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ANNEX VI – ICVS Annual Report 2018

University of Minho

ICVS | LIFE AND HEALTH SCIENCES RESEARCH INSTITUTE

SCHOOL OF MEDICINE
UNIVERSITY OF MINHO

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1. INTRODUCTION

1.1 DESCRIPTION OF THE FCT UNIT: ICVS/3B's ASSOCIATE LABORATORY (AL)

The ICVS/3B's Associate Laboratory (AL) was created in the University of Minho in 2011 as a result of the partnership established over the years between:

- The ICVS - a group on Biomedicine and Clinical Sciences, focusing its activities on Microbiology and Infection, Neurosciences and Surgical Sciences, member of the Clinical Academic Centre – Braga, Association (2CA-Braga);
- The 3B's - a group on Materials Science and Engineering, mainly focusing on Technologies Applied to Regenerative Medicine, including Biomaterials, Stem Cells, Tissue Engineering and Nanomedicine, leader of the European Institute of Excellence on Tissue Engineering and Regenerative Medicine (EXPERTISSUES EEIG).

The ICVS/3B's AL centers its activities in the Health Sciences, namely in Biomedical and Clinical Sciences, and in Engineering/Materials Science and Biomaterials. This interface Health-Sciences/Technologies fosters the generation of value through the development of innovative products and services, resulting from internationally highly competitive research.

The creation of the ICVS/3B's AL potentiated activities within different dimensions, namely: (1) Scientific and technological research and development of applied research in the interface Health Sciences/Technology; (2) Advanced education and training, providing research and training activities to undergraduate/postgraduate students and health professionals; (3) Services, consulting and technology transfer, by taking into consideration the vital importance of industrial/clinical partners; (4) Dissemination and fostering of public and scientific awareness of science.

The collaboration and complementarities between the ICVS and the 3B's also benefit from the: (1) established network of expertise in animal models in health sciences/technology; (2) clinical know-how and resources centered at the Clinical Academic Centre – Braga, Association (2CA-Braga), as well as within the network of Health institutions affiliated with the ICVS; and (3) the European Institute of Excellence on Tissue Engineering and Regenerative Medicine, coordinated by the 3B's.

New technologies, therapies and medical products are being developed the ICVS/3B's AL, including in the context of vaccination, diagnosis, regenerative medicine, minimally invasive therapeutic procedures, personalized treatments and nanomedicine. The ICVS/3B's AL has, therefore, the potential to cross the complete development pipeline, from the more fundamental in vitro research, testing in animal models and pre-clinical validation, to the clinical trial phase, therefore transposing innovative therapeutic solutions to the market.

2. RESEARCH GROUP: ICVS (LIFE AND HEALTH SCIENCES RESEARCH INSTITUTE)

2.1 OBJECTIVES AND ACHIEVEMENTS

2.1.1 OBJECTIVES

The Life and Health Sciences Research Institute (ICVS) - member of the ICVS/3B's AL - aims at improving human health through outstanding life-science research, cutting-edge medical innovation and delivery of specialized services.

The ICVS is a R&D Unit incorporated in an innovative medical school, the School of Medicine (EM) - University of Minho (UMinho) - strategically located in the Northern region of Portugal within a growing Cluster of Biomedical Science, Technology and Healthcare institutions.

The ICVS is organized around four interdisciplinary Research Domains with high critical mass: Microbiology and Infection, Neurosciences, Surgical Sciences and Population Health.

The strategy for the ICVS development has been centred in: i) establishing a research unit within an innovative Medical School, guided by international standards of excellence; ii) establishing a consortium with the research group 3B's - Biomaterials, Biodegradables and Biomimetics - a leading research group in Health Technology; and iii) fostering a key partnership with the Clinical Academic Centre – Braga, Association (2CA-Braga) and the affiliated Healthcare Institutions in the Minho region.

The ICVS is a growing group and represents an attractive research environment for young researchers, providing a state-of-the-art technological platform for Cell and Tissue Culture, Electrophysiology, Biosafety Level 2 and 3, Molecular Biology, Imagiology, Microscopy Imaging, Neuroanatomy/Neuroimaging, Histology, Biological Resources, Cytometry, Endoscopy and Minimally Invasive Surgery, as well as a fully equipped Centre for Animal Experimentation and a Clinical Academic Centre.

THE ICVS AIMS TO ACHIEVE THE FOLLOWING GLOBAL GOALS:

- Promote original research on health sciences with high scientific outputs and recognized impact in the advance of knowledge on the biomedical, translational and clinical scopes;
- Participate in the development of novel products with medical application, including new diagnostic systems and new therapies, in collaboration with other R&D units from diverse technological fields;
- Encourage a wide-ranging interaction between research and medical undergraduate/graduate training, in partnership with the affiliated network of Healthcare Institutions;
- Promote the registration of patents and the creation of spin-offs on innovative medical products;
- Provide international advanced post-graduated programs in biomedicine and in clinical

sciences;

- Provide specialized clinical and scientific services to the community, including medical diagnosis and clinical trials, particularly in the context of the 2CA-Braga;
- Foment the public awareness of science;
- impact the society, as a nucleus to support the development of a national policy for scientific research in Biomedicine and Clinical Sciences.

THEREFORE, THE SPECIFIC DEVELOPMENTAL STRATEGIES FOR 2018 WERE TO:

- Develop flexible and integrated functional models that endorse multidisciplinary R&D projects, actively promoting the interplay Health-Sciences/Technologies – involving the ICVS researchers, health professionals from the 2CA-Braga, as well as researchers from the 3B's research group – on the Research Domains: i) Microbiology and Infection, ii) Neurosciences, iii) Surgical Sciences and iv) Population Health;
- Expand the activities of the 2CA-Braga, namely the development of clinical research, particularly with the capacity to accommodate clinical trials, aiming at reinforcing the leading position at the National level;
- Support the activities of the Spin-offs associated with the ICVS;
- Promote international post-graduate programs and courses on Medicine and Health Sciences, fostering and strengthening existing international collaborations, with a strong recruitment of foreign students (graduate, undergraduate and MDs);
- Support the ongoing EM/ICVS PhD and Master Programs, as well as the MD/PhD program in collaboration with the Thomas Jefferson and Columbia medical schools, USA;
- Provide specialized health services, particularly by developing clinical trials in the context of the 2CA-Braga;
- Stimulate the active participation of medical students in research projects, contributing to a MD training of excellence and fostering a “MD-scientist” profile among the EM graduates;
- Diversify the funding sources, particularly in projects on clinical sciences and at the international level;
- Offer a strong program of scientific seminars, namely through the ICVS International Seminar Seminars and the seminars “Ciência Falada”;
- Promote the public awareness on health sciences, contributing to the understanding of the importance of research, as well as to the general public health education and to healthier lifestyles.

2.1.2 MAIN ACHIEVEMENTS DURING THE YEAR OF 2018:

THE MAIN ACHIEVEMENTS IN 2018 WERE:

- The significant increase in the number of peer-reviewed international publications;
- The relevant increase in the competitive funding secured by the ICVS researchers through competitive calls;
- The increase in the number and in the impact of the clinical studies developed in the 2CA-Braga, including clinical trials;
- The increase in the number of contracts for research staff;
- The reinforcement of the network of collaborating R&D institutions such as the INL – International Nanotechnology Laboratory through a Hackathon and a Program of common grants;
- Launching of an initiative to build a new area for “Terminal Animal Experimentation Rooms” (SEAT), to be located close to the clean zone of the “Biotério”/rodent Animal Facility, in order to perform terminal procedures with rodents;
- The maintenance of a high number and impact of the Advanced Post-Graduation Courses.

SPECIFICALLY, IN 2018, THE ICVS WAS ABLE TO:

- Publish a total of 283 papers in international peer-reviewed journals (referenced in ISI, Scopus or in Pubmed), in addition to 14 international book chapters and 180 proceedings and communications in international meetings. Among the articles published in 2018, 263 were produced within the four research domains (Microbiology and Infection, Neurosciences, Surgical Sciences and Population Health), wherein 64% were in Q1-Q2, with 42% of these 263 in Q1. The average Impact Factor (IF) of these publications is 4.8, and includes 64 papers with IF between 3 and 5; 44 papers with an IF between 5 and 10; 14 papers with an IF between 10 and 20, 5 papers with an IF>20. Additionally, the ICVS published 20 articles in other fields.

Noteworthy, the average IF of the 100 articles published in the journals with higher impact was 8;

- Increase the amount of competitive funding from research grants, involving a total sum of about 22.3 million € in ongoing projects (3 years of accumulated value) from calls at the international and national levels, of which 8.1 million € correspond to funding obtained in 2018. Indeed, the level of funding granted through competitive sources and from contracts with leading industrial partners has been reinforced, namely through 84 ongoing projects (48 from FCT; 4 from NORTE2020; 3 from other national sources; 2 from H2020; 18 from other international sources and 9 from contracts with the national industry);
- Develop clinical research with a growing impact, through the 2CA-Braga, in partnership with the Medical School and Hospital of Braga, including clinical trials in collaboration with

international industrial leading partners. This strategy potentiated the capacity of the ICVS to provide specialized services by testing new therapies, with 187 clinical studies ongoing during 2018: 117 clinical studies were commercial-driven (90 clinical trials, 26 observational studies and 1 medical device study) and 70 clinical studies were investigator-driven (2 clinical trials, 54 observational studies and 14 validation studies of medical devices), assuming a leading position in the National context. The 2CA-Braga developed research projects in partnership with the ICVS and other research institutions from the UMinho (with projects funded by the European Commission and nationally, by the FCT and FEDER). As an important indicator, the 2CA recruitment rate of patients has been consistently above 85%;

- Increase the number of contracts for research staff. Indeed, although the total number of PhD researchers stabilized in recent years (from 93 in 2014 to 94 in 2018), the ICVS was able to define a policy of differentiation of its body of PhD researchers. In fact, their profile positively evolved, with an increase in the number of Post-docs that succeeded in competitive applications for researcher contracts – resulting in a growth of the total number of researcher contracts from 14 in 2014 to 20 in 2018 (funding sources such as FCT and P2020). Currently, taking advantage of the governmental policy defined for the “Scientific Employment”, the conditions are created for a new cycle of growth in the body of PhD researchers with contracts. In this context, we are planning to increase the number of researcher contracts in 2019 by at least 15 new contracts, including three positions for researchers with tenure. Additionally, the four spin-off companies associated with the ICVS are financially viable and, most importantly, generating alternative career pathways for researchers;

- Establish strategic partnerships with other research institutions based on complementarity and excellence in research. In this context, the INL | International Iberian Nanotechnology Laboratory was the focus of this policy in 2018, through the organization of a “Hackathon” initiative, from which emerged 7 collaborative projects supported by internal funding. Importantly, this interaction already resulted in 5 R&D projects with funding obtained from national and international competitive calls;

- Launch an initiative to build a new area for “Terminal Animal Experimentation Rooms” (SEAT), to be located close to the clean zone of the “Biotério”/rodent Animal Facility, in order to perform terminal procedures with rodents. It will include an animal preparation room, for anesthesia/sedation of animals, a room equipped for perfusion with hazardous chemicals and dissection, and a third room equipped for the preparation of primary cell cultures. These experimental rooms are essential for all research domains and follow a legal requirement to avoid the transportation of animals inside the research institute to laboratories away from the animal facilities;

- Pursue supporting the EM's Master Program in Health Sciences, as well as the four PhD Programs that have been granted with specific funding from the FCT;
- Continue fostering the Program of International Seminars Series that complemented the Seminars "Ciência Falada" (44 in total), involving the participation of leading scientists from foreign Institutions;
- Create the experimental conditions for the conclusion of 16 PhD thesis, including 5 from MDs;
- Foster collaborations between its researchers and partners from Biomedical Industries. In 2018, industry sponsored R&D activities was performed in areas of mutual interest with sponsors such as: BIOGEN PORTUGAL, FUNDAÇÃO BIAL, GILEAD SCIENCES, KARL STORZ and TECNIMEDE;
- Provide the Molecular Diagnostics Service (SDM), by offering genetic diagnostics of intellectual disability related disorders, with a CGH microarrays service for the screening of microdeletions and duplications of chromosome regions;
- Obtain 47 International and National scientific awards, including the "Prémio Santa Casa Neurociências – Melo e Castro" awarded by Santa Casa da Misericórdia de Lisboa; the MESCyT 2018 award for Achievement in Research, awarded by the Government of Dominican Republic; the 1st Prize - Ultrasound Imaging Prize 2018 by Grupo Português de Ultrassonografia Endoscópica (GRUPUGE); and the "Early Career Award", awarded by the Governing Board of the International Society of Behavioral Medicine;
- Submitted 2 patents, namely: "Guidance system, method and devices thereof" and "A novel oncogene biomarker, method and uses thereof";
- Support the expansion of the activities of the four spin-offs launched in the last years by the ICVS: iSurgical3D (<http://www.isurgical3d.com>), Bn'ML (<http://www.bnml.eu/bnml-pt>), iCognitus - IT Solutions, Ltd (<http://www.icognitus.com>) and Enlightenment, which reveals the ICVS interest of transferring the knowledge generated in the different domains into marketable products and services;
- Pursue a policy of fostering an active involvement of medical students and MDs within the ICVS research projects, involving an increasing number of MD students in research;
- Maintain the offer of a high number of Advanced Post-Graduation Courses/Workshops (38 in

2018), involving 1066 participants (including 78% MDs, 14% researchers from Biological Sciences fields, 3% other Health Professionals and 5% participants from other backgrounds);

- Foster the dissemination of knowledge and the promotion of scientific awareness and public perception of science. The activities organized by the ICVS counted with more than 1700 participants and involved the interaction with over 60 external institutions.

2.2 PRODUCTIVITY

2.2.1 PUBLICATIONS IN PEER-REVIEW JOURNALS

In 2018, the ICVS published 283 papers in international peer-reviewed journals (referenced in *ISI*, *Scopus* or in *Pubmed*).

Among the articles published in 2018, 263 were produced within the four research domains (Microbiology and Infection, Neurosciences, Surgical Sciences and Population Health), wherein 64% were in Q1-Q2, with 42% of these 263 in Q1. The average Impact Factor (IF) of these publications is 4.8, and includes 64 papers with IF between 3 and 5; 44 papers with an IF between 5 and 10; 14 papers with an IF between 10 and 20, 5 papers with an IF>20. Additionally, the ICVS published 20 articles in other fields.

In addition, the average IF of the 100 articles published in the journals with higher impact was 8.

SELECTED PAPERS IN PEER REVIEW JOURNALS:

- Leroy, F., Park, J., Asok, A., Brann, D. H., Meira, T., Boyle, L. M., Buss, E. W., Kandel, E. R., & Siegelbaum, S. A. (2018) A circuit from hippocampal CA2 to lateral septum disinhibits social aggression. *Nature*, 564(7735), 213-218. doi: 10.1038/s41586-018-0772-0
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2.2.2 ORGANIZATION OF COURSES/WORKSHOPS

TRAINING IN CLINICAL SCIENCES

- ETHICS IN MEDICAL PRACTICE
January 2018; 2nd Edition
- PREMIUM CATARACT SURGERY
January 2018; 8th Edition
- ERCP – THE ESSENCIALS
January 2018; 2nd Edition
- PSYCHIATRY AND MENTAL HEALTH
May 2018; 3rd Edition
- RESPIRATORY DISEASES
March 2018; 3rd Edition
- BASIC LAPAROSCOPY FOR RESIDENTS
May 2018; 14th Edition
- GYNECOLOGICAL LAPAROSCOPIC SURGERY
May 2018; 10th Edition
- FUNDAMENTALS IN ARTHROSCOPY
June 2018; 9th Edition
- ENDOSCOPIC SINUS SURGERY AND TRANSNASAL ENDOSCOPIC SKULL BASE
June 2018; 5th Edition
- FUNDAMENTALS IN RHINOSEPTOPLASTY
June 2018; 5th Edition
- SURGERY FOR SNORING AND OSAS
June 2018; 5th Edition
- APPLIED CLINICAL PSYCHOPHARMACOLOGY
June 2018; 1st Edition

- EVALUATION AND TREATMENT OF INFERTILE COUPLE
June 2018; 2nd Edition
- SULCI, GYRI, VENTRICLES AND DISSECTING FIBERS
August 2018; 16th Edition
- FETAL AND NEONATAL ENDOSCOPIC SURGERY
September 2018; 10th Edition
- HYPOSPADIAS REPAIR
September 2018; 2nd Edition
- CAPSULE ENDOSCOPY TRAINING PROGRAM
September 2018; 3rd Edition
- ESPGHAN ENDOSCOPY SUMMER SCHOOL
September 2018; 4th Edition
- MEDICAL ACUPUNCTURE
October 2018; 4th Edition
- BASIC ENDOSCOPY TECHNIQUES
November 2018; 1st Edition
- ADVANCED ENDOSCOPIC TECHNIQUES
November 2018; 1st Edition
- BASIC LAPAROSCOPY FOR RESIDENTS
November 2018; 15th Edition
- MINIMALLY INVASIVE SPINE SURGERY
November 2018; 7th Edition
- FOOT AND ANKLE SPORTS MEDICINE
December 2018; 4th Edition

TRAINING IN BIOMEDICAL SCIENCES AND OTHER AREAS

- BIostatISTICS IN HEALTH SCIENCES
January 2018; 8th Edition

- LABORATORY ANIMAL SCIENCE
January/March 2018; 13th Edition
- HANDS-ON THE RODENT BRAIN
February/March 2018; 2nd Edition
- PROGRESS TEST: INTEGRATING ASSESSMENT, FEEDBACK AND LEARNING
February 2018; 1st Edition
- EPIDEMIOLOGY
March 2018; 1st Edition
- BEING A BIO-ENTREPRENEUR
April 2018; 4th Edition
- TRANSFORMATIONAL HEALTH LEADERSHIP
April/June 2018; 2nd Edition
- NANO-BIOENGINEERING FOR MEDICINE
May 2018; 1st Edition
- FUNDAMENTALS IN NEUROSCIENCE
September 2018; 11th Edition
- FUNDAMENTALS IN IMMUNOLOGY AND INFECTION
October 2018; 10th Edition
- FUNDAMENTALS IN GENETICS, DEVELOPMENT AND NEOPLASIA
October 2018; 10th Edition
- INTENSIVE COMMUNICATION SKILLS COURSE
November 2018; 2nd Edition
- BIOINFORMATICS IN HEALTH SCIENCES
November 2018; 10th Edition
- RESEARCH METHODOLOGIES
December 2017; 10th Edition

2.2.3 INDUSTRY CONTRACT RESEARCH

In 2018, the ICVS had the following ongoing Research Contracts:

- TECNIMEDE - SOCIEDADE TÉCNICO MEDICINAL, SA: “Characterize the pharmacological activity of drugs in the control of pain in animals with traumatic neuropathy”;
- TECNIMEDE - SOCIEDADE TÉCNICO MEDICINAL, SA: “Study of Antidepressant properties of pirlindol an animal model Chronic Mild stress”;
- FUNDAÇÃO BIAL: “The role of astrocytes in complex cognitive processing”;
- FUNDAÇÃO BIAL: “Gliogenesis control of brain plasticity, neurophysiology and cognitive function”;
- FUNDAÇÃO BIAL: “Exploring the neural basis of motivation”;
- FUNDAÇÃO BIAL: “Developing a neurofunctional intervention for emotion regulation under stress”;
- GILEAD SCIENCES: “Impacto da diversidade genética do VIH-1 na imunodeciência”;
-
- GILEAD SCIENCES: “Relação entre as células T reguladoras e a hiperactivação imunológica que está associada às co-morbilidade dos doentes com infeção crónica por VIH”;
- BIOGEN PORTUGAL: “Impact of dimethyl fumarate on cognition: animal studies”.

2.2.4 INTERNATIONALIZATION

Reflecting the high level of internationalization of the ICVS, in 2018 the Institute's team included members from the following countries: Brazil, England, France, Greece, Iran and Istanbul.

Among the ICVS papers published in international peer-reviewed journals during 2018, over 54% resulted from partnerships involving research teams from leading foreign research institutions. In addition, ICVS members were involved in congresses and seminars in the context of international meetings outside Portugal during 2018 (generating 180 communications in international meetings).

In 2018, the ICVS was involved in international networks with specific funding, including:

- 2 European H2020 research projects;
- 17 grants funded by other international institutions.

Globally, in 2018, the ongoing projects funded by international sources represented a total amount of 1.8 million €. These collaborative networks involved the participation of institutions from the following countries: Austria, Belgium, Brazil, Denmark, Finland, France, Germany, Greece, Hungary, India, Israel, Italy, Netherlands, Norway, Slovenia, Spain, Sweden, Switzerland, United Kingdom and Turkey and United States of America.

The international recognition of the ICVS research activities is also reflected by the granting of 35 International scientific awards, including the MESCyT 2018 award for Achievement in Research, awarded by the Government of Dominican Republic; and the "Early Career Award", awarded by the Governing Board of the International Society of Behavioral Medicine.

The Post-graduation program of the ICVS/EM promoted 38 international post-graduation courses that included the participation of 121 foreign students.

Finally, the ICVS strategy of internationalization was also fostered by the digitalization and social networks, promoting not only interactions between scientists, but also among other professionals, students, associations, companies, etc., in different parts of the globe. As an example, the ICVS website and its social networks have more than 2000 followers and have been visited by users from 30 different countries, from all five continents.

3. ACTIVITIES

3.1 OUTREACH ACTIVITIES

The program of outreach activities implemented by the ICVS and the EM represents a joint strategy to promote scientific awareness in the surrounding community on: the importance of R&D on life and health sciences, advanced technologies in biomedicine, health education and healthier lifestyles.

The younger population was one of the priority targets in the community, involving the interaction with over 50 schools, since first year to the pre-university stage.

In 2018, the ICVS continued its strong activity in disseminating scientific awareness and public perception of science and technology. The activities were organized in 8 major events, involving more than 1700 participants and the interaction with over 60 external institutions, ranging from first year schools to senior universities and other non-governmental organizations.

The younger and older sectors of the society were the priority targets of the outreach events in different scientific themes: the “UMinho Open Week; th “ICVS Open Week”;; the “UMinho Best Student”; the “Health Olympics”; the “Summer in the *Campus*”; the “ICVS School Visit”; the “*Ciência Falada*3”; and the “International Seminars Series”. These initiatives included interactive talks in schools, experimental activities at the ICVS laboratories, exhibitions, guided tours to the ICVS facilities and seminars.

Additionally, the ICVS activities were highly publicized in a variety of media vehicles, including in most of the main Portuguese journals, radio stations, information websites, several magazines with high circulations, different TV programs and social media.

4. OTHER ACTIVITIES

4.1 INTERNAL SERVICES AND RESOURCES

At the ICVS facilities, all the scientific equipment from the installed technological platform is shared amongst Research Domains. In addition, this equipment is also available under request to the other research units of the University of Minho and to the Portuguese scientific community in general.

A laboratory management organizational plot is setup, including both Functional Core facilities - equipment with a team of dedicated technical staff that provides services for researchers in the ICVS - and Shared Technical facilities - equipment and infrastructures organized into dedicated spaces based on a particular usage/technique.

A web platform is available and constitutes the basis of the Quality Management System. The purpose of this platform is the on-line management of all information regarding equipment, labs and consumables.

Specifically, the ICVS provides: fully operational Functional Cores for Animal Housing, Microscopy, Histology, Molecular Biology and Endoscopy/Minimally Invasive Surgery, and Shared Technical Facilities for Cytometry, Cell and Tissue Culture, Bio Banking, Electrophysiology and Biosafety Level 2 and 3. Some of this Functional Cores, such as histology, microscopy and animal housing also provide external services.

4.2 EXTERNAL SERVICES AND RESOURCES

The ICVS provides services to the general and the clinical communities. These external services were born from the knowledge developed in house by the ICVS researchers, with emphasis to the Molecular Diagnostics Service (SDM) which is fully equipped for molecular diagnostics. During previous years, the ICVS has been providing genetic diagnostics of intellectual disability related disorders to both public and private entities.

The ICVS researchers have also provided services to the industry at the international level through confidential research contracts.

Additionally, through the 2CA-Braga - in partnership with the Hospital of Braga and the Eurotrials – the ICVS participated in clinical trials in collaboration with international industrial leading partners. The 2CA-Braga combines a team of researchers, physicians and other health professionals, to which is associated a team of project managers, nurses and clinical trials coordinators/monitors, which ensure a professional management structure.

5. RESEARCH LINE: MICROBIOLOGY AND INFECTION

5.1 OBJECTIVES AND ACHIEVEMENTS

5.1.1 GENERAL OBJECTIVES

The Microbiology and Infection Research Domain (MIRD) aims essentially at unravelling mechanisms involved in host-pathogen interaction, with a special focus on those underlying resistance and susceptibility to infectious diseases. Research strategies within MIRD range from bioinformatics to molecular and cellular mechanisms, exploring the implemented and consolidated cellular and animal models, and patients, to understand the molecular and cellular mechanisms regulating the host-pathogen interaction and defining the immune response to infection. In addition, the MIRD also aims to dissect virulence mechanisms and determinants of drug resistance, as well as the evolutionary properties of the pathogens, and their dynamic relationships with the host and the environment, allowing therefore a transversal understanding of the pathogenetic mechanism contributing to infection.

The research is organized in two research topics: 1) Cellular and Molecular Microbiology, mainly devoted to the comprehension of molecular mechanisms of virulence, resistance/susceptibility to antimicrobial drugs and evolution of pathogenic microorganisms and the use of microorganisms as models to study human diseases and to develop industrial applications; 2) Immunology of Infection, dedicated to diverse aspects of the immune response of the host to infection and related immune mechanisms. Projects in this research topic are devoted to unravelling genetic profiles associated with susceptibility to infection; immunological mechanisms relevant in the host-pathogen interaction; development of new prophylactic and diagnostic methods, as well as drug delivery systems for infectious diseases.

5.1.2 MAIN ACHIEVEMENTS

The MIRD has followed a policy of staff recruitment/differentiation, counting presently with a multidisciplinary team that includes 18 PhD integrated members with backgrounds in biological sciences, engineering and medicine.

Research within the MIRD was supported by 18 projects from FCT, 1 from contracts with the national industry and 6 from other international sources.

During the year of 2018, researchers from MIRD published 39 papers in international peer-reviewed journals, including 21 in Q1, with an average IF of 6.9, of which 6 papers were published in journals with an IF>10.

Researches within the MIRD were granted with 7 International and 1 National scientific awards, including: the MESCyT 2018 award for Achievement in Research, awarded by the Government of Dominican Republic, an EFIS-ACTERIA Travel Grant awarded by the European Federation of Immunological Societies, and an EMBO Short-term fellowship.

The MIRD organized 2 post-graduation course/workshop and graduated 1 PhD-student and 6 MSc-students. In addition, MIRD members were involved in 7 lectures/seminars in the context of international meetings and submitted 49 communications to International Conferences/Meetings.

In line with the previous year, the MIRD kept reinforcing the translational/clinical research by fortifying effective collaborations with researchers from Portugal, the Netherlands, France, Greece, Germany, India and Spain.

5.2 RESEARCH LINE OUTPUT

5.2.1 SELECTED PUBLICATIONS IN PEER REVIEW JOURNALS

- Stappers, M. H., Clark, A. E., Bidula, S., Amanianda, V., Reid, D. M., Asamaphan, P., Hardison, S. E., Dambuza, I. M., Valsecchi, I., Kerscher, B., Plato, A., Wallace, C., Yucel, R., Hebecker, B., Teixeira Sousa, M. G., Cunha, C., Liu, Y., Feizi, T., Brakhage, A. A., Kwon-Chung, K. J., Gow, N. A., Zanda, M., Piras, M., Zanato, C., Jaeger, M., Netea, M. G., van de Veerdonk, F. L., Lacerda, J. F., Campos, A. Jr., Carvalho, A., Willment, J. A., Latgé, J. P., & Brown, G. D. (2018). Recognition of DHN-melanin by a C-type lectin is required for protective immunity to *Aspergillus*. *Nature*, *555*(7696), 382-386. doi: 10.1038/nature25974
- Kyrmizi, I., Ferreira, H., Carvalho, A., Figueroa, J. A. L., Zampas, P., Cunha, C., Akoumianaki, T., Stylianou, K., Deepe, G. S. Jr., Samonis, G., Lacerda, J. F., Campos, A. Jr., Kontoyiannis, D. P., Mihalopoulos, N., Kwon-Chung, K. J., El-Benna, J., Valsecchi, I., Beauvais, A., Brakhage, A. A., Neves, N. M., Latge, J. P., Chamilos, G. (2018). Calcium sequestration by fungal melanin inhibits calcium-calmodulin signalling to prevent LC3-associated phagocytosis. *Nature Microbiology*, *3*(7), 791-803. doi: 10.1038/s41564-018-0167-x
- Gresnigt, M. S., Cunha, C., Jaeger, M., Gonçalves, S. M., Subbarao Malireddi, R. K., Ammerdorffer, A., Lubbers, R., Oosting, M., Rasid, O., Jouvion, G., Fitting, C., de Jong, D. J., Lacerda, J. F., Campos, A. Jr., Melchers, W., Lagrou, K., Maertens, J., Kanneganti, T. D., Carvalho, A., Ibrahim-Granet, O., van de Veerdonk, F. L. (2018). Genetic deficiency of NOD2 confers resistance to invasive aspergillosis. *Nature Communications*, *9*, 2636. doi: 10.1038/s41467-018-04912-3
- Cruz, M., Sánchez, I. M., Diaz, J., Cuevas, F., Silva, M., Disla, M., Ferreira, P. E., & Veiga, M. I. (2018). Dosage of single low-dose primaquine to stop malaria transmission. *Journal of Infectious Diseases*, *217*(11), 1849-1850. doi: 10.1093/infdis/jiy108

- Sampaio-Marques, B., Pereira, H., Santos, A. R., Teixeira, A., & Ludovico, P. (2018) Caloric restriction rescues yeast cells from alpha-synuclein toxicity through autophagic control of proteostasis. *Aging*, 10(12), 3821-3833. doi: 10.18632/aging.101675
- Miranda, M. S., Rodrigues, M. T., Domingues, R. M. A., Torrado, E., Reis, R. L., Pedrosa, J., & Gomes, M. E. (2018). Exploring inhalable polymeric dry powders for anti-tuberculosis drug delivery. *Materials Science & Engineering C-Materials for Biological Applications*, 93, 1090-1103. doi: 10.1016/j.msec.2018.09.004
- Mesquita, I., Ferreira, C., Barbosa, A. M., Ferreira, C., Moreira, D., Carvalho, A., Cunha, C., Rodrigues, F., Dinis-Oliveira, R. J., Estaquier, J., Castro, A. G., Torrado, E., & Silvestre, R. (2018). The impact of IL-10 dynamic modulation on host immune response against visceral leishmaniasis. *Cytokine*, 112, 16-20. doi: 10.1016/j.cyto.2018.07.001
- Gaifem, J., Gonçalves, L. G., Dinis-Oliveira, R. J., Cunha, C., Carvalho, A., Torrado, E., Rodrigues, F., Saraiva, M., Castro, A. G., & Silvestre, R. (2018). L-threonine supplementation during colitis induction impairs goblet cell number and delays disease recovery. *Frontiers in Physiology*, 9, 1247. doi: 10.3389/fphys.2018.01247

6. RESEARCH LINE: NEUROSCIENCES

6.1 OBJECTIVES AND ACHIEVEMENTS

6.1.1 GENERAL OBJECTIVES

The Neurosciences Research Domain (NERD) focus its activities to the study of the Central Nervous System with emphasis in three main research topics, organized in the following research lines: **Neurodevelopment**, **Neurodegeneration** and **Neuroimmunology**. Studies at the molecular, cellular and system levels are performed in physiological conditions covering from neurodevelopment to senescence, as well as in several human disorders, such as early- and late-onset degenerative diseases, neuroimmune disorders, depression, anxiety and chronic pain syndromes. These research questions are approached in an integrative approach, given that the NERD benefits from an extensive technical platform, conducting studies in parallel in humans and animal models, covering fundamental, translational and clinical research.

In line with the multimodal approach of research questions, the team is multidisciplinary; indeed, it is composed by members with a wide spectrum of backgrounds (MDs from neurology, neuroradiology, psychiatry, internal medicine, endocrinology, urology, surgery, neonatology, paediatrics, medical genetics, but also biochemists, molecular biologists, statisticians, mathematicians, biomedical and electronic engineers, psychologists, veterinaries, pharmacists). This broadness of expertise and technics provides a vibrant atmosphere to the Neurosciences Research Domain that allows to attract very good students and post-docs.

6.1.2 MAIN ACHIEVEMENTS

The NERD has followed a policy of staff recruitment/differentiation, counting presently with a multidisciplinary team that includes 38 PhD integrated members with backgrounds in biological sciences, engineering and medicine.

Research within the NERD was supported by 19 projects from FCT, 4 from other national sources, 2 from H2020, 8 from other international sources and 7 from contracts with the national industry.

During the year of 2018, researchers from NERD published 106 papers in international peer-reviewed journals, including 61 in Q1, with an average IF of 5,4 of which 11 papers were published in journals with an IF>10.

Researchers within the NERD were granted with 8 international and 3 national scientific awards, including: the “Prémio Santa Casa Neurociências – Melo e Castro” awarded by Santa Casa da Misericórdia de Lisboa.

The NERD organized 12 post-graduation course/workshop and graduated 10 PhD-students and 8 MSc-students. In addition, NERD members were involved in 18 lectures/seminars in the context of international meetings and submitted 42 communications to International Conferences/Meetings.

In line with the previous year, the NERD kept reinforcing the translational/clinical research by fortifying effective collaborations with researchers from Portugal, Brazil, Austria, Belgium, Denmark, Finland, France, Germany, Greece, Hungary, Israel, Italy, Netherlands, Norway, Slovenia, Spain, Sweden, Switzerland, United Kingdom and Turkey and United States of America.

6.2 RESEARCH LINE OUTPUT

6.2.1 SELECTED PUBLICATIONS IN PEER REVIEW JOURNALS

- Leroy, F., Park, J., Asok, A., Brann, D. H., Meira, T., Boyle, L. M., Buss, E. W., Kandel, E. R., & Siegelbaum, S. A. (2018) A circuit from hippocampal CA2 to lateral septum disinhibits social aggression. *Nature*, 564(7735), 213-218. doi: 10.1038/s41586-018-0772-0
- Meira, T., Leroy, F., Buss, E. W., Oliva, A., Park, J., & Siegelbaum, S. A. (2018). A hippocampal circuit linking dorsal CA2 to ventral CA1 critical for social memory dynamics. *Nature Communications*, 9(1). doi: 10.1038/s41467-018-06501-w
- Miranda, A. M., Lasiecka, Z. M., Xu, Y., Neufeld, J., Shahriar, S., Simoes, S., Chan, R. B., Oliveira, T. G., Small, S. A., & Di Paolo, G. (2018). Neuronal lysosomal dysfunction releases exosomes harboring APP C-terminal fragments and unique lipid signatures. *Nature Communications*, 9, 291. doi: 10.1038/s41467-017-02533-w
- Magalhães, R., Barrière, D. A., Novais, A., Marques, F., Marques, P., Cerqueira, J., Sousa, J. C., Cachia, A., Boumezbeur, F., Bottlaender, M., Jay, T. M., Mériaux, S., & Sousa, N. (2018). The dynamics of stress: a longitudinal MRI study of rat brain structure and connectome. *Molecular Psychiatry*, 23(10), 1998-2006. doi: 10.1038/mp.2017.244
- Ferreira, A. C., Santos, T., Sampaio-Marques, B., Novais, A., Mesquita, S. D., Ludovico, P., Bernardino, L., Correia-Neves, M., Sousa, N., Palha, J., Sousa, J., & Marques, F. (2018). Lipocalin-2 regulates adult neurogenesis and contextual discriminative behaviours. *Molecular Psychiatry*, 23(4), 1031-1039. doi: 10.1038/mp.2017.95
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7. RESEARCH LINE: SURGICAL SCIENCES

7.1 OBJECTIVES AND ACHIEVEMENTS

7.1.1 GENERAL OBJECTIVES

The Surgical Sciences Research Domain (SSRD) deals with diseases from the digestive, pulmonary and urogenital systems. An interdisciplinary team, including biologists, engineers and MDs, works together aiming to: understand the development mechanisms regulating time and space differentiation of cells/tissues (e.g. somites, limb and lung growth); evaluate genetic/molecular markers as risk and prognostic factors, as well as therapeutic strategies (e.g. congenital malformations and oncological diseases). As surgery has a strong technical dimension, in connection with industry the SSRD explore the possibility of scarless interventions through Natural Orifices Transluminal Endoscopic Surgery (N.O.T.E.S.). Using human body imaging (CT scan and laser) as a surrogate to develop three-dimensional constructs, it provides personalized prosthesis and surgical plans. As additional mission, the SSRD provides an extensive international hands-on program with courses on minimally invasive techniques.

7.1.2 MAIN ACHIEVEMENTS

The SSRD has followed a policy of staff recruitment/differentiation, counting presently with a multidisciplinary team that includes 19 PhD integrated members with backgrounds in biological sciences, engineering and medicine.

Research within the SSRD was supported by 5 projects from FCT (including 1 IF), 1 project from FCT/Austin, 1 project from ASPIC, and 1 from contracts with the international industry.

During the year of 2018, researchers from SSRD published 114 papers in international peer-reviewed journals, including 28 in Q1, with an average IF of 3.9, of which 4 papers were published in journals with an IF>10.

Researchers within the SSRD were granted with 18 International and 8 National scientific awards, including: the "Best oral communication Prizes", awarded by Gastro Update Europe 2018, International Workshop in Esophago-Gastric Surgery, XXXI Reunião Anual da Sociedade Portuguesa de Gastroenterologia, Hepatologia e Nutrição Pediátrica (SPGP); 1st prize - Ultrasound imaging prize 2018 by Grupo Português de Ultrassonografia Endoscópica (GRUPUGE); and one Fellowship form LPCC/Fundação PT.

The SSRD organized 17 post-graduation courses/workshops, participated in the organization of 19 external meetings and graduated 3 PhD-students and 10 MSc-students. In addition, SSRD

members were invited for 11 lectures/seminars in the context of international meetings and submitted 68 communications to International Conferences/Meetings.

In line with the previous year, the SSRD kept reinforcing the translational/clinical research by fortifying effective collaborations with researchers from Portugal, Brazil, Belgium, Germany, and the United Kingdom.

7.2 RESEARCH LINE OUTPUT

7.2.1 SELECTED PUBLICATIONS IN PEER REVIEW JOURNALS

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- Queirós, S., Morais, P., Dubois, C., Voigt, J., Fonseca, J. C., Vilaça, J. L., & D'hooge, J. (2018). Validation of a Novel Software Tool for Automatic Aortic Annular Sizing in Three-Dimensional Transesophageal Echocardiographic Images. *Journal of the American Society of Echocardiography*, 31(4), 515-525.e5. doi: 10.1016/j.echo.2018.01.007
- Fernandes, J., Libânio, D., Giestas, S., Araújo, T., Martinez-Ares, D., Certo, M., & Lopes, L. (2018). Giant symptomatic rectal lipoma resected by endoscopic submucosal dissection. *Endoscopy*, 50(03), E63-E64. doi: 10.1055/s-0043-123876
- Queiros, S., Morais, P., Barbosa, D., Fonseca, J. C., Vilaca, J. L., & D'Hooge, J. (2018). MITT: Medical Image Tracking Toolbox. *IEEE Transactions on Medical Imaging*, 37(11), 2547-2557. doi: 10.1109/tmi.2018.2840820
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8. RESEARCH LINE: POPULATION HEALTH

8.1 OBJECTIVES AND ACHIEVEMENTS

8.1.1 GENERAL OBJECTIVES

The Population Health Research Domain (PHRD) was created in January 2018. It represents a novel challenge assumed by the ICVS in face of new health paradigms in the society. In fact, it responds to the natural development of research interests resulting from the close cooperation between the ICVS/3Bs/Medical School/Clinical Academic Center (2CA-Braga) and the affiliated healthcare providers. As such, the mission of the PHRD is to generate data and action that will improve the health care to the populations in the Minho region, with repercussions at the national level. For that purpose, the PHRD includes MDs, psychologists, epidemiologists, mathematicians, computer scientists and nutritionists who will focus on research projects on epidemiology, prevention and intervention, health informatics, health policy and management, biostatistics and big data analyses. The starting goal of the strategy was to integrate the research work already in progress, to define priorities for the future and to maximize the resources available in the different partners. It is of notice that research developed in the past by researchers at the ICVS has considerably contributed to the field of Population Health. These include the current Portuguese health authority's guidelines for iodine supplementation of pregnant women; the definition of the prevalence and the identification of risk factors of high blood pressure, of tuberculosis and diabetes; the prevalence of asthma; the incidence of certain type of cancer and the identification of predictors of cognitive healthy ageing.

8.1.2 MAIN ACHIEVEMENTS

The PHRD has followed a policy of staff recruitment/differentiation, counting presently with a multidisciplinary team that includes 17 PhD integrated members with backgrounds in biological sciences, engineering and medicine.

Research within the PHRD was supported by 1 project from FCT and 5 from other international sources, 2 of these with the industry.

During the year of 2018, researchers from PHRD participated in 71 published papers in international peer-reviewed journals; from these 30 were published in research areas of Population Health with an average IF of 3.2.

Researchers within the PHRD were granted with 2 international scientific award, namely: the "Early Career Award", awarded by the Governing Board of the International Society of Behavioral Medicine in the 15th International Congress of Behavioral Medicine, Santiago, Chile; and the prize "Projetos de Investigação Clínica Centro Clínico Académico – Braga" awarded by the Clinical Academic Center – Braga (2CA-Braga).

The PHRD organized (or co-organized) 6 post-graduation courses/workshops, and graduated 1 PhD-student. In addition, PHRD members were involved by invitation in 2 lectures/seminars in the context of international meetings and submitted 11 communications to International Conferences/Meetings. Several members of the domain were actively involved in training activities for the acquisition of skills like English writing, systematic reviews and meta-analysis, data mining and basic notions on epidemiology.

An effort to reinforce the translational research was done by fortifying the effective collaborations with regional health providing institutions and other communities involved in the promotion of healthy habits as well as researchers abroad, in particular from France, Spain and Sweden.

8.2 RESEARCH LINE OUTPUT

8.2.1 SELECTED PUBLICATIONS IN PEER REVIEW JOURNALS

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