B.S.R.C. "Alexander Fleming" Report for 20182021 evaluation

Executive Summary

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 currently comprises the newly established Institute for Bioinnovation (IBI) and the Institute for Fundamental Biomedical Research (IFBR), evaluated together in this review. 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 their 21 group leaders collaborate within **distinct research directions** in Immunity & Inflammation, Neuroscience, Cancer Biology, RNA Biology & Epigenetics, and Bioinformatics & Computational Biology.

The last assessment by an international, GSRI-organized scientific committee in 2014, **ranked FLEMING first** among Greek Research Institutes active in biomedical sciences, based on excellence in research publications, grants and training record. 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** autoimmune diseases, cancer, neurodegenerative and neuropsychiatric disorders, learning disabilities, osteoporosis, pulmonary fibrosis, among others and the development of new approaches for their diagnosis and treatment.

To maintain its scientific excellence, **FLEMING has prioritized specific actions** for the coming period, including:

- Consolidation of the distinct, but complementary character of the two new Institutes
- Upgrade and enrichment of major scientific equipment
- Recruitment of expertise in accord to smart specialization directives
- Development of strategic alliances and participation in complementary programs with other institutions
- Development of the Biotechnopolis project, an innovative biotechnology hub for the Attica region
- Creation of new spin-off companies
- Enhancement of educational and outreach activities

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 capacities in Greece), as well as **Transgenesis and Cryopreservation**, **Genomics, Proteomics, Flow Cytometry, Bioimaging, MicroCT, Endoscopy and Histopathology Units**. Fleming coordinates the <u>InfrafrontierGR/Phenotypos</u>, a National Research Infrastructure (NRI) for generating, archiving and phenotyping of animal models of disease and <u>ELIXIR-GR</u> NRI for bioinformatics/biocomputing resources. To continue its successful trajectory, FLEMING will further upgrade its infrastructure and facilities through a **17.8 million euro grant from the EU Recovery & Resilience Fund**. An initial approval by the European Investment Bank for the Biotechnopolis building has also been obtained (total cost 40m euro). However, the anticipated great increase in space and infrastructure requires to be complemented with the **recruitment of new researchers**, in addition to these currently in non-tenure track junior researcher positions, which is not currently supported by the state. Importantly, funding is urgently required for the highly trained, but soft-funds-supported facility technicians, because the current lack of bridging grants will inevitably result in their attrition. It would then be exceedingly difficult to maintain the diversity and quality of services provided by our facilities. An increase in administration personnel is also required due to rising bureaucratic demands.

FLEMING follows **open and transparent recruitment procedures** for researchers, administrative and other personnel, based on merit and in full compliance with The Code of Conduct for Recruitment of Researchers of the European Commission. Moreover, FLEMING implements the principles of **equal opportunity and treatment** irrespective of gender, origin or physical limitations and is implementing a Gender Equality Plan. An established Ethics and Code of Conduct Committee resolves issues of research **ethics and bioethics** in compliance with the rules of the European Code of Conduct for Research Integrity.

To strengthen extroversion, FLEMING has developed a **strategic partnership with the Medical School of the University of Athens**, coordinating joint MSc and PhD programs and codeveloping infrastructures for Precision Medicine (<u>pMedGR</u>), as well as with Global Projects and Consortia on mammalian genetics and phenotyping, and is a full partner of the ESFRI Infrafrontier. Scientific communication is mediated via **open lectures** by internationally renowned scientists, and weekly internal seminars by all lab members. We hope that a Scientific Retreat, will become an annual event. Close collaborations between FLEMING research groups are evidenced by multiple **joint publications**. Moreover, the unique expertise and state-of-the-art facilities facilitate a large number of collaborations with other groups, both in Greece and abroad.

FLEMING researchers have an **excellent record in attracting competitive grants**, amounting to 15 million euro for the reporting period 2018-2021. With 40% success rate in HFRI grants it ranks first among all research institutions. While FLEMING has maintained a **low ratio of state budget to grant income**, its **bibliometric output is top-ranked** by the National Documentation Center in terms of relative impact factor and other metrics.

Training and educational activities are an integral part of all FLEMING researchers' work. PhD, MSc and importantly undergraduate research theses are performed in the laboratories of Fleming faculty. FLEMING co-coordinates the International MSc Programs in "Molecular Biomedicine" and "Neurosciences" with the University of Athens and participates in many similar programs.

The intellectual output from FLEMING's research programs, protection and exploitation of research results is monitored and mediated by the **Innovation and Entrepreneurship Unit**, 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. Significantly, it has overseen the establishment of Fleming's first spin-off company <u>Biomedcode Hellas SA</u>, which provides full preclinical drug evaluation services to pharmaceutical companies worldwide, commercializing proprietary animal models of chronic inflammatory diseases.

Περίληψη

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. Επί του παρόντος περιλαμβάνει το νεοσύστατο Ινστιτούτο Βιοκαινοτομίας (IBK) και το Ινστιτούτο Βασικής Βιοϊατρικής Έρευνας (IBBE), τα οποία θα κριθούν μαζί στην παρούσα αξιολόγηση. 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 οι 21 επικεφαλής των ομάδων τους συνεργάζονται στο πλαίσιο διακριτών ερευνητικών κατευθύνσεων στους τομείς της ανοσίας και της βιοπληροφορικής και υπολογιστικής βιολογίας.

Η τελευταία οργανωμένη από τη ΓΓΕΚ αξιολόγηση από διεθνή επιστημονική επιτροπή το 2014, κατέταξε το ΦΛΕΜΙΓΚ στην πρώτη θέση μεταξύ των ελληνικών ερευνητικών ινστιτούτων που δραστηριοποιούνται στις βιοϊατρικές επιστήμες, με βάση την αριστεία στις ερευνητικές δημοσιεύσεις, τις ανταγωνιστικές χρηματοδοτήσεις και το εκπαιδευτικό έργο του. 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 αυτοάνοσων ασθενειών, καρκίνου, νευροεκφυλιστικών και νευροψυχιατρικών διαταραχών, μαθησιακών δυσκολιών, οστεοπόρωσης, και πνευμονικής ίνωσης, καθώς και την ανάπτυξη νέων προσεγγίσεων για τη διάγνωση και τη θεραπεία τους.

Για να διατηρήσει την επιστημονική του αριστεία, **το ΦΛΕΜΙΓΚ έχει θέσει ως προτεραιότητα** συγκεκριμένες δράσεις για την επόμενη περίοδο, μεταξύ των οποίων:

- Παγίωση του διακριτού, αλλά συμπληρωματικού χαρακτήρα των δύο νέων Ινστιτούτων
- Αναβάθμιση και εμπλουτισμός του κύριου επιστημονικού εξοπλισμού
- Πρόσληψη ερευνητών σύμφωνα με τη Στρατηγική Έξυπνης Εξειδίκευσης
- Ανάπτυξη στρατηγικών συνεργασιών και συμμετοχή σε προγράμματα άλλων ιδρυμάτων
- Ανάπτυξη της ΒΙΟΤΕΧΝΟΠΟΛΗΣ, ενός καινοτόμου κόμβου βιοτεχνολογίας για την Αττική
- Δημιουργία νέων εταιρειών spin-off
- Ενίσχυση των δραστηριοτήτων εκπαίδευσης και προβολής

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 έναν Οίκο Πειραματοζώων (επί του παρόντος το μεγαλύτερο στην Ελλάδα), καθώς και Μονάδες Διαγένεσης και Κρυοσυντήρησης, Γονιδιωματικής, Πρωτεωμικής, Κυτταρομετρίας Ροής, Βιοαπεικόνισης, MicroCT, Ενδοσκόπησης και Ιστοπαθολογίας. Το ΦΛΕΜΙΓΚ συντονίζει την InfraforntieGR/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.

Για να συνεχίσει την επιτυχημένη πορεία του, το ΦΛΕΜΙΓΚ θα αναβαθμίσει περαιτέρω τις υποδομές και τις εγκαταστάσεις του μέσω επιχορήγησης ύψους **17,8 εκατομμυρίων ευρώ από το Ταμείο Ανάκαμψης και Ανθεκτικότητας της ΕΕ**. Έχει επίσης ληφθεί μια αρχική έγκριση από την Ευρωπαϊκή Τράπεζα Επενδύσεων για το κτίριο στέγασης της ΒΙΟΤΕΧΝΟΠΟΛΗΣ (συνολικό κόστος 40 εκατ. ευρώ). Ωστόσο, η αναμενόμενη μεγάλη αύξηση των χώρων και των υποδομών πρέπει να συμπληρωθεί με την **πρόσληψη νέων ερευνητών**, πέραν αυτών που βρίσκονται σήμερα σε θέσεις νέων ερευνητών χωρίς μονιμότητα, και οι οποίες δεν υποστηρίζονται επί του παρόντος από το κράτος. Σημαντικό είναι

ότι απαιτείται επειγόντως χρηματοδότηση για τους άρτια καταρτισμένους, αλλά υποστηριζόμενους από έργα τεχνικούς του κέντρου, διότι η σημερινή έλλειψη επιχορηγήσεων-γέφυρα θα οδηγήσει αναπόφευκτα σε συρρίκνωση και θα είναι εξαιρετικά δύσκολο να διατηρηθεί η ποικιλία και η ποιότητα των υπηρεσιών που παρέχει το κέντρο μας. Απαιτείται επίσης αύξηση του διοικητικού προσωπικού λόγω αυξανόμενων γραφειοκρατικών απαιτήσεων.

Το ΦΛΕΜΙΓΚ ακολουθεί **ανοικτές και διαφανείς διαδικασίες πρόσληψης** ερευνητών, διοικητικού και λοιπού προσωπικού με βάση τα προσόντα και σε πλήρη συμμόρφωση με τον Κώδικα Δεοντολογίας για την Πρόσληψη Ερευνητών της Ευρωπαϊκής Επιτροπής. Επιπλέον, το ΦΛΕΜΙΓΚ εφαρμόζει τις αρχές των **ίσων ευκαιριών και της ίσης μεταχείρισης** ανεξαρτήτως φύλου, καταγωγής ή φυσικών περιορισμών και εφαρμόζει Σχέδιο Ισότητας των Φύλων. Μια θεσμοθετημένη επιτροπή ηθικής και δεοντολογίας και δυρωπαϊκού Κώδικα Δεοντολογίας του Ευρωπαϊκός επιλύει ζητήματα ερευνητικής δεοντολογίας και βιοηθικής σύμφωνα με τους κανόνες του Ευρωπαϊκού Κώδικα Δεοντολογίας για την Ακεραιότητα της Έρευνας.

Για την ενίσχυση της εξωστρέφειας, το ΦΛΕΜΙΓΚ έχει αναπτύξει **στρατηγική συνεργασία με την Ιατρική Σχολή του Πανεπιστημίου Αθηνών**, συντονίζοντας κοινά προγράμματα μεταπτυχιακών και διδακτορικών σπουδών και αναπτύσσοντας κοινές υποδομές για την Ιατρική Ακριβείας (pMedGR), καθώς και με διεθνή προγράμματα και κοινοπραξίες για τη γενετική και την φαινοτύπηση των θηλαστικών, ενώ είναι πλήρης εταίρος του ESFRI Infrafrontier. Η επιστημονική επικοινωνία επιτυγχάνεται μέσω **ανοικτών διαλέξεων** από διεθνώς αναγνωρισμένους επιστήμονες και εβδομαδιαίων εσωτερικών σεμιναρίων από τα μέλη όλων των εργαστηρίων. Ελπίζουμε επίσης, ότι η Επιστημονική Εκδρομή του κέντρου, θα γίνει ετήσιο γεγονός μετά την πανδημία. Οι στενές συνεργασίες μεταξύ των ερευνητικών ομάδων του ΦΛΕΜΙΓΚ αποδεικνύονται από πολλαπλές κοινές δημοσιεύσεις. Επιπλέον, η μοναδική τεχνογνωσία και οι υπερσύγχρονες εγκαταστάσεις διευκολύνουν ένα μεγάλο αριθμό συνεργασιών με άλλες ομάδες, τόσο στην Ελλάδα όσο και στο εξωτερικό.

Οι ερευνητές του ΦΛΕΜΙΓΚ έχουν **εξαιρετική επίδοση στην προσέλκυση ανταγωνιστικών** επιχορηγήσεων, ύψους 15 εκατομμυρίων ευρώ για την περίοδο αναφοράς 2018-2021. Με ποσοστό επιτυχίας 40% στις επιχορηγήσεις του ΕΛΙΔΕΚ κατέχει την πρώτη θέση ανάμεσα στα ερευνητικά ιδρύματα. Παράλληλα, το ΦΛΕΜΙΓΚ έχει διατηρήσει μια χαμηλή αναλογία κρατικού προϋπολογισμού προς τα έσοδα από επιχορηγήσεις, ενώ η βιβλιομετρική του παραγωγή κατατάσσεται στην πρώτη θέση από το Εθνικό Κέντρο Τεκμηρίωσης όσον αφορά τον σχετικό συντελεστή απήχησης και άλλους δείκτες.

Οι **δραστηριότητες κατάρτισης και εκπαίδευσης** αποτελούν αναπόσπαστο μέρος της εργασίας όλων των ερευνητών του ΦΛΕΜΙΓΚ. Διδακτορικές, μεταπτυχιακές και προπτυχιακές ερευνητικές εργασίες πραγματοποιούνται στα εργαστήρια του ω, που συμμετέχει επίσης στο συντονισμό των διεθνών προγραμμάτων MSc στη "Μοριακή Βιοϊατρική" και στις "Νευροεπιστήμες" με το Πανεπιστήμιο Αθηνών, ενώ συμμετέχει και σε πολλά άλλα παρόμοια προγράμματα.

Η επιστημονική γνώση που προέρχεται από τα ερευνητικά προγράμματα του ΦΛΕΜΙΓΚ και η προστασία και η εκμετάλλευση των ερευνητικών αποτελεσμάτων παρακολουθείται και διαχειρίζεται από τη **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 <u>Biomedcode Hellas SA</u>, η οποία παρέχει πλήρεις υπηρεσίες προκλινικής αξιολόγησης φαρμάκων σε φαρμακευτικές εταιρείες παγκοσμίως, αξιοποιώντας ιδιόκτητα ζωικά μοντέλα χρόνιων φλεγμονωδών παθήσεων.

1 Introduction and Background

1.1 Brief History of the Institute

The Biomedical Sciences Research Center "Alexander Fleming" is a top-ranked Greek nonprofit research organization focusing on scientific and technological excellence, training, and innovation in biomedical sciences. The Center was established in 1998 in honor of the Nobel laureate Alexander Fleming and operates under the supervision of the General Secretariat for Research and Innovation (GSRI) of the Hellenic Ministry of Development. The Center is housed in a 6,000 sq.m. building in Vari, Attica. Competitive funding each year amounts to approx. 75% of the total budget, an achievement that underlies FLEMING's strategic prioritization of research and innovation that conforms tightly with Europe 2020 priorities.

The initial plan for the center was to house 5 Institutes (Immunology, Molecular Biology & Genetics, Molecular Oncology, Developmental Biology, and Microbiology & Virology). The first 4 become operational gradually during the initial 10-year period. However, due to government actions in response to the financial crisis, the Institutes were amalgamated into one in 2012, the Institute of Biomedical Sciences "Alexander Fleming". Former institutes however, continued to operate as distinct Departments. In recognition of FLEMING's top performance in research and innovation, and upon a positive evaluation by the National Council for Research and Innovation, in 2018 the government approved the establishment of two Institutes: the Institute for Bioinnovation (IBI) and the Institute for Fundamental Biomedical Research (IFBR). The IBI's vision is to advance basic research discoveries towards innovation in the area of biotechnologies and drug development, while the main focus of IFBR is unravelling the molecular and cellular basis of disease and the development and validation of animal models that mimic human pathologies. The two institutes share all facilities and have close collaborations in the areas of Immunity & Inflammation, Neuroscience, Cancer Biology, RNA Biology & Epigenetics, and Bioinformatics & Computational Biology. Since the institutes are new and appointment of an IBI director is still pending, the current evaluation concerns both institutes as a single entity, herein abbreviated as FLEMING.

FLEMING specializes in internationally relevant areas of biomedical sciences and biotechnology and is consistently exhibiting top research performance among its peers in Greece, reaching international best practice levels in key academic and research excellence indicators, which include (over the last 20 years):

- Over 600 publications (1999-2021) in peer-reviewed journals (average Impact Factor 8)
- 11 patent applications in translational research and over 600 outgoing Material transfer agreements for mouse models and other research tools produced in the Institute
- More than 160 competitive research grants from national, European, and international sources (EU, HFSP, USA-NIH and others) amounting to 65M€
- 4 ERC grant awards (2 Advanced and 2 Starting) among a total of 18 eligible group leaders
- Coordination of 5 EC projects
- Coordination of two national research infrastructures
- A strong record in training students (participation in over 10 EC training networks, coordination of an International MSc Program with the Medical School of Athens) and founding role in another (Athens International Master's in Neurosciences Program).

In the last evaluation by an international scientific committee organized by the GSRI in 2014, **FLEMING was ranked first** among Greek Research Institutes active in biomedical sciences.

1.2 Mission, Scientific Identity and Distinctive Character of the Institute

The cornerstones of FLEMING's mission are 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
- actively engage in technology transfer and innovation

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**. Research at FLEMING spans a range of topics: i.e., the immune system and autoimmune disease, cancer, genetic and epigenetic regulation, memory/learning and neurodegenerative diseases, and is advanced using transdisciplinary approaches and technologies that include functional genomics, transcriptomics, proteomics and state-of-the art bioimaging and bioinformatics.

FLEMING has gained international recognition for its pioneering research towards understanding the molecular and cellular basis of human diseases, such as autoimmune diseases, cancer, neurodegenerative disorders, osteoporosis, pulmonary fibrosis and others, and the development of new approaches for their diagnosis and treatment. FLEMING currently hosts 21 highly competitive teams. It is **internationally recognized for its projects in translational research on pathway, target and biomarker identification and validation, preclinical evaluation of therapeutics in animal models and novel drug development and screening**. FLEMING's strength and international visibility lies on its focus and success in developing and characterizing **animal models that mimic human disease**, and the Institute has consequently invested heavily on related infrastructures.

Since its inception, a distinctive feature of FLEMING has been the emphasis on establishing **state-of-the-art facilities** that offer services for biomedical research internally, but also to researchers and companies in Greece and abroad. They include an Animal House (currently with the highest capacities in Greece), as well as Transgenesis and Cryopreservation, Genomics, Proteomics, Flow Cytometry, Bioimaging, MicroCT, Endoscopy and Histopathology Units. FLEMING is the Coordinator of two National Research Infrastructures: InfrafrontierGR/Phenotypos and ELIXIR-GR, active in the areas of generation, archiving and phenotyping of animal models of disease (including CRISPR/Cas9 technologies) and bioinformatics/biocomputing resources, respectively.

Our major goal is to foster excellent research with a focus on innovation. FLEMING has already established 11 patent portfolios around core Fleming technologies, more than 600 MTAs and a number of licensing contracts with industry. In 2006, Fleming established the spin-off company **Biomedcode Hellas SA**, a CRO company providing full preclinical drug evaluation services to small and large pharmaceutical companies worldwide, commercializing proprietary animal models of chronic inflammatory diseases.

1.3 Scientific Orientation of the Institute

a. Current scientific directions and thematic priorities

FLEMING has established 5 main research directions or programs that are covered by the work of its group leaders and serve as links between the two newly formed Institutes. Researchers can be active in more than one program depending on their current priorities and needs.

1. Immunity & Inflammation

The aim of the Immunity & 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 modelling and systems-level profiling. Researchers of this 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. Researchers active in this field are:

- <u>G. Kollias</u> Molecular and cellular mechanisms of chronic inflammation and cancer
- <u>V. Aidinis</u> Molecular pathophysiology of pulmonary inflammation, fibrosis and cancer
- <u>M. Armaka</u> Molecular and cellular pathogenesis mechanisms of inflammatory diseases of the joints with emphasis on the role of mesenchymal cells.
- <u>E. Douni</u> Mouse Functional Genetics for bone, immune and neurological diseases
- <u>V. Koliaraki</u> Origin, plasticity and function of the intestinal microenvironment in health and disease
- <u>D. Kontoyiannis</u> Post-transcriptional modules of gene expression in physiology and disease
- <u>A. Matralis</u> Development of bioactive molecules against complex human diseases
- <u>M. Tsoumakidou</u> Tumor immunology and immunotherapy
- <u>M. Verykokakis</u> Development and function of innate T lymphocytes

2. Neuroscience

The Neuroscience Program aims to advance high quality fundamental research in cutting edge areas of current Neuroscience. The aim is to understand normal development and function of the brain and peripheral nervous system and developmental aberrations and dysfunction characterizing disabilities and diseases in vertebrate and invertebrate model systems. In addition, projects emphasize the potential for innovative diagnostic and translational approaches to ameliorate debilitating conditions such as cognitive and learning disabilities, dementias, neurodegenerative and psychiatric 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. External members of the Program include adjunct researchers, Dr Antonis Stamatakis, 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, and Dr Luca Turin, Professor, Faculty of Medicine University of Buckingham UK Neurophysics and Quantum Biology and Dr Panos Roussos an Associate Professor of Psychiatry, Genetics and Genomics at the Icahn School of Medicine at Mount Sinai NY. Researchers active in this field are:

- M. Denaxa Development and Function of Cortical Interneurons
- <u>K. Papanikolopoulou</u> Neurobiology of Neurodegenerative Tauopathies
- M. Skoulakis Molecular Cognitive Neuroscience
- <u>L. Turin</u> Quantum Neurobiology

3. Cancer Research

The main aim is 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. Researchers active in this field are:

- G. Kollias Molecular and cellular mechanisms of chronic inflammation and cancer
- <u>V. Aidinis</u> Molecular pathophysiology of pulmonary inflammation, fibrosis and cancer
- <u>E. Douni</u> Mouse Functional Genetics for bone, immune and neurological diseases
- <u>M. Fousteri</u> Regulatory (epi)genomics in cancer and aging related diseases
- <u>P. Hatzis</u> RNA-mediated transcriptional and epigenetic regulation in carcinogenesis
- <u>V. Koliaraki</u> Origin, plasticity and function of the intestinal microenvironment in health and disease
- D. Kontoyiannis Post-transcriptional modules of gene expression in physiology and disease
- <u>V. Kostourou</u> Blood vessel morphogenesis and function
- <u>A. Matralis</u> Development of bioactive molecules against complex human diseases
- <u>G. Panayotou</u> Molecular Analysis of Signal Transduction Pathways
- <u>M. Tsoumakidou</u> Tumor immunology and immunotherapy

4. RNA biology & Epigenetics

The RNA biology & 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. Researchers active in this field are:

- <u>A. Dimas</u> genomic architecture of complex traits in humans
- M. Fousteri Regulatory (epi)genomics in cancer and aging related diseases
- <u>P. Hatzis</u> RNA-mediated transcriptional and epigenetic regulation in carcinogenesis
- <u>P. Kafasla</u> Nuclear Ribonucleoprotein complexes (RNPs) in immune response and cancer
- D. Kontoyiannis Post-transcriptional modules of gene expression in physiology and disease

5. Bioinformatics & Computational Biology

The aim of the Bioinformatics & Computational Biology program is to use and develop stateof-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-throughput data such as genomics, proteomics and metabolomics while we simultaneously provide bioinformatics solutions as services to nonexperts. 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. Researchers active in this field are:

- <u>C. Nikolaou</u> Computational genomics
- <u>G. Pavlopoulos</u> Bioinformatics & integrative biology
- <u>P. Moulos</u> statistical algorithms for NGS

b. Support schemes for the reported directions and priorities

- Investment in infrastructures that may be relevant to particular research directions
- Targeted recruitment of young researchers (semi-independent) or new group leaders, when possible, to enhance capacities and critical mass of specific programs
- Encouragement of joint grant applications for program members
- Participation in specialized MSc programs to attract students interested in the relevant research field.

1.4 Self-assessment and Future Planning

a. Assessment of current strengths and weaknesses (SWOT analysis)

Strengths

- Top-ranked Institute, internationally recognized leaders in the field, top in comparative productivity indices
- Node for European and National Research Infrastructures: Strategic partnership with ESFRI Infrafrontier and ELIXIR, lead partner is Greek node of EMMA since 2009
- State-of-the-art facilities, used by international researchers and industry; highly skilled personnel, know-how in state-of-the-art technological platforms
- Wide range of research projects in translational science using the mouse as a model for human disease
- International standing High success rate in competitive grant applications, solid networking and integration with Centers of Excellence for mouse phenotyping and animal modeling
- Sound Technology Transfer and IP support
- Focus on innovation: Spin-off company (Biomedcode Hellas SA)
- Established links with regional and international stakeholders (including industry, hospitals and academia)
- Land available for further development in biomedical R&D
- Healthy administration, meritocracy and excellence

Weaknesses

- Small size marginal critical mass
- Aging building infrastructures and limited space already filled to capacity
- Distant location to universities & hospitals
- Limited access through public transport dissuades students and other staff
- Saturation of the capacities of existing facilities, due to high demand from users

Opportunities

- Mature strategic planning for further development in the area (Biotechnopolis business plan)
- 138 acres land available for further development of up to 10.000sqm buildings for Biomedical R&D
- Support by the EU Recovery and Resilience Fund to improve building infrastructures and acquire advanced instrumentation for our facilities
- Momentum for the establishment of new strategic partnerships both nationally and internationally
- Brain gain momentum for experienced high-level faculty through provision of favorable research environment
- Opportunity to exploit current infrastructures by complementing them with newer advanced technologies

Threats

• Cumbersome, time-consuming administrative processes due to bureaucratic hurdles imposed by the current national legal framework

- Extreme delays in degree accreditation by NARIC (National Academic Recognition information Center) hinders recruitment of foreign researchers (and Greeks with foreign degrees)
- Limitations and inflexibility in eligible cost categories in national grants and lengthy procurement processes
- Irregular governmental planning of funding opportunities and other support resulting in delays in acquiring technology platforms and retaining highly trained supporting personnel
- Intense competition for top quality highly trained personnel from well-funded institutions outside Greece (Brain Drain)

b. Summary of the actions to maintain and augment the scientific excellence of the Institute

Fleming's priorities for the upcoming period are to maintain scientific and technological excellence, provide new services in state-of-the-art technologies, support training of young researchers, and develop innovation in biomedical sciences. To that end, the upcoming period will focus on the following main directions:

1. **Consolidation of the distinct character of each new Institute**. The election of a Director for the Institute of Bioinnovation should be completed by April 2022 and this will allow the initiation of discussions with group leaders for the priorities and directions to be pursued. This process is already under way for the Institute for Fundamental Biomedical Research where Dr. E. Skoulakis has already taken on the role of Director.

2. Upgrade and enrichment of the **major scientific equipment** used by FLEMING's facilities and those used by individual laboratories.

3. Investigation, strategic discussions and plan drafting towards **attracting and recruiting expertise** (via ERA chairs, Marie Sklodowska Curie fellowships and others) in underrepresented scientific areas in Attica and Greece in general in accord to smart specialization directives.

4. **Strategic alliances** and participation with complementary Biomedical Research institutions and programs such as the Personalized Medicine Initiative in collaboration with the University of Athens Medical School.

5. Further development of the **Biotechnopolis project**. Half of the necessary funds has been secured from the European Investment Bank and there is strong interest by the supervising ministry to cover the rest from central government funds.

6. **New spin-off companies** by FLEMING researchers and/or recruiting innovative biotech companies at our premises.

7. Enhance **educational activities** to increase extroversion and FLEMING's participation in Master's Programs, public outreach activities and science popularization

c. Needs and assumptions for carrying out the envisioned plan

Infrastructures

Infrastructure upgrades are very important for FLEMING's development, given the emphasis on state-of-the-art facilities to provide advanced services to our researchers and elsewhere.

We have secured a grant of 17.8 million euro from the EU Recovery & Resilience Fund, which will be used to upgrade our building and acquire new scientific equipment. The FLEMING building is in urgent need of repairs, new electromechanical infrastructures, energy cost saving measures and lab refurbishments. In terms of scientific instruments, we will both upgrade or replace older equipment and acquire new instruments, including mass spectrometers, NMR, advanced microscopes, etc. We estimate that approximately **10-11** million will be spent on new equipment, mainly to support our common facilities, but also to upgrade equipment and capacities of individual labs.

Regarding our plan for Biotechnopolis, we have an initial approval of our request to the **European Investment Bank**, who will cover half the costs for the project, while the other half will be provided by as yet undefined means by the Greek government (total cost approx. 40 million euro).

New Researchers and Support personnel

Unfortunately, despite the very good support in terms of infrastructures that we are receiving from the State, as outlined above, this is not accompanied by parallel measures regarding personnel, and in particular new researchers and facility technicians. Research centers in Greece have not received any new researcher positions in the last 7 years. In FLEMING there is an urgent need for at least 4 positions and when the Biotechnopolis plan will be realized, there will be additional need for several more. Three of the positions we require are to cover group leaders who have been running their labs at Fleming for several years now, supported by a grant from the Stavros Niarchos Foundation. While all researchers recruited with this grant were at the level of Researcher C', we were not allowed to hire them as such due to government restrictions, and instead they were designated as SNF group leaders. They were all very successful in setting up their labs and also in attracting some additional funding, although their unofficial position meant they were not eligible for most Greek and EU grants. For these reasons they are not able to cover their salaries at the moment and we are facing the risk of their departure, either to a university (where new positions are more readily available) or abroad. An additional position at the level of Specific Operations Scientist (ELE) is required for the Genomics Facility, where again we face a risk of losing highly trained personnel that has been running the facility for many years.

Several **highly trained and specialized technicians** at our facilities have been supported up to now by large infrastructural grants (Infrafrontier, Elixir, Bioimaging-GR, SNF, etc.) that have concluded at the end of 2021, and their renewal has been severely delayed. This makes it very difficult to keep these valuable personnel, some of which have already gone abroad. Only two will be supported by government-approved positions, which are yet to be finalized.

Finally, our **administration** is understaffed, while **bureaucratic demands are rising**. Moreover, at least half of our admin staff are supported by grant overheads, i.e. they are not covered by the state budget. We have urgent needs for at least two grants' officers to handle the complex management tasks for most grants, technical support staff, such as electricians, and accountants. While 5 such positions have been approved since 2017, they have not yet materialized due to cumbersome public hiring procedures – in any case, at least twice as many are required to ease pressure on our overhead budget.

2 Organizational Structure

2.1 Institute Organogram



2.2 Research Groups

Institute for Fundamental Biomedical Research

- Maria Armaka
- Maria Fousteri
- Pantelis Hatzis
- Panagiota Kafasla
- Vassiliki Koliaraki
- Dimitris Kontoyiannis
- Panagiotis Moulos
- George Pavlopoulos
- Efthimios Skoulakis
- <u>Michael Verykokakis</u>

Institute for Bio-Innovation

- Vassilis Aidinis
- Antigone Dimas
- Eleni Douni
- George Kollias
- Vasso Kostourou
- <u>Christoforos Nikolaou</u>
- <u>George Panayotou</u>

- Maria Tsoumakidou
- Babis Savakis (emeritus)

Stavros Niarchos Foundation researchers

- <u>Myrto Denaxa</u>
- <u>Alexis Matralis</u>
- <u>Katerina Papanikolopoulou</u>
- Luca Turin (departed 2020)

2.3 Research Facilities and Support Units

Fleming has established **state-of-the-art facilities** that offer services for biomedical research internally, but also to researchers and companies in Greece and abroad. Support for the establishment and running of these facilities has come from a variety of Greek and EU grants. Among them, Fleming is the **Coordinator of 2 National Research Infrastructures (NRI)**: InfrafrontierGR/Phenotypos and ELIXIR-GR, active in the areas of generation, archiving and phenotyping of animal models of disease, and bioinformatics/biocomputing resources, respectively. 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** <u>pMedGR</u>, in collaboration with the Medical School of Athens.

All the facilities listed below are available to scientists in other institutes and universities, as well as to companies, either through collaborative grants or as contract services. While the relative usage for internal and external access varies considerably for each facility, in general external services account for approximately 20% of total.

Fleming facilities

Animal House: <u>https://www.fleming.gr/services/facilities/animal-house</u>

& Phenoclinic: <u>https://www.fleming.gr/our-facilities/phenoclinic-services</u>

Since 2001, the Animal House of BSRC "Alexander Fleming" provides high quality breeding and experimental environment and animal models to the biomedical research community, promoting animal welfare, excellence and scientific interaction.

Animal Supply: The FLEMING Animal House provides mouse research models of the highest quality. Animals are bred and maintained under strict barrier conditions, that guarantee specific pathogen free status. Animal models include a variety of inbred and outbred strains, as well as models for human disease.

Experimental Services: The Animal House provides state of the art installation, phenotyping equipment, specialized personnel and animal models for research protocols, ensuring high standards of experimentation and reproducibility. All services provided are in accordance with the National Legislation and the European Legal Framework.

Education & Training: The Animal House holds an education and training program, in line with legislation, ensuring competency of personnel involved in the care, breeding and use of animals for scientific procedures. It participates in tours and seminars, organized for schools and academic foundations.

PhenoClinic Services:

Endoscopy

- Ultrasound imaging
- In vivo optical / X-ray Imaging
- Irradiation
- Metabolic/Behavioral Phenotyping
- Metabolic Cage housing

Transgenics facility: https://www.fleming.gr/services/facilities/trangenesis

The Transgenics & Gene Targeting Facility at the BSRC Al. Fleming was established in 2001 to integrate transgenic technologies in the mouse for cutting-edge biomedical research. We provide services for BSRC Al. Fleming investigators as well as for collaborating scientists in academic Institutes or biotech/pharmaceutical companies worldwide.

ES Cell Technology Services: Our services support the generation of mice carrying a disrupted or mutated specific genetic locus. Generation of transgenic mice is achieved through: Embryonic Stem Cell Gene Targeting, Blastocyst Injection, Chimera Production, Germline transmission.

DNA microinjection Service: Our services support the generation of transgenic mice carrying an inserted cassette in their genome through DNA microinjection in the pronucleus and generation of founders. The service is certified with ISO 9001:2000 since 2008.

Archiving Services: The facility is a member of the European Mouse Mutant Archive network since May 2010. It has more than 350 lines deposited in a CryoBank. It offers storage, archiving and transportation of mutant strains through embryo rederivation, cryopreservation and recovery of mouse embryo and sperm.

Proteomics facility: https://www.fleming.gr/services/facilities/proteomics

The Proteomics facility offers services for the quantitative analysis of proteins and the characterization of their interactions and post-translational modifications. A Thermo Scientific Q Exactive HF-X Hybrid Quadropole-Orbitrap mass spectrometer and an LTQ Orbitrap XL Hybrid Ion Trap are available, providing outstanding tools for advanced proteomics. Both instruments are coupled to specialized RSLCnano systems for peptide separation.

Services:

- Protein identification by nano Ultra LC–mass spectrometry
- Differential proteomics of complex samples using label-free quantification (LFQ)
- Protein quantification using isotopic labeling (SILAC) or reporter ion labeling (iTRAQ, TMT)
- Characterization of protein complexes
- Targeted proteomic analysis
- Identification of post-translational modifications
- Quantitative phospholipid analysis

Genomics facility: https://www.fleming.gr/services/facilities/genomics

The BSRC Al. Fleming Genomics Facility was established in 2008. The Facility operates an Ion Proton[™] System coupled to Ion Torrent[™] Ion Chef[™] System, for next generation sequencing-based experimental protocols.

Services:

- Genome Sequencing: gDNA-Seq (de novo, re-sequencing)
- Targeted/Exome sequencing: In solution Hybridization (TargetSeq), or PCR based amplification (AmpliSeq)
- Transcriptome Sequencing: RNA-Seq, smallRNA-Seq.
- Chip/FAIRE-Seq.

Micro CT Imaging: <u>https://www.fleming.gr/services/facilities/microct-imaging</u>

Advanced micro-CT imaging services and support are available at BSRC Fleming for research involving ex vivo analysis of selected tissues derived from small animals (mineralized biomaterials, grafts, implants, composites etc). The recently acquired SkyScan1172 high-resolution micro-CT delivers high quality images and can be used by researchers for X-ray scans of selected regions of small animals followed by 3D visualization. Quantitative bone density and bone micro-architecture are a few of the available services provided. **The services provided include** micro-CT analysis and histomorphometric analysis of bone tissue.

Histopathology: https://www.fleming.gr/services/facilities/histopathology

BSRC Fleming's histopathology lab has more than 12 years of experience to provide state-ofthe-art research histology services. Specialized staff offers a full array of services including evaluating the user's needs in histology and advice on using the most appropriate techniques. Included in the range of services available are cutting (including bone) and staining as well as cryostat sectioning. Assistance can also be provided to mouse biology research scientists in processing tissue samples for routine histochemical and immunostaining procedures.

Services:

- Histology
- Frozen sections
- Soft organ and tissue sections
- Immunohistochemistry & in situ hybridization

Flow cytometry & Cell sorting: https://www.fleming.gr/services/facilities/flow-cytometry

The BSRC Fleming Flow Cytometry and Cell Sorting Facility is equipped with the BD FACS Canto II analyzer capable for up to 8-colour analysis and high-throughput applications and the BD FACS Celesta analyzer capable for up to 12-colour analysis as well as an 18-colour BD FACS Aria III cell-sorting unit operating under BSL-2 with enhanced precautions (during sorting operations). The Facility also offers services for analysis of clinical-chemical and hematological parameters. It is equipped with Mindray BC5000Vet, a 5Diff Hematology analyzer capable of mouse blood analysis and the Beckman Coulter AU480 Biochemical analyzer.

Services:

Flow Cytometry

- Multiparametric flow cytometric analysis
- Flow cytometric functional assay analysis (such as cell cycle, apoptosis and proliferation)
- Multiplex bead-based immunoassay analysis *Cell Sorting*
- Isolation of Cellular subsets for functional assays

- Isolation of Cellular subsets for sequencing
- Single cell sorting *Clinical chemistry and Hematology*
- Complete 5 population mouse blood count.
- Detection and quantification of common mouse serum/plasma and urine electrolytes, metabolites and enzymes. *Customized services*
- Assays for the identification of cellular and molecular perturbations during phenotyping or disease modelling using cells in biological fluids (e.g., blood/sera) or tissues
- Establishment and optimization of customized cell sorting platforms

Bioimaging unit: <u>https://www.fleming.gr/services/facilities/bioimaging</u>

The Imaging Unit provides expertise and state-of-the-art equipment for modern multidimensional biomedical imaging applications using modern microscopy methods, digital image processing and computational image analysis. Imaging equipment include a Leica TCS SP8X White Light Laser confocal system, a PicoQuant FLIM system with two external APD detectors, a Zeiss LightSheet Z1 Imaging System and several fluorescent microscopes and stereoscopes.

Services include:

- High resolution dynamic fluorescent imaging in 2D and 3D
- Multi Fluorescent Protein detection (Spectral Unmixing)
- co-localisation and ratiometric analysis
- light and fluorescent imaging
- fast live cell imaging
- FRAP (Fluorescent recovery after photobleaching)
- FRET (Fluorescent resonance energy transfer)
- FLIM (Fluorescent lifetime Imaging microscopy)
- Live dynamic imaging

Bioinformatics services: <u>https://www.fleming.gr/services/facilities/bioinformatics-e-resources</u>

The facility offers high-quality, state-of-the-art scientific software for various types of analyses. Through their implementations, they maintain an active presence in respective communities such as Bioconductor, bio.tools, ELIXIR and others. Current software and resources (databases, portals) developed by the Bioinformatics and Computational Biology Program are:

- Biological networks: NORMA, NAP, VICTOR, Arena3Dweb
- Databases and portals: Fibromine, NMPfaDB
- Genomics: SeqCVIBE, recoup, scanner, FLAME
- Text mining: OnTheFly

At the moment, the local computational infrastructure at BSRC "Alexander Fleming" includes 13 servers which in total consist of 292 computing cores, 1,83TB memory and 671TB disk storage. Moreover, BSRC "Alexander Fleming" has full access to the GRNET cloud infrastructure platform and resources (~okeanos, ~okeanos-knossos, ARIS) for high performance computing, parallelization and big data analyses.

2.4 Scientific Council

The Scientific Council (SC) provides recommendations and advice to the Director of the Institute and the Board of Directors, as required, on issues related to scientific policy and assessment, research personnel recruitment (proposes research directions and evaluation committees), provides opinions for the Institute's strategic development and assesses any scientific matters that may arise. It is consulted for the development or restructuring of laboratories, divisions or facility units.

For the first two years of the review period (2018-19), the Institute's Scientific Council was composed of the following:

- Dr. George Panayotou, Researcher A', BSRC Fleming Elected President of the Scientific Council
- Dr. Dimitris Kontoyiannis, Associated Researcher, Professor of Biology, Aristoteleion University of Thessaloniki
- Dr. Efthimios Skoulakis, Researcher A', BSRC Fleming
- Dr. Ioannis Talianidis, Researcher A', BSRC Fleming (currently Director of the Institute of Molecular Biology and Biotechnology, FORTH)
- Dr. George Kollias, Associated Researcher, Professor of Physiology at National and Kapodistrian University of Athens
- George Papathanassiou, non-voting member, as personnel representative

Following the establishment of the two Institutes, the respective Scientific Councils were elected as follows:

Institute for Fundamental Biomedical Research

- Dr. Dimitris Kontoyiannis, Associated Researcher, Professor of Biology, Aristoteleion University of Thessaloniki – Elected President of the Scientific Council
- Dr. Maria Fousteri, Researcher B', BSRC Fleming
- Dr. Pantelis Hatzis, Researcher B', BSRC Fleming
- Dr. George Pavlopoulos, Researcher B', BSRC Fleming
- Dr. Martin Reczko, Specific Operations Scientist A', BSRC Fleming

Institute for BioInnovation

- Dr. Vasso Kostourou, Researcher B', BSRC Fleming Elected President of the Scientific Council
- Dr. Eleni Douni, Associated Researcher, Associate Professor of Biotechnology, Athens Agricultural University
- Dr. Christoforos Nikolaou, Researcher B', BSRC Fleming
- Dr. Martina Samiotaki, Specific Operations Scientist A', BSRC Fleming
- Dr. Maria Tsoumakidou, Researcher B', BSRC Fleming

2.5 Personnel

Table 2-1: Permanent Researchers

Researcher Name	Position ¹	Year joining the Institute	Year departing from the Institute	Year(s) of promotion
Vasilis Aidinis	Researcher A	2001		2012
George Panayotou	Researcher A	1999		2006
Efthimios Skoulakis	Researcher A	2002		2013
Maria Fousteri	Researcher B	2009		2015
Pantelis Hatzis	Researcher B	2010		2018
Vassiliki Kostourou	Researcher B	2007		2018
Christoforos Nikolaou	Researcher B	2020		
George Pavlopoulos	Researcher B	2018		
Maria Tsoumakidou	Researcher B	2017		2019
Maria Armaka	Researcher C	2016		
Antigone Dimas	Researcher C	2016		
Panagiota Kafasla	Researcher C	2016		
Vassiliki Koliaraki	Researcher C	2016		
Panagiotis Moulos	Researcher C	2017		2021
Mihalis Verykokakis	Researcher C	2017		2021
Martina Samiotaki	ELE A	2000		2019
Martin Reczko	ELE A	2019		2019
Sofia Grammenoudi	ELE B	2016		2020
Vasileios Ntafis	ELE B	2017		2020

¹ Research personnel A, B, C (this includes Researchers and Specific Operations Scientists (ELE))

Table 2-2a: Affiliated Researchers

Researcher Name	Position ²	Year joining the Institute	Year departing from the Institute	Year(s) of promotion
George Kollias	Professor	2000		NA
Dimitris Kontoyiannis	Professor	2001		NA
Babis Savakis	Emeritus Prof.	2012		NA
Eleni Douni	Associate Prof.	2001		NA

Table 2-3c: Stavros Niarchos Foundation Researchers

Researcher Name	Position ³	Year joining the Institute	Year departing from the Institute	Year(s) of promotion
Myrto Denaxa	SNF researcher	2018		NA
Alexis Matralis	SNF researcher	2018		NA
Katerina Papanikolopoulou	SNF researcher	2018		NA
Luca Turin	SNF researcher	2016	2020	NA

² Research personnel A, B, C (this includes Researchers and Specific Operations Scientists (ELE))

³ Research personnel A, B, C (this includes Researchers and Specific Operations Scientists (ELE))

Table 2-4: All Personnel

Personnel Totals 2018			2019		2020		2021	
reisonner rotais	Male	Female	Male	Female	Male	Female	Male	Female
Researchers	6	6	6	7	7	7	8	7
Collaborating University								
Faculty	2	1	2	1	2	1	3	1
Adjunct, part-time,								
visiting Researchers	4	3	4	2	2	3	1	2
Staff Scientists and								
Technicians	6	10	9	11	11	12	14	12
Post-doctoral								
Researchers (on contract)	14	17	13	18	15	25	16	22
Research Associates (on								
contract)	1	1	1	1	2	1	1	1
PhD Students (on								
contract)	8	25	10	23	9	28	4	25
Administrative Personnel								
(permanent or on								
contract)	13	10	13	10	12	8	9	7
Master and								
Undergraduate Students	1	3	2	8	2	10	8	12
Other Personnel	7	8	5	8	6	8	5	9
Total	62	84	65	89	68	103	69	98

3 Administration and Management Policies and Practices

a. Policies and practices for financial management and Access policies to Facilities.

Overhead policy: Overhead applicable to grants or services is used to cover administrative personnel costs (grants manager, accountants, IT, etc.), utility bills, building maintenance, common equipment repairs and various other running expenses. The amount of overhead is determined by each grant. In cases where no overhead is available or it is considerably less than 20%, we ask researchers to cover some additional general costs from their grants, provided they are eligible. For services offered by our facilities to outside partners, we charge a 25% overhead. The same is applied to Matching Funds provided by the state for eligible EU grants.

Budget allocation: The government grant allocated to FLEMING is used to cover the salaries of Researchers and Specific Operations Scientists (ELE), a small number of central administrative and technical support personnel and a fraction of utility bills. Institutes do not have their own admin or support staff, as they are all provided by the Center.

Concerning **Matching Funds** and other awards relevant to EU grants, although the Center has full control on their allocation, these are always given to the researchers that have secured the EU grant, minus a 25% overhead.

Common Facilities: FLEMING has a number of facilities (see 2.3 above) offering services to internal and external users and these are administered centrally, i.e. they are not part of any specific institute (see organogram at 2.1 above). For most facilities, a Specific Operations Scientist (ELE) oversees day-to-day running, while a Researcher is responsible for scientific matters and development strategies. Other staff include technicians or other support employees, a small percentage of which are covered by the government grant, while the rest are supported by infrastructure grants, overheads, or income of the facility from external users.

The **fees charged for facility services** are based on detailed costing and differ for internal and external users. The cost for external users is calculated based on personnel costs (man-hours), consumables, instrument depreciation and servicing, as well as a 25% overhead to cover utilities, management and other costs. On the other hand, internal users are not charged for personnel covered by the state budget, for instrument depreciation or for central admin or utility costs (electricity etc.), leaving consumables as the main cost and in particular cases technical personnel salaries that cannot be covered otherwise.

b. Management of the Human Potential

FLEMING follows strict and transparent procedures for the recruitment of researchers, as well as administrative and other personnel, always based on merit. All available positions are advertised as broadly as possible. Depending on the type of personnel, this includes calls for expression of interest or job announcements <u>at our website</u> and the <u>EURAXESS network</u>, emails to lists of collaborators or potential candidates, local job-finding websites, etc. Our calls clearly outline the selection process, evaluation criteria and the process for redress of grievances. In this way, FLEMING is in full compliance with the general principles and requirements of **The Code of Conduct for Recruitment of Researchers** of the European Commission, concurrently respecting national legislation for open recruitment procedures.

Regarding Researcher positions, informal procedures are usually arranged before announcement of the position, including an initial call for expression of interest, informal enquiries to colleagues abroad, invitation of potential candidates to a seminar and discussions with other researchers. For the formal procedure, the Institute's Scientific Council initially makes a recommendation on the scientific area of interest for the strategic development of the Institute. The position is then announced and advertised as above. A pre-selection of the best candidates by the recruitment recommendation committee is followed by seminars and discussion with the recruitment evaluation panel before final candidate recommendation to the Board. The criteria for researcher selection are **academic excellence**, **contribution to the development of new research areas, synergy with existing groups and potential for innovation**. The Institute's Scientific Council advises the Director on researcher recruitment and may prioritize specific research areas for development. It also selects the members of the candidate evaluation committees. In addition, FLEMING has adopted the approach of recruiting and supporting **Junior Researchers** to set up their own independent groups through funding from various sources (e.g. 6 Stavros Niarchos Researchers, 7 ELIDEK Postdoc Researchers, 2 Marie Curie Fellows). This gives the opportunity both to test the abilities of the recruits as group leaders and to provide the necessary time-frame for securing new government researcher positions, which are allotted intermittently and in small numbers.

The recruitment of **post-doctoral or pre-doctoral researchers and technicians** is the responsibility of each group leader, although common policies are followed to conform with best practices and law requirements. Positions are advertised for at least 15 days. Selection is carried out by a committee consisting of three group leaders, who grade candidates on several qualitative and quantitative criteria, clearly defined in the call. A similar procedure is followed for **administrative staff**.

While **start-up funding** is not guaranteed, we aim to recruit new researchers when opportunities for such support arise, for example through central institutional grants, excellence awards, large infrastructural projects, etc. Depending on the funds available, start-ups usually include the purchase of small equipment, 1–2-person salary support and consumables. Subsidized costs for using our central facilities are also an important part of the support offered.

Mentoring is very important for new researchers and actively practiced by institute directors. Apart from scientific directions and approaches, mentoring is especially important for guiding new recruits to navigate the complex and highly competitive grant landscape in Greek and EU research. This will include not only advice for each individual grant opportunity, but also inclusion of the new researcher in joint applications for larger collaborative grants.

Postdocs and graduate students are very important for the work done by all FLEMING researchers and therefore we place particular emphasis not only in their recruitment procedure, but especially in their training as scientists during their stay and in ensuring the best possible outcome in terms of their future career. In particular, their performance is regularly assessed through internal seminars, where they can get comments and advice on their projects. They are also encouraged to participate in local and international conferences, presenting their work and getting acquainted with future employers. Regarding PhD students, it is strongly advised that group leaders support them with funding throughout their studies, especially when it is deemed necessary that they stay beyond the normal timeframe of 3-4 years. PhD Students are also encouraged and supported to apply for scholarships to national and international foundations thus gaining further experience in fund raising.

c. Measures for promoting Equality, Diversity and Inclusion

FLEMING strives to implement the principles of equal opportunity and treatment for all employees, irrespective of gender, origin or physical limitations. Indicative respective data: 60% of total FLEMING personnel are female 50% of total FLEMING researchers are female Physical limitations / Special needs employees comprise 2% of total personnel

FLEMING has prepared a <u>Gender Equality Plan</u> (GEP), adopting the European Commission's Gender Equality Strategy 2020-2025 which covers all Union policies, including Research and Innovation policy. The implementation of this strategy will follow a two-pronged approach: taking targeted measures to achieve gender equality combined with stronger gender mainstreaming.

Working conditions

We ensure that the working conditions for all staff, including disabled people, provide the flexibility deemed essential for successful research performance in accordance with existing national legislation. We aim to provide working conditions which allow both women and men to successfully combine family and work, children and career.

Accessibility for People with disabilities

The current building has three floors plus a basement. The main entrance is accessible to wheelchair users. To facilitate entrance accessibility, a 5% slope ramp has been constructed. There are two clearly demarcated parking slots reserved for vehicles of disabled persons next to the ramp in the front parking lot, by the main entrance. Moreover, 2m wide corridors ensure accessibility for disabled people within the building and appropriate lifts provide access to all floors. There is a fully configured WC with adequate space for people with mobility problems on the ground floor of the building, where all materials, design and equipment are aligned to the legal national requirements.

d. Policy and Regulations enforcing Ethics in Research and Scientific Integrity

The **Ethics and Code of Conduct Committee** advises on issues of bioethics and ethics that arise when carrying out research work at FLEMING and provides recommendations on ethical issues in the context of research programs proposed and implemented at the institute.

The structure of the Committee is as follows:

- Maria Armaka, Chairman of the Committee, Researcher C' BSRC Fleming
- Vasileios Ntafis, Vice-Chairman, Staff Scientist B'-Veterinarian, BSRC Fleming
- Dimitris Kletsas, Member, Director of the Institute of Biosciences and Applications, NCSR "Demokritos"
- Michael Koutsilieris, Member, Professor of Experimental Physiology, Medical School, University of Athens
- Mata Hatzipetrou, Member, Legal Counsellor

The Committee addresses issues of compliance with the rules of the **Code of Conduct for Research** and provides recommendations to the competent bodies of the Center. In particular, the responsibilities of the Committee include:

- Provides recommendations on issues related to Bioethics and Research Ethics
- Reviews proposed research and approves research protocols, as required to ensure that studies meet the requirements of National and International Regulations
- Monitors compliance with rules on use of biological samples and protection of personal data resulting from investigations.
- Prepares and periodically updates the Center's Code of Conduct for Research.
- Creates and updates the corresponding website of the Center to inform Center members on the basic principles and rules of research ethics.
- The Committee proposes to the Board of Directors the suspension or termination of a research project, if any violation of the law and the Code of Ethics for Research occurs.
- Prepares and periodically updates the Center's Code of Conduct.

FLEMING's Board of Directors, following the recommendation by the Scientific Council, adopted the **European Code of Conduct for Research Integrity** of the European Federation of Academies of Sciences and Humanities (ALLEA), which is available at:

https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/guidance/european-code-of-conduct-for-researchintegrity horizon en.pdf

Furthermore, the Board adopted the **European Charter & Code for Researchers**, available at:

https://euraxess.ec.europa.eu/sites/default/files/am509774cee_en_e4.pdf .

Both documents are uploaded on the Center's Intranet and can be accessed by all FLEMING staff.

Conflict resolution in cases of scientific misconduct, authorship disputes, harassment, or discrimination:

For scientific misconduct issues FLEMING has upgraded its Bioethics Committee renaming it **Bioethics and Research Ethics Committee** and broadening its scope to issues of general scientific code of conduct and research ethics. Additionally, it has implemented the updated "European Code of Conduct for Research Integrity" (ALLEA, see above). Finally, we are evaluating electronic systems for recording research results and have assigned a working group to examine the best available technical solutions.

Authorship disputes that cannot be resolved within a research group are referred to the Institute Scientific Council.

FLEMING has zero tolerance towards any form of physical harassment – any form of violence is reason for immediate dismissal. Verbal, psychological or other non-physical harassment or discrimination is dealt at varying levels, depending on severity and circumstances, i.e., by the group leader if it regards members of their group or the institute director in cases involving group leaders. If escalation is required, all staff can forward grievances to an independent committee that has been established to deal with these issues, consisting of:

1. The representative of researchers at the Board (currently Dr. Vasso Kostourou)

2. The representative of other staff at the Board (currently Mr. George Papathanasiou)

3. FLEMING's Legal Councilor (currently Ms. Mata Hatzipetrou).

Depending on the initial outcome, the issue can be further referred to the FLEMING Board of Directors.

As mentioned above, a Scientific Data Management Plan is under construction. Concerning GDPR, we conform to Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC.

e. Partnerships, strategic alliances

FLEMING has developed a strategic partnership with the **Medical School of the University of Athens**, which consists of the coordination of joint MSc and PhD programs as well as co-development of infrastructures for Precision Medicine (<u>pMedGR</u>) and translational research through mouse models of human disease (<u>InfrafrontierGR</u>).

As a full partner of the ESFRI Infrafrontier, FLEMING has direct connectivity and strategic partnerships to Global Projects and Consortia on mammalian genetics and phenotyping, including the International Knock-out consortium (IKMC), the European conditional mutagenesis program (EUCOMM), the International Mouse Phenotyping Consortium (IMPC), the coordination action InfraCoMP, and others.

FLEMING has also signed a MoU with the National Bank of Greece sharing the common vision of fostering innovation and entrepreneurship in emerging areas of modern research. This partnership also involves two more Greek research organizations and aims to contribute to the translation of scientific achievements into clinical practice and the development of innovative products of high added value.

f. Scientific exchanges and collaborations

Internal seminars take place every Wednesday, giving the opportunity to postdocs and PhD students to present informally their current work, discuss their findings and get useful feedback. The schedule is such that everyone presents at least once every year.

Once or twice a month, FLEMING organizes **open lectures** by internationally renowned scientists in the field of immunology, functional genomics, neurobiology, cutting edge technologies and other areas of interest. These lectures were attended by FLEMING personnel and scientists from other institutions. A full list of the FLEMING invited lectures is available here: <u>https://www.fleming.gr/dissemination/external-seminars</u>).

In April 2019, a two-day <u>Scientific Retreat</u> was organized for all FLEMING research staff at the island of Evia. The main aim of this event was to promote the exchange of scientific knowledge within the FLEMING community and to strengthen the

collaborations among the different disciplines. The retreat featured a mix of science and social activities, providing the opportunity to highlight current research performed by all members, including Faculty, post-doctoral fellows, facility personnel and graduate students, through informal talks and poster presentations. It also allowed informal team bonding activities. It was attended by 112 members of the institute. Due to the Covid-19 pandemic, this event was not repeated in the following years and is tentatively scheduled again for 2023.



Scientific Retreat 2019

FLEMING has always placed an **emphasis on complementarity** when recruiting researchers. Together with the relatively small size of the institute, this has resulted in very close collaborations between different groups. The proximity of lab spaces and the sharing of facilities is also a contributing factor. Joint applications for funding, in the case of collaborative or large infrastructure grants, is common among our researchers. As a result, there are many publications arising with **joint authorship** by different group leaders:

- Sfikakis PP, Verrou KM, Ampatziadis-Michailidis G, Tsitsilonis O, Paraskevis D, Kastritis E, Lianidou E, Moutsatsou P, Terpos E, Trougakos I, Chini V, Manoloukos M, <u>Moulos</u> <u>P, Pavlopoulos GA</u>, <u>Kollias G, Hatzis P</u>, Dimopoulos MA. 2021, "Blood Transcriptomes of Anti-SARS-CoV-2 Antibody-Positive Healthy Individuals Who Experienced Asymptomatic Versus Clinical Infection", **Front. Immunol.**, 05 October 2021
- Baltoumas F.A., Zafeiropoulou S. Karatzas E., Koutrouli, M., Thanati F., Voutsadaki K., Gkonta M., Hotova J., Kasionis, I., <u>Hatzis P., Pavlopoulos G.A.</u> 2021, "Biomolecule and Bioentity Interaction Databases in Systems Biology: A Comprehensive Review", **Biomolecules**, 2021, 11, 1245
- 3. Elisa De Crignis, Tanvir Hossain, Shahla Romal, Fabrizia Carofiglio, <u>Panagiotis Moulos</u>, Mir Mubashir Khalid, Shringar Rao, Ameneh Bazrafshan, Monique Ma Verstegen, Farzin Pourfarzad, Christina Koutsothanassis, Helmuth Gehart, Tsung Wai Kan, Robert-Jan Palstra, Charles Boucher, Jan Nm IJzermans, Meritxell Huch, Sylvia F Boj,

Robert Vries, Hans Clevers, Luc Jw van der Laan, <u>Pantelis Hatzis</u>, Tokameh Mahmoudi. 2021, "Application of human liver organoids as a patient-derived primary model for HBV infection and related hepatocellular carcinoma.", **Elife.**, 2021 Jul 30; 10:e60747. doi: 10.7554/eLife.60747

- Kostaki EG, <u>Pavlopoulos GA</u>, Verrou KM, Ampatziadis-Michailidis G, Harokopos V, <u>Hatzis P</u>, <u>Moulos P</u>, Siafakas N, Pournaras S, Hadjichristodoulou C, Chatzopoulou F, Chatzidimitriou D, Panagopoulos P, Lourida P, Argyraki A, Lytras T, Sapounas S, Gerolymatos G, Panagiotakopoulos G, Prezerakos P, Tsiodras S, Sypsa V, Hatzakis A, Anastassopoulou C, Spanakis N, Tsakris A, Dimopoulos MA, Kotanidou A, Sfikakis P, <u>Kollias G</u>, Magiorkinis G, Paraskevis D. 2021, "Molecular Epidemiology of SARS-CoV-2 in Greece Reveals Low Rates of Onward Virus Transmission after Lifting of Travel Restrictions Based on Risk Assessment during Summer 2020.", mSphere., 2021 Jun 30: e0018021. doi: 10.1128/mSphere.00180-21
- Koutrouli M, Karatzas E, <u>Papanikolopoulou K</u>, <u>Pavlopoulos GA</u>. 2021, "NORMA: The Network Makeup Artist - A Web Tool for Network Annotation Visualization.", **Genomics Proteomics and Bioinformatics.**, 2021 Jun 22: S1672-0229(21)00130-3. doi: 10.1016/j.gpb.2021.02.005
- Theodorakis V., Antonakis AN., Baltsavia I., <u>Pavlopoulos GA.</u>, <u>Samiotaki M.</u>, Amoutzias G., Theodosiou T., Acuto O., Efstathiou G., Iliopoulos I. 2021, "ProteoSign v2: A faster and evolved user-friendly online tool for statistical analyses of differential proteomics", **Nucleic Acids Res.**, 2021 May 8: gkab329. doi:10.1093/nar/gkab329
- Georgios C Stefos, Eszter Szantai, Dimitris Konstantopoulos, <u>Martina Samiotaki</u>, <u>Maria Fousteri</u>. 2021, "aniFOUND: analysing the associated proteome and genomic landscape of the repaired nascent non-replicative chromatin", **Nucleic Acids Research**, gkab144 https://doi.org/10.1093/nar/gkab144
- Zannikou M, Barbayianni I, Fanidis D, Grigorakaki T, Vlachopoulou E, Konstantopoulos D, <u>Fousteri M</u>, Nikitopoulou I, Kotanidou A, Kaffe E, <u>Aidinis V</u>. 2021, "MAP3K8 Regulates Cox-2-Mediated Prostaglandin E 2 Production in the Lung and Suppresses Pulmonary Inflammation and Fibrosis.", **J Immunol**, 2021 Feb 1; 206(3):607-620
- Verrou KM, Vlachogiannis NI, Ampatziadis-Michailidis G, <u>Moulos P</u>, <u>Pavlopoulos GA</u>, <u>Hatzis P</u>, <u>Kollias G</u>, Sfikakis PP. 2021, "Distinct transcriptional profile of blood mononuclear cells in Behcet's disease: insights into the central role of neutrophil chemotaxis", **Rheumatology** (Oxford), 2021 Jan 25; keab052. doi: 10.1093/rheumatology/keab052
- 10. <u>Koliaraki V</u>, Prados A, Armaka M, <u>Kollias G</u>. 2020, "The mesenchymal context in inflammation, immunity and cancer.", **Nat Immunol.**, 21(9): 974-982
- Christodoulou-Vafeiadou E, Geka C, Ntari L, Kranidioti K, Argyropoulou E, Meier F, <u>Armaka M</u>, Mourouzis I, Pantos C, Rouchota M, Loudos G, Denis MC, Karagianni N, <u>Kollias G</u>. 2020, "Ectopic bone formation and systemic bone loss in a transmembrane TNF-driven model of human spondyloarthritis.", **Arthritis Res Ther.**, 22(1):232
- Engie Prifti, Eleni N Tsakiri, Ergina Vourkou, George Stamatakis, <u>Martina Samiotaki</u>, <u>Katerina Papanikolopoulou</u>. 2020, "The two Cysteines of Tau protein are functionally distinct and contribute differentially to its pathogenicity in vivo", J Neurosci., 2020 Dec 15; JN-RM-1920-20. doi: 10.1523/JNEUROSCI.1920-20.2020
- 13. Keramidis I, Vourkou E, <u>Papanikolopoulou K</u>, <u>Skoulakis EMC</u>. 2020, "Functional Interactions of Tau Phosphorylation Sites That Mediate Toxicity and Deficient Learning in Drosophila melanogaster.", Front Mol Neurosci. , 2020 Oct 21; 13:569520
- Magkrioti C, Kaffe E, Stylianaki EA, Sidahmet C, Melagraki G, Afantitis A, <u>Matralis AN</u>, <u>Aidinis V.</u> 2020, "Structure-Based Discovery of Novel Chemical Classes of Autotaxin Inhibitors.", Int J Mol Sci., 2020 Sep 23; 21(19):7002.

- Marianthi Gioulbasani, Alexandros Galaras, <u>Sofia Grammenoudi</u>, <u>Panagiotis Moulos</u>, Alexander L Dent, Mikael Sigvardsson, <u>Pantelis Hatzis</u>, Barbara L Kee, <u>Mihalis</u> <u>Verykokakis</u>. 2020, "The transcription factor BCL-6 controls early development of innate-like T cells", Nat Immunol., 2020 Sep; 21(9):1058-1069. doi: 10.1038/s41590-020-0737-y. Epub 2020 Jul 27
- Roulis M, Kaklamanos A, Schernthanner M, Bielecki P, Zhao J, Kaffe E, Frommelt LS, Qu R, Knapp MS, Henriques A, Chalkidi N, <u>Koliaraki V</u>, Jiao J, Brewer JR, Bacher M, Blackburn HN, Zhao X, Breyer RM, <u>Aidinis V</u>, Jain D, Su B, Herschman HR, Kluger Y, <u>Kollias G</u>, Flavell RA. 2020, "Paracrine orchestration of intestinal tumorigenesis by a mesenchymal niche.", **Nature**, 580(7804) :524-529
- Ninou I, Sevastou I, Magkrioti C, Kaffe E, Stamatakis G, Thivaios S, <u>Panayotou G</u>, Aoki J, <u>Kollias G</u>, <u>Aidinis V</u>. 2020, "Genetic deletion of Autotaxin from CD11b+ cells decreases the severity of experimental autoimmune encephalomyelitis.", **PLoS One**, 15(4) :e0226050
- <u>Papanikolopoulou K</u>, <u>Skoulakis EMC</u>. 2020, "Altered Proteostasis in Neurodegenerative Tauopathies", Adv Exp Med Biol., 2020; 1233: 177-194. doi: 10.1007/978-3-030-38266-7_7
- <u>Koliaraki V</u>, Henriques A, Prados A, <u>Kollias G</u>. 2020, "Unfolding innate mechanisms in the cancer microenvironment: The emerging role of the mesenchyme.", J Exp Med., 217 (4)
- Koutrouli M, <u>Hatzis P, Pavlopoulos GA</u>. 2020, "Exploring networks in the STRING & REACTOME database", in Systems Medicine: Integrative, Qualitative and Computational Approaches. Reference Module in Biomedical Sciences, 13 January 2020 ISBN:9780128012383, doi:0.1016/B978-0-12-801238-3.11516-8
- Papadaki M, Rinotas V, Violitzi F, Thireou T, Panayotou G, Samiotaki M, Douni E. 2019, "New Insights for RANKL as a Proinflammatory Modulator in Modeled Inflammatory Arthritis", Frontiers in Immunology, : 10:97. 2019
- Daras G, Rigas S, Alatzas A, <u>Samiotaki M</u>, Chatzopoulos D, Tsitsekian D, Papadaki V, Templalexis D, Banilas G, Athanasiadou AM, <u>Kostourou V</u>, <u>Panayotou G</u>, Hatzopoulos P. 2019, "LEFKOTHEA Regulates Nuclear and Chloroplast mRNA Splicing in Plants", **Developmental Cell.**, 12. pii: S1534-5807(19)30630-6. 2019
- 23. Foteini Violitzi, Vasiliki-Iris Perivolidi, Trias Thireou, Ioannis Grivas, Sylva Haralambous, <u>Martina Samiotaki</u>, <u>George Panayotou</u>, <u>Eleni Douni</u>. 2019, "Mapping interactome networks of DNAJC11, a novel mitochondrial protein causing neuromuscular pathology in mice", **J Proteome Res.**, 18(11): 3896-3912. 2019
- 24. Roussou IG, <u>Papanikolopoulou K</u>, Savakis C, <u>Skoulakis EMC</u>. 2019, "Drosophila Bruton's Tyrosine Kinase Regulates Habituation Latency and Facilitation in Distinct Mushroom Body Neurons.", **J Neurosci.**, 2019 Oct 30; 39(44):8730-8743
- 25. <u>Katerina Papanikolopoulou</u>, Jean Gouzi, Ilianna Roussou, Martina Samiotaki and <u>Efthimios Skoulakis</u> 2019, "Drosophila Tau negatively regulates translation and olfactory Long-Term Memory, but facilitates footshock habituation and cytoskeletal homeostasis", **Journal of Neuroscience.**, 39, 8315-8329
- 26. Polykratis A, Martens A, Eren RO, Shirasaki Y, Yamagishi M, Yamaguchi Y, Uemura S, Miura M, Holzmann B, Kollias G, Armaka M, van Loo G, Pasparakis M. 2019, "A20 prevents inflammasome-dependent arthritis by inhibiting macrophage necroptosis through its ZnF7 ubiquitin-binding domain.", Nat Cell Biol., 2019 May 13. doi: 10.1038/s41556-019-0324-3
- <u>Matralis AN</u>, Afantitis A, <u>Aidinis V</u>. 2019, "Development and therapeutic potential of autotaxin small molecule inhibitors: From bench to advanced clinical trials", **Med Res Rev.**, 2019 May; 39(3):976-1013

- Krishna-Subramanian S, Singer S, <u>Armaka M</u>, Banales JM, Holzer K, Schirmacher P, Walczak H, <u>Kollias G</u>, Pasparakis M, Kondylis V. 2019, "RIPK1 and death receptor signaling drive biliary damage and early liver tumorigenesis in mice with chronic hepatobiliary injury", **Cell Death Differ.**, 2019 Apr 15. doi: 10.1038/s41418-019-0330-9
- Kerdidani D, Chouvardas P, Arjo AR, Giopanou I, Ntaliarda G, Guo YA, Tsikitis M, Kazamias G, Potaris K, Stathopoulos GT, Zakynthinos S, Kalomenidis I, Soumelis V, <u>Kollias G</u>, <u>Tsoumakidou M</u>. 2019, "Wnt1 silences chemokine genes in dendritic cells and induces adaptive immune resistance in lung adenocarcinoma.", Nat Commun., 2019 Mar 29; 10(1):1405
- <u>Papanikolopoulou K</u>, Mudher A, <u>Skoulakis E</u>. 2019, "An assessment of the translational relevance of Drosophila in drug discovery.", **Expert Opin Drug Discov**, 2019 Jan 21: 1-11. doi: 10.1080/17460441.2019.1569624
- Koliaraki V, Chalkidi N, Henriques A, Tzaferis C, Polykratis A, Waisman A, Muller W, Hackam DJ, Pasparakis M, <u>Kollias G</u>. 2019, "Innate Sensing through Mesenchymal TLR4/MyD88 Signals Promotes Spontaneous Intestinal Tumorigenesis.", Cell Rep., 2019 Jan 15; 26(3):536-545.e4. doi: 10.1016/j.celrep.2018.12.072
- 32. Kadas D, <u>Papanikolopoulou K</u>, Xirou S, Consoulas C, <u>Skoulakis EMC</u>. 2018, "Human Tau isoform-specific presynaptic deficits in a Drosophila Central Nervous System circuit", **Neurobiol Dis.**, 2018 Dec 8; 124:311-321. doi: 10.1016/j.nbd.2018.12.004
- Henriques A, <u>Koliaraki V</u>, <u>Kollias G</u>. 2018, "Mesenchymal MAPKAPK2/HSP27 drives intestinal carcinogenesis", **Proc Natl Acad Sci U S A.**, 2018 Jun 12; 115(24):E5546-E5555. doi: 10.1073/pnas.1805683115
- Melagraki G, Leonis G, Ntougkos E, Rinotas V, Papaneophytou C, Mavromoustakos T, Kontopidis G, <u>Douni E</u>, <u>Kollias G</u>, Afantitis A. 2018, "Current Status and Future Prospects of Small-molecule Protein-protein Interaction (PPI) Inhibitors of Tumor Necrosis Factor (TNF) and Receptor Activator of NF-κB Ligand (RANKL).", **Curr Top Med Chem.**, 2018; 18(8):661-673. doi: 10.2174/1568026618666180607084430
- 35. <u>Papanikolopoulou K, Grammenoudi S, Samiotaki M, Skoulakis</u> <u>EMC.</u> 2018, "Differential effects of 14-3-3 dimers on Tau phosphorylation, stability and toxicity in vivo.", **Hum Mol Genet.**, 2018 Apr 12. doi: 10.1093/hmg/ddy129
- 36. <u>Turin L, Skoulakis EMC.</u> 2018, "Electron Spin Resonance (EPR) in Drosophila and General Anesthesia.", **Methods Enzymol.**, 2018;603: 115-128. doi: 10.1016/bs.mie.2018.01.020. Epub 2018 Mar 8
- 37. <u>Armaka M</u>, Ospelt C, Pasparakis M, <u>Kollias G</u>. 2018, "The p55TNFR-IKK2-Ripk3 axis orchestrates arthritis by regulating death and inflammatory pathways in synovial fibroblasts", **Nat Commun.**, 12;9(1):618

FLEMING's state-of-the-art facilities are also the means for very productive collaborations with other institutes and universities. The recent partnership with the Medical School of the University of Athens to develop the **pMedGR infrastructure** has resulted in many common projects and is already starting to bear fruit in terms of collaborative publications (e.g., 1, 2, 4 above, among others).

4 Financial Situation of the Institute

Table 4-1: Governmental Funds

	2018	2019	2020	2021
Regular Budget	1,253,130.00	1,252,700.00	1,252,000.00	1,252,000.00
Matching Funds	1,588,101.00	1,252,444.71	553,224.11	0.00
TOTAL	2,841,231.00	2,505,144.71	1,805,224.11	1,252,000.00

Table 4-2: Competitive Grants

	2018	2019	2020	2021
Greek Programs	2,909,954.40	3,202,317.29	2,442,961.00	1,197,554.48
EC Programs	188,935.52	1,009,662.28	139,954.23	652,572.25
Other International	263,361.86	298,561.29	192,447.94	262,080.29
Private Funding	162,456.92	434,663.39	394,283.47	165,654.42
Other	123,565.30	208,340.75	120,094.36	165,469.06
TOTAL	3,648,274.00	5,153,545.00	3,289,741.00	2,443,330.50

Table 4-3: Common Expenses (not including Salary Costs)

	2018	2019	2020	2021
Operational costs (electricity, water etc.)	231,947.00	247,996.00	278,549.00	333,736.17
Buildings & maintenance	15,728.85	76,898.98	38,108.52	25,998.79
Instruments & maintenance	5,937.50	35,879.08	65,027.40	5,858.04
Educational (e.g. invited speakers, journal subscription etc.)	6,276.77	11,067.64	929.70	776.06
Travel	3,085.33	4,532.97	5,175.07	1,599.28
Other	56,873.17	127,914.73	138,128.26	247,345.55
TOTAL	319,848.62	504,289.40	525,917.95	615,313.89

	2018	2019	2020	2021
Salary cost from Central Budget	948,586.13	939,444.00	958,043.41	980,398.83
Salary cost of non-permanent staff	2,214,966.87	2,565,999.00	2,625,900.59	2,642,574.14
Instruments & maintenance	131,167.50	1,252,913.92	374,019.60	125,918.96
Consumables	452,206.00	591,022.00	762,889.00	688,171.10
Other	193,305.88	360,365.68	102,742.45	87,798.08
TOTAL	3,940,232.38	5,709,744.60	4,823,595.05	4,524,861.11

Table 4-4: Operational Costs for Facilities and Infrastructures

Note: Table 4-5 below is added as supplementary to distinguish between operational costs for the whole institute (shown in Table 4-4) and those relating only to research facilities & support units (animal house, etc., see section 2.3)

Table 4-5: Operational Co	ts for Research Facilities	and Support Units (also	o included in Table 4-4)
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	2018	2019	2020	2021
Salary cost from Central Budget	183,072.30	183,169.22	192,523.84	195,353.87
Salary cost of non-permanent staff	58,364.76	58,364.76	58,364.76	58,364.76
Instruments & maintenance	107.04	2,363.31	1,378.73	411.29
Consumables	103,533.70	113,703.29	42,739.05	105,236.29
Other	22,945.04	79,673.52	20,550.40	16,352.05
TOTAL	368,022.84	437,274.10	315,556.78	375,718.26

As reported in the recent evaluation of the Hellenic Foundation for Research and Innovation, which is the main source for basic research grants in Greece, FLEMING has achieved the highest success rate in grant applications to this foundation, averaging over 40%, among all eligible institutions in medical and life sciences, as shown in the following graph:



Success rate in HFRI grants

5 Results & Achievements

5.1 Bibliometric Output

Table 5-1: Bibliometric Output

	2018	2019	2020	2021	TOTAL
Journal Publications	37	42	37	85	201
International conference proceedings	19	18	10	12	59
Other conferences	12	47	7	20	86
Book chapters	0	1	3	0	4
Books - monographs	0	1	0	0	1
TOTAL	68	109	57	117	351
Citations	3060	3617	3748	4596	15021

Average Journal Impact Factor for 2018-21: 9

FLEMING achieves very high scores in all relevant markers recorded by the National Documentation Center. The latest data (2018) show that FLEMING has the highest Relative Impact Factor as well as the highest percentage of publications attracting citations among other GSRI centers in the field of Medical and Health Sciences, as shown in the following figures:





Percentage of publications attracting citations for each GSRI research center

5.2 Training and Educational Activities

a. PhD Programs

PhD students perform their thesis research in the laboratories of Fleming faculty, often in collaborative projects with other labs in the Centre. They are encouraged to seek such collaborations and interact with the Facilities personnel as necessary for their specific projects. They are required to present their work once a year on average in the Centre-wide Wednesday seminar series and lab or research area specific research presentations. In total, 17 PhD students supervised by FLEMING Researchers were awarded their degree during the assessed period.

a. MSc Programs

Students of various MSc programs (listed below), but mostly from the Molecular Biomedicine and Athens International Master's program in Neurosciences perform their MSc thesis research in the laboratories of Fleming faculty. They participate in and present in lab or research area specific research presentations and events. In total, 47 MSc students supervised by FLEMING Researchers were awarded their degree during the assessed period.

b. Undergraduate Students, Internships

Undergraduate students from different Greek Universities perform their undergraduate thesis research in the laboratories of Fleming faculty for 6-12 months or shorter practical training exercises for 2-3 months. They participate in and present in lab or research area specific research presentations and events. In total, 40 undergraduate theses have been supervised by FLEMING Researchers during the assessed period.

c. Other Mentoring activities and actions to support career development of the trainees

LAS CORE Modules Course

Since 2020, FLEMING has been organizing the annual Laboratory Animal Science (LAS) Core Modules Course, a two-day intensive training event for research personnel working with laboratory animals. The Course content includes the Core Modules, as described in the European Commission's "Working Document on the development of a common education and training framework to fulfil the requirements under the Directive 2010/63/EU".

Core Modules represent the basic theoretical training for all personnel performing any of the Functions A-D of Article 23 (Directive 2010/63/EU) and Article 22 (P.D. 56/2013, national legislation). Completion of all Core Modules is compulsory for staff carrying out procedures on animals (function A), designing procedures and projects (function B), taking care of animals (function C) or killing animals (function D).

FLEMING's Training and Educational approach and philosophy

FLEMING's teaching activities greatly enhance its role in shaping modern biomedical research in Greece. We are focused on providing stat of the art training to students and scientists of all levels through formal educational programs (e.g., Marie Curie programs, joint MSc and PhD programs in cooperation with Greek university departments), "training through research" hosted in its laboratories and facilities, a systematic conference and seminar activity, as well as through the Fleming Museum, which operates in its premises, and promotes Alexander Fleming's heritage

FLEMING, provides state-of-the-art research infrastructures and facilities, coupled with highly regarded researchers and a strong emphasis in innovation in biomedical sciences, all factors that contribute to its attractiveness as a host for students at various levels.

Students recognize and seek the unique and stimulating research environment and rigorous academic training at FLEMING. Through its programs, infrastructures and personnel, students have the opportunity to:

- Gain strong cross-disciplinary research backgrounds in disease modelling, translational and clinical research, bioinformatics, immunology, genetics, molecular and cellular biology, functional genomics, and epigenetics.
- Develop expertise in cutting edge methodologies and research tools, including transgenic technologies (CRISPR-Cas9), NGS, proteomics, multi system mouse phenotyping and advanced imaging.
- Perform independent research across several disease areas and model systems to discover and validate novel targets for mechanistic understanding of disease and innovative drug development.
- Obtain a variety of transferable, complementary skills, which will enhance their career prospects in academic as well as non-academic routes.
- Be exposed to the international scientific and industrial community.
- Interact with the private sector to gain experiences in drug development and evaluation platforms, biomarker development, and a deep insight into how fundamental discoveries and advances are translated to successful investments, thus fostering a culture of entrepreneurship.
- Acquire the ability to communicate with a professional environment, the scientific community or society in general about basic questions of science and science policy.

Furthermore, career prospects for graduates are promising, since upon completion of the program, students are fully equipped to tackle the future challenges of modern biology, its applications and implications, and to pursue successful careers in science, industry, health and public engagement sectors.

Specifically, FLEMING alumni students usually:

- 1. Pursue academic careers in top research labs (Research Assistant, PhD, Postdoc)
- 2. Staff research infrastructures in Greece or abroad
- 3. Work in R & D departments in pharmaceutical or biotechnology companies
- 4. Establish their own innovative SME companies

A Memorandum of Understanding on Establishing a **Joint Doctoral Program (JDP)** has been signed between FLEMING and the Medical School of the National and Kapodistrian University of Athens in 2012. The two leading academic institutions jointed forces in order to perform training and forefront research in the field of biomedicine, focused on the understanding of medical physiology and disease pathogenesis and translation to novel therapeutic approaches. Graduates from recognized Universities will are registered under the JDP

program upon approval of the JDP Committee. These students are awarded the Doctoral degree by Med-UoA jointly with FLEMING according to Med-UoA requirements.

The above-mentioned MoU facilitates FLEMING Researchers in recruiting PhD Candidates but is not restrictive.





Since 2016 FLEMING coordinates the 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. The Program aims to place students in the forefront of modern biomedical research and to lay the foundation for the development of innovation and entrepreneurship in the field of biomedicine and biotechnology. The MSc provides the opportunity to perform research in leading labs in the field, and offers innovative, multidisciplinary training, combining practical experience and theoretical knowledge in disease mechanisms, state-of-the-art technologies, animal

modeling, clinical validation, large scale omics analysis, advanced imaging platforms, as well as complementary training in innovation, entrepreneurship, and technology transfer.

The program provides state-of-the-art training towards deep mechanistic understanding of disease pathogenesis combined with a systemic, integrated view of pathophysiology and tools for the development of novel approaches for disease management, preparing students to pursue successful research careers in the new era of personalized medicine. The program accepts students from various disciplines aiming to create a vibrant environment where students will interact and gain a broad perspective of the current scientific questions.

Intra-departmental International MSc Program in Neurosciences



FLEMING participates since 2016 in the Intradepartmental International MSc Program in **<u>Neurosciences</u>** coordinated by the Biology Department of the National and Kapodistrian University of Athens. FLEMING is a member of the highest administrative body of the program with an equal vote. The program offers spherical training on the neuronal systems of many organisms including the anatomy and the development of the nervous system, offers and deep insight the neurobiological of diseases, neuropharmacology, neuroimmunology, neuroendocrinology, as well as in computational neuroscience, while in parallel offers training on the

state-of-the-art technologies required to address scientific questions related to the nervous systems.

Participation in other MSc programs

Further to the above-mentioned programs, where most FLEMING Researchers participate as lecturers and thesis supervisors, FLEMING Researchers also participate in **other MSc programs** as listed below:

- Interdepartmental MSc in Clinical Biochemistry and Molecular Diagnostics, Department of Biology, National and Kapodistrian University of Athens
- MSc in Translational Research in Biomedicine, Demokritos University of Thrace
- MSc in Life Sciences and Biomedicine Informatics, University of Patras
- MSc in Methodology of Research in Basic Medical Sciences, Medical School, University of Patras.
- MSc in Molecular and Applied Physiology, Medical School, National and Kapodistrian University of Athens.
- MSc in Introduction of Research Methodology, Medical School, National and Kapodistrian University of Athens
- MSc in Biotechnology and Applications in Agricultural Sciences, Department of Agricultural Biotechnology, Agricultural University of Athens
- MSc in System Biology, Department of Agricultural Biotechnology, Agricultural University of Athens.
- MSc in Current topics in Biosciences, Department of Biology, Aristotle University of Thessaloniki.
- MSc in Information Technologies in Medicine and Biology, Department of Informatics and Telecommunications, National and Kapodistrian University of Athens
- MSc in Microbial Biotechnology, Department of Biology, National and Kapodistrian University of Athens
- MSc in Molecular Medical Biopathology, Medical School, National and Kapodistrian University of Athens.
- MSc in The Molecular Basis of Human Disease, University of Crete Medical School
- MSc in Translational Research in Biomedicine, Department of Molecular Biology & Genetics of the Democritus University of Thrace
- MSc in Applications in Biology, Department of Biology, Aristotle University of Thessaloniki
- MSc in Translational research in molecular biology and genetics, Dept. Molecular Biology and Genetics, Democritus University of Thrace
- MSc in Applied Genetics and Biotechnology. Dept. Biology, Aristotle University of Thessaloniki
- MSc in Molecular Biology-Biomedicine, Department of Biology, University of Crete
- MSc in Basic Medical Sciences, Faculty of Medicine, Univ. of Patras. (2015)
- MSc in Molecular Biopathology, Medical School, National and Kapodistrian University of Athens.
- MSc in Clinical Biochemistry Molecular Diagnostics Department of Biology, National and Kapodistrian University of Athens.
- MSc in The Science of Stress and Promotion of Health, Medical School, National and Kapodistrian University of Athens

5.3 Innovation and Intellectual Property

FLEMING's Innovation and Entrepreneurship Unit (IEU) was first established in 2005 under a grant from General Secretariat for Research and Technology and has been wholly supported by the Centre since then. The IEU is staffed with qualified personnel who have brought their work experience from abroad, and it is further supported by a network of external professionals (patent lawyers, business development consultants etc.). The IEU monitors FLEMING intellectual output from its research programs, providing advice on optimal means of protecting and exploiting key outputs.

During the review period, the IEU has facilitated/lead the following key activities:

- Full range of contractual services, including drafting and negotiation of material transfer agreements (MTAs), service agreements, collaboration agreements, research agreements and license agreements. In the reporting period, the IEU has continuously reviewed and updated the FLEMING contract portfolio to ensure that contractual terms and conditions offer the best possible legal protection of FLEMING's intellectual assets.
- Negotiated, as part of the European Mouse Mutant Archive (EMMA) consortium, a key commercial license that allows FLEMING to create and distribute transgenic mice using the innovative and patented CRISPR technology. The license further cements FLEMING's unique position as Greece's leading repository and expert base in transgenic mice, and it allows FLEMING to continue to operate as a local distribution node for the EMMA network. FLEMING's participation in the EMMA network is key to maintaining and building on our reputation for cutting edge research among the international mouse community. During the evaluation period, FLEMING generated, on behalf of both its own and external researchers, thirteen new transgenic mice for use in the general research community. Seven of these mice were generated using the new CRISPR technology. Eleven of the mice were generated for academic researchers, while two were created for Industry.
- Around 160 MTAs were signed in the reporting period, approx. 100 of which were for non-FLEMING researchers wishing to use our mice and reagents, and the reach of the MTAs extended to Korea the USA and throughout Europe. MTA compliance continues to be monitored carefully and a number of serious cases of MTA breach have been pursued and rectified wherever possible.
- FLEMING is developing a **new patent family** with a key collaborator in the Greek pharmaceutical industry, Unipharma, concerning the development of autotaxin inhibitors. The patent family currently consists of seven Greek national patents (filed in 2020, all granted) and one PCT stage application that is currently under examination by the European patent office (filed in 2021).
- Continued and growing support to FLEMING service units, both as standalone service provision and as part of the Phenotypos infrastructure. A total of 45 service contracts have been signed during the evaluation period, with a total value of approximately 145,000 Euros (of which, 62k was to academic institutions and 83k to companies). With a customer base that extends throughout Europe, the steady growth in services provision is a reflection of the quality of FLEMING's research, continuously updated end upgraded facilities and the standing and reputation of resident researchers and scientists.

- **Out-licensed antibodies** have generated a small but steady income of around 6k Euros during the reporting period, while out-licensed mice have generated an income of greater than 15k Euros (excluding 2021 data not yet reported by licensee).
- Representation of FLEMING in the HBio Greek Biotechnology Cluster.
- Promoting and raising visibility of FLEMING's intellectual property portfolio and tech transfer services in various events in Greece.

The IEU continues to **support BioMedCode S.A**., FLEMING's spin-off company, and its relationship with Biomedcode continues to be positive and productive. Specific mouse licenses have been renewed during the reporting period.

5.4 Awards and Distinctions

(selected)

Dr Eleni Douni was elected as an Executive Board Member of the International Bone Marrow Adiposity Society, joined the Editorial Board of the Journals "Genes" and "Bone Reports" and was elected at the Dean's Committee of the School of Applied Biology and Biotechnology, AUA.

Dr George Kollias was appointed Director at the Department of Physiology, Medical School, University of Athens, was elected as a member of the Steering Advisory Board of the National Centre for Biotechnology (CNB), Madrid, Spain, and became an Associate Editor of 'Physiological Reviews'.

Dr Dimitris Kontoyiannis became Director of the Department of Genetics, Developmental and Molecular Biology at the School of Biology, AUTH and was elected at the General Assembly of the Hellenic Foundation for Research and Innovation (HFRI).

Dr George Panayotou was appointed as an Associate Member of the Biomedical Sector Scientific Council, National Council for Research and Innovation (2018-20).

Dr Efthimios Skoulakis was appointed as Basic Science Board Member of the Hellenic Initiative Against Alzheimer's Disease, and became Associate Editor of 'Frontiers in Cell and Developmental Biology for Molecular Medicine' and Academic Editor of the 'International Journal of Molecular Sciences'

5.5 Societal Impact

Through its high-quality research, FLEMING's scientific team has achieved **significant and tangible social impact**, towards better understanding of disease mechanisms, as well as the development of diagnostic and therapeutic tools. We therefore place significant emphasis on disseminating the impact of our work to the general public and in particular to young people. In 2021, FLEMING was awarded a grant (95k euro) from the Hellenic Foundation for Research & Innovation for the promotion and dissemination of our research output, which will significantly improve our outreach activities by developing various multimedia presentations, demonstration actions, interactive exhibitions, development of the <u>Alexander Fleming</u> <u>Museum</u> and preparation of printed informational material.

School Educational Program

In order to increase public awareness, inspire the next generation of biologists and publicize its research programs, FLEMING organizes visits to its premises for **High School students** who have an interest in Life Sciences. A typical school visit accommodates 12-15 students, has three hours duration and includes, among others, a visit to the Alexander Fleming Museum, short presentations and videos describing issues of modern Biological Research and demonstration of laboratories and experimental research models.

Student visits take place during the academic year, once per month and our schedule is always fully booked – with an exception during Covid-19 restrictions. We accept students attending the final year of High School from both public and private sector schools (Greek or English speaking), as well as from universities and other higher education institutions. Notably, students visit from outside of the immediate Athens area, as well as nearby locations. The school visits are publicized in our website for interested parties to apply.

Advisory roles to the State

FLEMING Researchers hold several positions in advisory roles to the Greek government. Indicatively:

- **George Kollias** is Member of the Attica Regional Council on Research and Innovation (PSEK) 2017 present) and has served as Chair of the Assembly of Presidents of Greek Research Centers (2017 2018).
- **Dimitris Kontoyiannis** is Member of the General Assembly of the Hellenic Foundation for Research and Innovation (HFRI) since 2017 and Member of "Innovation and Entrepreneurship" platform on "Health and Medicines" run by the General Secretariat for Research Technology (GSRT).
- **George Panayotou** served as Associate Member of the Biomedical Sector Scientific Council, National Council for Research and Innovation (2018-2020).
- **Babis Savakis** is Vice Chair of the National Council for Research and Innovation since 2016, Member of the National Bioethics Commission since 2014 and Member of the National Commission of Human Rights since 2015.

FLEMING participated in the following **open events for the general public in 2019.** No further events were attended till now because of the Covid-19 pandemic restrictions:

- <u>Athens Science Festival 2019</u>, where we organized three educational activities in the fields of Biology and Biomedicine for all ages, aiming to bring science closer to the public.
- <u>Researchers' Night 2019</u>, where we presented interactive demonstrations including a) the microscopic observation of animal cells from various organs, b) interactive experiments to understand electromuscular activity, and c) projection of a video presenting the research activities of the institute.

Highlights, Press releases, Video Gallery, Social Media

FLEMING regularly publishes important news (including major publications, grants, events etc.) on its website (<u>https://www.fleming.gr/research/fleming-highlights</u> and <u>https://www.fleming.gr/dissemination/fleming-news</u>) and has an active video gallery, which

includes taped lectures from FLEMING Researchers or guests. Our presence in social media is on the rise, with active accounts in Twitter (<u>@BSRC_Fleming</u>), <u>LinkedIn</u> and <u>YouTube</u>.

Distinguished Affiliated Scholar (DAS) Program

In 2014 FLEMING introduced the Distinguished Affiliated Scholar Program with the aim to establish synergies with distinguished international scholars from the Humanities, Arts, Sciences and Technologies, in order to spark innovative and 'out of the box' thinking. FLEMING's goal was to organize and host a series of events and lectures that aim to foster interactions beyond conventional boundaries. As part of this newly established Program, during this reporting period, FLEMING hosted three Distinguished speakers.

Major achievements of socioeconomic impact

Through its high-quality research, FLEMING's scientific team has achieved significant and tangible social impact, towards the **better understanding of disease mechanisms**, as well as the development of **diagnostic and therapeutic tools**. Furthermore, through participation in large EU infrastructure networks (e.g., Infrafrontier, ELIXIR), FLEMING is playing a pivotal role in bringing **access to state-of-the-art biotechnology platforms** to Greece as well as the Balkans region.

In parallel to - and as a result of - the core research work, FLEMING's focus on innovation has already led to the establishment of **a successful spin-off company, Biomedcode**, located within FLEMING premises and leveraging the Center's facilities, which focuses **on preclinical drug evaluation services.** Moreover, the Center's innovation-related activities are supported by an experienced Technology Transfer Office, which aims to support the commercialization of research work and establish strong links with the local and international industry in line with international practice.

Through its diverse set of activities and on top of its valuable contribution to the global scientific excellence, FLEMING already generates multiple economic benefits for the Greek State. FLEMING has been generating on an annual level:

- Employment contribution of ~140 directly employed personnel and at least twice as many personnel as indirect contribution (source: McKinsey Business plan for Biotechnopolis).
- Positive contribution to the **national trade balance**, as a result of the inflow of international funds
- Positive contribution to the **fiscal balance**, as a result of employer and employee contributions and taxes