INSPIRING DISCOVERIES

BIOMEDICAL
SCIENCES
RESEARCH CENTER
“ALEXANDER FLEMING”

"ALEXANDER FLEMING"
Biomedical Sciences Research Center

H.F.R.I.
Hellenic Foundation for Research & Innovation

"Science and Society"
"Research, Innovation and Dissemination Hubs"

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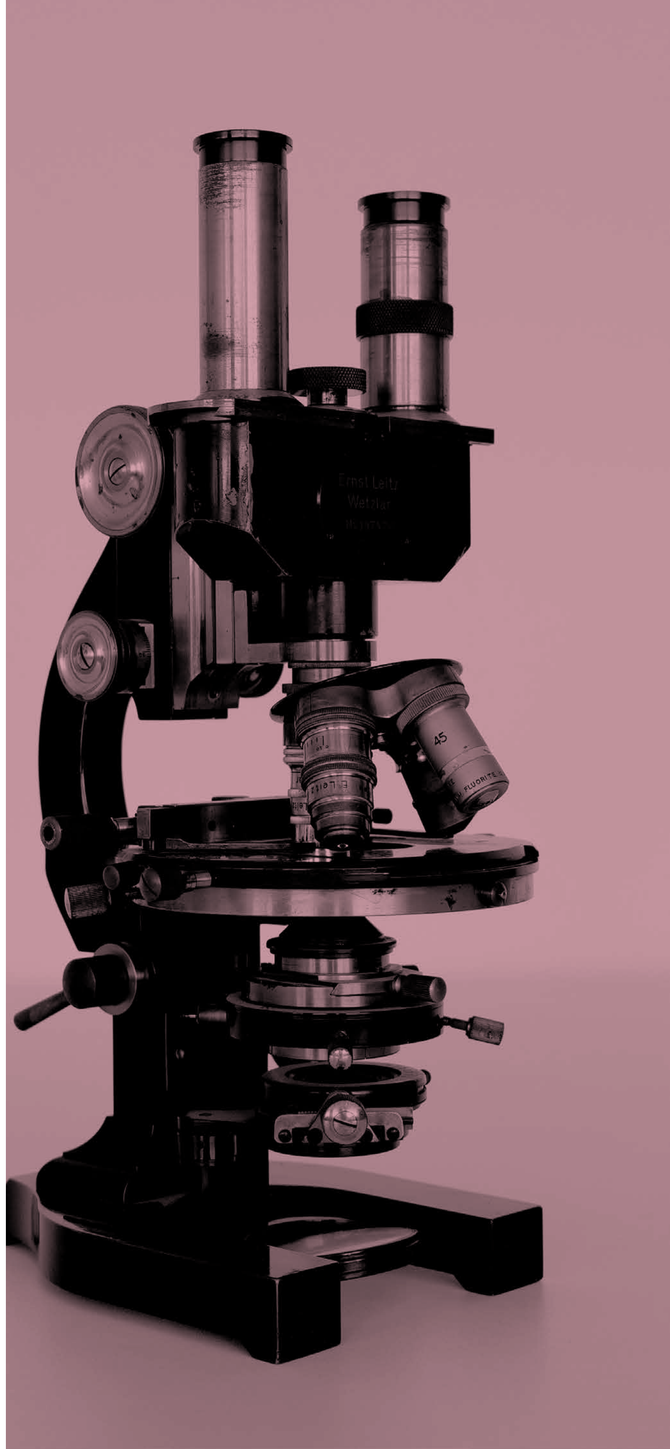
The **Biomedical Sciences Research Center "Alexander Fleming" (FLEMING)** is a top-ranked non-profit research organization with a mission to perform cutting edge **basic and translational research** in biomedical sciences, provide state-of-the-art **training and mentorship** to scientists and students of all levels, offer high-end scientific and technological services, and engage in **technology transfer and innovation.**

It comprises the newly established Institute for Bioinnovation (IBI) and the Institute for Fundamental Biomedical Research (IFBR). While the main focus of IFBR is unravelling the molecular and cellular basis of disease via novel animal models of human pathologies, IBI's vision is to advance fundamental research achievements towards innovative translational biotechnologies and drug development. The Institutes share all facilities, and collaborate within **distinct research directions** in Immunity & Inflammation, Neuroscience, Cancer Biology, RNA Biology & Epigenetics, Bioinformatics & Computational Biology and Biomolecular Engineering & Synthetic Biology.

The last assessment by an international General Secretariat for Research and Innovation (GSRI)-organized scientific committee, concluded that FLEMING is **at the top of research institutes in Greece** considering its publications, funding, and appointments of world-caliber investigators. FLEMING researchers are established in their fields, have an excellent record in attracting research funding, including highly competitive grants from sources such as the European Research Council (ERC). FLEMING's bibliometric output is top-ranked by the National Documentation Center and its training and educational activities are of a very high standard and form an integral part of all FLEMING researchers' work.



“FLEMING was and remains one of the Top institutes in Greece and it is actually based right at the Top if one considers specific metrics.

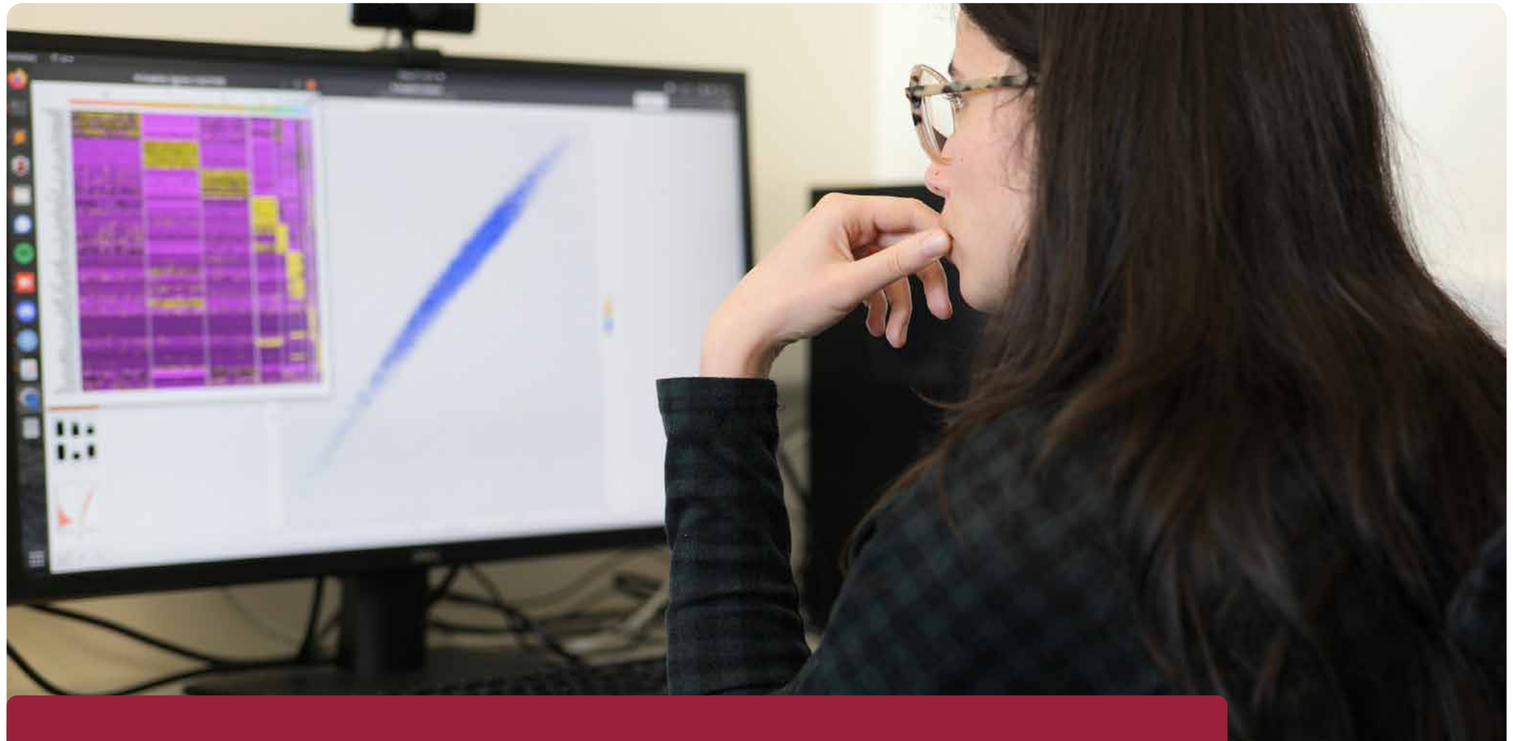
The institute maintains a number of world-caliber established investigators who continue to lead and at the same time publish and attract funding.

FLEMING also has a number of younger potential future stars that could take over in the next few years and be the next leaders of the institution and research not only in FLEMING but also Greece”

(Excerpt from the Center’s 2022 International Scientific Committee evaluation report)

FLEMING's strength and international recognition arises from pioneering research towards understanding the **molecular and cellular basis of human diseases,** and development and validation of **relevant animal models of** chronic inflammatory diseases, neurodegenerative disorders, metabolic diseases, cancer and autoimmune syndromes among others and the development of new approaches for their diagnosis and treatment, using transdisciplinary approaches and state-of-the art technologies.

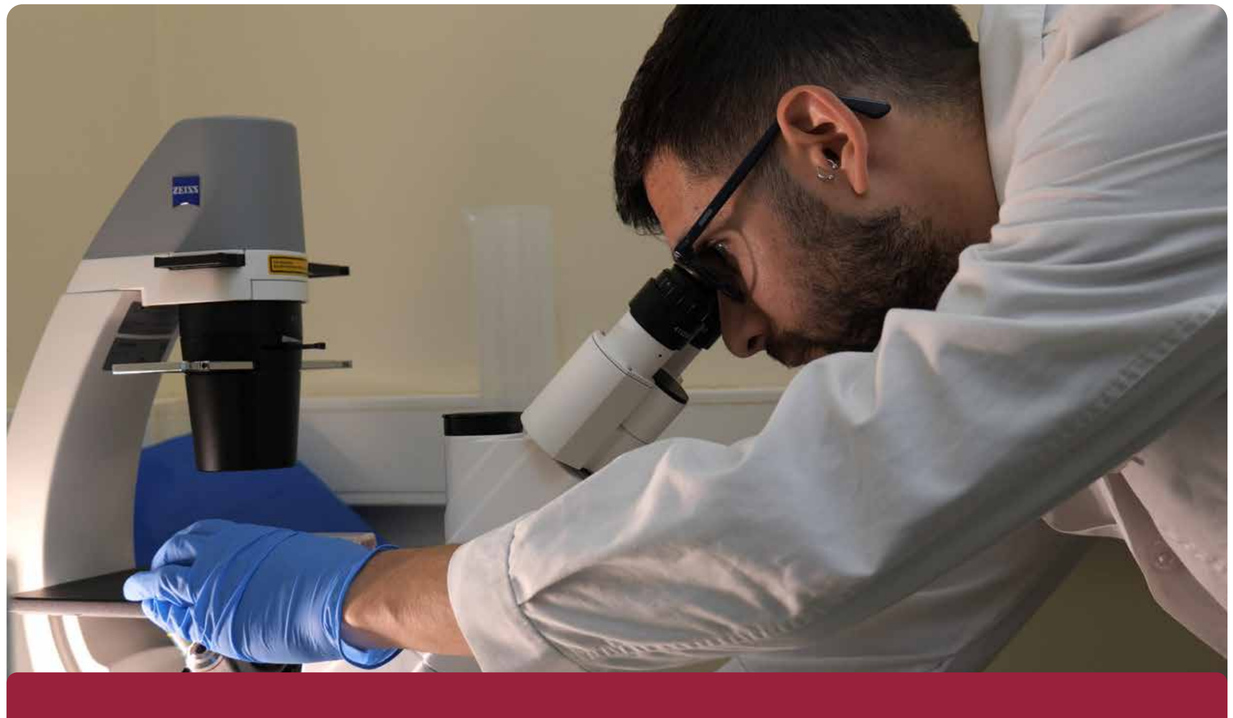
The excellent work of FLEMING research teams would not be possible without the **active involvement of our support staff** who ensure the seamless operation of the Center. They include the administrative, financial and procurement personnel, human resources team, the legal service, the grant management officers, the tech support and IT support officers, the technology transfer experts, the press office, the facilities' personnel, the health and safety teams, and the maintenance and janitorial personnel.



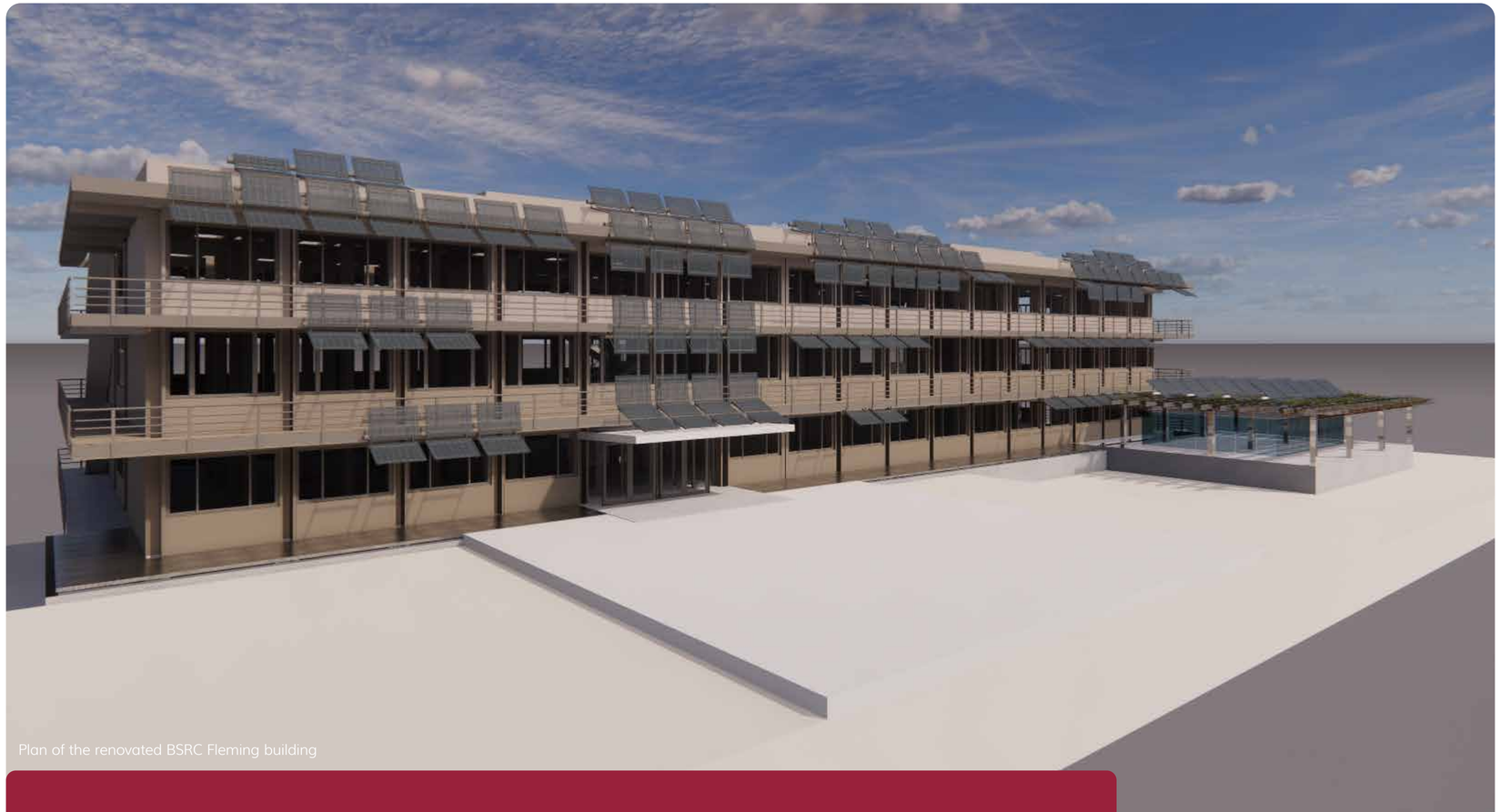
FLEMING places particular emphasis on establishing, maintaining, and continuously updating the **state-of-the-art facilities** that offer services for biomedical research internally, but also to researchers and companies locally and abroad.

They include an **Animal House** (currently with the highest capacity in Greece), as well as a **PhenoClinic**, and **Transgenesis, Gene Targeting and Cryopreservation**, **MicroCT Imaging**, **Histopathology**, **Bioimaging**, **Flow Cytometry**, **Single Cell Analysis**, **Genomics**, **Proteomics** and **Bioinformatics** Units.

FLEMING coordinates the **InfrafrontierGR/Phenotypos**, a National Research Infrastructure (NRI) for generating, archiving and phenotyping of animal models of disease, as well as the **ELIXIR-GR** NRI for bioinformatics/biocomputing resources. FLEMING also participates in the **Bioimaging-GR** NRI that aims to provide high quality imaging services for examining fundamental biological processes, as well as the NRI for Personalised Medicine **pMedGR**, in collaboration with the Medical School of Athens and the oncology network NRI **Oncology Precision Medicine**.



To continue its successful trajectory, FLEMING will **further upgrade its infrastructure and facilities** through a grant from the EU Recovery & Resilience Fund. The renovation of the building will include new safety, energy and environmental efficiency standards and equipment upgrading to state-of-the-art instrumentation. In addition, FLEMING has obtained an initial approval by the European Investment Bank for construction of the **Biotechnopolis Park** for Science, Arts and Technology – an innovative biotechnology hub for the Attica region which will cover approximately 12,000 sq.m. of laboratory and office space for startups, R&D units, research labs and facilities.



Plan of the renovated BSRC Fleming building

The intellectual output from FLEMING's research programs, protection and exploitation of research results is monitored and mediated by the **Innovation and Entrepreneurship Unit (IEU)**, which has already established 11 patent portfolios around core Fleming technologies, finalized more than 600 outgoing MTAs worldwide for mouse models, genetic tools and other innovations and has concluded several licensing contracts with industry. Furthermore, the IEU has overseen the establishment of Fleming's first spin-off company, **Biomedcode**, which provides full preclinical drug evaluation services to pharmaceutical companies worldwide, commercializing proprietary animal models of chronic inflammatory diseases, as well as the recently established spin-off company, **MABY**, which develops novel monoclonal antibodies for the pharmaceutical industry and academia.

FLEMING PERSONNEL:
OUR MOST IMPORTANT ASSET

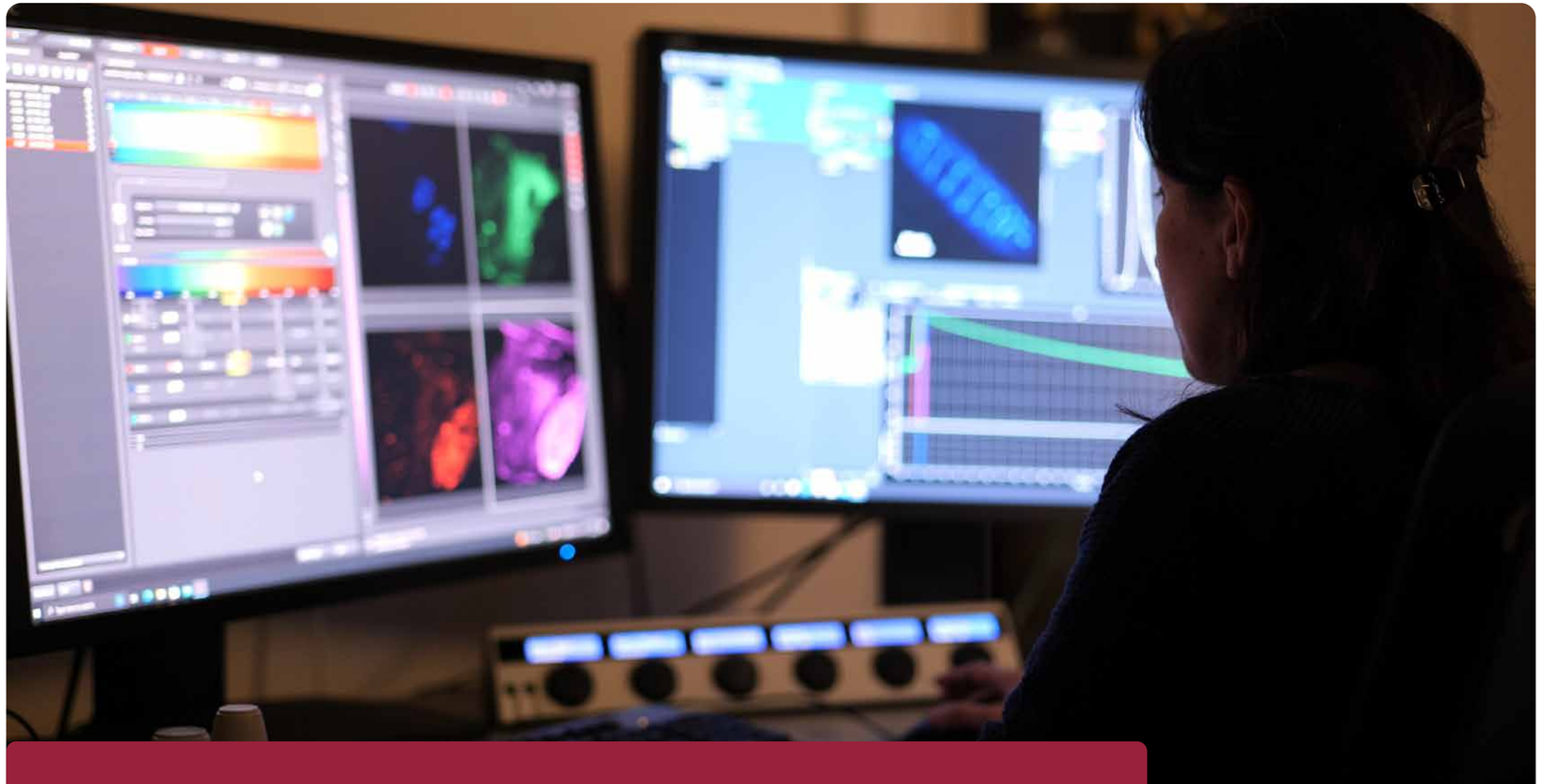
ΛΙΓΑ ΛΟΓΙΑ ΓΙΑ ΕΜΑΣ

Το Ερευνητικό Κέντρο Βιοϊατρικών Επιστημών “Αλέξανδρος Φλέμιγκ” είναι ένας κορυφαίος μη κερδοσκοπικός ερευνητικός οργανισμός με αποστολή να διεξάγει **βασική και μεταφραστική έρευνα** αιχμής στις βιοϊατρικές επιστήμες, να παρέχει υψηλού επιπέδου **εκπαίδευση και καθοδήγηση** σε επιστήμονες και φοιτητές όλων των επιπέδων, να προσφέρει ποιοτικές **επιστημονικές και τεχνολογικές υπηρεσίες** και να ασχολείται με τη **μεταφορά τεχνολογίας και την καινοτομία.**

Περιλαμβάνει το νεοσύστατο Ινστιτούτο Βιοκαινοτομίας (IBK) και το Ινστιτούτο Βασικής Βιοϊατρικής Έρευνας (IBBE). Ενώ ο κύριος στόχος του IBBE είναι η αποκάλυψη της μοριακής και κυτταρικής βάσης των ασθενειών μέσω νέων ζωικών μοντέλων ανθρώπινων παθολογιών, το όραμα του IBK είναι να προωθήσει τα επιτεύγματα της βασικής έρευνας προς καινοτόμες μεταφραστικές εφαρμογές στη βιοτεχνολογία και την ανάπτυξη φαρμάκων. Τα Ινστιτούτα μοιράζονται όλες τις εγκαταστάσεις και συνεργάζονται στο πλαίσιο διακριτών **ερευνητικών κατευθύνσεων** στους τομείς της ανοσίας και της φλεγμονής, της νευροεπιστήμης, της βιολογίας του καρκίνου, της βιολογίας RNA και της επιγενετικής, της βιοπληροφορικής και υπολογιστικής βιολογίας, και της βιομοριακής μηχανικής και συνθετικής βιολογίας.

Η εξαιρετική απόδοση των ερευνητικών ομάδων του ΦΛΕΜΙΓΚ δεν θα ήταν δυνατή χωρίς την **ενεργή συμμετοχή του υποστηρικτικού προσωπικού**, που εγγυάται την αδιάλειπτη λειτουργία του Κέντρου. Σε αυτό περιλαμβάνεται το διοικητικό προσωπικό και οι οικονομικές υπηρεσίες, το γραφείο προσωπικού, το τμήμα προμηθειών, το γραφείο υποστήριξης ερευνητικών προγραμμάτων, η τεχνική υπηρεσία και το γραφείο πληροφορικής, η νομική υπηρεσία, το γραφείο μεταφοράς τεχνολογίας, το γραφείο τύπου και επικοινωνίας της επιστήμης, το προσωπικό των μονάδων, οι ομάδες υγιεινής και ασφαλείας και το προσωπικό συντήρησης και καθαριότητας.

Η τελευταία αξιολόγηση από διεθνή επιστημονική επιτροπή που οργάνωσε το ΓΓΕΚ το 2014, **κατέταξε το ΦΛΕΜΙΓΚ στην πρώτη θέση** μεταξύ των ελληνικών ερευνητικών ινστιτούτων που δραστηριοποιούνται στις βιοϊατρικές επιστήμες, με βάση την αριστεία σε ανταγωνιστικές χρηματοδοτήσεις, ερευνητικές δημοσιεύσεις και εκπαιδευτικό έργο. Οι ερευνητές του ΦΛΕΜΙΓΚ έχουν εξαιρετικές επιδόσεις στην προσέλκυση ερευνητικής χρηματοδότησης, συμπεριλαμβανομένων **ιδιαίτερα ανταγωνιστικών επιχορηγήσεων** από πηγές όπως το Ευρωπαϊκό Συμβούλιο Έρευνας (ERC). Η **βιβλιομετρική παραγωγή του ΦΛΕΜΙΓΚ** κατατάσσεται στην κορυφή της κατάταξης από το Εθνικό Κέντρο Τεκμηρίωσης και οι **δραστηριότητες κατάρτισης και εκπαίδευσης** είναι πολύ υψηλού επιπέδου και αποτελούν αναπόσπαστο μέρος της εργασίας όλων των ερευνητών του ΦΛΕΜΙΓΚ.



«Το ΦΛΕΜΙΓΚ ήταν και παραμένει ένα από τα κορυφαία ιδρύματα στην Ελλάδα και στην πραγματικότητα βρίσκεται ακριβώς στην κορυφή, αν λάβει κανείς υπόψη του συγκεκριμένες μετρήσεις. Το Ινστιτούτο διατηρεί έναν αριθμό καταξιωμένων ερευνητών παγκόσμιου βεληνεκούς που συνεχίζουν να ηγούνται και ταυτόχρονα να δημοσιεύουν και να προσελκύουν χρηματοδότηση.

Το ΦΛΕΜΙΓΚ διαθέτει και έναν αριθμό νεότερων εν δυνάμει μελλοντικών αστέρων, που θα μπορούσαν να αναλάβουν τα επόμενα χρόνια και να αποτελέσουν τους επόμενους ηγέτες του ιδρύματος και της έρευνας όχι μόνο στο ΦΛΕΜΙΓΚ αλλά και στην Ελλάδα»

(Απόσπασμα από την έκθεση αξιολόγησης Διεθνούς Επιστημονικής Επιτροπής για το Κέντρο το 2022)

Η ισχύς και η διεθνής αναγνώριση του **ΦΛΕΜΙΓΚ** απορρέει από την πρωτοποριακή έρευνα για την κατανόηση της **μοριακής και κυτταρικής βάσης των ανθρώπινων ασθενειών** και την ανάπτυξη και επικύρωση **σχετικών ζωικών μοντέλων** χρόνιων φλεγμονωδών ασθενειών, νευροεκφυλιστικών διαταραχών, μεταβολικών ασθενειών, καρκίνου και αυτοάνοσων συνδρόμων μεταξύ άλλων, καθώς και την ανάπτυξη νέων προσεγγίσεων για τη διάγνωση και τη θεραπεία τους, χρησιμοποιώντας διεπιστημονικές προσεγγίσεις και τεχνολογίες αιχμής.

Το ΦΛΕΜΙΓΚ δίνει ιδιαίτερη έμφαση στη δημιουργία, τη διατήρηση και τη συνεχή αναβάθμιση των **υπερσύγχρονων υποδομών** που προσφέρουν υπηρεσίες για τη βιοϊατρική έρευνα στους ερευνητές του ΦΛΕΜΙΓΚ, αλλά και σε εξωτερικούς ερευνητές και εταιρείες σε τοπικό και διεθνές επίπεδο.

Περιλαμβάνουν Εγκαταστάσεις Ζώων Εργαστηρίου (επί του παρόντος τις μεγαλύτερες στην Ελλάδα), μια Φαινοκλινική, καθώς και Μονάδες Διαγένεσης και Κρυοσυντήρησης MicroCT Απεικόνισης, Ιστοπαθολογίας, Βιοαπεικόνισης, Βιοπληροφορικής, Κυτταρομετρίας Ροής, Ανάλυσης Μοναδιαίων Κυττάρων, Πρωτεωμικής και Γονιδιωματικής.

Το ΦΛΕΜΙΓΚ συντονίζει την InfrafrontierGR/Phenotypos, μια Εθνική Ερευνητική Υποδομή (ΕΕΥ) για την παραγωγή, αρχειοθέτηση και φαινοτυποποίηση ζωικών μοντέλων ασθενειών, καθώς και την ELIXIR-GR, για τη διαχείριση και επιμέλεια δεδομένων βιοπληροφορικής/βιοϋπολογιστικής. Το ΦΛΕΜΙΓΚ συμμετέχει επίσης στην υποδομή Bioimaging-GR, η οποία στοχεύει στην παροχή υψηλής ποιότητας υπηρεσιών απεικόνισης για την εξέταση θεμελιωδών βιολογικών διεργασιών, καθώς και στην υποδομή εξατομικευμένης ιατρικής pMedGR σε συνεργασία με την Ιατρική Σχολή Αθηνών, και το δίκτυο ογκολογίας Oncology Precision Medicine.

Για να συνεχίσει την επιτυχημένη πορεία του, το ΦΛΕΜΙΓΚ **θα αναβαθμίσει περαιτέρω τις υποδομές και τις εγκαταστάσεις του** μέσω επιχορήγησης από το Ταμείο Ανάκαμψης και Ανθεκτικότητας της ΕΕ. Επιπλέον, το ΦΛΕΜΙΓΚ έχει λάβει αρχική έγκριση από την Ευρωπαϊκή Τράπεζα Επενδύσεων για την κατασκευή της **ΒΙΟΤΕΧΝΟΠΟΛΗΣ** – ενός καινοτόμου βιοτεχνολογικού κόμβου για την περιοχή της Αττικής.

Την επιστημονική γνώση που προέρχεται από τα ερευνητικά προγράμματα του ΦΛΕΜΙΓΚ αλλά και την προστασία και εκμετάλλευση των ερευνητικών αποτελεσμάτων παρακολουθεί και διαχειρίζεται η **Μονάδα Καινοτομίας και Επιχειρηματικότητας**, η οποία έχει ήδη δημιουργήσει 11 χαρτοφυλάκια διπλωμάτων ευρεσιτεχνίας γύρω από βασικές τεχνολογίες του ΦΛΕΜΙΓΚ, έχει ολοκληρώσει περισσότερες από 600 εξερχόμενες Συμφωνίες Μεταφοράς Υλικού παγκοσμίως για μοντέλα ποντικών, γενετικά εργαλεία και άλλες καινοτομίες και έχει συνάψει πολυάριθμες συμβάσεις αδειοδότησης με τη βιομηχανία. Ιδιαιτέρως σημαντικό είναι το γεγονός ότι έχει επιβλέψει τη δημιουργία της πρώτης spin-off εταιρείας του ΦΛΕΜΙΓΚ, της **Biomedcode**, η οποία παρέχει πλήρεις υπηρεσίες προκλινικής αξιολόγησης φαρμάκων σε φαρμακευτικές εταιρείες παγκοσμίως, αξιοποιώντας ιδιόκτητα ζωικά μοντέλα χρόνιων φλεγμονωδών παθήσεων, καθώς και της πρόσφατα ιδρυθείσας spin-off εταιρείας **MABY**, που αναπτύσσει νέα μονοκλωνικά αντισώματα για τη φαρμακευτική βιομηχανία και τον ακαδημαϊκό κόσμο.

OUR HISTORY

SIR ALEXANDER FLEMING AND THE DISCOVERY OF PENICILLIN

Sir Alexander Fleming (1881-1955) was a Scottish physician and bacteriologist working at St. Mary's Hospital in London.

While serving in a hospital during World War I, Fleming witnessed the death of hundreds of soldiers from sepsis due to untreatable wound infections. At the same time, in those years infectious diseases such as cholera, diphtheria and pneumonia could easily lead to death. Fleming returned to his laboratory after the war in search of substances with bactericidal activity to protect against such infections.

In 1928, while conducting research on pathogenic bacteria of the Staphylococcus family, he noticed that one of his laboratory cultures had been contaminated by a fungus, and that bacterial growth near the fungus had been inhibited. He identified the fungus as a member of the genus Penicillium and named its potent substance "penicillin". A powerful new weapon against contagious diseases had just been born: antibiotics.

For his contribution, Fleming was knighted in 1944 and a year later was awarded the Nobel Prize in Physiology or Medicine (jointly with Howard Florey and Ernst Chain at the University of Oxford for its development). The name of Alexander Fleming became famous all over the world and will remain in history as the man who discovered the cure for diseases such as syphilis, pneumonia and meningitis.

AMALIA FLEMING AND THE BSRC “ALEXANDER FLEMING”

Amalia Koutsouri-Fleming (1912-1986) was an acclaimed Greek physician specialized in microbiology.

In 1947, she was awarded a fellowship from the British Council to work in the laboratory of the Nobel laureate Sir Alexander Fleming in London. Amalia worked in Fleming’s laboratory for several years doing research on antimicrobial agents and antibiotic resistance, authoring nine publications from 1947 to 1952.

Alexander and Amalia Fleming were married in 1953. Amalia was a woman of great humanitarian spirit who made an immense contribution to the field of sciences in Greece, as well as a passionate activist for democracy and human rights. After Fleming’s death, Amalia founded in his memory the Greek Foundation for Basic Biological Research “Alexander Fleming” in 1965.

In 1966, an area of 12.8 hectares in Vari was granted to the foundation by the Church for the attainment of its goals. After many years of efforts, interrupted by the military dictatorship and hampered by political events, – including the imprisonment of Amalia during the military junta – a modern building occupying a total of 6,000 sq.m. was built on this site, financed mainly by the 1st EU Framework Program. Construction of the building finished in 1993. In 1995, the Biomedical Sciences Research Center “Alexander Fleming” was established.

The Center is under the supervision of the General Secretariat of Research and Technology (GSRT) of the Greek Ministry of Development and Investments. It started its operation in 1998 with the appointment of the first Director, Prof. John Volanakis, followed by the appointment of the first investigators in 1999.

The establishment of our Center was the result of Amalia Fleming’s vision for a Greek Center of Scientific and Technological Excellence, which would attract young Greek researchers and be based on meritocracy, excellence and innovation.

MILESTONES

1965
Amalia Fleming establishes the Hellenic Foundation for Basic Biomedical Research "Alexander Fleming"

1966
HFBBR acquires 12.8 hectares of land in Vari, Attica

1968
Building foundations laid

1971
Construction is interrupted after the arrest of Amalia Fleming for actions against the military junta

1975
Construction resumes at a slow pace

1986
Amalia Fleming dies

1993
Building construction ends

1995
Establishment of B.S.R.C. "Alexander Fleming"

1998
Appointment of the first Scientific Director

1999
Appointment of the first investigators

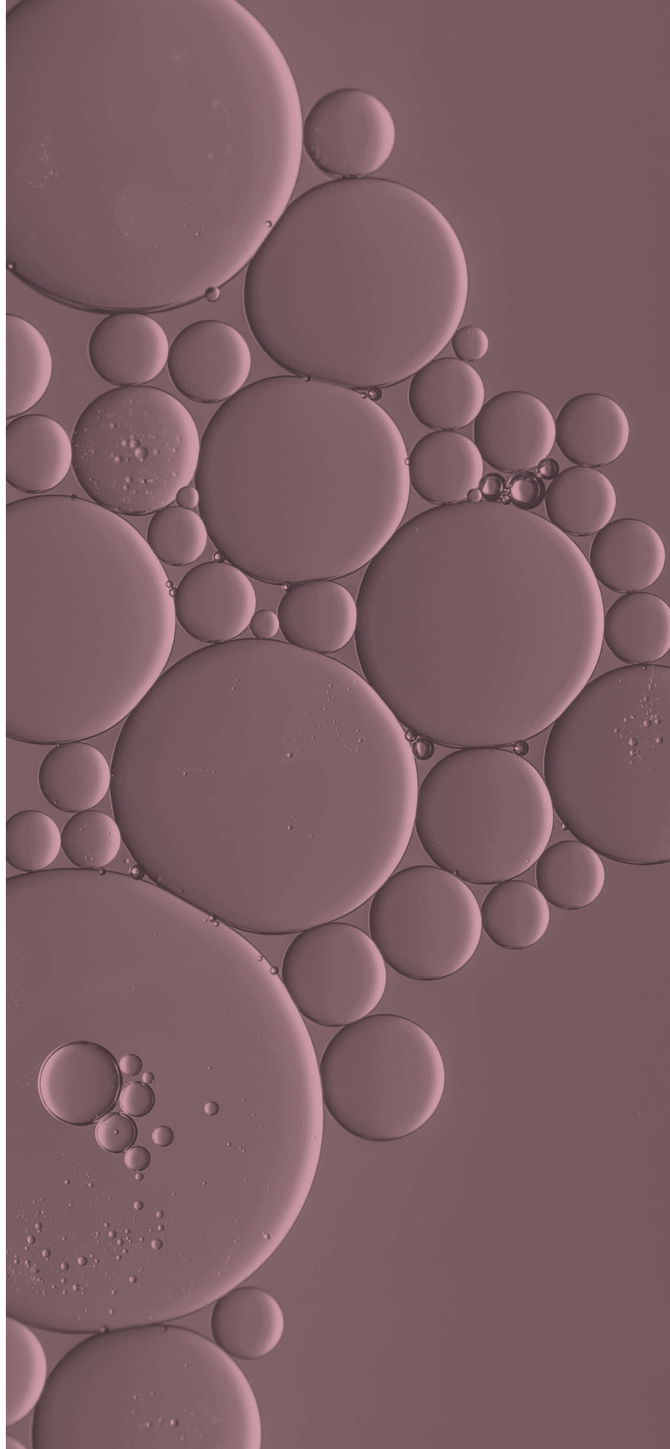
OUR MISSION

OUR MISSION

FLEMING's central mission is to conduct pioneering research in the field of biomedical sciences. Our goal is to understand at the molecular and cellular level the mechanisms and principles that drive complex biological processes in health and disease and to translate this knowledge into innovative solutions for diagnosis and therapy, focusing on immunity and inflammation, cancer and neurodegenerative diseases.

The cornerstones of FLEMING's mission are to:

- **perform cutting edge basic and translational research in biomedical sciences,** recruiting talented investigators capable of leading independent, internationally competitive research teams, and promoting a thriving scientific environment based on academic principles, the exchange of ideas, openness, and peer-based evaluation.
- **provide state-of-the-art training and mentorship** to scientists and students of all levels.
- **offer high-end scientific and technological services.**
- **actively engage in technology transfer and innovation,** exploiting research findings to develop new products that can improve the prevention, diagnosis, and therapy of human diseases.
- **disseminate its research findings** to patient groups, clinicians, and the general public.



RESEARCH DIRECTIONS

FLEMING has established 6 main research directions or programs that are covered by the work of its group leaders and serve as links between the IFBR and the IBI Institutes. Researchers can be active in more than one program depending on their current priorities and needs.

IMMUNITY & INFLAMMATION

The mission of the Immunity and Inflammation Program is to advance knowledge on complex immunological diseases such as rheumatoid arthritis, inflammatory bowel disease, pulmonary diseases, multiple sclerosis and cancer using a variety of approaches, including transgenesis, biochemistry, imaging, computational modeling and systems-level profiling. Researchers at the Program focus on the development of animal models to dissect the molecular and cellular mechanisms that underlie disease pathogenesis, aiming at the establishment of innovative translational platforms for the discovery and validation of novel therapeutics and biomarkers.

CURRENT PROGRAM MEMBERS:

V. Aidinis
Molecular pathophysiology of pulmonary inflammation, fibrosis, and cancer

M. Armaka
Molecular and cellular pathogenesis mechanisms of inflammatory diseases of the joints, with emphasis on the role of mesenchymal cells

E. Douni
Mouse Functional Genetics for bone, immune, and neurological diseases

V. Koliaraki
Origin, plasticity, and function of the intestinal microenvironment in health and disease

G. Kollias
Molecular and cellular mechanisms of chronic inflammation and cancer

D. L. Kontoyiannis
Post-transcriptional modules of gene expression in physiology and disease

A. Matralis
Development of bioactive molecules against complex human diseases

M. Tsoumakidou
Tumor immunology and immunotherapy

M. Verykokakis
Development and function of innate T lymphocytes

NEUROSCIENCE

The Neuroscience Program aims to advance high quality fundamental research in cutting edge areas of current Neuroscience towards understanding the development and function of the brain and peripheral nervous system in vertebrate and invertebrate model systems. In addition to basic research, current and future projects emphasize the potential for innovative diagnostic and translational approaches to combat debilitating conditions which disrupt the function of the nervous system such as cognitive and learning disabilities, dementias, psychiatric, and neurodegenerative disorders. Furthermore, the Program reaches out to Greek and International companies operating in the area of pharmaceuticals that target the nervous system, with the aim of joint projects and strategic partnerships.

CURRENT PROGRAM MEMBERS:

M. Denaxa
Development and Function of Cortical Interneurons

K. Papanikolopoulou
Neurobiology of Neurodegenerative Tauopathies

M. Skoulakis
Molecular Cognitive Neuroscience

B. Savakis
(Emeritus)

External members of the Program include adjunct researchers, Dr. Antonis Stamatakis, Associate Professor of Biology in the School of Nursing at the University of Athens, who contributes his expertise on mouse behavioral analyses, Dr. Christos Consoulas, an Associate Professor of Experimental Physiology at the University of Athens Medical School who collaborates in the area of Neurophysiology, Dr. Ioannis Sotiropoulos, a Researcher at the University of Minho in Braga Portugal, on Tauopathies, and Dr. Panos Roussos, an Associate Professor of Psychiatry, Genetics and Genomics at the Icahn School of Medicine at Mount Sinai, NY.

CANCER BIOLOGY

The Cancer Biology program aims to achieve excellence in Cancer Research by employing multi-disciplinary approaches to understand fundamental mechanisms that regulate cell growth and promote carcinogenesis. Research findings are exploited to develop new products that can improve prevention, diagnosis and therapy of cancer.

CURRENT PROGRAM MEMBERS:

V. Aidinis
Molecular pathophysiology of pulmonary inflammation, fibrosis and cancer

E. Douni
Mouse Functional Genetics for bone, immune and neurological diseases

M. Fousteri
Regulatory (epi)genomics in cancer and aging related diseases

P. Hatzis
RNA-mediated transcriptional and epigenetic regulation in carcinogenesis

V. Koliaraki
Origin, plasticity, and function of the intestinal microenvironment in health and disease

G. Kollias
Molecular and cellular mechanisms of chronic inflammation and cancer

D. L. Kontoyiannis
Post-transcriptional modules of gene expression in physiology and disease

V. Kostourou
Blood vessel morphogenesis and function

A. Matralis
Development of bioactive molecules against complex human diseases

G. Panayotou
Molecular Analysis of Signal Transduction Pathways

M. Tsoumakidou
Tumour immunology and immunotherapy

RNA BIOLOGY AND EPIGENETICS

The RNA Biology and Epigenetics Program aims to advance knowledge on the mechanisms driving regulation of gene expression at the transcriptional, post-transcriptional, and epigenetic levels, using cutting-edge molecular biology and biochemical approaches, including high-throughput functional assays and single-cell NGS technologies, transgenic systems, animal models of disease, and patient-derived material. We are endeavoring to elucidate these molecular regulatory mechanisms at the fundamental level, but also to understand how their perturbation is involved in the development and progression of inflammatory disorders, degenerative diseases, and cancer. We also aim towards translational exploitation of our results for the development of diagnostic tools and therapies targeting the relevant essential regulatory processes.

CURRENT PROGRAM MEMBERS:

A. Dimas
genomic architecture of complex traits in humans

M. Fousteri
Regulatory (epi)genomics in cancer and aging related diseases

P. Hatzis
RNA-mediated transcriptional and epigenetic regulation in carcinogenesis

P. Kafasla
Nuclear Ribonucleoprotein complexes (RNPs) in immune response and cancer

D. L. Kontoyiannis
Post-transcriptional modules of gene expression in physiology and disease

BIOINFORMATICS AND COMPUTATIONAL BIOLOGY

The mission of the Bioinformatics and Computational Biology division is to use and develop state-of-the art software, applications, databases, and pipelines to tackle complex biological problems. Living in the big-data era, we utilize high performance computing to process and analyze various -Omics high-thoughput data such as genomics, proteomics and metabolomics while we simultaneously provide bioinformatics solutions as services to non-experts. While the focus of the division is to aid researchers in understanding the mechanisms behind immunological diseases, our activities can cover a wider spectrum of problems, varying from personalized medicine to fundamental biology research and environmental studies.

CURRENT PROGRAM MEMBERS:

C. Nikolaou
Computational genomics

G. Pavlopoulos
Bioinformatics & integrative biology

M. Reczko
RNA modeling, Computational metabolomics, coordination of ELIXIR-GR

P. Moulos
Statistical algorithms for NGS

BIOMOLECULAR ENGINEERING & SYNTHETIC BIOLOGY

The activities of this program lie at the interfaces of biology, chemistry and engineering. The Laboratory of Biomolecular Engineering & Synthetic Biology (BESB) is a multi-disciplinary group employing researchers with different types of expertise, such as molecular biology, engineering, chemistry and agricultural sciences. The main goal of BESB is the development of engineered microbial cells with the ability to perform novel and complex functions by employing principles of Synthetic Biology. The lab utilizes simple organisms, such as the bacterium *Escherichia coli* and the yeast *Saccharomyces cerevisiae* as "biological chassis" and seeks to evolve them into efficient cell factories for the production of valuable chemical and biological products, and for the performance of industrially important processes, such as drug sensing and discovery, bio-transformations etc. Genetic engineering techniques are applied in order to redesign and rearrange the genome of the organism of interest, while protein engineering (directed protein evolution) and synthetic biology approaches are utilized so as to introduce novel functions in the cell. A key aspect of the work that is carried out is the design and development of high-throughput screening systems, which are used to isolate the rare biomolecules and microbial strains that execute the desired function among large combinatorial libraries comprising hundreds of millions of variants.

CURRENT PROGRAM MEMBERS:

G. Skretas
Innovative biotechnologies for protein misfolding and aggregation diseases

INSTITUTE FOR FUNDAMENTAL BIOMEDICAL RESEARCH (IFBR)

Efthimios Skoulakis
Director of the IFBR

NEUROSCIENCE

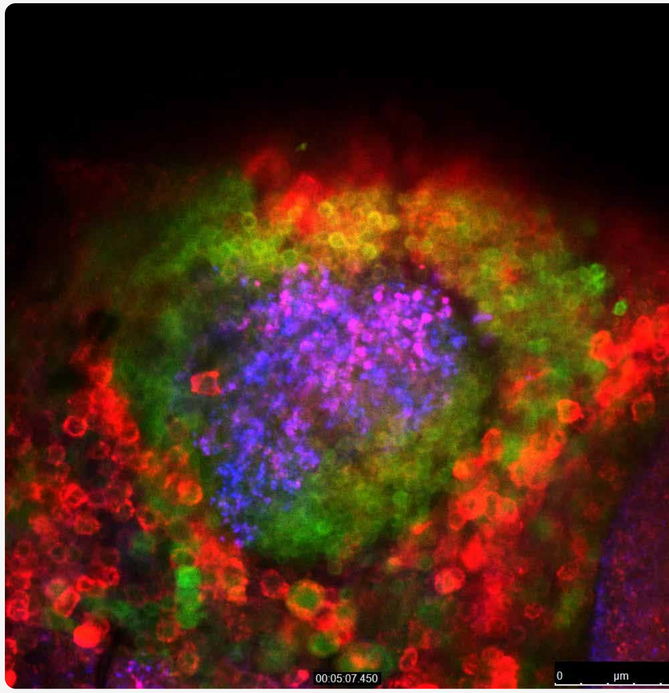
EFTHIMIOS SKOULAKIS RESEARCH GROUP

Molecular Cognitive Biology

It can be argued that the large capacity to learn, remember and use the acquired information in novel ways is the defining characteristic of our species. The long-term research goal of the Skoulakis laboratory is to define molecular mechanisms employed by neurons to acquire, store and retrieve information, and how these are altered in cognitive, neurodegenerative, and psychiatric diseases using Drosophila and mouse models. Overall, the research program concentrates on four main avenues:

First, exploring and defining the molecular and cellular mechanisms of habituation as the process(es) by which the nervous system assigns importance or ignores stimuli, a prerequisite for attention, learning and memory. Failed habituation is a schizophrenia endophenotype in humans, and we have demonstrated that Drosophila mutants in homologs, or orthologs of GWAS linked-schizophrenia loci present defective habituation, which can be rescued with specific typical and atypical antipsychotics. We have also identified a number of novel mutants that either fail to habituate or do so prematurely, the latter being potential attention deficit models.

Second, we are investigating the molecular mechanisms affected by loss of the Ras activity regulator Neurofibromin 1, and underlie the cognitive deficits associated with Neurofibromatosis 1. We have demonstrated that this implicates activation of the receptor Tyrosine Kinase Alk, which can be targeted pharmaceutically to treat these deficits. Nf1 loss also results in excess GABA signaling to neurons essential for learning. We are currently focusing on understanding the diverse genotype to phenotype relationships of mutations in the gene, modeling human mutations with largely cognitive phenotypes in Drosophila and mouse.



Third, we aim to determine the molecular mechanisms that underlie the protein synthesis independent memory (PSIM) in Drosophila, which our evidence suggests that mechanistically relies on modifications of the actin cytoskeleton, and have identified and are characterizing a number of genes essential for formation of this type of memory. In addition, we are endeavoring to define functional parameters and requirements of this type of memory, aiming to determine its relationship with vertebrate/human memory forms.

The fourth research track focuses on the molecular and cognitive neurobiology of a group of dementing neurodegenerative disorders known as Tauopathies, one of which is Alzheimer's. We use fly Tauopathy models and have shown that cognitive decline is predicted by particular Tau phosphorylations, clearly preceding neurodegeneration. We have demonstrated that Tau aggregation is protective to cognitive decline. We aim to define molecular events that promote Tau pathogenicity to identify early disease biomarkers and have focused on the effects of Tau-interacting proteins that enhance or suppress pathologies, the role of metal ions and redox in pathogenesis, as well as protocols that halt or reverse cognitive deficits.

Learning and Memory, Habituation, Tauopathies, Learning disabilities

LINK TO PUBLICATIONS

Vassilis Aidinis

IMMUNITY & INFLAMMATION

CANCER BIOLOGY

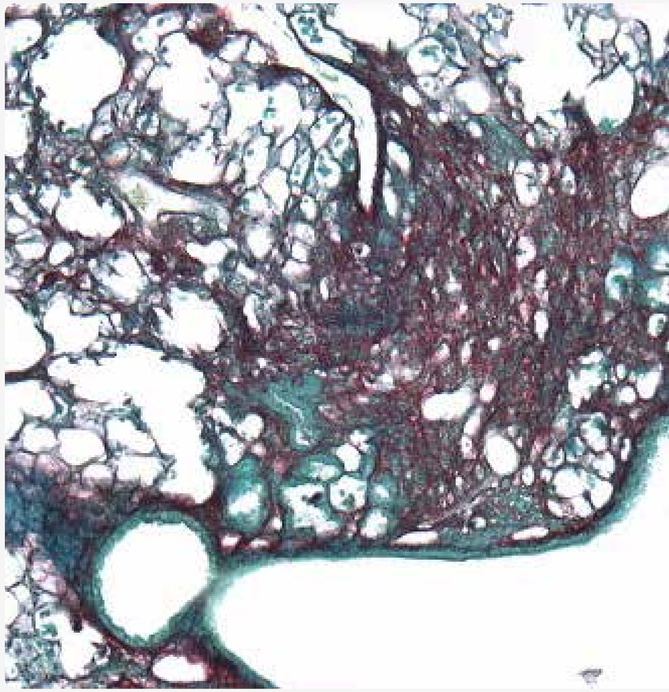
INSTITUTE
FOR FUNDAMENTAL
BIOMEDICAL RESEARCH
(IFBR)

VASSILIS AIDINIS RESEARCH GROUP

Key challenges for biology in the 21st century are the exploration of the structure and the dynamics of the complex inter- and intra- cellular web of interactions that contribute to the structure and function of a living cell. In this context and towards that end, we are implementing and integrating a variety of functional genomics (reverse genetics, expression profiling, and bioinformatics), methods and tools in holistic, multidisciplinary explorations of pathogenetic mechanisms. In this context, research @VART focuses on two pillars:

Molecular and genetic dissection of pathogenetic mechanisms in pulmonary inflammation and fibrosis

Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive, and usually lethal lung disorder of unknown etiology, and no proven therapies. Current research indicates that the mechanisms driving IPF reflect abnormal, deregulated wound healing within the lung, involving increased activity and possibly exaggerated responses by a spectrum of pro-inflammatory and pro-fibrogenic factors. To further dissect pathogenetic mechanisms of pulmonary fibrosis, we are utilizing the animal model of bleomycin-induced pulmonary inflammation and fibrosis, precision cut lung slices (PCLS), and 3D ECM fibroblast cell-based systems, to address the possible involvement of various mediators through genetic modifications and pharmacologic interventions, coupled with respiratory and metabolic functions, expression profiling, as well as translational research.



VASSILIS AIDINIS
RESEARCH GROUP

IMMUNITY & INFLAMMATION

CANCER BIOLOGY

INSTITUTE
FOR FUNDAMENTAL
BIOMEDICAL RESEARCH
(IFBR)

The role of ATX and LPA signaling in embryonic development, pathophysiology and cancer

Autotaxin (ATX, ENPP2) is a secreted glycoprotein, widely present in biological fluids, largely responsible for lysophosphatidic acid (LPA) production, a growth factor-like, signaling phospholipid. We have detected increased ATX and LPA levels, locally and/or systemically, in patients with different chronic inflammatory diseases and the corresponding animal models, including rheumatoid arthritis, hepatitis, as well as Idiopathic pulmonary fibrosis (IPF). With special regard to IPF, genetic or pharmacologic inhibition of ATX attenuated disease development in animal models, thus providing the proof of principle for therapeutic interventions and spurring three clinical trials. In this context, and using a combination of chemoinformatics and bioinformatics, rational design and targeted synthesis, dedicated enzymatic and ADMET assays, MS-based PK/PD analysis, as well as animal models and innovative delivery methods, we are developing a series of novel ATX inhibitors, currently at different pre-clinical characterization stages, protected by National and International patent applications in collaborations with the pharmaceutical industry.

Chronic Inflammation, Fibrosis, Autotaxin, Drug Development

LINK TO PUBLICATIONS

Marietta Armaka

INSTITUTE
FOR FUNDAMENTAL
BIOMEDICAL RESEARCH
(IFBR)

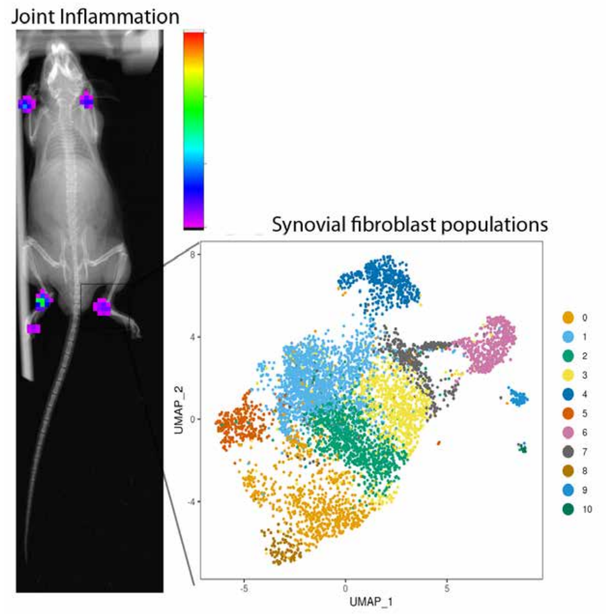
MARIETTA ARMAKA RESEARCH GROUP

Our group is dedicated in understanding the molecular signature of Synovial Fibroblasts (SFs) in homeostasis and arthritic diseases.

Synovial membrane is a thin membrane which encapsulates the joint surfaces and synovial fluid. It is populated mainly by SFs which maintain tissue integrity. In the inflammatory arthritides, such as Rheumatoid or Psoriatic arthritis, the synovial membrane is getting infiltrated by immune cells, and becomes hyperplastic due to activation of SFs which revert themselves into joint-destructing cells. The molecular mechanisms that dictate this reversion still remains poorly defined. Currently our group works towards two directions utilizing functional genetic and genomic approaches:

1. The identification of druggable molecular determinants in the TNF pathway which will cease the SF pathogenic autonomy

TNF has been causally linked with inflammatory arthritides. We have previously shown that pathogenic TNF primarily activates SFs to orchestrate modeled rheumatoid-like arthritis (JEM 2008). However, TNF can induce both inflammatory and death pathways. These pathways are interconnected and tightly regulated. We focus on reverting the inflammatory profile and death resistance of arthritic SFs with the SF-specific manipulation of the TNF-signaling components which act as checkpoints in the inflammatory and death responses (Nat Communications 2018).



2. The characterization and the functional significance of the synovial heterogeneity in homeostasis and chronic arthritic diseases

Accumulating evidence by both our and other labs, employing high-resolution transcriptomic analyses, suggests that the SFs segregate into different profiles with distinct functions in health and disease (Genome Med 2022). We have set forth the hypothesis that different types of SFs function for maintaining homeostasis or fueling arthritic diseases by their expansion and differential sensitivity to inflammatory stimuli, leading to disease-specific changes in the synovial membrane. Therefore, to explore the alterations of SF profiles among inflammatory joint pathologies, we generate and characterize the profiles of SFs in different chronic arthritides in murine arthritic models (Rheumatoid-like vs Psoriatic-like) with single-cell omic techniques.

Synovial Fibroblast, Animal Models,
Rheumatoid Arthritis,
Psoriatic Arthritis

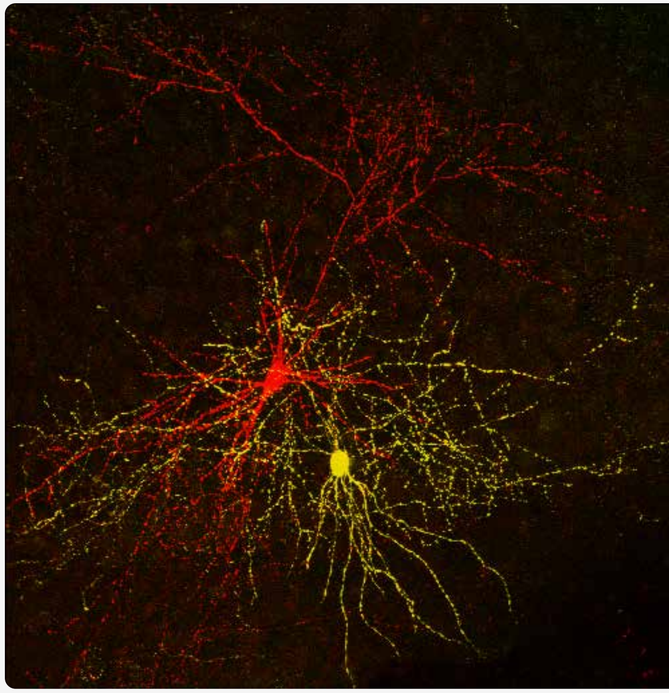
LINK TO PUBLICATIONS

Myrto Denaxa

NEUROSCIENCE

MYRTO DENAXA RESEARCH GROUP

INSTITUTE
FOR FUNDAMENTAL
BIOMEDICAL RESEARCH
(IFBR)



Mission and Research Focus

Cortical interneurons (cINs) are a relatively small but extremely diverse group of non-pyramidal GABA-expressing cells, which are critical for maintaining the balance between excitation and inhibition in the cerebrum, and play important roles in the pathogenesis of neurodevelopmental disorders, such as autism spectrum disorders and schizophrenia. My research group is interested in understanding how unique gene programs control the development of specific interneuron subtypes, and how these programs are modulated in response to environmental input. Our research is primarily focused on developmental processes occurring during postnatal stages, which define the mature properties of each IN type. We aim to define key steps implicated in interneuron differentiation and maturation, and understand how the perturbation of these processes results in brain dysfunction. We expect our work to provide fundamental biological insight and advance our understanding of the pathogenesis of major brain disorders.

Our Main Scientific Directions:

- Elucidate mechanisms controlling the differentiation and maturation of distinct interneuron populations.
- Generate and characterize relevant mammalian models for interneuropathies.

Cortical Development, Interneurons, Neurodevelopmental Disorders, Mammalian Animal Models

LINK TO PUBLICATIONS

Maria Fousteri

CANCER BIOLOGY

RNA BIOLOGY & EPIGENETICS

INSTITUTE
FOR FUNDAMENTAL
BIOMEDICAL RESEARCH
(IFBR)

MARIA FOUSTERI RESEARCH GROUP

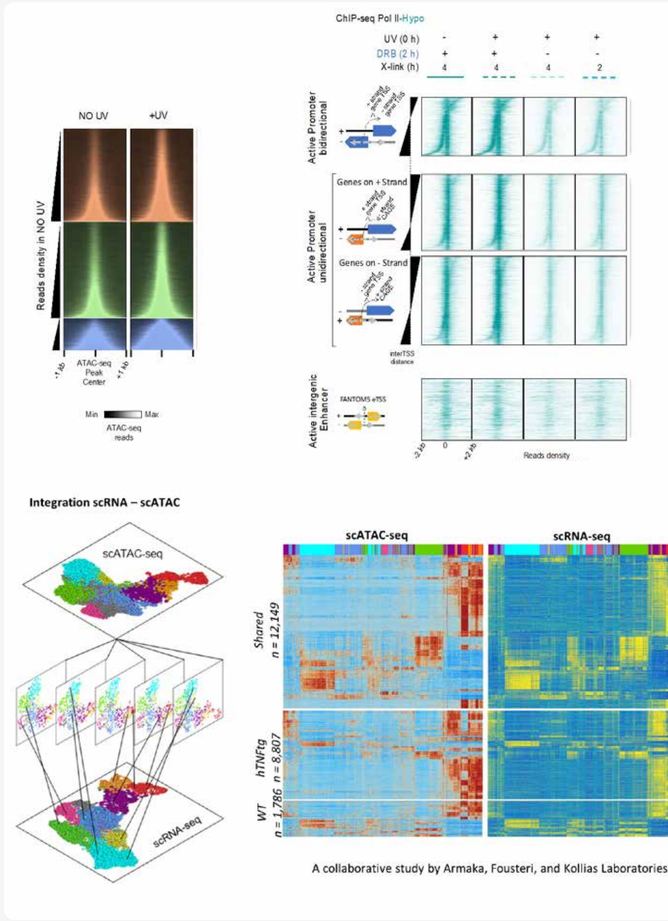
DECODING GENE AND (EPI)GENOME CONTROL IN HEALTH AND DISEASE CONDITIONS

Mission

By establishing a competitive and highly stimulating research environment for training young investigators, our mission is to gain in-depth knowledge of gene expression and (epi)genome regulatory programs, whose deviation leads to rare neurodevelopmental inborn conditions and cancer. We aim to reveal accurate disease biological processes and dissect therapy resistance mechanisms that may lead to the development of novel therapeutic approaches and improve patients' quality of life.

Research Focus

A major focus of our laboratory is to unravel the molecular mechanisms that regulate gene expression and chromatin landscape in humans in the face of various genotoxic stresses or in deficient situations. This line of investigation has broad significance due to the many rare genetic diseases as well as tumours that are associated with defects in genome maintenance mechanisms. We use cutting-edge biochemical, molecular and cellular biology methods and system biology approaches (bulk and single-cell transcriptomic and (epi)genomic analyses) to provide an in-depth understanding of the under study cellular processes.



CANCER BIOLOGY

RNA BIOLOGY & EPIGENETICS

In particular, our scientific directions include:

1. Elucidation of the genome surveillance mechanisms, transcription regulation events, and associated chromatin dynamics, whose perturbation gives rise to cancer or rare neurodevelopmental inborn disorders.
2. Investigation of the molecular paths, gene regulatory networks, spatiotemporal development and cellular heterogeneity that underlie disease-driven biological processes by single-cell Next Generation Sequencing approaches.

Genome surveillance mechanisms,
Spatial-temporal dynamics,
Epigenetics,
Gene Regulatory Networks

LINK TO PUBLICATIONS 1

LINK TO PUBLICATIONS 2

CANCER BIOLOGY

RNA BIOLOGY & EPIGENETICS

Pantelis Hatzis

INSTITUTE
FOR FUNDAMENTAL
BIOMEDICAL RESEARCH
(IFBR)

PANTELIS HATZIS RESEARCH GROUP

Mission

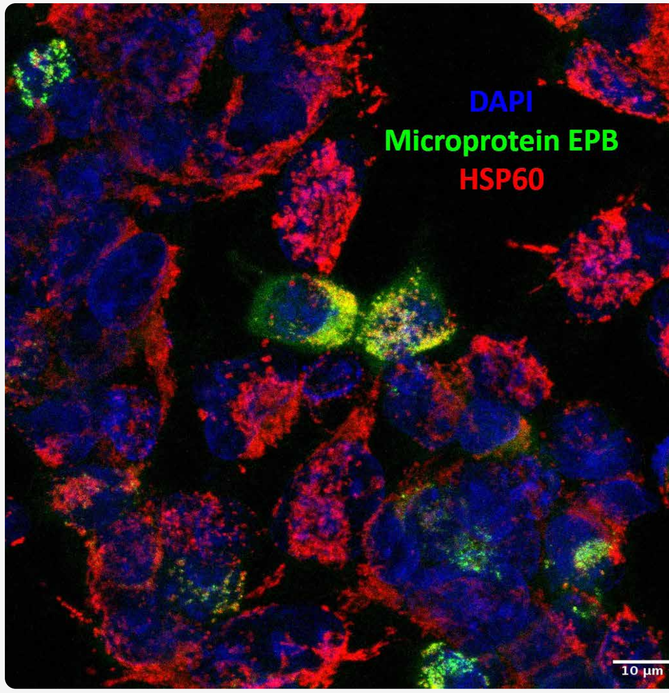
The Hatzis lab pursues fundamental questions regarding the function of the pervasive, previously unappreciated, transcriptional activity of the parts of the genome previously described as 'junk'. Our goal is to understand the functions of some of the tens of thousands of novel gene units termed "long non-coding RNAs", that have been uncovered in the past 15 years by new high-throughput approaches. Our work aims at uncovering novel molecules impacting cellular physiology and carcinogenesis and exploring their potential as prognostic and diagnostic markers and therapeutic targets.

Research Focus

Long non-coding RNAs have been shown to play prominent roles in a multitude of cellular functions, in both health and disease. Our research is aimed at uncovering the function of certain such lncRNAs we have identified, as well as their roles in normal homeostasis and carcinogenesis in the human intestinal epithelium and other tissues. Our particular focus partly lies on certain lncRNAs that we have identified as targets of the Wnt signaling pathway, which plays a central role in stem cell maintenance, differentiation, and proliferation in the intestinal epithelium. The Wnt-regulated lncRNAs we study are located in the nucleus, and regulate the epigenetic and transcriptional status of neighboring protein-coding genes in cis, affecting stemness, differentiation and, ultimately, carcinogenesis. Additionally, we have recently uncovered a small group of genes annotated as long-non coding RNAs which, in fact, appear to be coding: they appear to produce small proteins, the functions and importance of which in cell physiology and carcinogenesis we are trying to uncover.

Long non-coding RNAs,
Microproteins, smORFs

→ LINK TO PUBLICATIONS



Panagiota Kafasla

INSTITUTE
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BIOMEDICAL RESEARCH
(IFBR)

PANAGIOTA KAFASLA RESEARCH GROUP

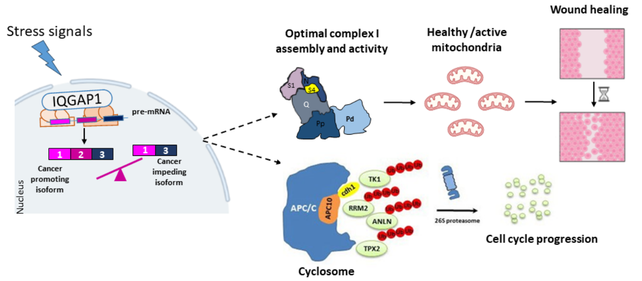
Mission

To study the assembly and the role of nuclear ribonucleoprotein complexes (RNPs) that control cancer development and progression in the gastrointestinal system. We also aim to dissect the way signals are transferred to the nucleus, and determine the composition and function of splicing regulating RNPs in tumour development and progression.

Our main research activities focus on:

1. Characterization of the composition of nuclear RNPs that regulate alternative splicing of pre-mRNA, and thus control development and progression of pancreatic neuroendocrine and gastric tumours.
2. Study of alternative splicing changes that happen in response to stress signals, such as heat-induced signals, cell cycle arrest, and mitochondrial stress.
3. Study of the control of the communication between mitochondria and the nucleus via alternative splicing (in collaboration with the Junior Researcher Z. Erpapazoglou, hosted in our laboratory).

Achievements: Since 2017, when our group was established, we have published three manuscripts in peer review journals: Birladeanu et al, *Oncogene*, 2021; Rogalska et al, *Metabolism, 2023*; Papadaki et al, *NAR cancer*, 2023. Our funding sources: Stavros Niarchos Foundation, Hellenic Foundation for Research and Innovation and the Neuroendocrine Tumour Research Foundation.



PANAGIOTA KAFASLA
RESEARCH GROUP

RNA BIOLOGY & EPIGENETICS

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(IFBR)

Our Future Plans include:

- Further experimentation on the AS deregulation that takes place during Pancreatic Neuroendocrine Tumour development, not only to understand the biological processes that are deregulated due to mis-splicing, but also to identify new targets for the development of therapeutic approaches.
- Development of mouse models of Pancreatic Neuroendocrine Tumours that will help us clarify the involvement of Alternative splicing deregulation in the development and progression of this disease.
- Identification of key components of the splicing machinery that are affected in response to stress signals.

RNA splicing,
Pancreatic Neuroendocrine Tumours

LINK TO PUBLICATIONS

Vasiliki Koliaraki

IMMUNITY & INFLAMMATION

CANCER BIOLOGY

INSTITUTE
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BIOMEDICAL RESEARCH
(IFBR)

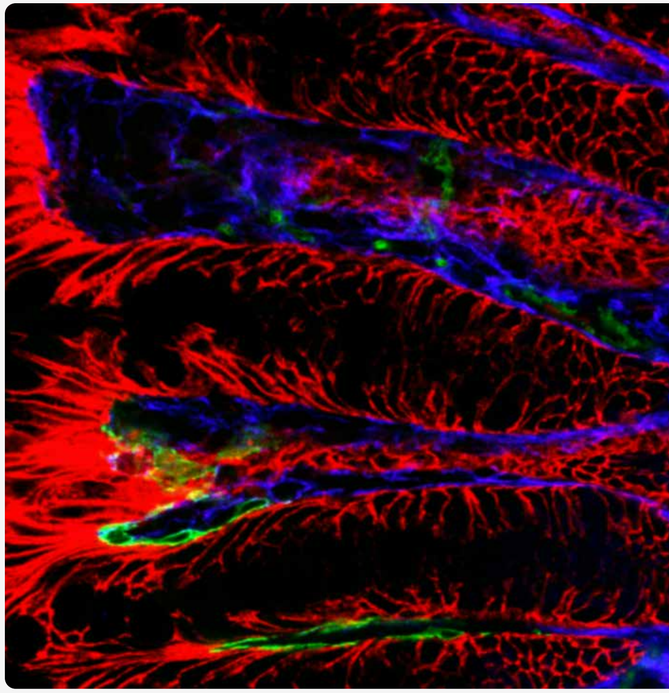
VASILIKI KOLIARAKI RESEARCH GROUP

Mission

Our lab's main goal is the delineation of the properties of intestinal mesenchymal cells and the molecular mechanisms that regulate their functions in homeostasis and disease. We are particularly interested in the pathways that drive fibroblast activation in intestinal regeneration and cancer, and the downstream mechanisms that orchestrate their communication with neighboring cells. To accomplish our goal, we combine genetic targeting in mice, lineage tracing studies, animal models of disease, and high-throughput technologies, including single-cell transcriptomics.

Our main scientific directions include:

1. Understanding the contribution of fibroblast heterogeneity and functions in intestinal damage and repair. We believe that fibroblasts play an important role in the orchestration of a regeneration-permissive microenvironmental milieu and the dictation of epithelial cell fate decisions. To this end, we aim to characterize the heterogeneity and the cellular and molecular alterations of the regenerating intestinal stroma, delineate the cellular fates of fibroblasts, and elucidate the molecular mechanisms underlying their functions following intestinal injury.
2. Identifying cancer-associated fibroblast (CAF)-specific cellular and molecular mechanisms that regulate tumour initiation and progression. Our aim is to elucidate the origin of intestinal CAFs, define the drivers and downstream pathways leading to their irreversible reprogramming, and study their downstream functions within the complex tumour microenvironment.



3. Describing age-associated changes in fibroblast subsets and properties and how they may affect intestinal cancer initiation. We are especially interested on how these changes could be influenced by age-associated dysbiosis and in turn affect immune homeostasis, epithelial turnover, and cancer cell proliferation.

With these studies we aim to provide insight into the biology of mesenchymal cells and their contribution to disease pathogenesis, and offer new potential for prognostic, diagnostic and therapeutic applications.

LINK TO PUBLICATIONS

Dimitris L. Kontoyiannis

INSTITUTE
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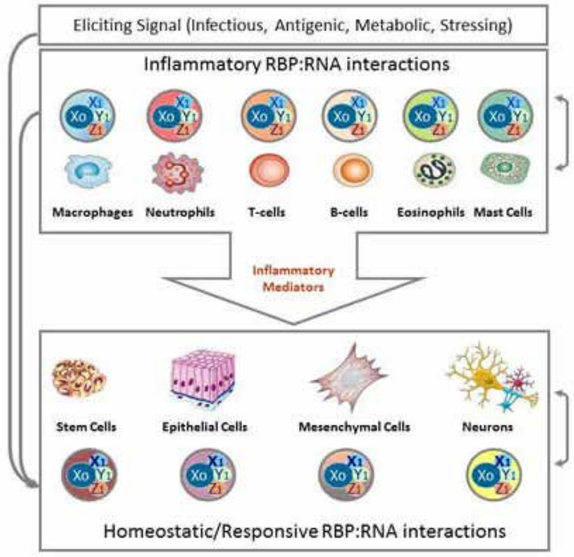
(IFBR)

DIMITRIS L. KONTOYIANNIS RESEARCH GROUP

Mission

The exploration of the RNA world has progressed significantly and already provides important biomedical solutions against viral infections and monogenic rare diseases. Along came our understanding of the selectivity of eukaryotic RNA usage by maturation, modification, editing, localization, translation, and destruction mechanisms that can modify cellular decisions and their misuse in disease. Central to the regulation of RNA usage are hundreds of RNA-binding proteins that sort and cluster functionally related RNAs in ribonucleoprotein complexes to coordinate their use as regulons for a given cellular response beyond its transcriptomic definition. The exploitation of RNA usage for the management of complex diseases stumbles upon our lack of knowledge on the roles of RBPs and RNPs: (a) in supporting tissue- or cell-specific transitions and (b) in remodeling their interactions while adapting to signals to promote such transitions. The group addresses such questions under the auspices of a hypothesis where the selectivity of RNA use is paramount for cellular adaptation by plasticity.



Research

In light of the above, the group analyzes members of selected hnRNPs and mRNPs to dissect their cellular functions *in vivo* via genetic or pharmacological means, assess their contextual protein and RNA partners in RNPs via relevant -omic platforms, and decipher targetable signal-to-RBP relationships supporting:

1. Macrophage heterogeneity and polarization arising due to adaptation upon infectious, metabolic, and immune signals of relevance to inflammatory degenerative diseases and pathologic tumor micro-environments

2. Mucosal epithelial degeneration and regeneration of particular relevance to intestinal diseases, including Inflammatory Bowel Diseases
3. Cardiovascular adaptations to metabolic or mechanical stress of relevance to cardiomyopathies and heart failure

Achievements

Since 2005, the group has highlighted the relevance of targeting the so-called "ARE-binding factors" (like, e.g., Elavl1/HuR, hnRNPD/AUF1, Zfp36, and TIA1) for the regulation of immunocellular reactions, developmental processes, epithelial and neuronal degenerations, as well as cancer. It also supported efforts in mammalian mutation generation and analysis and manages related national efforts under the European Research Infrastructure INFRAFRONTIER and its National counterpart InfrafrontierGR/Phenotypos. Dimitris L. Kontoyiannis is also a Professor at the School of Biology of the Aristotle University of Thessaloniki and acts to expand the educational activities of BSRC "Alexander Fleming" towards the undergraduate and postgraduate students of the School.

Coding and Non-coding Rnas,
RNA Binding Proteins,
RNP Networks, Gene Expression

→ LINK TO PUBLICATIONS

Panagiotis Moulos

BIOINFORMATICS AND COMPUTATIONAL BIOLOGY

PANAGIOTIS MOULOS RESEARCH GROUP

Overview

We live in the era of personalized medicine, where technological advancements provide the means to systematically and holistically investigate the human genome, and use the findings towards better healthcare and well-being. Such advancements, in combination with vast amounts of research data accumulated over the past couple of decades, offer unique opportunities for breakthrough discoveries through Bioinformatics, the realization of Data Science in Life Sciences, and the best of many worlds: Biology, Computer Science and Statistics.

Our lab's main mission is to scrutinize and harness the vast volumes of clinical genomics data and develop novel consensus algorithms for multiple data sources with the purpose of analytical harmonization in the clinical bioinformatics landscape. Our research focuses on the intelligent integration of current methods for -omics data analysis and multi-omics integration with mostly clinical focus, such as the derivation of multi-omic molecular signatures in cancer and other polygenic diseases, as well as health-related lifestyle traits. At the same time, we implement our integrative algorithms in sustainable and maintainable software, for the analysis of high-throughput genomics datasets including gene expression, protein-DNA interactions, and mutation detection, using modern Next Generation Sequencing data. Our software packages contribute to major Bioinformatics communities, such as Bioconductor and ELIXIR, and our integrated platforms have already contributed to colorectal cancer and kidney disease research.

PANAGIOTIS MOULOS
RESEARCH GROUP

BIOINFORMATICS AND COMPUTATIONAL BIOLOGY

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(IFBR)

We expect to harvest additional opportunities and use the nowadays extensive open public genomic data towards the derivation of novel combinatorial genetic signatures of disease, like the effect of non-coding RNAs to alternative transcription in cancer through the application of modern statistical and Machine Learning techniques. Furthermore, we continue to develop methodologies for the creation of harmonized disease-specific knowledge bases, which are deployed in national and international initiatives dedicated to personalized medicine and better healthcare for the individual.

Clinical Bioinformatics, Scientific Software Development, Multiomics Integration, Biological Big Data

LINK TO PUBLICATIONS

Katerina
Papanikolopoulou

NEUROSCIENCE

KATERINA PAPANIKOLOPOULOU RESEARCH GROUP

Overview

The microtubule-associated protein Tau is an enigmatic protein. Its phosphorylation plays a pivotal role in normal physiology, while its hyperphosphorylation occurs in neurodegenerative disorders like Alzheimer's disease, Pick's disease, and FTDP-17. As with other neurological diseases, *Drosophila melanogaster* allows the power of genetic analysis to help decipher the role of Tau in the disease process, and to probe molecular and genetic interactions that are important in preventing or enhancing its deleterious effects. We express transgenes encoding human Tau in the entire fly central nervous system, and, in combination with a powerful proteomic approach, we probe molecular interactions that are important in preventing or enhancing its deleterious effects. We further validate the results of the proteomic screens above by genetic and molecular analyses for the enhancement/suppression of Tau-dependent behavioral and neurodegenerative phenotypes. As we gain a deeper understanding of the cellular regulation mechanisms of Tau function, we will shed more light on the complex role of Tau in

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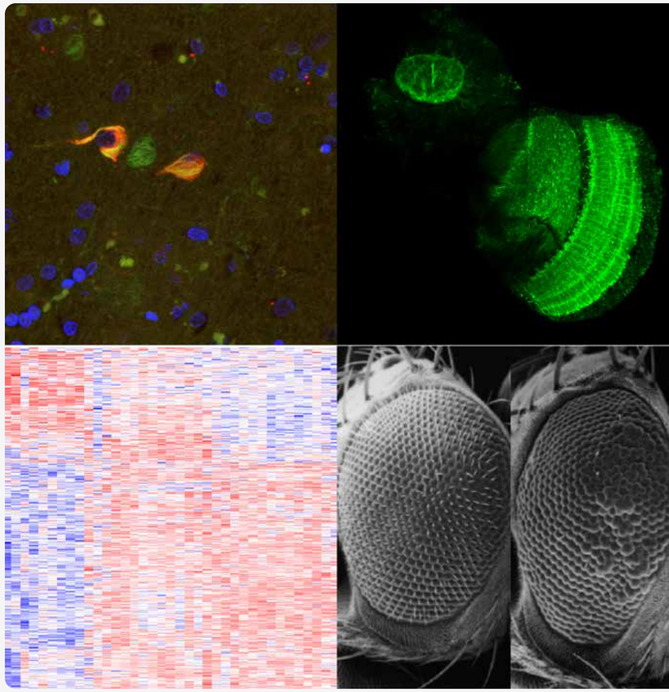

the aetiopathogenesis of neurodegeneration.

At the same time, we are trying to focus on the potential functional differences between Tau isoforms. When Tau is routinely studied, it is treated as if it was a single protein, whereas, in fact, it exists in six protein isoforms whose functions are not entirely understood. However, their differential involvement in particular Tauopathies raises the possibility that different Tau isoforms may possess some distinct functional capabilities in both physiology and pathology. To explore this, we compare the phenotypes induced by all six Tau isoforms in Drosophila (learning, memory, habituation, phosphorylation, aggregation, resistance to oxidative stress, etc.). Such isoform-specific differences are essential to understanding their apparent differential involvement in Tauopathies and contribution to neuronal dysfunction and toxicity.

Tau, isoforms, Drosophila,
Aggregation, Toxicity

LINK TO PUBLICATIONS

Georgios Pavlopoulos

BIOINFORMATICS AND COMPUTATIONAL BIOLOGY

GEORGIOS PAVLOPOULOS RESEARCH GROUP

In today's big-data era, the exponential growth of information caused by the latest advances of high-throughput technologies is indisputable. Therefore, efficient algorithms and tools for the extraction, analysis, exploration and representation of biological information are necessary.

The Bioinformatics and Integrative Biology Lab is located at the Institute for Fundamental Biomedical Research (IFBR) at BSRC 'Alexander Fleming' Research Institute, and hosts bioinformaticians and software engineers trying to create scalable and efficient applications dedicated to biological problem solving.

The main research interest of the group is to develop innovative bioinformatics solutions, as well as scalable tools and pipelines to integrate, visualize, and analyze biological and biomedical data to unravel Earth's microbial diversity.

The main domains of the group's research are: *Genomics, Metagenomics, Graph Theory, Parallel Programing, Biological Network Analysis, Data Integration, Text Mining, Artificial Intelligence, and Visualization.*

While our activities are applicable to many different areas varying from cancer research to environmental sciences, we mainly focus on network analysis, data integration, and multi-omics approaches, hoping to understand the function, the dynamics and the evolution of complex biological systems.

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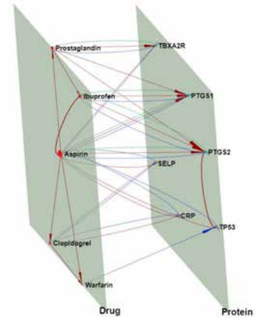

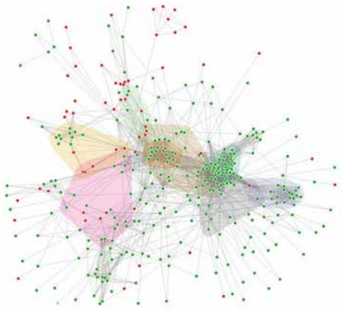

GEORGIOS PAVLOPOULOS
RESEARCH GROUP

BIOINFORMATICS AND COMPUTATIONAL BIOLOGY

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(IFBR)

Major achievements of the group include: *(i)* several publications in high impact journals such as Nature, Cell, Science, Nucleic Acid Research, Nature Biotechnology and others, *(ii)* a publication, nominated as finalist for the 2022 Gordon Bell Prize for innovation in applying high-performance computing to applications in science, engineering, and large-scale data analytics and, *(iii)* presence in the 2022 updated list ("**Updated science-wide author databases of standardized citation indicators**"), which includes the scientists who are placed in the top 2% of their field, worldwide.

Genomics/Metagenomics,
Biological Networks, Text Mining,
Data Integration and Visualization,
Knowledge Management
& Representation

→ **LINK TO PUBLICATIONS 1**

→ **LINK TO PUBLICATIONS 2**

Mihalis Verykokakis

MIHALIS VERYKOKAKIS RESEARCH GROUP

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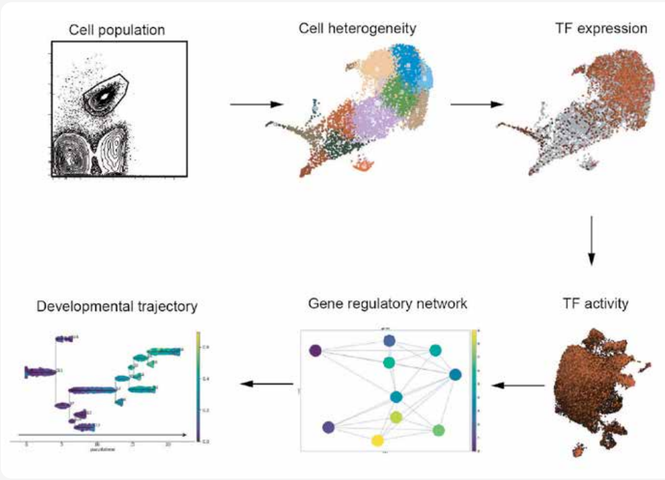
(IFBR)

Overview

Our research focuses on the molecular mechanisms that control cell fate decisions during T lymphocyte development and function, contributing to the generation of a self-tolerant and functionally competent immune system.

Part of our research explores the central hypothesis that unique gene expression programs, instructed by transcriptional regulatory networks, orchestrate the developmental pathway of progenitors as well as the homeostasis of mature cells and, at the same time, repress alternative programs. The stability or plasticity of cell identity is linked to the epigenetic chromatin organization that regulates transcription factor accessibility in space and time. Such circuits are characterized by cross-interacting molecular modules, which may be recurrently utilized in various immune cells. In lymphopoiesis, failure of the progenitors to execute their specified programs leads to aberrant differentiation and contributes to disease initiation.

A second line of our research aims at understanding the immune and molecular mechanisms involved in chronic inflammation-induced tumourigenesis. Although inflammation is largely a feature of the innate immune system, it is now clear that adaptive immune cells contribute to the perpetuation of inflammation, thus leading to disease. However, cancer development is associated with genetic alterations that lead to expression of tumour-associated antigens that are recognized by T lymphocytes, thus triggering an anti-tumour immune response. Therefore, tumourigenesis is a result of the balance between tumour-promoting inflammatory and tumour-fighting immune responses.



MIHALIS VERYKOKAKIS
RESEARCH GROUP

IMMUNITY & INFLAMMATION

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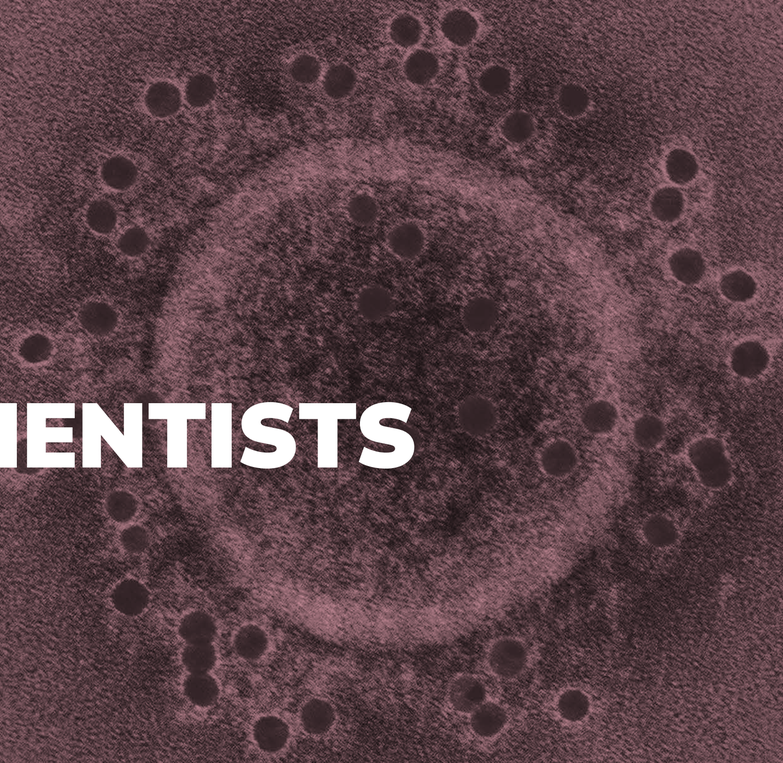
Our laboratory focuses on the function of T cells and the elucidation of the molecular mechanisms that control liver disease and the development of hepatocellular carcinoma. The concepts developed will help to reveal potent genetic and environmental factors that can predispose or protect individuals from disease, and in the long-term, may be utilized for the development of novel immunotherapeutic and vaccination strategies.

T Cell Development, Liver Cancer, Transcription, Epigenetics

LINK TO PUBLICATIONS

STAFF SCIENTISTS (IFBR)



BIOINFORMATICS AND COMPUTATIONAL BIOLOGY

Martin Reczko
Staff Scientist A'

MARTIN RECZKO RESEARCH GROUP

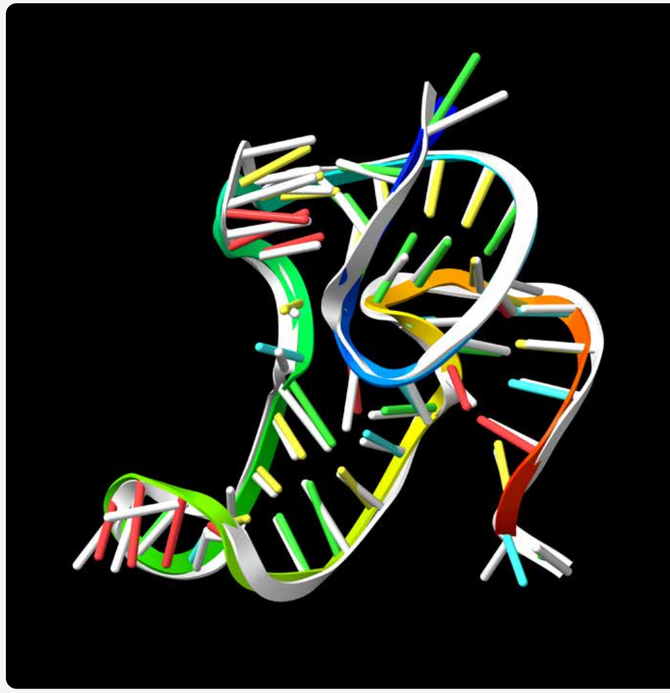
Research projects carried out by our team include the use of computational techniques to model biomolecular interactions, particularly those involving RNA and proteins.

We also work on computational metabolomics, delevoping methods for the genome-scale simulation of multispecies systems in different environmental conditions.

Additionally, we coordinate and support computational research infrastructures for all national life scientists within the European network ELIXIR. With ELIXIR, we deploy an efficient implementation of an infrastructure to support the safe archiving and retrieval of sensitive genomic data of Greek origin and promote its use by producers of such data.

We also conduct bioinformatics analysis for genomic and proteomic data, and operate part of the computational infrastructure of the institute.

We have devised and applied several novel machine-learning methods for biomedical research. Examples for these are a reinforcement learning algorithm for modeling biomolecular interactions and a novel transformer algorithm, which produces large language models that are used as question answering systems for biomedical topics. Our question answering system participated in the last two editions of the international competition “BioASQ,” and achieved twice the first place in one of the prediction rounds for answering “yes/no” questions.



MARTIN RECZKO
RESEARCH GROUP

BIOINFORMATICS AND COMPUTATIONAL BIOLOGY

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(IFBR)

For the prediction of the 3D structure of RNA given only its sequence, we employ an ensemble of established deep neural network systems, to predict a collection of 3d models, and score these models using a neural network that processes calculated physical properties of these models to select the most accurate prediction.

An example of a RNA structure predicted by our workflow is shown in white in the image here, overlaid with the experimentally determined structure of a non-coding RNA that controls gene expression.

LINK TO PUBLICATIONS

Sofia Grammenoudi
Staff Scientist B'

SOFIA GRAMMENOUDI RESEARCH GROUP

The main objective of our research is the development of infrastructures that provide integrated, standardized assays and services in biomedical research.

Our research focus is on the co-development, establishment and optimization of:

- Flow cytometric, hematological and clinical chemistry assays for the inflammatory phenotype monitoring of mouse disease models.
- Cutting-edge cell sorting platforms for high-throughput experiments, sequencing and functional assays.

Dr. Sofia Grammenoudi is responsible for the Scientific and Operational Management of the **Flow Cytometry and Cell Sorting Facility** and participates in the National Research Infrastructures **InfrafrontierGR/Phenotypos**, **pMedGR**, and **Bioimaging-GR**.

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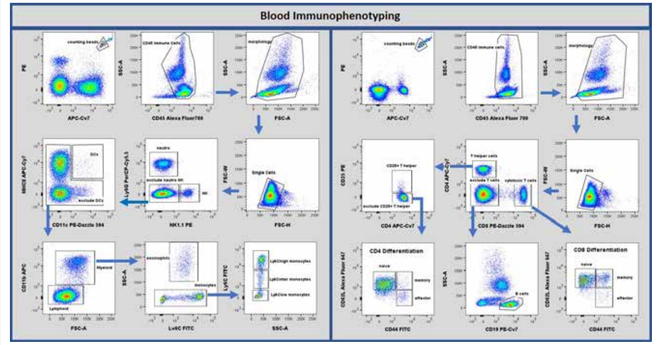

Flow Cytometry, phenotype monitoring, standardized assays

LINK TO PUBLICATIONS

Vasileios Ntafis
Staff Scientist B'

VASILEIOS NTAFIS RESEARCH GROUP

The care and use of live animals for scientific purposes is governed by internationally established principles of replacement, reduction and refinement (3Rs). Adopted in 2010, the Directive 2010/63/EU on the protection of animals used in research provides an appropriate framework, which should allow it to ensure appropriate standards of welfare through effective application of the 3Rs in the use, care, and breeding of animals.

The main objective of our research is to develop non-invasive and/or non-terminal phenotyping assays for animal models, ensuring that the number of animals used in projects is reduced to a minimum, without compromising the objectives of the project.

Our research focus is on the development of:

- In vivo imaging assays for small rodents, using X-rays, bioluminescence, fluorescence, endoscopy and ultrasound technologies
- Metabolic phenotyping assays for small rodents

Dr. Vasileios Ntafis is in charge of the **Animal House** and the **phenotyping services provided by Phenoclinic** and participates at the Infrastructures Program **InfrafrontierGR**.

In vivo imaging assays,
phenotyping assays, animal models

LINK TO PUBLICATIONS

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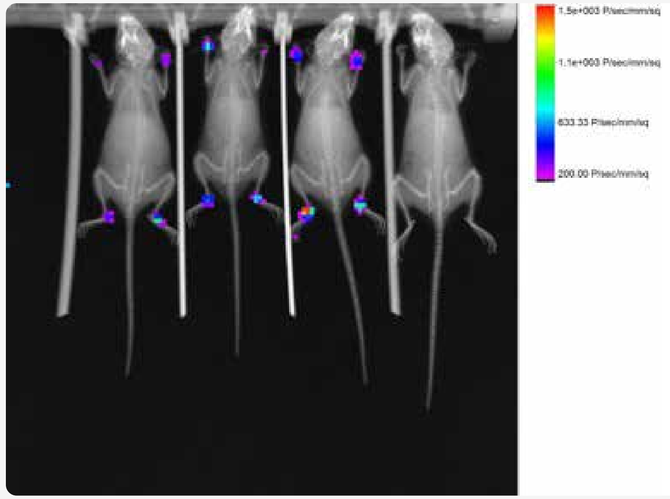

JUNIOR RESEARCHERS (IFBR)

CANCER BIOLOGY

RNA BIOLOGY & EPIGENETICS

Marianthi Kiparaki

MARIANTHI KIPARAKI RESEARCH GROUP

Elucidating the homeostatic mechanisms that safeguard tissue integrity and regulate organ size remains a major challenge in biology, necessary to acquire a deeper understanding of animal development and devise effective treatments for diseases. Cell competition constitutes a quality control mechanism wherein changes in cellular properties are sensed non-autonomously within mosaic tissues, culminating in the selective elimination of the "less-fit" population (losers). Demonstrated to be crucial for tissue homeostasis in both flies and mammals, cell competition serves as a regulatory mechanism that enhances tissue and organ fitness by removing suboptimal cells during both development and adult life. Moreover, cell competition has been implicated in processes such as regeneration, aging, and tumourigenesis. Nevertheless, the specific mechanisms governing cellular fitness and initiating competition remain elusive.

We have identified a stress response pathway that is activated in cells with heterozygous mutations in ribosomal protein genes (*Rp*+/- cells), leading to their elimination when surrounded by wild-type cells. This pathway is orchestrated by the transcription factor Xrp1, and has been also implicated in the elimination of aneuploid cells by cell competition during Drosophila development. In addition, the Xrp1 pathway is responsible for the majority of the autonomous responses of *Rp*+/- cells (i.e. reduced translation, slow growth), and for the developmental delay of the Rp+/- flies. In humans, mutations in many Rp genes lead to Diamond-Blackfan Anemia syndrome, characterized by bone-marrow defects, reduced growth, delayed maturity, skeletal malformations, and increased cancer predisposition. Similar to Xrp1 in Drosophila, p53 transcription factor is responsible for many aspects of *Rp*+/- induced phenotypes in mammals.

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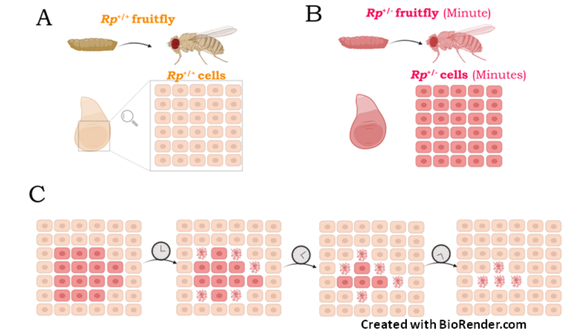

Figure
A,B. Flies with heterozygous mutations in Rp genes ($Rp^{+/-}$), which are called Minutes are viable and have no significant body size differences compared to wild type flies ($Rp^{+/+}$). In accordance $Rp^{+/-}$ mutant cells survive in homogenous environment, as wild type cells do ($Rp^{+/+}$).
C. In mosaic proliferative tissues (such as wing imaginal discs), $Rp^{+/-}$ cells undergo apoptosis when surrounded by wild type ($Rp^{+/+}$) cells.

CANCER BIOLOGY

RNA BIOLOGY & EPIGENETICS

Our future research goals include:

- Identification of the mechanisms driving cell competition.
- Elucidation of the autonomous and non-autonomous stress responses in both proliferative and post-mitotic *Rp*+/- cells.
- Investigation of the role of Transposable Elements in *Rp*+/- cells and in Cell Competition.

Cell competition, Development, Ribosome, Stress Response, Growth regulation

LINK TO PUBLICATIONS

Solenn Patalano

NEUROSCIENCE

BIOINFORMATICS AND COMPUTATIONAL BIOLOGY

INSTITUTE
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BIOMEDICAL RESEARCH
(IFBR)

SOLENN PATALANO RESEARCH GROUP

Mission

The main goal of the lab is to study how exposure to environmental endocrine disruptors affects cognitive functions.

Research directions

Our research model focuses on *Apis mellifera* honeybee societies. We study the impact of non-lethal pesticide exposure on honeybee memory, using high-throughput sequencing to describe transcriptomic and epigenetic changes during memory formation under field condition. This aims to identify key pathways in learning and memory, and provide insight into neuropathologies related to chronic exposure to pesticides. Additionally, we explore cellular resilience after chemical exposure, monitoring long-term effects and recovery. Furthermore, our lab optimizes honey metagenomics approaches to characterize species interacting with honeybees, aiming to describe the complexity and dynamics of the ecosystems influencing honeybee health and survival.

Achievements

Since she joined the Fleming Institute in 2018, Dr. Patalano secured significant European (H2020-MCSA) and Greek (ELIDEK, Fondation santé, Ministry of Agriculture) funding, while actively collaborating at both national and international levels that led to impactful research. Over the years, her lab is strongly committed to impacting society, and coordinates a citizen science project for Greece involving several hundreds of beekeepers for the international NGO "COLOSS". The results of her research at Fleming have been published in more than 10 international peer-reviewed journals and at international conferences.

Future plans

The recent research directions set by the European Union, specifically concerning habitat restoration and pollinator health protection, necessitate research implementation strategies involving not just scientists, but also the integration of local communities like beekeepers. Taking advantage of our citizen science networks, we intend to consolidate our research directions, primarily focusing on evaluating how transforming threatening environments can enhance bee health.

Brain and Memory, Epigenetics,
Phenotypic Plasticity,
Molecular Ecology, Adaptation

LINK TO PUBLICATIONS 1

LINK TO PUBLICATIONS 2

Nikolaos Vakirlis

NIKOLAOS VAKIRLIS RESEARCH GROUP

The lab is active in the wider research area of evolutionary genomics.

More specifically, our main goal is to understand molecular novelty and how it arises during evolution, that is how novel genes and protein functions originate. Not much is known about novel genes, also known as "orphans" or species-specific genes, but we do know that they contribute to the unique biology of each species, and can be crucial for adaptation and phenotypic diversification. Unique, novel genes can be found in the genome of every species, from E. coli to elephant. To understand how they evolved and what they do, we study them in genomes of organisms from across the tree of life, with a special focus on yeasts and human.

Another area of focus of the lab is that of "microproteins", short proteins that were until recently mostly ignored, but are now emerging as biologically important, including in human physiology and disease. We are developing new computational methodologies to accurately identify microproteins and elucidate their function, a challenging task, given that many of them are evolutionarily young and lack conservation. As a purely "dry" lab, we mine the vast quantities of publicly available biological data using cutting-edge computational molecular evolution, comparative -omics, phylogenetics and machine learning methodologies.

LINK TO PUBLICATIONS

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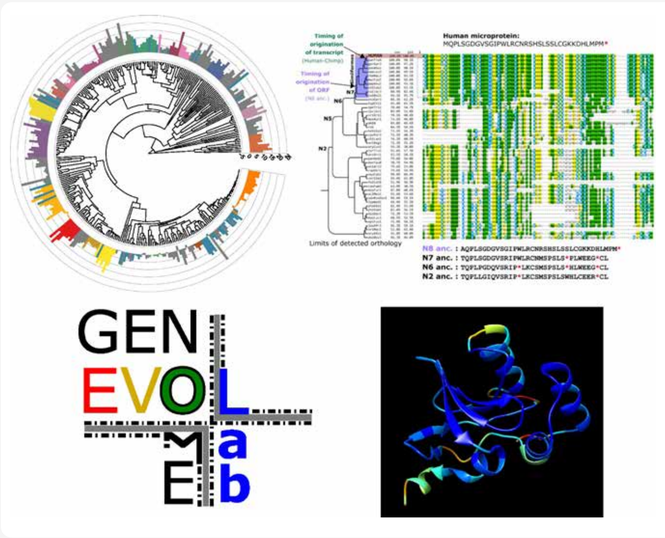
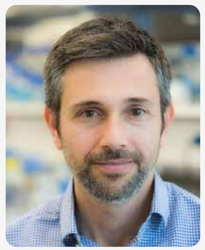


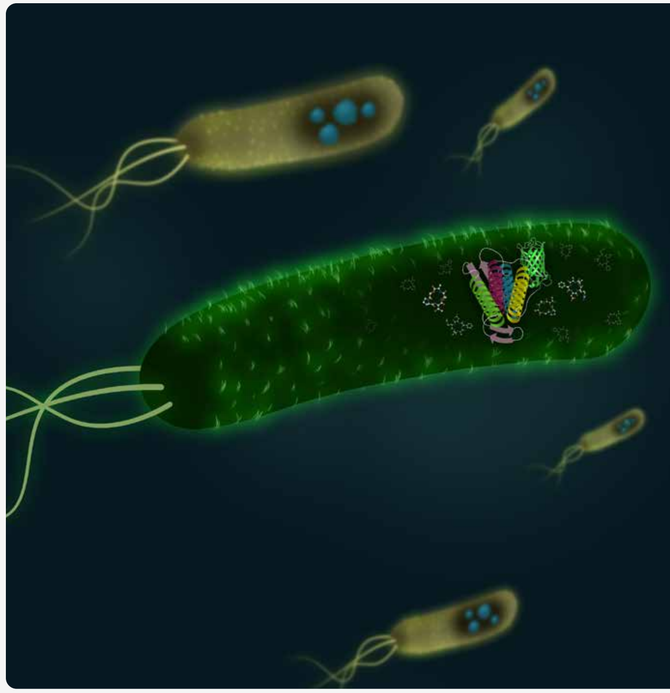
INSTITUTE FOR BIOINNOVATION (IBI)



Georgios Skretas
Director of the IBI

GEORGIOS SKRETAS RESEARCH GROUP

Our activities lie at the interface of biology, chemistry and engineering. The Laboratory of Biomolecular Engineering & Synthetic Biology (BESB lab; PI: Dr. Georgios Skretas) is a multi-disciplinary group employing researchers with different types of expertise, such as molecular biology, engineering, chemistry and agricultural sciences. The main goal of ESB is the development of engineered microbial cells with the ability to perform novel and complex functions by employing principles of Synthetic Biology. The lab utilizes simple organisms, such as the bacterium *Escherichia coli* and the yeast *Saccharomyces cerevisiae* as "biological chassis", and seeks to evolve them into efficient cell factories for the production of valuable chemical and biological products, and for the performance of industrially important processes, such as drug sensing and discovery, biotransformations, etc. Genetic engineering techniques are applied in order to redesign and rearrange the genome of the organism of interest, while protein engineering (directed protein evolution) and synthetic biology approaches are utilized, so as to introduce novel functions in the cell. A key aspect of the work that is carried out is the design and development of high-throughput screening systems, which are used to isolate the rare biomolecules and microbial strains that execute the desired function among large combinatorial libraries comprising hundreds of millions of variants.



BIOMOLECULAR ENGINEERING & SYNTHETIC BIOLOGY

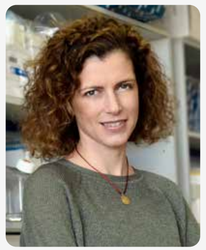
Currently, we have four main research directions underway:

1. Engineering bacteria as an early-stage drug discovery platform for diseases caused by protein misfolding & aggregation
2. Development of specialized microbial strains for high-level production of recombinant membrane proteins
3. Discovery of thermostable hydrolytic enzymes of industrial interest using bioinformatics and functional (meta)genomics
4. Development of protein-based tools for synthetic biology applications in biosensing and the programming of cell behavior

The BESB lab has secured significant funding from competitive sources and for various projects, including the ERC Consolidator Grant "ProMiDis", the ERA Chairs Project "Boost4Bio, and the Twinning project "Twin4Promis".

Recently, the BESB lab has established the spin-off company **ResQ Biotech**, which is applying innovative biotechnologies to discover and develop new and effective drugs against diseases caused by protein misfolding and aggregation, such as Alzheimer's disease and amyotrophic lateral sclerosis (ALS).

LINK TO PUBLICATIONS



Antigone Dimas

RNA BIOLOGY & EPIGENETICS

ANTIGONE DIMAS RESEARCH GROUP

Through our research we aim to understand how medically relevant, complex traits are shaped in humans. We seek to characterize the genetic architecture shaping disease risk and the molecular mechanisms underlying disease pathogenesis. We address the above aims by applying a muti-omics approach, combining genomics with the study of multiple molecular phenotypes including transcriptomes, proteomes, metabolomes, methylomes and gut microbiomes. We seek to characterize each biological level, but also to integrate data across molecular levels to obtain comprehensive biological signatures shaping higher-level phenotypes. We also complement our findings through dynamic experiments in cell culture to characterize the molecular pathways under study. Uncovering these signatures enables precision medicine approaches and empowers translation for disease management and treatment.

A central theme of our research is the impact of dietary restriction (DR) on biological pathways in the cell and on human health. In model organisms, DR extends health- and lifespan. In humans, although dietary interventions constitute a promising approach for the prevention and treatment of disease, performing rigorous dietary research remains challenging. We have established the **FastBio study** to address the molecular impact of DR in humans, in the form of periodic abstinence from animal products. FastBio comprises 200 periodic vegan individuals who alternate between an omnivorous and a vegan diet for religious reasons, in a highly consistent and temporally structured manner, and 211 non-vegan individuals

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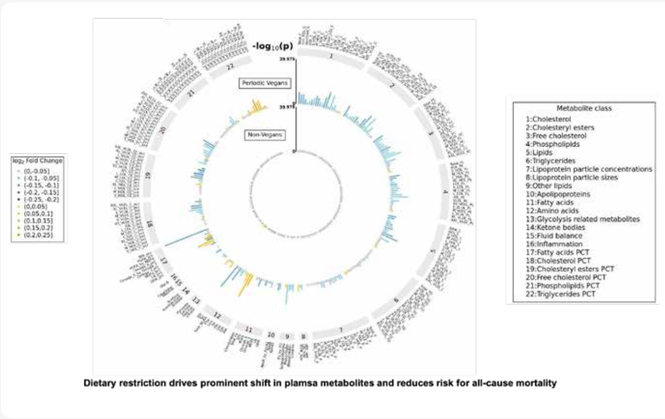

Dietary restriction drives prominent shift in plamsa metabolites and reduces risk for all-cause mortality

who are continuously omnivorous.

Through extensive molecular profiling, including measurements of blood biomarkers, RNA, the plasma proteome and metabolome, DNA methylation and characterization of the gut microbiome, we seek to identify pathways driven by DR and their link to health. We also address the pharmacological value of key molecular entities and characterize genetic variants that modify molecular responses to altering nutrient environments. Our work aims to underline the potential of dietary interventions for the prevention and treatment of chronic conditions (e.g. obesity) and disease, and to highlight the power of a food-as-medicine approach.

Multi-Omics, Human Functional Genomics, Translational, Immunometabolic, Food-As-Medicine, Primary Cells

LINK TO PUBLICATIONS

Eleni Douni

IMMUNITY & INFLAMMATION

CANCER BIOLOGY

ELENI DOUNI RESEARCH GROUP

Dr. Eleni Douni is Professor at the Biotechnology Department of the Agricultural University of Athens and Associate Researcher at the Institute for Bioinnovation of BSRC "Alexander Fleming". Our research group has long-lasting experience and expertise in the modeling of human diseases, using a broad range of *in vitro* and *in vivo* tools that reveal the underlying mechanisms of human diseases, with the ultimate aim of identifying novel therapeutic strategies. These approaches include molecular biology techniques, cell cultures, compound screening in cell assays, genetically engineered mice and establishment of breast cancer and bone metastasis mouse models. Our current research interests are focused on pathogenic and epigenetic mechanisms involved in osteoporosis, carcinogenesis, and bone metastasis, through the development and analysis of transgenic mouse models expressing human RANKL, the major inducer of osteoclastogenesis and bone resorption. Using RNA-Seq and proteomic analysis we have identified genes that are deregulated in RANKL-mediated osteoporosis and carcinogenesis, providing a plethora of potential novel biomarkers and disease targets that need further validation. Following a forward genetics approach, our group has also identified novel genetic causes of neurodegenerative diseases, the mitochondrial proteins DNAJC11 and SLC25A46, with critical role in mitochondrial biogenesis and central nervous system pathogenesis.

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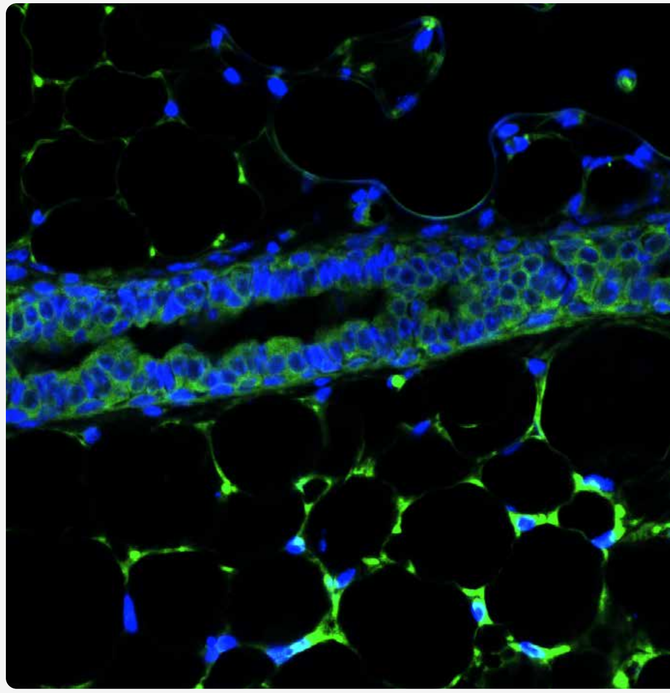

IMMUNITY & INFLAMMATION

CANCER BIOLOGY

Our research falls under the following thematic areas:

1. Pathogenic mechanisms and therapeutic approaches in Osteoporosis
2. The role of RANKL in mammary gland, breast cancer and bone metastasis
3. The role of the SLC25A46 outer mitochondrial protein in neurodegenerative diseases

Dr. Douni has more than 50 publications in peer-reviewed journals with over 3,000 citations according to Scopus, while she is regular reviewer in several scientific journals. She is member of scientific committees for a variety of conferences, including European Calcified Tissue Society (2020, 2024), Bone Marrow Adiposity Society (2022/president), and Hellenic Society for Biochemistry and Molecular Biology (2021, 2023/president). Dr. Douni is co-founder of the International Bone Marrow Adiposity Society and Biomedcode Hellas SA.

Transgenic mouse models, RANKL, osteoporosis, breast carcinogenesis, preclinical studies

LINK TO PUBLICATIONS

George Kollias

GEORGE KOLLIAS RESEARCH GROUP

The Kollias lab focuses on understanding the molecular and cellular mechanisms orchestrating complex phenotypes in chronic inflammation, immunity and cancer. The lab has revolutionized our understanding of cytokines and their pivotal role in chronic inflammatory diseases, firmly establishing Tumour Necrosis Factor (TNF) as a central molecule in the development of several inflammatory conditions.

In 1991, the lab demonstrated that deregulated TNF production causes chronic polyarthritis in a transgenic animal model, and that anti-TNF antibody treatment effectively alleviates the disease. This pivotal discovery catalyzed the development of the first successful clinical trials with anti-TNF antibodies for conditions like rheumatoid arthritis, Crohn's disease, psoriasis, and others.

More recently, the lab introduced a novel principle for the key pathogenic role of fibroblasts in chronic inflammatory disease, by demonstrating that mesenchymal cells are pathogenic targets of TNF, necessary and sufficient to orchestrate complex chronic inflammatory joint and gut pathologies. Subsequent work provided seminal mechanistic insights and novel concepts, establishing that subsets of fibroblastic mesenchymal cells play distinct and significant roles in tissue homeostasis, immunity, chronic inflammation, tumourigenesis and fibrosis. The lab uses **frontier technologies** to provide cues on how the functional heterogeneity of stromal cells can be translated to therapeutic innervations.

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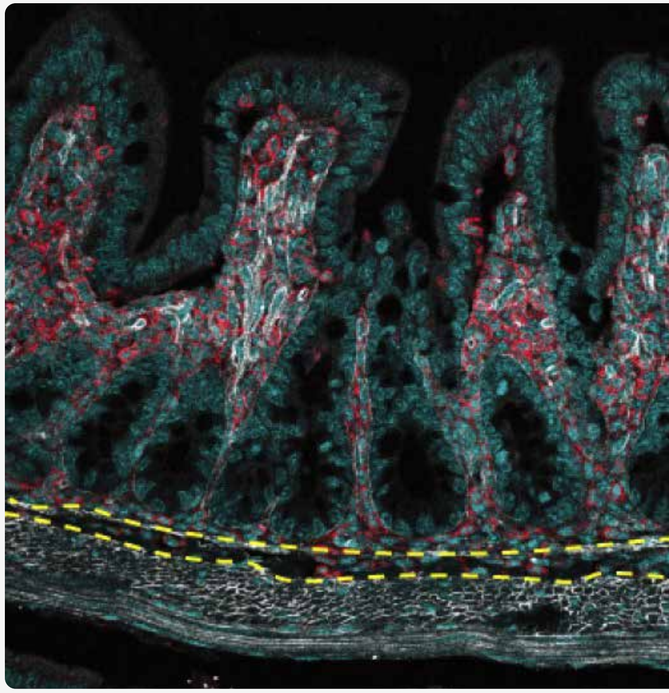

IMMUNITY & INFLAMMATION

CANCER BIOLOGY

Supported by several national and European grants, including two Advanced ERC grants (MCs-inTEST 2014 and BecomingCausal 2021), and industry partnerships, the lab has spearheaded major research infrastructures like **InfrafrontierGR** and **pMedGR**, advancing imaging and single-cell multi-omic analyses in Greece. They've filed over 10 patent applications and facilitated over 400 MTAs for global research projects. Their biotech spin-off, **Biomedcode Hellas SA,** provides preclinical drug evaluation services to the global pharma industry. The lab has trained numerous students and postdocs and coordinates the International MSc in **Molecular Biomedicine** in co-operation with the Medical School of Athens.

In their quest to identify new pathways, targets, and biomarkers, the lab team seek to transform disease prognosis, prevention, and therapy. They explore the functional diversity of stromal cells, especially fibroblasts, for future therapeutic innovations.

Animal Models, Fibroblasts, Mesenchymal Cells, Chronic Inflammation, Cancer, Single-Cell Multiomic Analysis

→ LINK TO PUBLICATIONS

Vasso Kostourou

VASSO KOSTOUROU RESEARCH GROUP

Endothelial Pathobiology and Tissue Microenvironment

The mission of the Kostourou lab is to discover the fundamental principles governing blood vessel biology and the cross-talk of the vascular network with tissue environment in health and disease. Our research focuses on endothelial cell adhesions, namely cell-extracellular matrix and cell-cell adhesions, which act as molecular organisers to integrate biochemical and mechanical signals of the extracellular microenvironment and regulate blood vessel function. Over the years, we have established strengths in combining the use of endothelial-specific inducible knockout mice with specific angiogenesis assays (retina angiogenesis, aortic ring sprouting), advanced cellular assays (live endothelial cell invasion assay), biophysical methods (traction force microscopy), and system biology approaches (proteomics), to examine how endothelial adhesions guide cellular responses and shape pathological microenvironments, including cancer. Expanding previous lab work on the role of focal adhesion kinase (FAK) in tumour angiogenesis, we investigate the functional significance of key cell-extracellular matrix adhesion proteins, including Talin, ILK and PINCH, in tumour growth and angiogenesis. Recently, we established that endothelial talin is a key mechanosensor in vivo to drive and sustain the growth of vascular network and fuel cancer progression.

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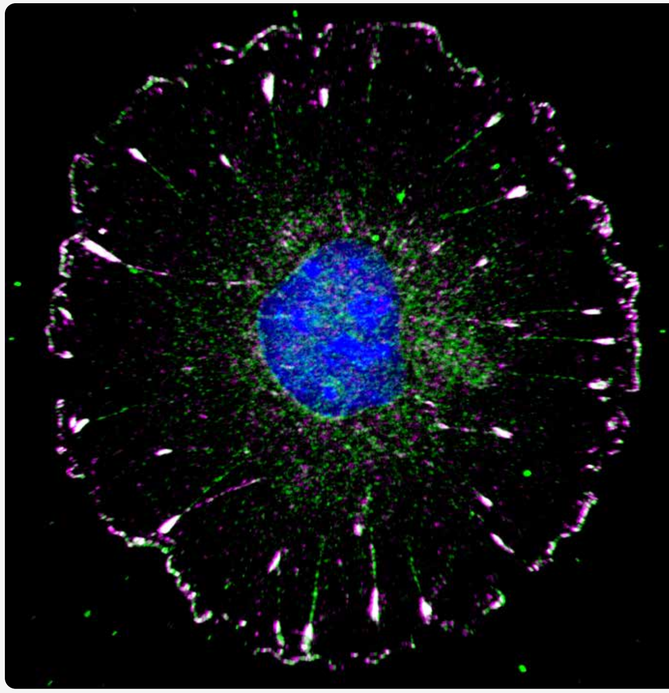


These findings shed light into the molecular mechanisms of cell mechanotransduction, and underpinned the significance of mechanical signals in regulating vascular morphology and ultimately modulating cancer progression. Also, in a collaborating project, we established a splice-variant in the *TLN1* gene as the genetic link of Systemic Capillary Leak Syndrome (SCLS), a rare life-threatening human disease with unknown cause and only symptomatic treatment. To gain the medical perspective and facilitate the translation of our findings, we are closely collaborating with clinicians. Specifically, we investigate the mechanobiology of human tumour microenvironment, and the impact of vascular morphology and function in cancer malignancy and resistance to therapy.

Our research aims to identify specific targets that can be used to modify blood vessel growth and function and provide novel therapeutic approaches for vascular-related pathologies, and to discover key factors of tumour microenvironment for innovative diagnostic and therapeutic interventions.

Cancer, cell adhesion, mechanobiology, endothelial cells, tumour microenvironment

LINK TO PUBLICATIONS

IMMUNITY & INFLAMMATION

CANCER BIOLOGY

ALEXIS MATRALIS RESEARCH GROUP

The research interest of my lab focuses on the development (design, synthesis and pharmacological evaluation) of novel bioactive molecules addressing to the inhibition of key-proteins involved in the onset and progression of complex human diseases, such as chronic inflammatory diseases, fibroproleferative diseases, and tropical diseases. Specifically, the expertise of my lab is related to the identification of "hit" compounds using either Differential Scanning Fluorimetry (DSF) or NMR techniques, and then the conduct of Structure-Activity Relationship Studies (SAR) using organic synthesis, aiming at the optimization of these "hits" to advanced leads. The lead compounds are evaluated in a multitude of in vitro and cell-based assays for their activity, and the most promising compounds are tested in terms of their therapeutic effect in vivo in different experimental animal models. Furthermore, our lab in collaboration with the proteomics facility of "Fleming" performs target identification studies (chemoproteomics) with the purpose of finding the main target protein(s) of bioactive compounds having exhibited a promising phenotypic activity against a disease. Lastly, our lab has a keen interest in drug repurposing area which aspires to the identification of already known drugs that could be able to be used for the treatment of a different disease.

Current efforts in our lab are focused on the following Drug Development projects:

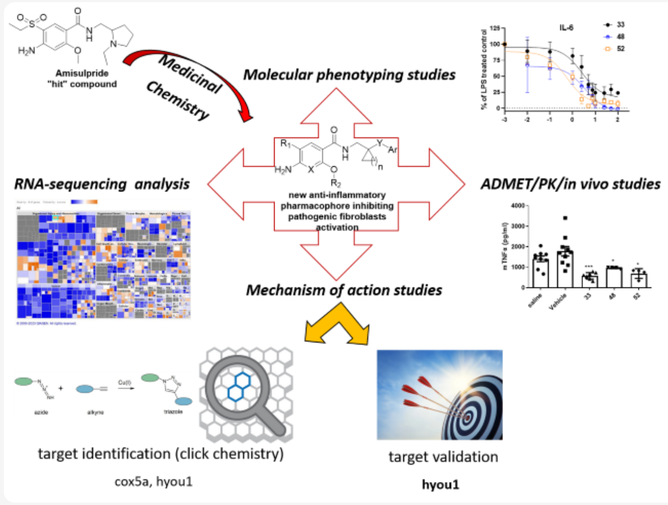
a. *Development of small molecules targeting the activation of pathogenic fibroblasts for the treatment of chronic inflammatory diseases.*

b. *The circadian clock core component RORα as a novel target in Fibroproliferative Diseases*

c. *Highlighting the role of SRPK-2 protein kinase in developing a new generation of potent fast-killing antimalarial drugs.*

d. *Design, synthesis and pharmacological evaluation of novel dual-targeting PPARγ-Autotaxin modulators against Idiopathic Pulmonary Fibrosis.*

INSTITUTE
FOR BIOINNOVATION
(IBI)



Medicinal Chemistry,
Drug Development, Chemical Biology

LINK TO PUBLICATIONS

Christoforos Nikolaou

CHRISTOFOROS NIKOLAOU RESEARCH GROUP

Our group was formed in May 2020. Our mission is to deploy computational and bioinformatics approaches to analyze, model and predict the relationship between eukaryote genome architecture and gene regulation.

We make use of both bulk and single cell -omics data, combined with high resolution imaging outputs, to answer fundamental questions related to how gene expression programs are affected by chromatin and chromosomal positional constraints in both one and three dimensions.

In this framework we are interested in a) understanding the constraints that underlie the positional preferences of genes and regulatory sequences in eukaryotes, b) linking chromatin structure with gene regulation, and c) modeling gene expression dynamics in development and disease. The Fleming environment is allowing us to explore questions related to the above in the contexts of inflammatory and auto-immune diseases, cancer, and cell development. At the same time, we approach all of the above under the lens of genome evolution.

INSTITUTE
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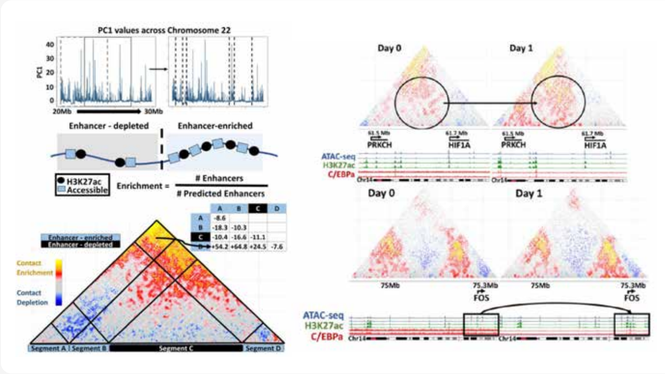


BIOINFORMATICS AND COMPUTATIONAL BIOLOGY

Positional Constraints in Gene Expression

We explore the way gene expression may be reflecting underlying positional constraints in eukaryotic genomes when challenged in certain pathological contexts. In the past, we have introduced the concepts of "domains of focal deregulation" and "domains of coordinated expression" as areas of linear chromosomes where gene de-/co-regulation is positionally constrained.

Chromatin-guided Gene Regulation

We aim at defining mechanisms through which chromatin structure may guide gene regulation in the contexts of disease and development. We are particularly interested in models that explain enhancer-promoter rewiring and the formation of molecular, transcriptional condensates, and how these may be perturbed under inflammation.

Evolution of Genome Architecture

We study the evolution of genome organization in both unicellular and multicellular eukaryotes. We have introduced the concept of "genomic niches", whereby eukaryote genomes appear to be compartmentalized in self-contained structural regions that reflect an underlying optimization at both functional and evolutionary levels.

Genome Organization, Transcription,
Evolution of Genome Architecture,
Chromatin Structure,
Genomic Sequence Constraints

LINK TO PUBLICATIONS

George Panayotou
Director &
Chairman of the Board

GEORGE PANAYOTOU RESEARCH GROUP

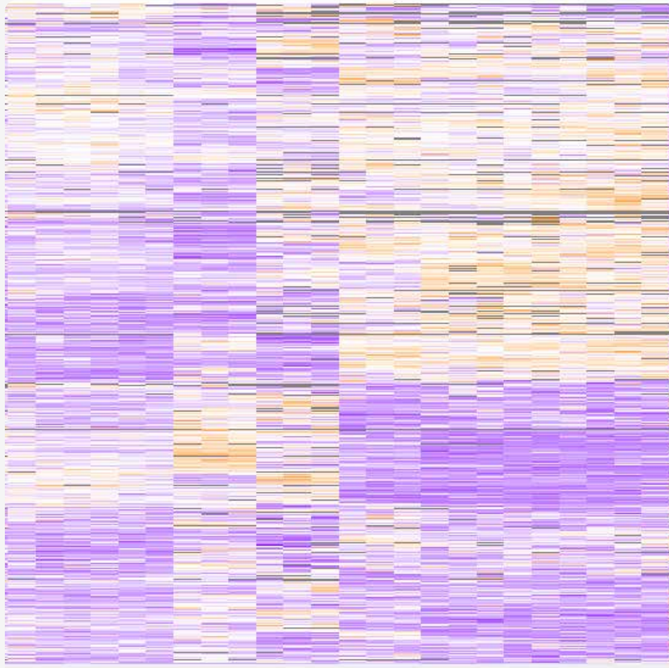
George Panayotou was the first researcher recruited at the BSRC "Alexander Fleming" in 1998. He has been present throughout its development, and has helped shape the distinctive character of FLEMING. He was particularly involved in setting up the center's advanced facilities in 1999, as well as in their subsequent upgrade and enrichment. He is currently the Center's Director and Chairman of the Board.

Mission

The mission of the Panayotou lab is to uncover determinants of specificity in signal transduction processes involved in human disease. The laboratory primarily employs proteomic technologies in order to understand the role of specific signaling pathways in cancer development.

Research Focus

The lab has two main research directions: a) to study the complex signaling pathways that are activated in mammalian cells upon their stimulation by extracellular stimuli or stress, and b) to develop and implement proteomic technologies.



Main Scientific Directions

The role of dual-specificity phosphatases in MAP kinase signaling pathways.
We are investigating the mechanisms of regulation of the dual-specificity phosphatase DUSP8 – a JNK and p38 specific phosphatase - aiming for a better understanding of the role of this enzyme in cell physiology and disease processes.

Development of proteomic methodologies
We develop and implement proteomic methodologies to identify differences in protein expression or post-translational modifications in a variety of projects, both relevant to the lab's directions, and in collaboration with other groups within FLEMING and other institutions. We are currently in the process of upgrading the proteomics facility instrumentation as part of FLEMING's infrastructure renovation.

Signal transduction, phosphatases, oncogenic signaling, proteomics

LINK TO PUBLICATIONS

Maria Tsoumakidou

IMMUNITY & INFLAMMATION

CANCER BIOLOGY

INSTITUTE
FOR BIOINNOVATION
(IBI)

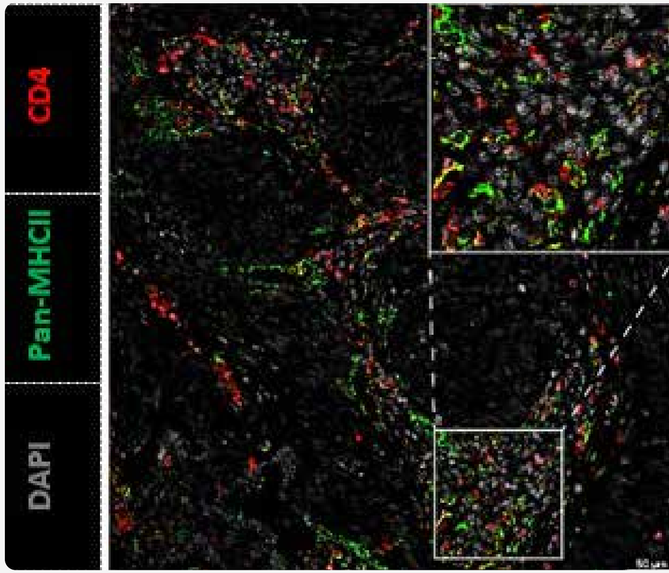
MARIA TSOUMAKIDOU RESEARCH GROUP

Mission: Towards efficient cancer immunotherapies: deciphering the landscape of antigen-presenting cells.

Anti-cancer immunity depends on efficient presentation of tumour antigens and co-stimulatory signals by antigen-presenting cells to anti-tumour T cells. The **overarching goal** of the lab is to decipher the landscape of antigen-presenting cells in cancer patients, with the ultimate aim to develop more effective and precise immunotherapies. The laboratory has strong clinical links and works simultaneously with the mouse and human system. By using state of the art -omic technologies, cancer mouse models, patient-derived xenografts, and advanced culture systems, such as cancer organ chips, we study cell subtypes, signaling pathways, genes, regulatory modules and interactions that control antigen presenting cells in cancer.

Among the pioneering questions, we are interested in are:

- How do dendritic cells change as they transition from homeostasis to tumour and tumour draining lymph node microenvironments?
- How do non-hematopoietic cells, such as fibroblasts, evolve and acquire their exclusive antigen presenting signatures in the tumour microenvironment?
- Which are the cardinal interactions that signal for T cell priming in tumour-draining lymph nodes and tumour tissues?



Signal transduction, phosphatases, oncogenic signaling, proteomics

LINK TO PUBLICATIONS

STAFF SCIENTISTS (IBI)

Martina Samiotaki
Staff Scientist A'

MARTINA SAMIOTAKI RESEARCH GROUP

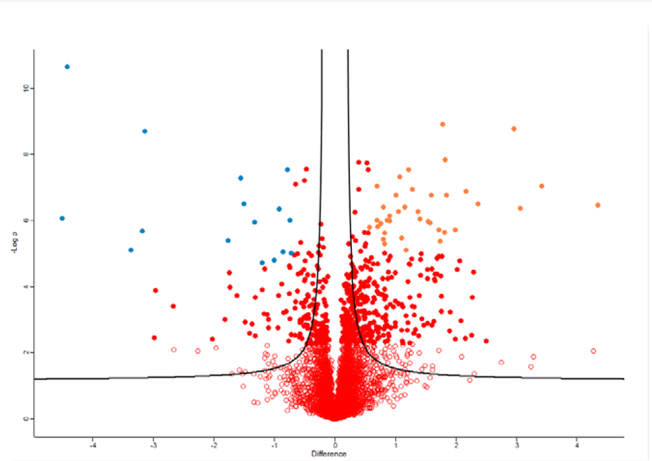
Our research aim is to set up and perform high quality analyses addressing questions mainly in the field of proteomics.

We are continuously trying to improve our mass-spectrometry platform with new methodological, instrumental and software tool developments for the:

- Analysis of proteins in any organism, in any tissue or cell type, using variable sample preparation methods depending on the research question.
- Targeted as well as untargeted proteomic workflows. Label free quantification of proteomes. Labeled based quantification using variable reporter ion chemistries.
- Generation of sensitive results from limited initial material, such as FACS sorted cells and isolated exosomes.
- Studying of protein interaction networks and their visualization.
- Finding and characterizing protein modifications using "Open searches" such as PTM Shepard.
- Characterization of microbial populations taxonomically using metaproteomic platforms, as well as functional characterization of altered microbial proteomes.
- Elucidation of drug interactions with proteomes chemo-proteomic approaches.
- Clinical and pre-clinical proteomic projects, as well as the proteogenomic-assisted analysis of samples.
- Numerous software solutions often used in parallel in order to extract the most from the experimental data. Main tools in usage are DIA-NN, Proteome Discoverer 2.4 (Thermo), MaxQuant/Perseus, Skyline, MSFragger, EpiProfile, iMetaLab, MSStats.

Dr. Martina Samiotaki is responsible for the Scientific and Operational Management of the Proteomics Facility and participates in the National Research Infrastructure pMedGR.

INSTITUTE
FOR BIOINNOVATION
(IBI)



Proteomics, Mass spectrometry

LINK TO PUBLICATIONS

FACILITIES

Vasileios Ntafis
Head of Facility,
Designated Veterinarian

ANIMAL HOUSE

Since 2001, the Animal House of BSRC "Alexander Fleming" provides a high-quality breeding and experimental environment for animal models towards the biomedical research community. At the same time, it promotes animal welfare, excellence, and scientific interaction. The Animal House covers an area of approximately 900 sqm, it provides mouse husbandry - approximately 22.000 animals - and is one of the largest facilities in terms of number and variety of mice in Greece.

The Animal House operates in accordance with the National and European legislation and are registered by the Official Veterinary Service of the Prefecture of Athens as Breeding, Supplying and Experimental Establishment in accordance with the National Legislation, under the Code Numbers EL 09 BIO 04, EL 09 BIO 06, EL 09 BIO 05, respectively.

Currently the Animal House comprises 6 different Facilities of SPF status, a Core Breeding-Barrier Unit, 4 Phenotyping Units (one of which is a BSL-2 Unit) and a Quarantine.

Similar to its operation, the services provided by the Animal House of BSRC "Alexander Fleming" are in accordance with the National Legislation and the European Legal framework (on the protection of animals used for scientific purposes), as well as the current guidelines of the Federation of European Laboratory Animal Science Associations (FELASA).

Animal House services include mouse hosting and supply, education and training, as well as experimental support for mouse phenotyping. Regarding education and training, in-house seminars, and LAS (laboratory animal science) courses are provided to all users designing projects and performing procedures on animals. Additionally, upon agreement, Animal House provides installation, personnel, and mouse phenotyping services for research protocols.

FACILITIES

Facility affiliated with

InfrafrontierGR/PHENOTYPOS

Mouse, hosting,
phenotyping services

LINK TO FACILITY

PHENOCLINIC

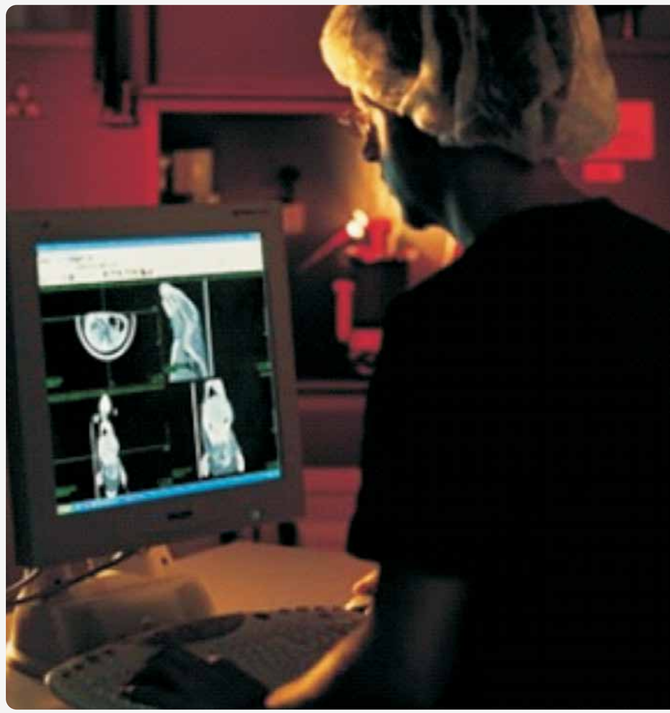
Vasileios Ntafis
Head of Facility,
Designated Veterinarian

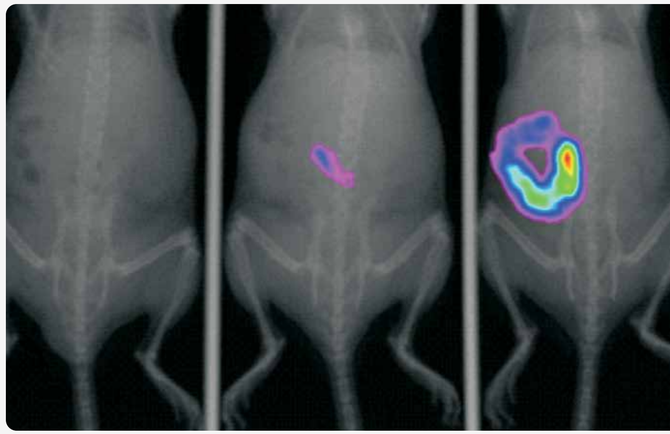
In 2019, the PhenoClinic was established by the support of Stavros Niarchos Foundation and INFRAFRONTIER-GR to maximize the phenotypic and preclinical services provided by BSRC" Alexander Fleming" and by the National INFRAFRONTIER activities. The PhenoClinic is supervised by the authorities of BSRC's Animal House and offers modalities for non-invasive/non-terminal in vivo imaging, metabolic, behavioral phenotyping and transplantation services to the scientific and industrial communities.

The *in vivo* imaging unit is equipped with an in vivo optical/x-ray system (**In-Vivo Xtreme, Bruker**), an endoscopy system (**Mainz COLOVIEW System, Karl Storz**) and an ultrasound imaging system (**Vevo 3100 Imaging System, FUJIFILM VisualSonics)**.

The metabolic and behavioral unit is equipped with a metabolic and behavioral measurement system, the **Promethion Core System (Sable Systems International), metabolic cages (Tecniplast)** and state-of-the-art equipment for behavioral phenotyping from **Ugo Basile**.

Moreover, irradiation services and of transplantation studies are also provided by the PhenoClinic, which is equipped with the **MDS Nordion Gammacell 3000 Elan irradiator** for small animals.





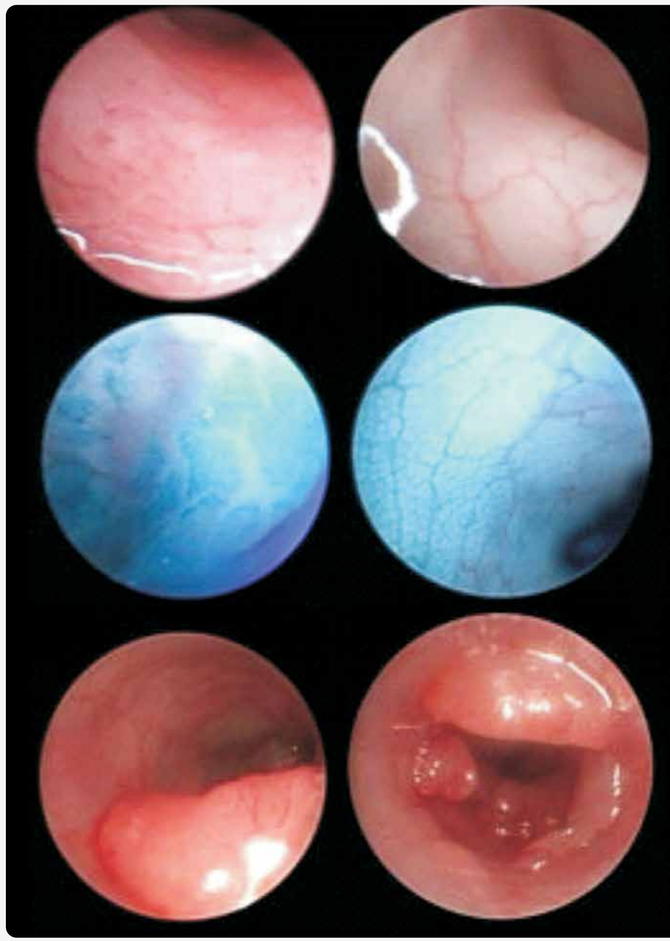
Facility affiliated with

InfrafrontierGR/PHENOTYPOS

Units are supported by dedicated and trained personnel to offer custom-made services upon request, such as:

- X-ray imaging - primary phenotyping
- X-ray imaging - bone density monitoring
- Bioluminescence for acute/chronic inflammation monitoring
- Bioluminescence/Fluorescence for tumor models monitoring
- Cardiovascular phenotyping
- Tumor detection and analysis in animal models (liver cancer, bladder cancer etc.)
- Colonoscopy in experimental models - high quality data acquisition
- Colorectal implantation of tumor cells and monitoring
- Primary metabolic phenotyping
- Primary and advanced behavioral phenotyping

FACILITIES



LINK TO FACILITY

Dimitris L. Kontoyiannis
Facility Manager

Kostas Bozonelos
Head of Operations

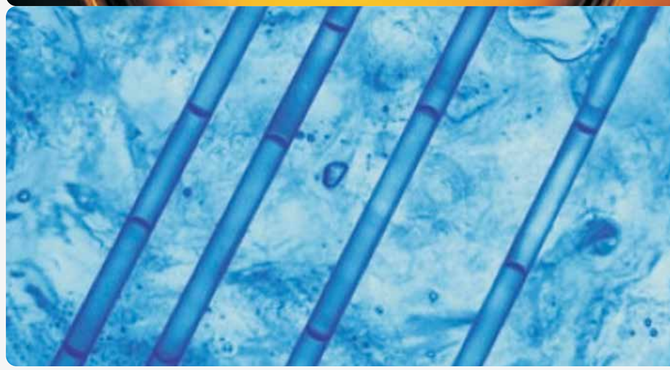
TRANSGENIC FACILITY, ARCHIVING & DISTRIBUTION SERVICES

The Transgenic Facility was established in 2001 as the first open-access unit of B.S.R.C. "Al. Fleming" to provide services in gene modification and the generation of rodent models used in cutting-edge biomedical research. It has a rich track record in providing such services beyond Fleming and towards academic institutes, biotech, and pharmaceutical companies worldwide. The facility's international standing provided a first basis for establishing B.S.R.C. "Al. Fleming" as a leader in animal models for human diseases, and as a key partner of the ESFRI Infrastructure INFRAFRONTIER.

Currently the facility offers services in two areas:

1. **Induction of any type of mutation** in rodents using specialized instrumentation and protocols for conventional and novel methodologies such as:
   - » Gene addition, via the microinjection of modified DNA constructs into the pronucleus of fertilized oocytes.
   - » Gene targeting or replacement for knock-out, conditional knock-out, and knock-in gene models via the targeted manipulation of mouse embryonic stem cells, subsequent implantation in blastocyst embryos and chimera production.
   - » CRISPR/Cas9 mediated gene editing for the induction of precision and clinically relevant mutations using a variety of methods (embryo/uterine electroporation, microinjection).

The abovementioned services are supplemented with the mutation design, provision of genotyped cohorts and logistical support for distribution.



EMMA mouse repository

Facility affiliated with

INFRAFRONTIER

TRANSGENIC FACILITY, ARCHIVING & DISTRIBUTION SERVICES

2. Archiving by Cryopreservation and Distribution

The Facility acts as the official national node of Europe's largest repository of mutant mouse strains - **the European Mutant Mouse Archive (EMMA).** As part of the European Landmark Research Infrastructure (RI) INFRAFRONTIER, EMMA nodes archive, distribute or revive regional strains following commonly agreed standards and service protocols. In doing so they provide economical and ethical solutions in mouse handling.

The Transgenic Facility abides to EMMA principles to offer services in:

- Sperm & Embryo Cryopreservation
- Long-term deposition in a state-of-the-art Biobank located at B.S.R.C. "Al. Fleming" with a capacity to store 1300 lines placed as mirror duplicates.
- Cataloging for Distribution via EMMA or independently
- Shipment of Cryopreserved material using the dedicated dry-shipper containers of the Facility
- Revival by In Vitro Fertilization, Embryo thawing or Embryo Rederivation of Live mice
- Consulting and Training

Transgenic, mouse, cyopreservation, archiving

LINK TO FACILITY

LINK TO PUBLICATIONS

Marietta Armaka
Head of Facility

MICROCT IMAGING

The microCT Facility of BSRC Alexander Fleming is equipped with a SkyScan1172 high-resolution ex vivo micro-CT scanner, which delivers 3D image datasets of X-ray attenuation throughout a sample, allowing 3D visualization and analysis. Our equipment permits the visualization over a range of spatial scales from <1μm to 35 μm, with dynamically variable acquisition geometry for shortest scan at any magnification utilized. Cross-section images are generated in a wide range of formats up to 8000 x 8000 pixels. The maximum object size could reach 50 mm in diameter and 70mm in height.

The facility has 10 years' experience, and can provide advanced micro-CT imaging services and support for research involving ex vivo analysis of selected tissues derived from small animals (bone, mineralized biomaterials, grafts, soft tissues, etc.).

We commonly provide 2D and 3D bone histomorphometric analyses, 2D and 3D imaging of mineralized and soft tissues (surface and volume rendering), while customized analysis and imaging protocols can be designed on-site. Since 2016, we have established several National and Transnational collaborations (Universities of Athens, Thessaloniki, Thessaly, Greece; Ghent University and VIB, Belgium; Cologne University, Germany, etc.).

LINK TO FACILITY

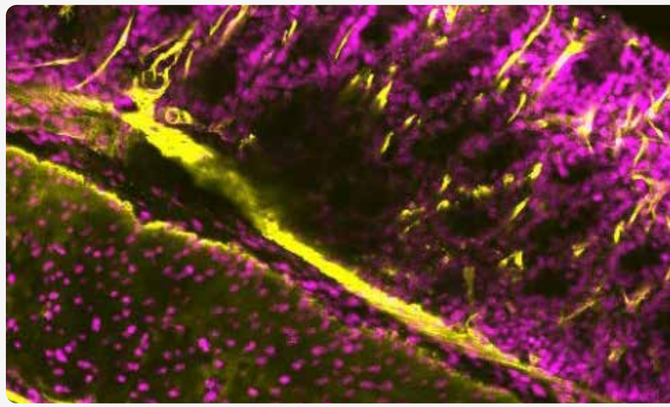
HISTOPATHOLOGY

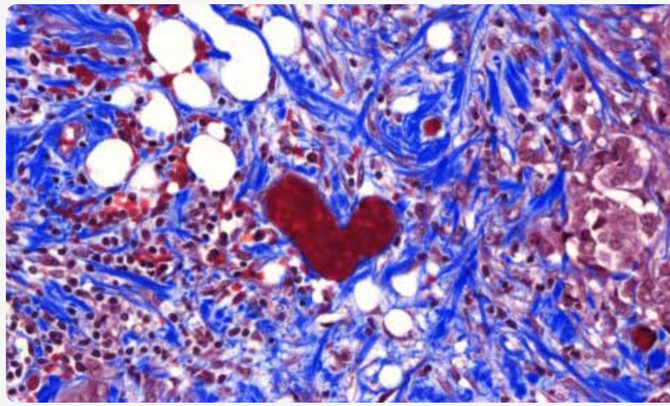
BSRC Fleming's Histopathology Unit provides state-of-the-art histology services, including tissue fixation, sectioning, and high quality staining for research applications.

The Unit is equipped with a Leica TP1020 **automated tissue processor**, a Leica RM2125 **microtome**, a VT 1200 **vibratome**, a CM1950 **Cryostat** and a ST5010 **automated slide stainer** combined with a CV5030 Robotic coverslipper. The Unit recently acquired an **Olympus SlideView VS200 slide scanner**, which captures high resolution images for quantitative analysis and facilitates sharing and archiving of histopathology data.

The Unit offers open access services to the research community, including standard mouse tissue processing and fixation, paraffin coating/embedding, microtome and cryo-sectioning, bone processing including decalcification, H/E or tissue staining with specialized dyes on paraffin-embedded or frozen sections, vibratome sectioning as well as Immunohistochemistry (IHC) and in situ hybridization (ISH). The Unit also offers assistance and custom solutions for histopathological analysis.

FACILITIES





Facility affiliated with

InfrafrontierGR/PHENOTYPOS

LINK TO FACILITY

Vasso Kostourou
Head of Facility

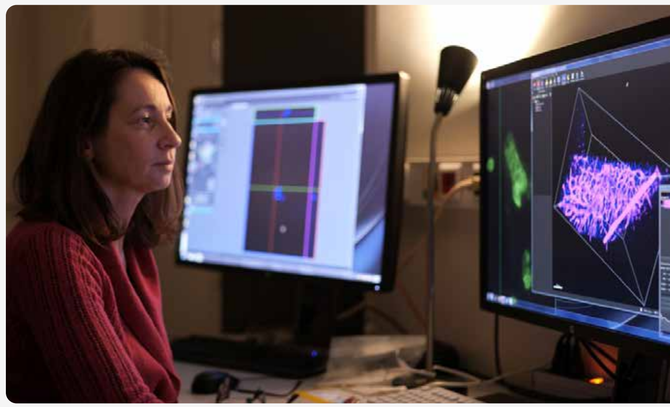
BIOIMAGING

The BSRC Fleming BioImaging Facility provides expertise and state-of-the-art equipment for modern multidimensional biomedical imaging applications using cutting-edge microscopy methods, digital image processing and computational image analysis. The scientific personnel can provide expert guidance to scientists and assistance for projects requiring highly specialized image processing and analysis.

The BioImaging facility is equipped with **Leica TCS SP8X White Light Laser confocal** system, **PicoQuant FLIM** system with two external APD detectors, **Zeiss LightSheet Z1** Imaging System, **AxioObserver 3** Fluorescent Microscope, **Leica DM2000** Fluorescent Microscope, **Nikon E800** upright widefield/fluorescent microscope, **Nikon TE300** widefield with Hoffman optics/ fluorescent microscope, Nikon fluorescent stereoscope, **Leica SMZ800** fluorescent stereoscope and Imaging analysis software, including **IMARIS 10** with automated detection, measurements and statistics, visualization and group comparison, tracking in 2D/3D and lineage, Filaments, and automated tracing.

Trained personnel could offer the **following services** upon request:

- High-resolution dynamic fluorescent imaging in 2D and 3D
- Multi - Fluorescent Protein detection (Spectral Unmixing)
- 3D visualisation
- unlimited selection of excitation and emission wavelengths in visible light
- automated multi-position acquisition
- co-localisation and ratio-metric analysis
- FRAP (Fluorescent recovery after photobleaching)
- FRET (Fluorescent resonance energy transfer)
- FLIM (Fluorescent lifetime Imaging microscopy)
- Live dynamic imaging
- Deep tissue and organ fluorescent imaging
- Methods for clearing large tissue and organs for 3D multi-view imaging.



LINK TO FACILITY

Sofia Grammenoudi
Flow Cytometry and Cell Sorting Facility Scientific and Operational Manager

FLOW CYTOMETRY & CELL SORTING
Hematology and Clinical Chemistry

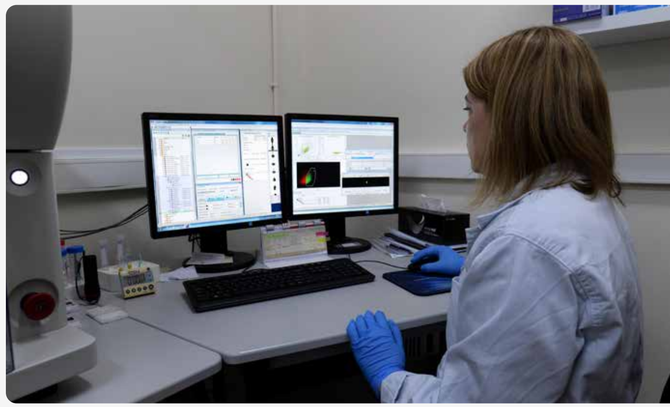
Overview

The BSRC Fleming Flow Cytometry and Cell Sorting Facility provides investigators with access to multiparametric flow cytometric analysis and cells sorting, as well as analysis of clinical-chemical and hematological parameters. The facility is a key participant in the National Research Infrastructure InfrafrontierGR/Phenotypos.

The Facility personnel offer maintenance of the instruments, training and assistance on instrument usage and running of cell sorting, clinical chemistry, and hematology experiments. Protocol design and establishment, as well as troubleshooting and results analysis and interpretation are also provided, depending upon the researcher's knowledge and requirements. Flow cytometric analysis, data analysis, cell sorting, sample preparation clinical chemistry and hematology services are also available to external scientists from the academic or industrial sector.

Infrastructure/Capabilities

- **BD FACS CANTO II:** A two lasers (488nm and 633nm) Flow Cytometry analyzer capable of detecting up to 8 colors simultaneously.
- **BD FACS CELESTA:** A three lasers (405nm, 488nm and 633nm) Flow Cytometry analyzer capable of detecting up to 12 colors simultaneously.
- **BD FACS ARIA III:** A five lasers (375nm, 405nm, 488nm, 561nm and 633nm) cell sorter capable of measuring up to 18 colors simultaneously. The sorter can operate under BSL-2 with enhanced precautions (during sorting operations). It is also equipped with an ACDU module for single cell and index sorting in 96 and 348 well pates and slides.



Facility affiliated with

InfrafrontierGR/PHENOTYPOS

FLOW CYTOMETRY & CELL SORTING

- **Mindray BC5000Vet:** A 5Diff Hematology analyzer equipped with the appropriate software to allow a 23-parameter mouse blood analysis. The instrument is operated by the facility members.
- **Beckman Coulter AU480:** An open, fully automated high throughput chemistry analyzer. Currently optimized for the analysis of 30 mouse serum/plasma parameters and 14 mouse urine parameters.

Ongoing Infrastructure expansion Plans

State-of-the-art spectral cytometry analyzer (5 laser > 30 colors) and spectral 6 way cell sorter (5 laser > 30 colors)

Flow cytometry, cell sorting, immunophenotyping, functional assays, clinical chemistry

→ LINK TO FACILITY

→ LINK TO PUBLICATIONS

George Kollias
Head of Facility

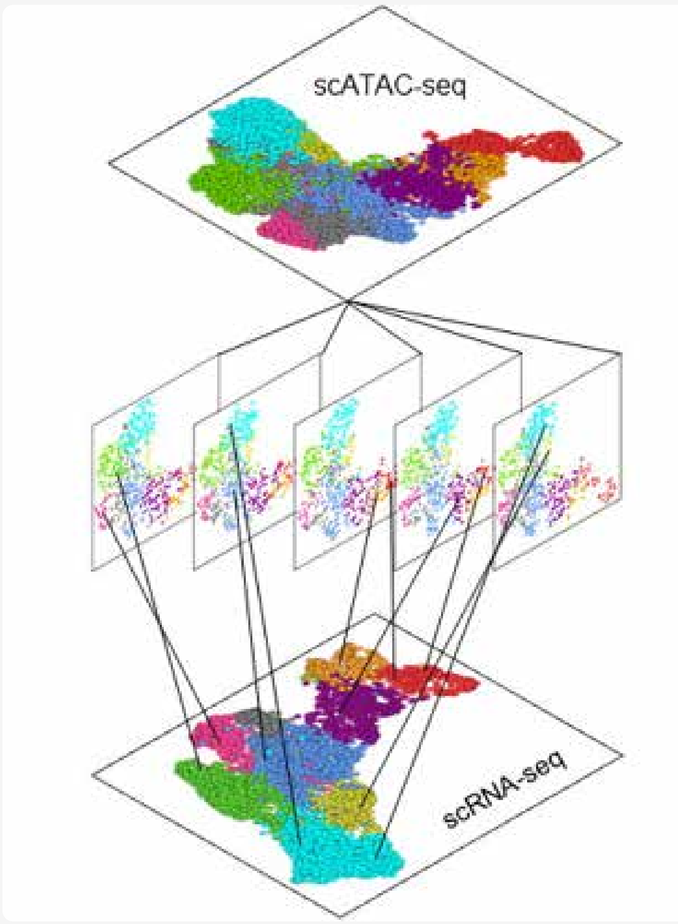
SINGLE CELL ANALYSIS UNIT

The Single Cell (sc) Analysis Unit is a new core facility initiative developed in the Kollias lab, with the mission to provide analysis services and technical support to researchers that wish to conduct single cell Next Generation Sequencing (scNGS) studies. The Unit offers expertise and computational space to support users' research by providing analysis services for a wide range of single cell assays including scRNA-seq (single cell profiling of the transcriptome), scATAC-seq (single cell profiling of the epigenome), and spatial transcriptomics.

The Unit offers end-to-end single-cell analysis solutions, using state-of-the art bioinformatics methodologies and in-house analysis pipelines, offering structured, high quality and reproducible analysis deliverables. The Unit provides easy access to primary analysis solutions, and develops novel algorithms for the interpetation of the high-dimensional single-cell information in order to answer complex biological questions.

The team has recently developed SCALA (Single Cell AnaLysis for All), an R/Shiny web application and stand-alone toolkit, that handles the analysis of scRNA-seq and scATAC-seq datasets. It offers various modes of analysis including quality control, normalization, dimensionality reduction, differential expression/accessibility analysis, cell clustering, functional enrichment analysis, trajectory inference, ligand – receptor analysis, gene regulatory network inference, and visualization.

The Unit is currently equipped with the 10X Genomics Chromium X, designed to enable high-throughput single-cell sequencing and genomics applications, and recently acquired the Visium CytAssist system that allows spatial profiling of RNA expression for more than 18,000 genes in human and mouse FFPE samples with high resolution across entire tissue sections.



SINGLE CELL ANALYSIS UNIT

The Unit closely collaborates and exchanges know-how and expertise with the Single Cell analysis Unit of the pMedGR Research infrastructure, established at the Medical School of the University of Athens by the Kollias lab at the Department of Physiology.

The Unit has been supported by the Hellenic Foundation for Research & Innovation (HFRI) ELIDEK; 1st Call for H.F.R.I. Research Projects to Support Faculty Members & Researchers and Procure High-Value Research Equipment (Grant ID: 3780) to George Kollias.

Pantelis Hatzis
Head of Facility

GENOMICS

Next Generation Sequencing (NGS) has revolutionized genomics, offering a wide range of novel applications on a high throughput, genome-wide level. NGS enables massively parallel sequencing of nucleic acid fragments to address a variety of experimental questions, such as SNP and mutation discovery, detection of structural variants, genome-wide measurement of mRNA transcript levels, alternative splicing events, microbiota compositions, and a number of other applications.

The Fleming Genomics Facility was established in 2008. The Facility currently operates an **Ion Proton™ System coupled to Ion Torrent™ One Touch™** and **Ion Chef™ System**, as well as an **MGI DNBSEQ-G400** for next generation sequencing-based experimental protocols.

A broad variety of experimental protocols are supported by the Genomics Facility, such as whole genome sequencing, shotgun sequencing, targeted/exome sequencing, mRNA-seq, RNA-seq, 3′ mRNA-seq, ChIP-seq, 16S RNA sequencing, methylation sequencing, etc.

The Genomics Facility, through the Fleming Computational Biology and Bioinformatics groups, additionally offers bioinformatics support at various levels, including basic bioinformatics processing spanning basic quality control and alignment to reference genomes, as well as basic statistical analysis for most projects, up to more advanced bioinformatics analytics based on collaboration agreements.

→ LINK TO FACILITY

→ LINK TO PUBLICATIONS

Martina Samiotaki
Proteomics Operational Scientist

PROTEOMICS

Diverse Applications of Proteomics in Advancing Biomedical Sciences

Cutting-edge Technologies: At our Proteomics Facility, we are committed to staying at the forefront of proteomics research. Our facility has recently invested in state-of-the-art mass spectrometry equipment and advanced data analysis software. These technological advancements enable us to identify and quantify proteins with unprecedented precision and efficiency, ensuring that your research projects reach new heights. Our current instrumentation platform is the Q Exactive HF-X Orbitrap (Thermo).

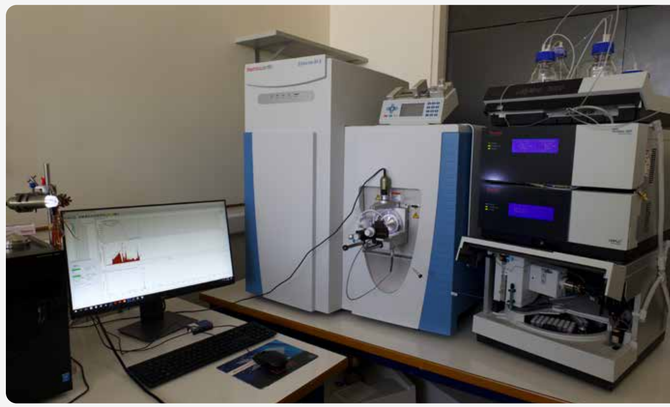
Research Highlights: Our researchers are working on various proteomics projects leading to discoveries in fields like cancer research, neurodegenerative diseases, immunopeptidome, metaproteome, autoimmunity, and personalized medicine, resulting in numerous high quality publications (Publications).

Training: To foster knowledge exchange, we have constantly been educating researchers and students in the latest proteomic technologies and workflows, as well as in data analysis and results visualization.

We are very excited to announce the ongoing expansion of our proteomics facility adding more analytical capabilities in order to enable **single-cell proteomics** workflow. This will generate data for more than 6,000 proteins/cell.

Collaborations and Partnerships: Collaboration is at the heart of scientific progress. We take immense pride in our collaborative projects with numerous research institutions and industry partners, in Greece and abroad. These partnerships enable us to tackle complex scientific challenges and provide our researchers with unique opportunities to exchange knowledge and expertise.

FACILITIES



Facility affiliated with

InfrafrontierGR/PHENOTYPOS

Proteomics,
Mass spectrometry

→ LINK TO FACILITY

→ LINK TO PUBLICATIONS

Georgios Pavlopoulos
Head of Facility

BIOINFORMATICS/E-RESOURCES

The bioinformatics facility at BSRC 'Alexander Fleming' is equipped with state-of-the-art computational resources, software tools, and expertise dedicated to the field of bioinformatics. Bioinformatics is an interdisciplinary field that combines biology, computer science, and data analysis to extract meaningful information from biological data, particularly DNA, RNA, and protein sequences, as well as other high-throughput -omics data like genomics, transcriptomics, proteomics, and metabolomics.

The current facility comes with:

- **A High-Performance Computing cluster (HPC)** that consists of multiple interconnected servers or nodes with powerful processors, ample memory, and high-speed storage. It enables researchers to perform complex and computationally intensive analyses, such as sequence alignment, molecular modeling, and phylogenetic tree construction.
- **Data Storage** to store large datasets, including genomic sequences, experimental results, and reference databases.
- **Bioinformatics software, databases, and services** to assist researchers with their computational needs. Genomics, Metagenomics, Integrative Biology, Text-Mining, Network Biology, Proteomics, and Expression analysis are a few of the current activities.
- **Data Analysis and Visualization Tools**, which offer a range of options to assist researchers in interpreting their results.
- **Expertise**: a team of skilled bioinformaticians, computational biologists, and data scientists who collaborate with researchers to guide experimental design, data analysis strategies, and troubleshoot computational challenges.
- **Training and Workshops** to help researchers and students develop their bioinformatics skills.

LINK TO FACILITY

INFRASTRUCTURES

George Kollias
Co-ordinator of InfrafrontierGR/Phenotypos

Dimitris L. Kontoyiannis
General Manager of InfrafrontierGR/Phenotypos

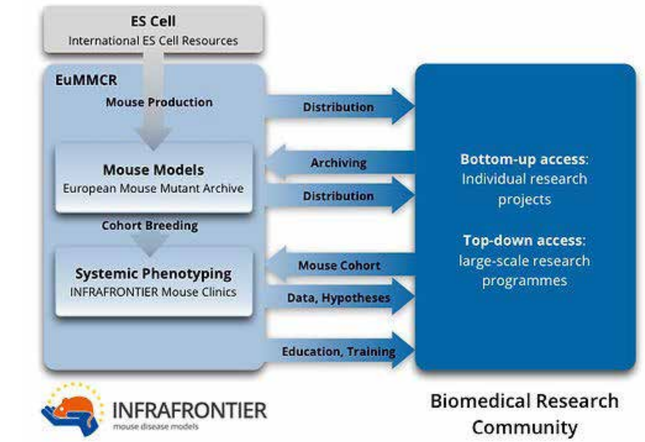
Head of the Hellenic Node of INFRAFRONTIER

INFRAFRONTIER & InfrafrontierGR/Phenotypos

BSRC Fleming is a founding and full member of the European Landmark Research Infrastructure (RI) INFRAFRONTIER dedicated in advancing disease prevention and therapies through the generation and analysis of appropriate models. Since 2014, BSRC Fleming acts as a member of its management entity, Infrafrontier GmbH, which is currently transitioning to a European Research Infrastructure Consortium (ERIC) status. As the appointed Hellenic Node of the European RI, BSRC Fleming is coordinating the National Infrastructure InfrafrontierGR/Phenotypos encompassing the activities of five National Research and Academic Institutions to supplement the portfolio of the European RI in specialized and preclinical services for Chronic Degenerative Diseases.

The Hellenic Node and National Infrastructure provide a unique set of open-access, cost-effective biomedical services to national and international users, which include:

1. Access to INFRAFRONTIER's **European Mouse Mutant Archive – EMMA,** the 3rd largest resource of its kind in the world. Under EMMA and since 2009, the Hellenic node offers standardized services for the collection, archiving (via cryopreservation) and distribution of relevant mutant rodent strains essential for biomedical and preclinical research.
2. **State-of-the-art genome manipulation services (gene addition, targeting and editing)** for the induction of clinically relevant mutations and the creation **of rodent models that mimic physiological and pathological processes.**
3. Access to equipment-based **procedures for the phenotypic, diagnostic and clinical monitoring** of rodent models through advanced imaging modalities (Endoscopy, Ultrasound, Optical and X-ray Micro-Computed Tomography, Positron Emission Tomography), Hematology, Clinical Biochemistry, Specialized Flow Cytometry and Cell sorting, Histopathology and Immunohistochemistry, as well as targeted Proteomics.



InfrafrontierGR/PHENOTYPOS

INFRAFRONTIER

INFRAFRONTIER & INFRAFRONTIERGR/ PHENOTYPOS

4. **Custom-made pipelines** for the preclinical evaluation of mutations or therapeutics **relating to complex, communicable and non-communicable diseases,** such as:
   - » Bacterial Infections, Inflammatory Bowel Diseases, Arthropathies, Neurodegenerative & Neuro-cognitive disorders, Cardiovascular and Liver diseases, and several types of Cancer.
5. Harmonization of services with the **European quality standards**, ethical principles and animal welfare, including 4Rs principle (Reduction, Replacement, Refinement, Reusability), as well as Data FAIRification.
6. Consulting services and Training Courses.

Over the last 10 years, InfrafrontierGR has offered:

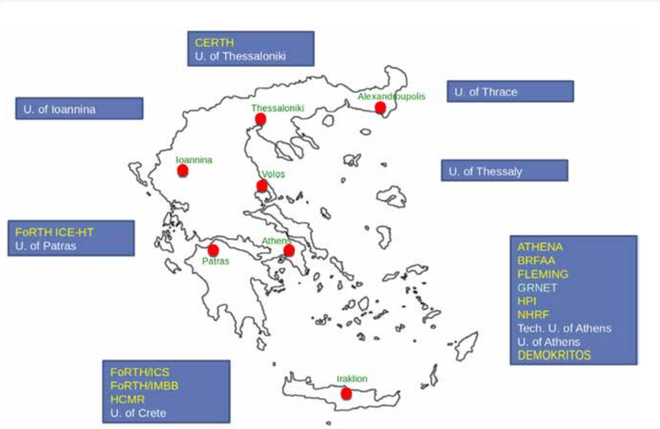
- *Open and easy access through a centralized electronic platform*
- *Archiving of more than 500 models and distribution of more than 300 models covered by Material transfer agreements*
- *Over 550 completed phenotyping and preclinical services*
- *Support to more than 40 high impact publications*

Martin Reczko
Head of Node

ELIXIR-GR

ELIXIR-GR is the Greek National Node of the ESFRI European Research Infrastructure ELIXIR, a distributed infrastructure that will allow the life science research community across Europe to process, share and store their research data as part of an organized network. Its goal is to bring together Europe's laboratories and data centers to help coordinate the collection, quality control and storage of large amounts of biological data produced by life science experiments. ELIXIR-GR offers a collection of unique tools and databases that focuses primarily on biomedical research and marine biology, and will be continually expanded. Training is offered to all stakeholders in the form of hands¬-on workshops and web¬-based training courses.

Bioinformatics and biocomputing are, by their nature, both scientific and technological activities. ELIXIR -GR enhances the potential of the Greek bioinformatics community to offer open, easily accessible and state-of-the-art services to the Greek and the international academic community and other stakeholders, such as industry and the health sector. By providing these services, the infrastructure facilitates discoveries in the field of the life-sciences, having strong spill-over effects in promoting innovation in sectors such as discovery of new drug targets and development of novel therapeutic agents, development of innovative diagnostics, personalized medicine, and development of innovative biotechnological products and processes.



Resources offered

- **Compute resources**. ELIXIR-GR provides large-scale computing resources for data-intensive tasks needed to store, analyze and process big biological data, such as molecular sequence and bioimaging data.
- **Data resources**. ELIXIR-GR stores, safeguards and provides access to biological databanks for which the Greek R&D life science community has high levels of appropriate domain expertise.
- **Standards/Interoperability.** In compliance with the standards of ELIXIR-EUROPE, ELIXIR-GR addresses requirements for unified programming access to databanks and services.
- **Training**. ELIXIR-GR provides training for life scientists and other stakeholders in the use of the bioinformatic and biocomputing services available at ELIXIR and other international RIs.
- **Tools**. In collaboration with other ELIXIR Nodes and the ELIXIR Hub, ELIXIR-GR offers a catalog of tools and services provided by the scientific community for biological data management and analysis.

elixir-greece.org

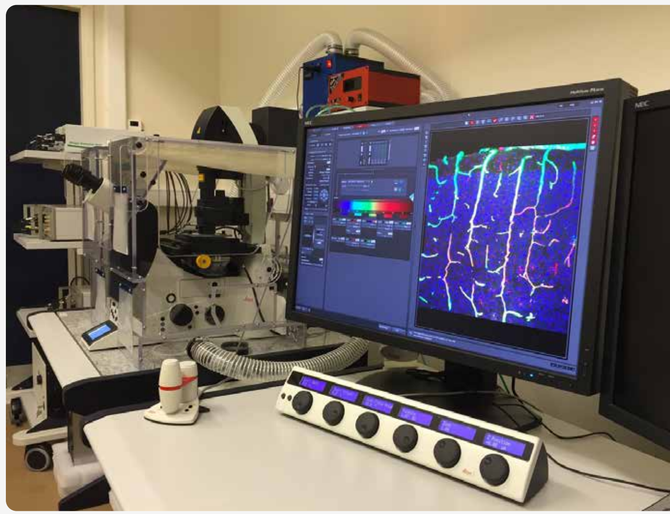
BIOIMAGING-GR

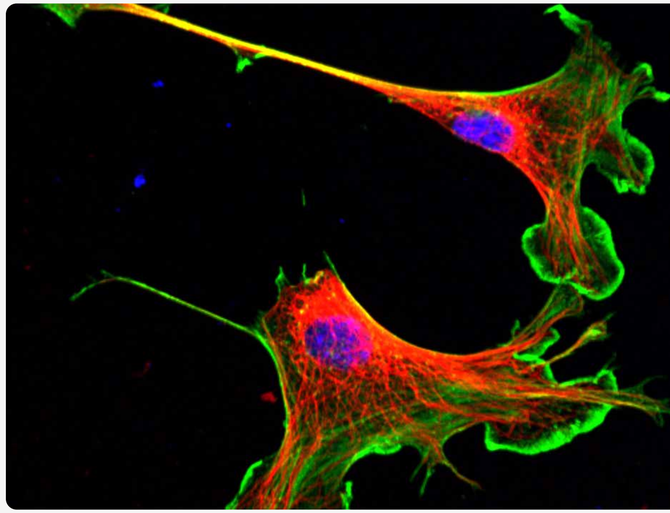
BioImaging-GR is a distributed research infrastructure for **open-access, high-end biological imaging** providing a range of imaging methods to scientists in Greece and neighbouring countries.

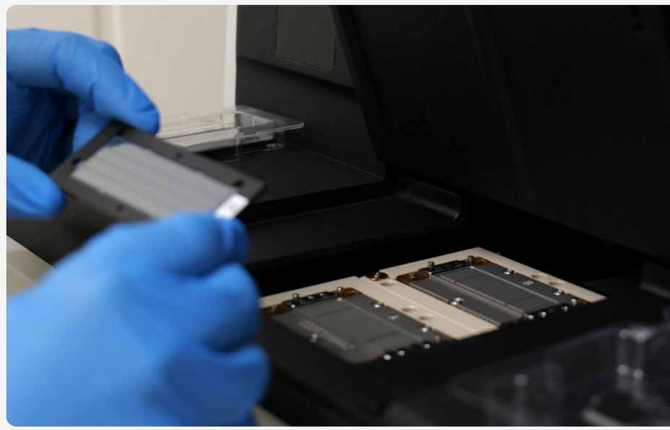
BioImaging-GR has a central coordinating **Hub**, serving as a single point of entry to the national infrastructure, and distributed partner **Nodes** that provide access to high-end Bioimaging instrumentation and services in a coordinated and harmonized manner, by pursuing the following 3 main objectives:

1. Expand existing and establish new BioImaging facilities: such as next-generation fluorescence microscopy, electron microscopy (both TEM and SEM), PET, Micro CT, fMRI, intravital imaging, microfluidics, ratiometric imaging, super-resolution microscopy, and others.
2. Provide training and imaging services to the research community and industrial users in Greece and neighbouring countries, using cutting-edge BioImaging technologies.
3. Enhance the research and innovation potential of the Greek biomedical research community, by networking and coordinating existing facilities, which operate at different centers, towards maximum complementarity and minimum redundancy.

bioimaging.gr







ONCOLOGY PRECISION MEDICINE

THE MEDICINE OF THE FUTURE IN ONCOLOGY

WHO WE ARE

EDIMO was established on 30 May 2022 by decision of the General Secretariat for Research & Innovation. The network is nationwide in scope, and serves the needs of both patients and their families, as well as doctors and participating laboratories, clinics and hospitals. It is a partnership of Greek research centers, university institutions, hospital clinics and laboratories, which are active in cutting-edge research in the fields of molecular oncology and precision medicine.

WHAT WE DO

The network offers genetic/molecular oncology services and is the coordinating body for a range of research activities in precision medicine and oncology. The data collected from the services offered by the network are stored in databases and, in turn, lead to new research, diagnostic technologies and treatments in oncology.

OUR PROJECT

The network harnesses the scientific potential and expertise available in the country, based on a new approach to prevention, diagnosis and treatment of diseases, taking into account what has been called ‘personalized medicine’ or ‘precision medicine’, in other words, the differences between individuals in terms of their genetic characteristics, their lifestyle, and the environment in which they live.

edimo.gr

pMedGR

THE GREEK RESEARCH INFRASTRUCTURE FOR PERSONALIZED MEDICINE

MISSION

Fleming is a key partner of the Greek Research Infrastructure for Personalized Medicine (pMedGR) coordinated by the Medical School of the University of Athens. pMedGR is the first Greek Infrastructure developed in the field of Personalized Medicine and provides research services in cutting-edge technologies that serve public health and form the basis for competitive research, education, and innovation. **Its mission is to enable research on precision prognosis, diagnosis & therapy through advanced biotechnology platforms.**

pMedGR has been fully operational since February 2020, establishing and maintaining **six new high-technology Units** that have supported research projects related to chronic inflammatory and autoimmune diseases, cancer, neurological disorders, genetic syndromes, as well as COVID-19, through high-level genomic, transcriptomic and proteomic analyses.

The infrastructure currently offers the following research services:

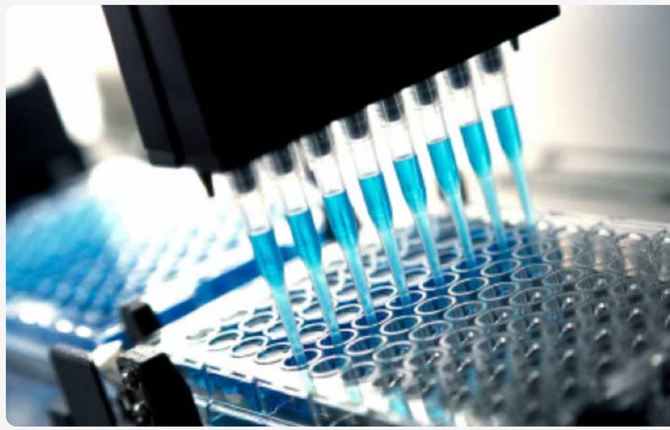
- Personalized Genomic and Transcriptomic Analysis (gDNA-Seq, targeted/exome seq, mRNA/smallRNA seq, Chip/FAIRE/ATAC-Seq)
- Single Cell Multiomic Analysis, Sorting & Barcoding
- Mass Cytometry (CyTOF)
- Quantitative Proteomics
- Bioinformatic Analysis (Exome, Whole genome, RNA-seq, scRNAseq)
- Quality control and processing of clinical samples

PMEDGR

pMedGR offers **open and easy access** to the provided services through **a centralized electronic platform**. Users to date come from several Universities, Hospitals, and Research Centers from all over Greece, as well as from private pharmaceutical companies. pMedGR aims to capitalize on its close proximity, access and interactions with hospitals and research clinics, to serve as **a regional hub for personalized medicine approaches** in the region.

precisionmedicine.gr

TECHNOLOGY TRANSFER



INNOVATION & ENTERPRISE UNIT

BSRC Alexander Fleming researchers work across a range of biomedical research disciplines in the broad areas of Immunology, Molecular Biology, Genetics, Molecular Oncology, Neuroscience, Bioinformatics and Computational Biology. Our balanced portfolio includes both basic and applied research that is relevant to the needs of the biopharmaceutical industry and other end-users.

BSRC Fleming's dedicated Innovation and Enterprise Unit (IEU) is a one-stop-shop for all aspects of the successful exploitation of inventions and technologies arising from Fleming research. Its mission is to guide and assist researchers, and work with external collaborators to ensure Fleming science is transferred to the wider community for best use, both socially and economically. Established in 2005, to date the IEU has:

- Established patent portfolios around core Fleming technologies.
- Overseen the establishment of Fleming's spin-out company, BiomedCode.
- Established streamlined procedures to manage Fleming intellectual property (IP).
- Concluded important contracts with industry.
- Main IEU responsibilities:
- To draft, negotiate and manage IP agreements between Fleming and third parties. For example: Material Transfer Agreements, Service Agreements, Research Agreements, Collaboration Agreements and Confidentiality Agreements.
- To evaluate the patentability and commercial potential of Fleming IP, relying on a strong network of collaborators with expertise in IP protection and business development.
- To support spin-off establishment.
- To support Fleming researchers in fostering common development projects with industry.
- To promote Fleming's IP portfolios, technologies and expertise through participation in external events and exhibitions.

TRAINING

FLEMING's teaching activities greatly enhance its role in shaping modern biomedical research in Greece. The Center is focused on providing state-of-the-art training to students and scientists of all levels through various formal educational programs.

PHD TRAINING PROGRAMS

(In cooperation with Greek University departments)
PhD students perform their thesis research in the laboratories of Fleming faculty, often in collaborative projects with other labs in the Center.

INTERNATIONAL MSC PROGRAM IN MOLECULAR BIOMEDICINE

Mechanisms of Disease, Molecular and Cellular Therapies and Bioinnovation
(In collaboration with the Medical School of the National and Kapodistrian University of Athens)

molecularbiomedicine.gr

INTRA-DEPARTMENTAL INTERNATIONAL MSC PROGRAM IN NEUROSCIENCES

(Coordinated by the Biology Department of the National and Kapodistrian University of Athens)

masterneuroscience.biol.uoa.gr

UNDERGRADUATE STUDENTS & INTERNSHIPS

Undergraduate students from different Greek Universities conduct their undergraduate thesis research in the laboratories of Fleming faculty for 6-12 months, or take part in shorter practical training exercises for 2-3 months. The Center also accepts students for short-term training or for research projects required for a university post-graduate degree.

SCHOOL VISITS & FOREIGN STUDENT VISITS

In order to increase public awareness and publicize its research programs, FLEMING provides a tour of its premises to students attending the senior year of High School. A typical school visit includes a visit to the Alexander Fleming Museum, short presentations and/or videos describing issues of modern Biological Research, and demonstration of laboratories and experimental research models.

FLEMING also has the pleasure to host visits from International Master-program students in the Biomedical Sciences. Graduate students are given a guided tour of the laboratories and facilities, attend talks by FLEMING researchers, and have the opportunity to discuss with students of the institute, exchange experiences, and network.

THE ALEXANDER FLEMING MUSEUM

THE ALEXANDER FLEMING MUSEUM

The Fleming Museum of Contemporary Science is housed in the premises of the BSRC Fleming.

The core of the Museum is Alexander Fleming's original archival material and personal effects, which were donated by Amalia Fleming, and include photographs of the actual Petri dishes on which Fleming discovered penicillin, a turning point in 20th century pharmaceutical science.

A new space is currently under development for the relocation and exhibition of the Alexander Fleming archives. These archives will provide the basis for the presentation of modern scientific thought and technology through the Museum's exhibitions.

The Alexander Fleming archives contain:

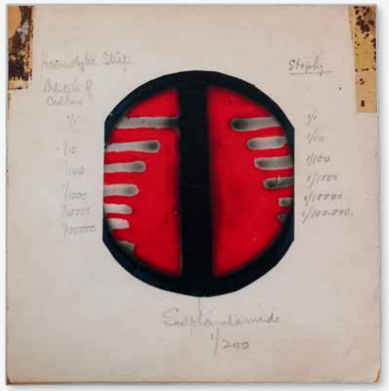
- Fleming's original laboratory notebooks and hand-drawn representations of his research results
- Scientific notes, lectures, books, leaflets, photographs and letters
- Reprints of his main scientific publications after 1908
- Articles in the international press
- Scientific instruments, microscopes and various personal effects
- Prizes, awards, photographs, correspondence and material about Amalia Fleming.

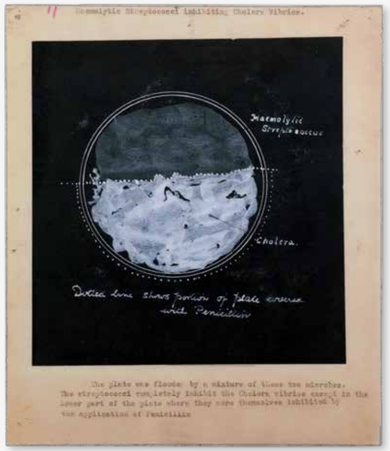
The main objectives of the museum are:

- to digitize and preserve the collection's archives,
- to evaluate its scientific relevance, and
- to publicize Alexander Fleming's unique achievements.

Education plays a central role in our mission

The Museum, which is the only science and biomedical research museum in Greece housed in a research center, will attract visitors from diverse backgrounds, such as school children, university students, researchers and the general public. Through the selection and use of innovative new technologies (multimedia), a major emphasis will be placed on education, engaging visitors of all levels, and encouraging them to take an active part in learning about biomedical research and technology and their applications. In addition to the permanent exhibition that will link Fleming's work with modern research, there will also be temporary exhibitions that will employ innovative educational methods to approach diverse themes of science and society.





Museum Curator: Myrta Perraki

Further information about the items in the Alexander Fleming collection can be obtained by contacting **perraki@fleming.gr**

"ALEXANDER FLEMING"
Biomedical Sciences Research Center

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