID:* KIN_IMMUNMD_V in the framework of the *14th Call for Production Projects Accessing the supercomputer system ARIS* @ GRNET (P.I.: M. Vlassi). Proposal submitted: January 2023; Approved: March 2023 (pr014038). Duration: March 2023-March 2024.
Total computing resources: 500.000,0 core-hours/thin nodes + 500.000,0 core-hours/gpu nodes (for 2023: 750.000,0 total core-hours)

CENTRAL PROJECTS
IBA

Beyond the already described activities of each Lab, part of IBA's personnel continued to be engaged in the networks of three National Research Infrastructures (NRIs). In particular:

IBA is the **coordinating institute** of 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), with Coordinator the Director of IBA. OPENSCREEN-GR aims at the implementation of medium to large-scale molecular target-based screening of existing libraries of synthetic small molecules, but also natural products, by means of the necessary equipment, as well as, trained personnel for employing 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). Beyond IBA's researchers participating in OPENSCREEN-GR, a collaborator was hired in 2023 with permanent contract assuming the responsibilities of coordinating all network activities and supervising the NRI's equipment. 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.

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

OPENSCREEN-GR is interconnected with the corresponding European Research Infrastructure Consortium (ERIC) EU-OPENSCREEN, through the participation in the European project EU-OPENSCREEN-DRIVE (Driving forward long-term Sustainability of Excellence in Chemical Biology within Europe and beyond) coordinated by EU-OPENSCREEN and encompassing 34 partners from 15 EU member states or associated countries. The project was selected for funding within the framework of the call H2020-INFRADEV-2018-2020/H2020-INFRADEV-2018-1 (Grant Agreement: 823893) with a total budget of 2,485,600.80 €, from which 16,875.00 € were allocated to IBA. Aim of the project is the support of EU-OPENSCREEN through dissemination activities targeting possible users, as well as, through the enhancement of the collaborations among the project partners. EU-OPENSCREEN-DRIVE is very important for IBA, keeping the communication channels with EU-OPENSCREEN open until the final integration of OPENSCREEN-GR into the ERIC.

IBA participates also in 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 many IBA researchers and the Imaging Unit operator, a collaborator hired in 2023 with permanent contract.

Finally, IBA is 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). 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.

An important development regarding the above-mentioned networks was their evaluation by an external independent expert committee, appointed by the Directorate-General for Research and Innovation of the European Commission (Horizon Europe Policy Support Facility: PSF). The outcomes of this evaluation were communicated to the Hellenic General Secretariat for Research and Innovation, which – following the prompts for ensuring the sustainability of the NRIs – announced in 2023 a call for expressions of interest to update the funding of the NRIs. IBA took part to all relevant proposals, with the aim to ensure the extension of the funding all three above-mentioned networks and to support their unconstrained functionality, as well as, their further development.

SERVICE UNITS

- ✓ ***LABORATORY FOR DOPING CONTROL AND METABOLIC STUDIES***
- ✓ ***HUMAN TISSUE BANK***
- ✓ ***EXPERIMENTAL ANIMAL FACILITY***
- ✓ ***LASER CONFOCAL MICROSCORY***
- ✓ ***HISTOLOGY UNIT***
- ✓ ***CIRCULAR DICHROISM (CD) LABORATORY***
- ✓ ***LABORATORY OF CELL-BASED ASSAY SYSTEMS AND BIOACTIVE COMPOUNDS***

LABORATORY FOR DOPING CONTROL AND METABOLIC STUDIES

Personnel
Dimitris Kletsas, Institute Director,
Laboratory Administrative Director
Christoforos Christoforidis, PhD, Laboratory Scientific Head
(from 5/4/2023 to 31/12/2023)
Emilia Makrygianni, MSc, Quality Manager
Ioannis Angelis, PhD, Research Division Head
Argiro Fragkaki, PhD, Analyst
Athanasia Kioukia-Fougia, PhD, Analyst
Polyxeni Kiousi, PhD, Analyst
Olga Goula, Chemist, MSc student, Analyst
Panagiotis Sakellariou, PhD, Analyst
Fotini Chlapana, Technician (Retired 9/2023)
Stella Loui, Technician
Maria Filippidou, Secretary
Maria Vlachou, Secretary (Retired 9/2023)
Maria Pavlaki, Support Staff
Vasiliki Tzouvara, Support Staff
Sofia Karnava, Postgraduate Student

Research Interests

The primary mission of the Doping Control Laboratory (DCL) is to analyze human and equine samples for the presence of doping substances. The laboratory is fully equipped with the necessary infrastructure and expertise. The DCL also undertakes various anti-doping research projects, some funded by the World Anti-Doping Agency (WADA), others by anti-doping organizations like the Cyprus Anti-Doping Agency (CYADA), or independently by the former hosting organization (Olympic Athletic Center of Athens, OAKA).

The results of these studies have been published in peer-reviewed journals and presented at international anti-doping conferences. Several postgraduate and doctoral theses have also been conducted in the laboratory's facilities under the supervision of its scientific personnel in collaboration with local universities.

The DCL is dedicated to advancing scientific research in human and equine doping control, improving existing detection methods, developing new ones, and conducting metabolic studies. Future research objectives include enhancing research activities by collaborating with other laboratories at IBAfor molecule characterization, protein and metabolic studies, and cell and animal model experiments.

Progress in 2023

The laboratory was designated as a WADA candidate lab in September 2022 and continued its efforts toward achieving probationary and, eventually, full accreditation status. On April 5, 2023, Dr. Christoforos Christoforidis was appointed as the new scientific director, and his credentials were approved by WADA.

The DCL maintained its ISO17025:2017 accreditation from the National Accreditation System (ESYD) for doping control in humans and horses. On July 4, 2023, the laboratory underwent ESYD supervision per the ELOT EN ISO/IEC 17025:2017 standard, considering the requirements of the WADA International Standard for Laboratories (ISL) 2021. The supervision focused on reviewing the new scientific director and the Quality Management System, achieving positive results.

The laboratory successfully renewed its equine doping control accreditation from the Association of Official Racing Chemists (AORC) for 2023 (July 2023). Additionally, three laboratory personnel members achieved professional membership status following an official examination (August 2023). The laboratory also provided services through an annual contract for analyzing biological samples (urine and blood) for the Hellenic Equestrian Federation (EOI).

Following the procurement of two new GC-MS/MS instruments (November 2022), a new GC-IRMS system was delivered on March 7, 2023, complementing the earlier acquisition of a new HPLC with a fraction collector (September 2022). Training provided by representatives of ThermoScientific in Greece (MetroLab) occurred immediately after the installation, with additional training from an external trainer provided on March 27-30, 2023.

Validation of analytical methods continued for WADA reaccreditation for athlete doping control, including ITP screening and confirmations. Additionally, the annual quantitative determination reviews of selected compounds in biological materials from humans and horses were conducted as usual.

In July 2023, the laboratory successfully upgraded its building's HVAC and water heating systems with new, energy-efficient units funded by OAKA's energy upgrade program. Battery systems supporting the UPS and a new UPS system for analytical instrument support during power outages were also installed. The computer network was upgraded with modern access control, antivirus detection, and data recovery/storage software (backup) to ensure electronic security. The building was connected to a fiber-optic network and directly linked to the Demokritos research center network. Collaboration with Demokritos technical services for building maintenance (fire detection/fire safety systems, security grids on windows, electrical work, cooling/freezing equipment support, and outdoor area maintenance) continued.

Laboratory members attended the annual Manfred Donike Workshop on Doping Analysis, gaining insights into developments and scientific needs in the doping control community. A postgraduate thesis by a student from the University of Athens (Sofia Karnava) focused on preparatory processes for biological samples from humans and horses for detecting banned substances.

Research activities continued as part of a WADA-funded project. Two earlier WADA-funded research studies from 2016 and 2021 were completed:

A) Chemical derivatization of intact phase II metabolites of AASs for confirmatory purposes.

B) Synthesis of the main long-term dihydroxylated metabolite of LGD 4033 as a reference material for doping control analysis.

Publications

Angelis Y.S., Fragkaki A.G., Kiousi P., Sakellariou P., Christophoridis, "LC-MS/(MS) confirmatory doping control analysis of intact phase II metabolites of methenolone and mesterolone after Girard's Reagent T derivatization," Drug Testing and Analysis, 15 (6), 2023.

Articles in Press

Sakellariou P., Kiousi P., Petrou M., Angelis Y.S., "Simultaneous quantitation and identification of intact Nandrolone phase II oxo-metabolites based on derivatization and inject LC–MS/(HRMS) methodology," Drug Test Anal., Apr 2024.

Angelis Y.S., Sakellariou P., Fragkaki A.G., Karnava S., Goula O., Kiousi P., Kioukia-Fougia N., Georgakopoulos C., Loui S., Chlapana F., Kletsas D., "New long-standing metabolites of 17α-methyltestosterone are detected in HepG2 cell in vitro metabolic model and in human urine," Drug Test Anal., Jun 2024.

HUMAN TISSUE BANK

Personnel
Helen Vavouraki Senior Researcher, Scientific Responsible
Yiannis Ninios, Research Collaborator (PhD)
Charalampos Voudommatis, Research Collaborator (MSc)
Eleutherios Kosmidis, Scientific Collaborator (MSc)
Milena Tselia, Technician

Laboratory Description – Research Interests
A) Development activity
Human Tissue Bank (HTB) of NCSR "DEMOKRITOS" is one of the Labs of the Institute with both development and research activities**.** These activities include, in particular, the collection and storage of various tissues of human origin, their processing and the production of sterile allografts for medical use.

It follows international standards and the specifications of the relevant European Directives 23/2004, 17/2006 and 86/2006, as updated and harmonized with Greek Legislation, for each stage of tissue graft preparation.

HTB is licensed to operate at NCSR "DEMOKRITOS", under the scientific responsibility of. Dr. H. Vavouraki (Government Gazette 768, 26/2.2021) and unique EU TE Code GR013836.

It is the only Bank of its kind in Greece, applying its "knowhow" in the processing of a great variety of human tissues and its expertise that has gradually developed in each procedure (procurement, tissue processing, irradiation sterilization and disposal of tissue grafts) is unique and constantly improving.

During the many years of its continuous operation, it has distributed more than 55,000 tissue grafts without ever reporting a problem that could be attributed to the quality of its products.

The quality system followed by the Bank is based on Presidential Law 26/2008, regarding scientific documentation, and applies the International Standard ISO 9001/2015 in terms of its management.

The grafts produced are available in hospitals, health clinics and medical laboratories throughout the country.

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

Regarding the design of research and development of new innovative bone graft products, the study of manufacturing products in paste / putty form continues. Putty is a new pharmaceutical form of allografts that includes components other than bone substance, such as special excipients, hyaluronic acid, antibiotics, possibly growth factors and/or BMPs.

The Laboratory plans to develop an original formulation based on the assay of combinations of excipients and other substances at various concentrations, in order to select the one that provides a composition (pharmacoform) with the desired properties, e.g. physical form, grain size, malleability and plasticity.

There are differences presented in the international literature, concerning the effectiveness in bone regeneration of various marketed products, which have been attributed to the different methods of processing bone substance. Therefore, experiments were conducted to study the

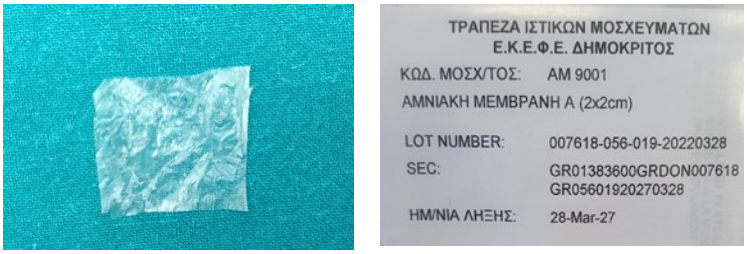
processing stage of the relevant bone allograft (lyophilized or not, demineralized or not) that will participate in the formulation.

The comparative study of demineralized and non-demineralized bone material requires the production of demineralized cancellous bone following a protocol previously studied at the Bank. The form (solution or powder) and concentration of the added hyaluronic acid were examined so that the product obtained had the desired pharmaceutical properties (paste viscosity, homogeneity and malleability).

Studies are ongoing to finalize the concentrations of the various components, although the first experimental findings tend to lead us to establish the use of specific percentages of hyaluronic acid, demineralized bone and PBS as basic components of the final product under formulation (confirmatory experiments are expected to consolidate the use of these components in these proportions).

At the same time, we are in the process of implementing the initial experiments to search for the ideal radiation dose that our product (bone graft/paste) can receive without affecting both its organoleptic abilities and structure.

The team continued to work on the study of development and implementation of new protocols for the preparation of membrane grafts from fetal membranes, with multiple uses in Reconstructive Regenerative Medicine (Collaboration with Drs. M. Leventis and Or. Vassiliadis dentists-implantologists).



The new products are safe and effective, help reduce surgical and recovery time, make use of additional materials, and excel in terms of better fit and use.

The production of improved and customized (special type) products also continues (Collaboration with Dr. Sp. Lazarou. Face-maxillofacial surgeon for infants and children).

For the implementation of our research activities there are collaborations with universities and hospitals that enable the assurance and supply of tissues - "raw materials", the processing of new tissues and application of new techniques that lead to constantly improving products evolving know-how and promoting Public Health.

Progress in 2023

In 2023, HTB collected tissues from various hospitals, with which there are relevant contracts in accordance with European and National Legislation. 6 new contracts were renewed or concluded with respective Public and Private Hospitals.

The tissues to be processed were taken from 309 living donors. They were collected in accordance with the applicable European Protocols and were stored and processed. We have also prepared 17 cranium grafts - autologous living.

995 bone grafts were prepared and made available for dental, neurosurgical and orthopaedic use. In addition, 20 amniotic membrane grafts were also delivered.

Announcements /Participation in Congresses
Conference of the Scientific Society of Oral Surgery 2023
Modern therapeutic approaches in dental clinical practice with emphasis on aesthetic restoration
Athens, 11 February 2023

Workshop of the Hellenic Transplant Organization (ETO)
"Modern Procedures and Quality of Transplantation in Greece"
Athens, 14 December 2023
Presentation (HTB, El. Vavouraki) as a "model body" (Decision of the Board of Directors of ETO, 12-09-2023, determining the Human Tissue Bank of the Institute of Biosciences and Applications "Demokritos", for the development of the quality-safety-biovigilance framework in the field of bone graft transplantation).
Co-funded NSRF Action, Subproject 2 "Development and implementation of a quality-safety-biovigilance management framework in health units and other bodies of the transplant system"

Online participation / attendance of Workshops/Events/Conferences
"Research in Greece in the 21st century: Needs and Prospects"
Online Conference of the Union of Greek Researchers (UGS), 13 March 2023

"Contemporary issues of ethics and law in Biological Sciences and Medicine"
3rd Hybrid Workshop of NCSR Research Ethics Committee
NCSR "Demokritos", 29 November 2023

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

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

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

Scientific Coordinator of YGEIA Innovations, spinoff of NCSR "D"

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

Member of the European Network of Tissue and Cell Bank Inspectors

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

Cooperation with the Ministry of Health and the HellenicTransplant Organization

Other Activities at IBA and NCSR "D"
Quality Manager of the Bank according to standard 9001/2015. Annual renewal of certification.

Member of the Centre's Committee on Health, Hygiene and Safety of Employees.

Working Groups of the Gender Equality Committee. framework of the Communication Action for the International Day of Girls and Women in Science.

Member - President Committee for the receipt and evaluation of offers of a Biopathologist – Microbiologist at NCSR "D".

Member of the election committee for the election of members of the Board of Directors of the Association of Researchers "D".

Member of Evaluation Committees of scientific collaborators in research projects in "D".

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

Organization of a two-day conference - 2nd Transnational Project Meeting. -within the framework of the above program at NCSR "Demokritos" 15 and 16 June 2023.

The meeting was co-organized with the research team of Dr. Omiros Papadopoulos, ICT Scientist Researcher. Project Manager for "D".

Educational activities
Teaching at the MSc of the University of Patras "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products",
Course Title: Research and Development of Tissue Grafts

Participation in the Annual Postgraduate Program of Implantology of the Hellenic Society of Oral and Maxillofacial Surgery:
Basic Principles of Implant Surgery and Prosthetics
Lecture Title: TISSUE GRAFTS IN DENTISTRY/IMPLANTOLOGY - LATEST DEVELOPMENTS, 28/1/2023, Athens

Member of the Advisory Committee/Supervision of postgraduate thesis within the framework of the Postgraduate Program: "Biomedical and Molecular Sciences in the Diagnosis and Treatment of Diseases", Democritus University of Thrace, Department of Medicine/TEI

Academic Advisor to postgraduate students in the framework of the MSc of the University of Patras "Applied Biochemistry: Clinical Chemistry, Biotechnology, Evaluation of Pharmaceutical Products"

Participation of the Laboratory in the educational program of the students/visitors of the Center entitled: DEMOKRITOS -A tour in the heart of Research.

Citations 2023 (without self- citations): 6

Total Citations 2019-2023 (without self- citations): 34

h-index: 10 (Scopus)

Current External Funding
The external funding of the Human Tissue Bank is based on private resources and research programs.

EXPERIMENTAL ANIMAL FACILITY

Personnel

Dimitris Kletsas, Research Director, Scientific and Administrative Responsible
Giannis Zafeiropoulos, Laboratory Animal Technician
George Doulgeridis, Laboratory Animal Caretaker
Lykourgos Klamarias, Veterinarian

Laboratory Description

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

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

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

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

Animal strains

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

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

During 2023, the Animal House supplied the following laboratory animals:

Users	Rats WISTAR	Mice SKH1	Mice CFW	Mice C57Bl/6J	Rabbits NZW	Mice SCID	Total
IBA	**0**	**36**	**164**	**314**	**10**	**143**	**667**
INRASTES	**25**	**0**	**123**	**0**	**0**	**160**	**308**
External users	**95**	**12**	**44**	**32**	**18**	**50**	**251**
Total disposal of laboratory animals	**120**	**48**	**331**	**346**	**28**	**353**	**1.226**

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

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

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

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

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

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

D. Kletsas is a Member of the National Committee for the Wellbeing of Laboratory Animals.

During 2023

The required laboratory animal procedure permissions were approved and issued, eighteen (18) protocols for animal experimentation were modified, renewed and executed in the Facility of Use of EL25BIOexp039.

Required health examinations of the animals of the Animal House were carried out in domestic and foreign specialized laboratories. The annual microbiological and chemical test of water was carried out and the necessary certificates were received.

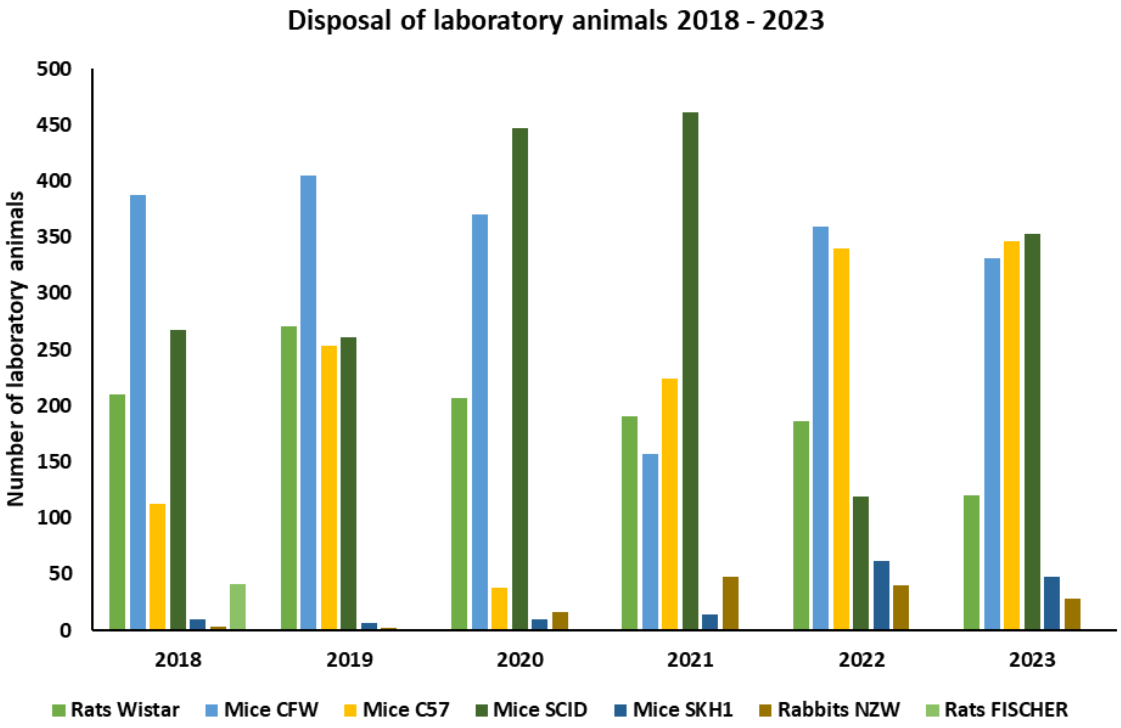
The breeding-disposal of the New Zealand (NZW) rabbit colony was extended to external users.

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

The Animal House regained accreditation of the Quality Management System to ELOT EN ISO 9001:2015. The Safety Regulation and the Regulation of Medical Inspection have been renewed.

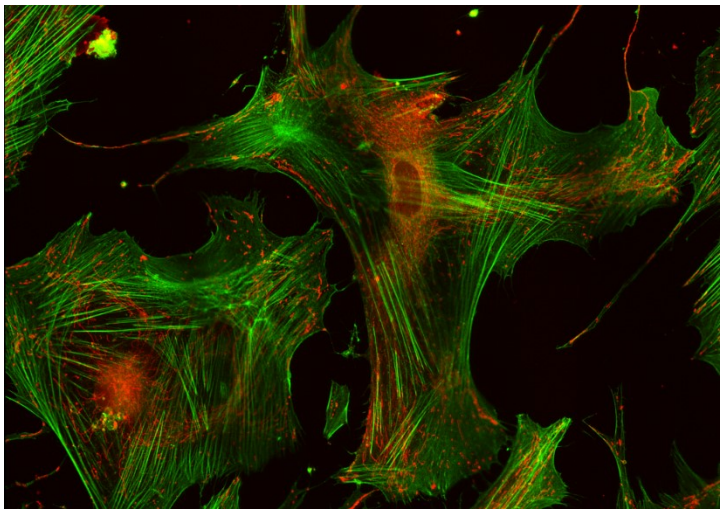
The contract with the company "LOCATE ITS" of the telemetry control system was renewed, for the recording, surveillance and immediate restoration of the mechanical equipment of temperatures and fresh air flow on a 24-hour basis. Building and mechanical upgrading of the facility and equipment of the Animal House continued. An air purification device was installed in the common areas of the Animal House.

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


Disposal of laboratory animals 2018 - 2023
Number of laboratory animals
500
450
400
350
300
250
200
150
100
50
0
2018
2019
2020
2021
2022
2023
Rats Wistar
Mice CFW
Mice C57
Mice SCID
Mice SKH1
Rabbits NZW
Rats FISCHER

LIGHT MICROSCOPY UNIT

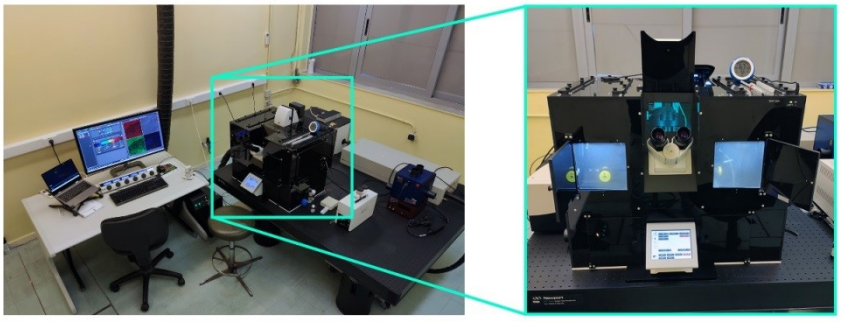
Personnel
Dimitris Kletsas, Research Director, Institute Director, Scientific and Administrative Responsible
Vassiliki Labropoulou, Research Director
Harris Pratsinis, Senior Researcher
Marina Sagnou, Senior Researcher
Alexandros Athanasopoulos, Scientific Staff



Laboratory Description – Progress during 2023

The Optical Microscopy Unit of the Institute of Biosciences and Applications (IBA) at NCSR "Demokritos" has been operational since July 2016 and is equipped with state-of-the-art instruments. These resources serve the imaging needs of the Institute's research laboratories, other institutes at NCSR "D", as well as external research centers, hospitals, and universities, including the National and Kapodistrian University of Athens (NKUA), the National Technical University of Athens (NTUA), the Agricultural University of Athens, and the University of Thessaly.

Leica TCS SP8 MP



The unit houses a confocal scanning microscope, equipped with a Nikon E600 upright optical microscope, and a cutting-edge Leica TCS SP8 MP multiphoton confocal microscope with a fully automated motorized stage. The system includes a climate-controlled chamber for strict management of environmental parameters (humidity, temperature, and gases such as CO_2, O_2, and N_2). The capabilities of the unit cover a wide range of optical microscopy applications, such as:

- Multi-channel confocal fluorescence microscopy, spanning ultraviolet, visible, and infrared spectra.
- Multicolor three-dimensional imaging (3D imaging).
- Live-cell imaging.
- Two-photon confocal microscopy.
- Second Harmonic Generation (SHG) imaging protocols.
- Förster/Fluorescence Resonance Energy Transfer (FRET) protocols for monitoring molecular interactions in live and fixed cells.
- Fluorescence Recovery After Photobleaching (FRAP) protocols.
- Colocalization analysis in cells and tissues.
- Calcium ion imaging.
- Differential Interference Contrast (DIC) microscopy, also known as Nomarski microscopy.
- Image processing and analysis: Specialized software such as ImageJ/Fiji and Imaris (Bitplane) is used for image and data analysis. Additionally, machine learning and deep learning techniques are employed for advanced bioimage analysis, encompassing structure recognition and classification, anomaly detection, and quantitative measurement of biological markers.

The Multiphoton Confocal Microscopy Unit recorded 1140 operational hours in 2023, a significant portion of which involved collaborations with external research centers and universities. The unit collaborated with research teams from the IBE and the INN, as well as with academic institutions, on protocols that included:

- Studying new chemical compounds aimed at discovering novel active agents or selective imaging substances.
- Investigating the induction of genotoxic damage and cellular aging.
- Examining the expression of specific proteins associated with the mechanisms of age-related disorders such as dyslipidemia, diabetes mellitus, and Alzheimer's disease.
- Researching the functional mechanisms of opioid receptors.
- Imaging and cellular localization of new dendrimers, liposomal formulations, and nanocarriers for the delivery of bioactive substances.
- Imaging biofilms in the nasal mucosa of patients with chronic rhinosinusitis and correlating them with the clinical characteristics of the patients.

The activities of the Microscopy Unit support the scientific work of multiple research teams, contributing to scientific publications, the completion of doctoral theses, and the development of collaborations among the unit's users. Additionally, the unit actively supports various educational programs at NCSR "Demokritos" by participating in presentations, conferences, and seminars across all educational levels.

Furthermore, the IBE participates in the project "Hellenic Research Infrastructure for Imaging and Monitoring of Fundamental Processes in Biology and Medicine (BIOIMAGING-GR)", funded by the General Secretariat for Research and Technology (GSRT). Alongside the IBE, this project involves ten additional institutions (universities and research centers).

HISTOLOGY UNIT

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

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.

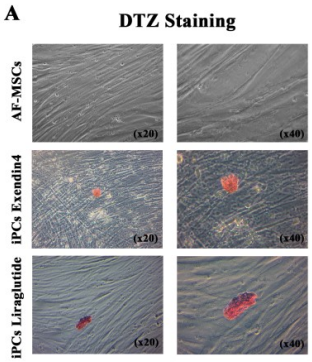
The HU supports the scientific work of several research groups and focuses on the investigation and phenotypic analysis at the tissue level of human and animal model specimens that are related to several pathologies, many of which derive from the Experimental Animal Facility of IBA.

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 2023 IBA HU, participated in research protocols regading the following:

- Mechanisms of pancreatic β-cells' apoptosis in Type II Diabetes Mellitus.
- The mode of action of liraglutide in the survival of glomerular podocytes of β-pancreatic cells.
- The protective role of the secretome of mesenchymal stem cells in the progression and treatment of Diabetic Nephropathy.
- Differentiation of insulin producing cells (IPCs) by mesenchymal stem cells
- Intervertebral disc degeneration
- Skin ageing
- Cancer development in experimental animal models



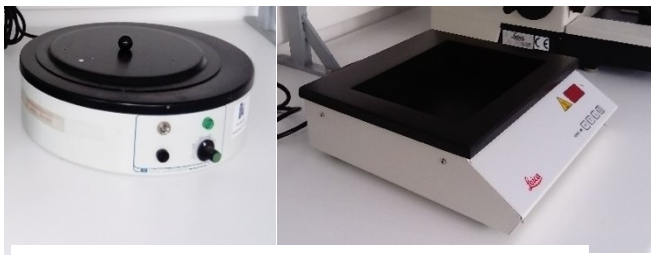
The main equipment of IBA HU consists of:

Cryostat Leica CM1850

Microtome Leica

Vibratome Leica

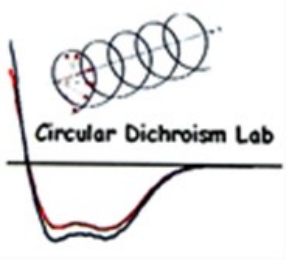
Water Baths Leica



Embedding oven (Jouan Percision)

CIRCULAR DICHROISM (CD) LABORATORY

Personnel
Metaxia Vlassi, Research Director
Maria Pelecanou, Research Director
Angeliki Panagiotopoulou, Functional Research Scientist B'



User Committee
Dr. Metaxia Vlassi
Dr. Maria Pelecanou
Dr. Angeliki Chroni
Dr. Georgios Nounesis (INRASTES)

Laboratory Description - Object
The equipment of the Circular Cichroism Laboratory (CD) includes a JASCO-715 spectropolarimeter equipped with Peltier system for temperature control. This CD infrastructure was acquired in 1998 within the framework of the "Center for Crystallographic Studies of Macromolecules (CCM)", which was financed through a grant (EPET) from the General Secretariat for Research and Technology as a network of three Institutes of NCSR "Demokritos" (the former Biology, Physical Chemistry, Radioisotopes & Radiodiagnostics Products) and other Greek academic institutions. It is located at room Y-35 of the Institute of Biosciences & Applications and is operating under the supervision of IB-A scientists. Since 2013 (13/06/2013), the CD Lab is included in the category of Specialized Services of NCSR "D", whereas in 2018, after re-categorization, the service was classified in the category of Specialized Services with Research Activity (decision of the Board of Directors 28-03-2018, Protocol # 010/2018-299 4/4/2018).

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

- Conformational analysis of biological macromolecules (e.g. proteins)
- Investigation of protein-protein interactions as well as interaction/complexation of proteins with various ligands, metals, stabilizers, inhibitors, drugs, etc.
- Monitoring conformational changes of biological macromolecules under different conditions
- Comparative structure-thermal stability studies of proteins under various conditions

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

Progress in 2023
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 2023, as in previous years, the CD Lab has supported research projects of six groups of the three participating NCSR "D" Institutes (IB-A, INRASTES, INN) and other Greek academic institutions, such as the National and Kapodistrian University of Athens (Pharmaceuticals, and Chemistry Depts), the University of Patras (Biology Dept), the Aristotle University of Thessaloniki (Chemistry

Dept), the University of Thessaly (Biochemistry & Biotechnology Dept) and the Agricultural University of Athens (Biotechnology Dept).

Like in the previous years, income from the provision of services is solely used to cover the operation and repair needs of the spectrophotometer. More specifically, in March 2023 the equipment was sent to Jasco Europe in Italy, for repair. All expenses (transport to/from Italy, successful repair) were covered partly by the CD lab income and by grants of the researches in charge of this service.

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

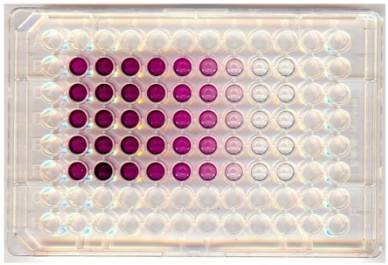
LABORATORY OF CELL-BASED ASSAY SYSTEMS AND BIOACTIVE COMPOUNDS

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

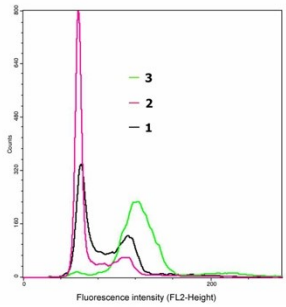
Description
The activities of the Laboratory comprise the isolation of primary somatic or mesenchymal stem cells, and the development of the appropriate cell assay systems for the evaluation of synthetic or natural bioactive products regarding their wound healing, anti-ageing, and anti-cancer properties.

2023 Findings
During 2023, the service lab concluded its collaboration with the company UNI-PHARMA SA for the study of compounds with putative senolytic or senomorphic activity, while it continued the collaboration 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.

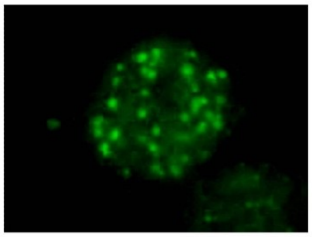
CYTOTOXICITY ASSESSMENT



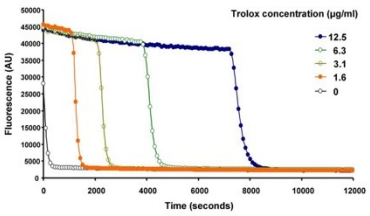
CELL-CYCLE ANALYSIS



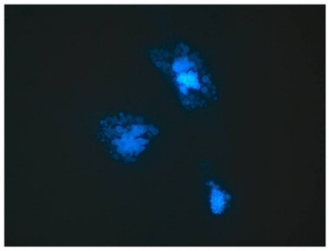
DNA DAMAGE ANALYSIS



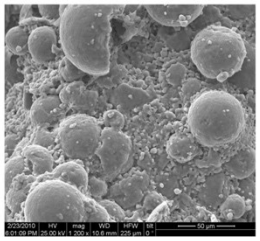
ANTIOXIDANT ACTIVITY ASSAY



STUDY OF APOPTOSIS



ORGANOTYPIC CELL CULTURES



EDUCATIONAL ACTIVITIES

EDUCATION

The Institute of Biosciences and Applications has continued the successful implementation of a variety of educational programs and activities in 2023, which include:

a) training of postdoctoral researchers
b) training of undergraduate students and the supervision of postgraduate (PhD, MSc and diploma) students to successfully complete their projects,
c) organization of postgraduate level seminars,
d) participation of IBA researchers in courses and lectures within the framework of postgraduate programs of several Greek Universities
e) participation of IBA researchers as instructors in the Annual Summer School of NCSR "Demokritos" for undergraduate and graduate students,
f) organization of Summer Schools for Lyceum students
g) 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 2023, **12** postdoctoral researchers were trained at IBA, while, **15** PhD students and **18** 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, 13 undergraduate students from Greek Universities performed their final year project at IBA. Additionally, 6 undergraduate students undertook research practice in IBA laboratories.

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

- Lecture entitled "Molecular mechanisms of carcinogenesis and pharmaceutical inhibition of selected therapeutic cellular targets" in the framework of the Post-Graduate Specialization Diploma "Drug development: Research, commercialization and accessibility" (**Dr. G. Voutsinas**, Medical School, University of Athens)
- Lecture entitled "Molecular mechanisms of carcinogenesis and pharmaceutical inhibition of selected therapeutic cellular targets" in the framework of the Post-Graduate Specialization Diploma "Applications of Biology in Medicine" (**Dr. G. Voutsinas**, Department of Biology and Medical School, University of Athens)
- 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 "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 "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 *"Tissue imaging applications"* in the framework the Postgraduate Master’s Degree "Musculoskeletal Oncology: Diagnosis-Treatment-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 “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) " Stress Science and Health Promotion", (**Dr. I. Sotiropoulos**, Medical School, National and Kapodistrian University of Athens)
- Teaching at the postgraduation (Master) course (4 hours) “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/per course) 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) (**Dr. I. Sotiropoulos**).
- 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)
- Teaching in the framework the Postgraduate Master’s Degree “Current Trends in Agricultural Pharmacology” (**Dr. M. Konstantopoulou**, Agricultural 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 2023, within the framework of the 56th NCSR “Demokritos” Summer School, IBA researchers delivered a series of lectures on various frontier subjects of biological interest (see list below).

In 2023, the operation of the Interdepartmental 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" continued. 12 Students were enrolled in this MSc Programme. They have completed the courses and are currently performing 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 “*Lateral compartmentalization and function of plasma membrane: eisosomes*
    and transmembrane transporters” (**Dr. V. Sophianopoulou & Dr. C. Gournas**)

- Molecular Pharmacology – Immunology
  - Lecture entitled *“Viral Immunology & Pharmacology (focus on SARS-CoV-2 and COVID-19)”* **(Dr. L. Swevers**)
  - Lecture entitled *“Enzymes, receptors and drugs”* **(Dr. A. Papakyriakou)**
  - Lecture entitled *“DNA: structure, function and binding of drugs”* **(Dr. M. Sagnou)**
  - Lecture entitled “*GPCRs in health, disease and drug development*” **(Dr. Z. Georgoussi)**
  - Lecture entitled “*New therapeutic approaches for Alzheimer's disease: pathobiology, biomarkers and new targets”* **(Dr. I. Sotiropoulos)**

- 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 *"Cardiavascular diseases and current therapeutic approaches"* **(Dr. A. Chroni)**

Furthermore, in 2023 the IBA researchers **Drs. Z. Georgoussi** and **I. Sotiropoulos** participated for another year in the joined MSc Programme **"Athens International Master's Programme in Neurosciences"**

In 2023, the Institute organized the 3rd Summer School for Lyceum students. The two-week school (26/6/2023 - 7/7/2023), which was attended by 19 students from various schools in Attica, included a series of visits to the Institute's laboratories and information about the research activities of the Institute and gave the opportunity to the students to get in touch with modern molecular, cellular and biochemical experimental techniques. The students were divided into groups and carried out two research projects (one per week) in laboratories of the Institute. Upon completion of the research projects the students presented their results to the members of the IBE, as well as to their teachers and parents. The Institute's researchers that participated in the Summer School were: **Drs. G. Drossopoulou, P. Kitsiou, V. Sofianopoulou, G. Voutsinas, D. Kletsas, H. Pratsinis, E. Mavrogonatou, Z. Georgoussi, I. Sotiropoulos, A. Chroni, A. Papakyriakou, M. Pelekanou, M. Sagnou, L. Swevers** and **V. Labropoulou**.

Additionally, weekly guided tours and briefings of High School and Lyceum students, as well as University students about the research activities of the Institute were performed by **Drs. H. Pratsinis** and **A. Prombona**.

COMPLETION/AWARD OF DOCTORAL THESES IN 2023

POSTGRADUATE STUDENT	TITLE OF MSc THESIS	IBA SUPERVISOR	UNIVERSITY
Maria Angelopoulou	*Study of antioxidant and photoprotective action of natural products*	D. Kletsas	Pharmacy Department, NKUA
Eleni Liakou	*Study of paracrine interactions between stromal and breast cancer cells. The role of cellular senescence.*	D. Kletsas	Chemistry Department, University of Patras
Amalia Megarioti	*The organization of the fungal plasma membrane in the quiescent state*	C. Gournas	Biology Department, NKUA
Nastazia-Lemonia Lesgidou	*Studies of disease-associated proteins structure and dynamics through Molecular Dynamics simulations.*	M. Vlassi	Department of Molecular Biology and Genetics, Democritus University of Thrace

COMPLETION OF MASTER THESES IN 2023

POSTGRADUATE STUDENT	TITLE OF MSc THESIS	IBA SUPERVISOR	UNIVERSITY
Maria Karanikou	*Applications of plant-derived vesicles to human cells: cytotoxicity and cell proliferation studies*	H. Pratisnis	Dep. Mechanical Engineering, Western Macedonia Univ.
Anastasia Kypreou	*Study of Interleukin 6 expression in normal (young and aged) and cancer cells*	D. Kletsas	Interdepartmental MSc Programme NCSRD/U. Patras
Marina Kavellari	*Study of Interleukin 8 expression in aged and cancer cells as a biomarker of inflammatory response*	D. Kletsas	Interdepartmental MSc Programme NCSRD/U. Patras
Daphne-Alexandra Kavoura	*Bioactivity of carob and its seeds in human skin cells: a comparative study of two Cretan varieties*	H. Pratisnis	Pharmacy Department, NKUA
Dimitris Lymperopoulos	*Effect of polyphenolic-rich Corinthian currant extract on the expression and activity of the antioxidant enzyme paraoxonase 1 (PON1): Association with Alzheimer's disease*	A. Chroni	Biology Department, NKUA
Spyros Gerostathis	*Study of subcellular localization and antifungal properties of polymeric nanoparticles in the hyphomycete A. nidulans*	V. Sophianopoulou	Interdepartmental MSc Programme NCSRD/U. Patras

IBA LECTURES' CONTRIBUTION TO THE 2023 SUMMER SCHOOL

DATE	SPEAKER	TITLE
14/7/2023	**Dr. L. Swevers**	Virus infection of the insect brain and modification of larval behavior
14/7/2023	**Dr. A. Chroni**	Dyslipidemia: the great enemy of the heart and blood vessels
14/7/2023	**Dr. E. Mavrogonatou**	The cell biology of intervertebral disc degeneration and aging
14/7/2023	**Dr. H. Pratsinis**	In vitro studies of natural and synthetic bioactive products
14/7/2023	**Dr. A. Papakyriakou**	The discovery of the antiviral drug PAXLOVID: How Pfizer brought a compound to clinical trials in less than 12 months
14/7/2023	**Dr. M. Sagnou**	The drug development roadmap: from bench to clinic

2023 INVITED SPEAKERS SEMINARS

DATE	SPEAKER	TITLE
27/10/2023	**Prof. Dimitris Kardassis** School of Medicine, University of Crete	Fatty Liver & Risk of Cardiovascular Disease: New data from genetic studies in animal models

COLLECTIVE DATA

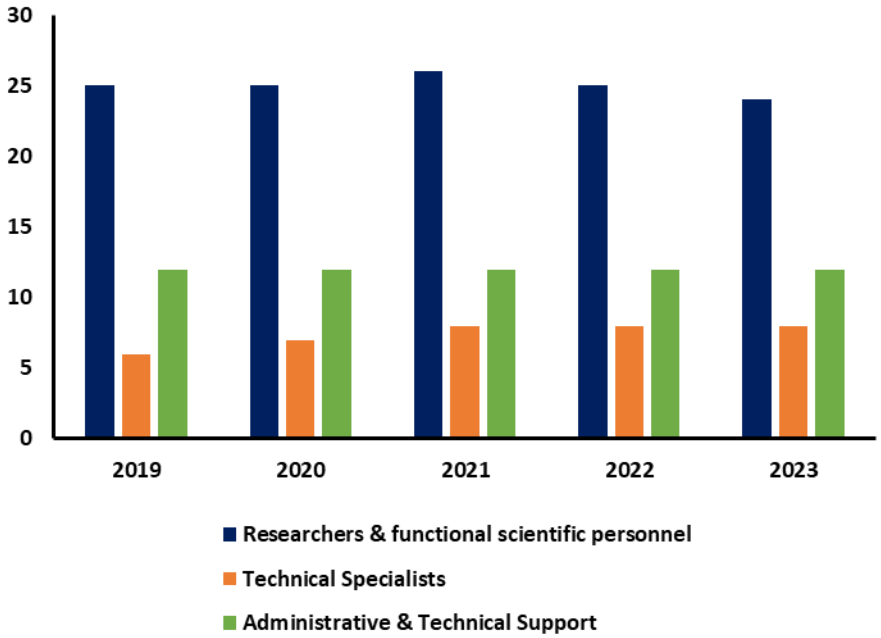
SUMMARIZED DATA ON THE PRODUCTIVITY OF SCIENTIFIC PROGRAMMES

	PROGRAMME			
	A	**B**	**C**	**INSTITUTE**
Researchers & functional scientific personnel	10	7	6	24[a]
Technical Specialists	1	1	-	8[b]
Collaborating & Emeritus Scientists	3	1	0	7[c]
Postdoctoral Fellows	8	2	1	12[d]
PhD candidates	8	5	2	15
MSc students	14	1	2	18[e]
Graduate Research Associates	7	4	3	16[f]
Undergraduate and other training students	17	3	4	24
Administrative and Technical Support	-	-	-	12
Total Personnel	**68**	**24**	**18**	**138**
Publications in Peer-Reviewed Journals	**14**	**19**	**11**	**45[g]**
Cumulative Impact Factor in Peer-Reviewed Journals	**129.700**	**37.000**	**56.271**	**225.571[g]**
Proceedings in Conferences	**3**	**1**	**-**	**4**
Total Publications				**49**
Citations	**2161**	**722**	**724**	**4337[h]**
International Patents	**-**	**-**	**1**	**1**
Greek Patents	**-**	**-**	**-**	
Presentations in International Conferences	**25**	**5**	**4**	**34**
Presentations in National Conferences	**27**	**1**	**2**	**33[i]**
Total Number of Presentations in Conferences	**52**	**6**	**6**	**56[i]**

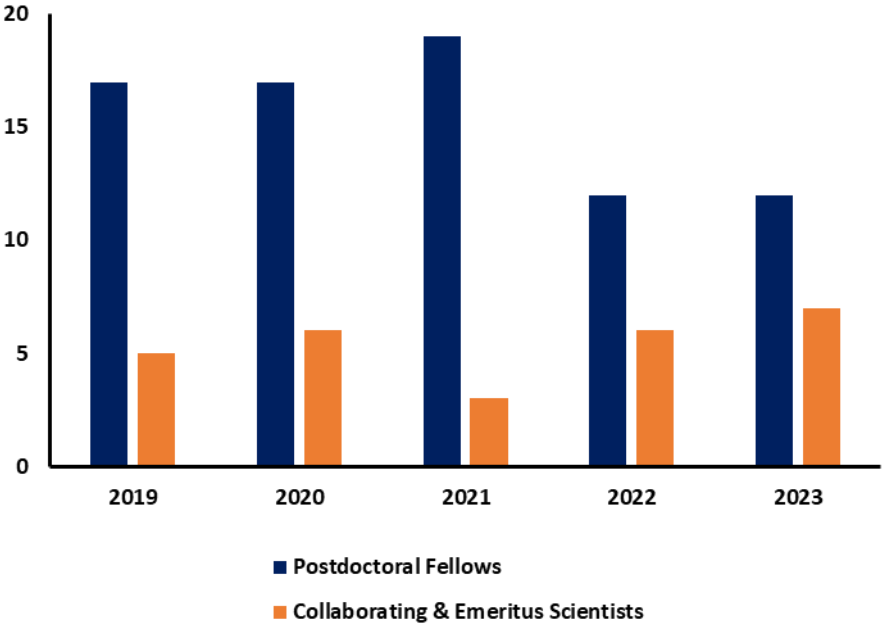
[a] 1 Scientist of the Human Tissue Bank included
[b] 4 Technical Specialists of the Laboratory for Doping Control and Metabolic Studies and 2 Technical Specialists of the National Infrastructure OPENSCREEN-GR included
[c] 3 Collaborating Scientists of the Human Tissue Bank included
[d] 1 Postdoctoral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

CHANGES IN IBA STAFF DURING 2019-2023

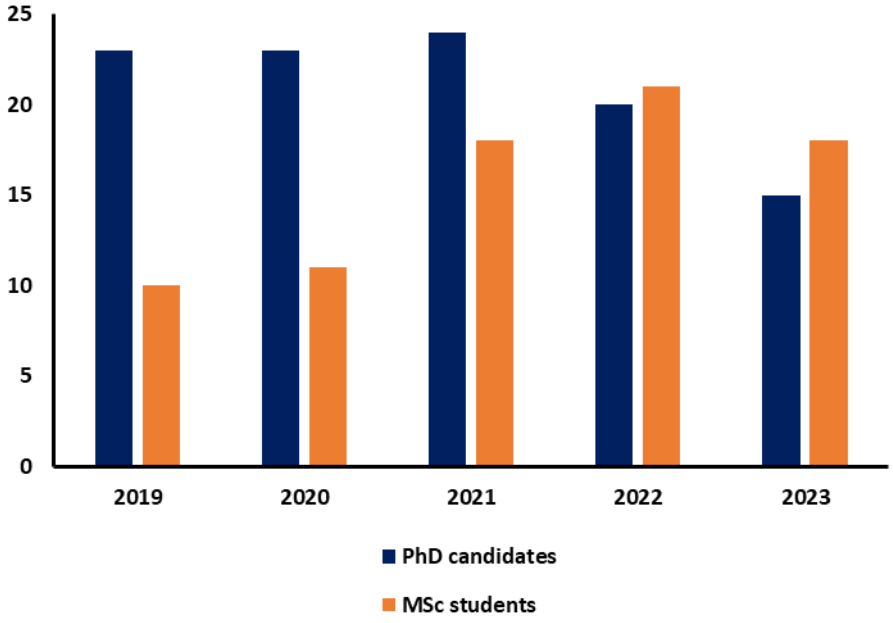
Tenured Staff



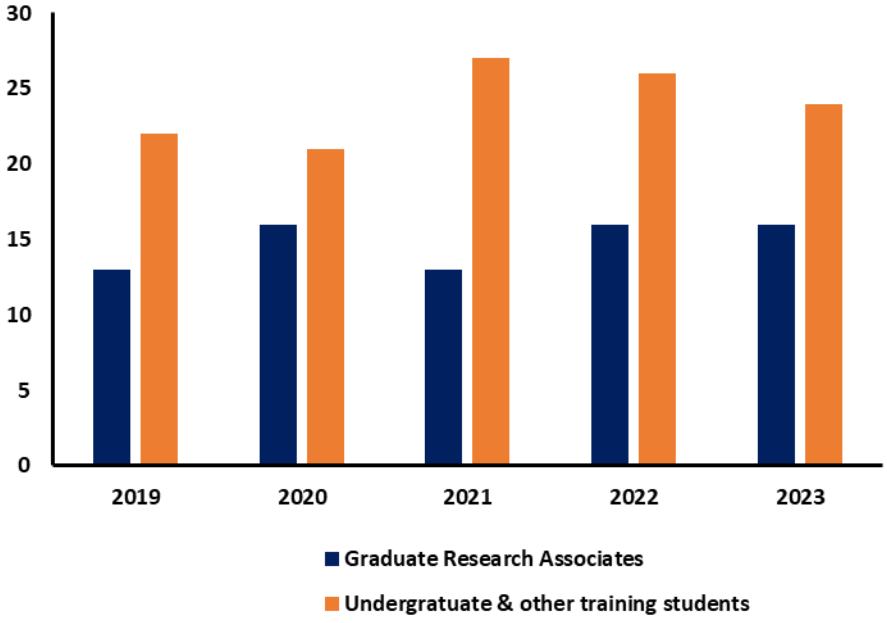
Postdoctoral fellows/ Emeritus & Collaborating Scientists



PhD candidates / MSc students

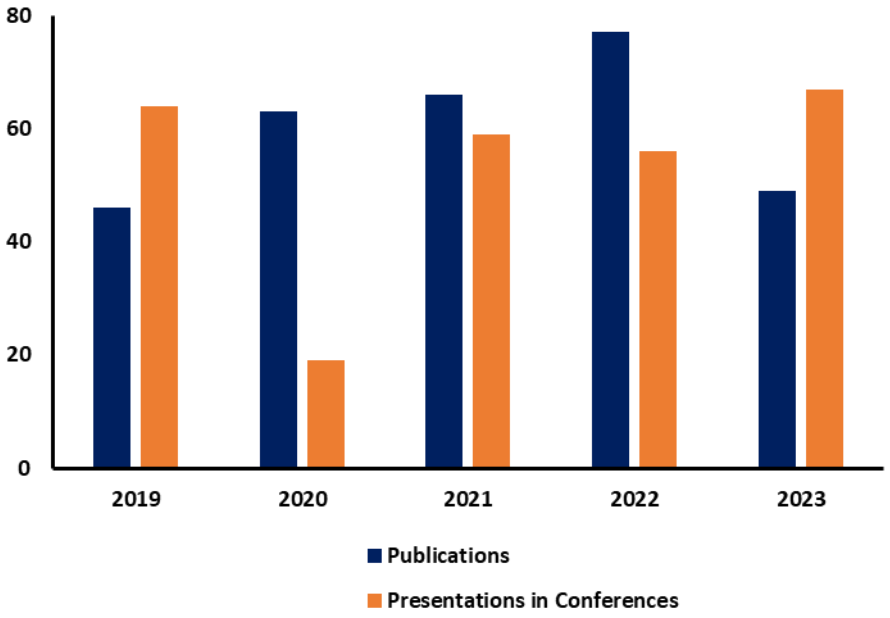


Graduate Research Associates / Undergratuate & other training students



QUALITATIVE AND QUANTITATIVE DATA ON IBA PUBLICATIONS DURING 2019-2023

Publications in peer-reviewed Journals / Presentations in Conferences



Citations