

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, to provide 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 in 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 to the market innovative therapeutic solutions.

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 three interdisciplinary Research Domains with high critical mass: Microbiology and Infection, Neurosciences and Surgical Sciences and two Pilot Research Lines, on Community Health and on Education on Life and Health Sciences.

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 strategic 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;
- promote 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 2017 WERE TO:

- develop flexible and integrated functional models that endorse multidisciplinary R&D projects, actively promoting the interplay Health-Sciences/Technologies - involving the ICVS's researchers, health professionals from the 2CA-Braga, as well as researchers from the 3B's research group, on: i) the Research Domains Microbiology and Infection, Neurosciences, and Surgical Sciences and; ii) the Pilot Research Lines on Community Health and on Education on Life and Health Sciences;
- Continue the installation of maintenance and scientific equipment in the new "Biotério" animal facility in the adjacent area of the EM/ICVS building;
- 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 courses on Medicine and Health Sciences, fostering and strengthening existing international collaborations, with a strong recruitment of foreign students (graduate, undergraduate and MDs);
- provide for advanced post-graduation activities, organized as an International Program;
- provide specialized health services to the community, particularly in fields not covered in the Minho region, such as in the area of genetics, as well as 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 excellent level and fostering a "MD-scientist" profile among the EM graduates;
- 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;
- 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 2017:

THE MAIN ACHIEVEMENTS IN 2017 WERE:

- the significant increase in the number of peer-reviewed international publications;
- 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 PhD students that successfully completed their Doctorate.
- the reinforcement of the network of collaborating R&D institutions, with the launching of a Hackathon and a Program of common grants within the partnership with the INL – International Nanotechnology Laboratory;
- the continuation of the installation of maintenance/scientific equipment in the new animal facility “Biotério”;
- the involvement of an increasing number of MD students in the ICVS research activities;
- the maintenance of a high number and impact of the Advanced Post-Graduation Courses;

SPECIFICALLY, IN 2017, THE ICVS WAS ABLE TO:

- Publish a total of 236 papers in international peer-reviewed journals (referenced in ISI, Scopus or in Pubmed), in addition to 9 international book chapters and 220 proceedings and communications in international meetings. Among the articles published in 2017, 208 were produced within the three research domains (Microbiology and Infection, Neurosciences and Surgical Sciences), corresponding to 70% in Q1-Q2, with 44% in Q1, with an average Impact Factor (IF) of 5.7 (including articles with IF between 3 and 5 = 61 papers; IF between 5 and 10 = 30 papers; IF between 10 and 20 = 16 papers; and IF>20 = 5 papers); and 7 additional articles in the fields of Medical Education and Public Health; 9 in the fields of Community Health and 14 in other fields;. In addition, the average IF of the 100 articles published in the journals with higher impact was 8.3.
- Develop clinical research with a growing impact, through the 2CA-Braga, in partnership with the Hospital of Braga and the Eurotrials, 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 83 clinical trials ongoing in 2017, assuming a leading position in the National context, since in Portugal the number of trials/year is of 140. Additionally, the 2CA-Braga developed 56 clinical studies, including research projects in partnership with the ICVS and other research institutions from the UMinho (with projects funded by the European Commission or nationally, by the FCT and FEDER), 14 observational studies and 1 validation study of medical devices. As an important indicator, the 2CA recruitment rate of patients has been consistently above 85%;
- 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 that complemented the Seminars “Ciência Falada” (43 in total), involving the participation of leading scientists from foreign Institutions;
- Create the experimental conditions for the conclusion of 20 PhD thesis, including 6 from MDs;
- Foster collaborations between its researchers and partners from Biomedical Industries. In 2017, industry sponsored R&D was performed in areas of mutual interest with sponsors such as: TECNIMEDE; FUNDAÇÃO BIAL and KARL STORZ;
- 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 42 International and National scientific awards, including the Medalhas de Honra L'Oréal Portugal para as Mulheres na Ciência by L'Oréal Portugal, a Comissão Nacional da UNESCO e a Fundação para a Ciência e a Tecnologia (FCT); Prémio Thomé Villar by Boehringer Ingelheim; Prémio Santa Casa Neurociências - Melo e Castro by Santa Casa da Misericórdia de Lisboa;
- Reinforce the level of funding obtained from competitive sources and from contracts with leading industrial partners, through 51 ongoing projects (21 from FCT; 4 from NORTE2020; 3 from other national sources; 2 from H2020; 14 from other international sources and 7 from contracts with the national industry);
- Attract competitive funding, involving 18.2 million € in ongoing projects (3 years of accumulated value), of which 6.7 million € correspond to funding obtained in 2017;
- Register 2 patents namely: “Visual choice selection concealment computing device and method of operation” and “Antimicrobial peptide-loaded hyaluronic acid-based formulations, method of production 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, including 43 Option Projects and 13 MD/PhD Laboratory Rotations;

- Maintain the offer of a high number of Advanced Post-Graduation Courses/Workshops (42 in 2017), involving 1098 participants (including 78% MDs, 16% researchers from Biological Sciences fields, 4% other Health Professionals and 2% 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 1750 participants and involved the interaction with over 60 external institutions.

2.2 PRODUCTIVITY

2.2.1 PUBLICATIONS IN PEER-REVIEW JOURNALS

In 2017, the ICVS published 236 papers in international peer-reviewed journals (referenced in *ISI*, *Scopus* or in *Pubmed*).

Among the articles published in 2017, 208 were produced within the three research domains (Microbiology and Infection, Neurosciences and Surgical Sciences), corresponding to 70% in Q1-Q2, with 44% in Q1, with an average Impact Factor (IF) of 5.7 (including articles with IF between 3 and 5 = 61 papers; IF between 5 and 10 = 30 papers; IF between 10 and 20 = 16 papers; and IF>20 = 5 papers); and 7 additional articles in the fields of Medical Education and Public Health; 9 in the fields of Community Health and 14 in other fields.

In addition, the average IF of the 100 articles published in the journals with higher impact was 8.3.

SELECTED PAPERS IN PEER REVIEW JOURNALS:

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- Marques F, Sousa JC, Brito A, Pahnke J, Santos C, Correia-Neves M, Palha JA. The choroid plexus in health and in disease: Dialogues into and out of the brain. *Neurobiology of Disease* 107:32-40 (2017)

2.2.2 ORGANIZATION OF COURSES/WORKSHOPS

TRAINING IN CLINICAL SCIENCES

- PREMIUM CATARACT SURGERY
January 2017; 7th Edition
- MENTAL HEALTH
January 2017; 3rd Edition
- ETHICS IN MEDICAL PRACTICE
March 2017; 1st Edition
- VIDEO-ASSISTED EXTRAPERITONEAL RADICAL PROSTATECTOMY
April 2017; 6th Edition
- INNOVATIONS IN MINIMALLY INVASIVE UROLOGIC SURGERY
April 2017; 2st Edition
- SONOANATOMY APPLIED TO PERIPHERAL NERVE BLOCK
April 2017; 10th Edition
- HIP ARTHROSCOPY
May 2017; 1st Edition
- PRACTICAL AND ESSENTIAL ASPECTS OF PALLIATIVE CARE
May 2017; 1st Edition
- SULCI, GYRI, VENTRICLES AND DISSECTING FIBERS
May 2017; 15th Edition
- MICROSURGICAL ANASTOMOSIS
May 2017; 8th Edition
- BASIC LAPAROSCOPY FOR RESIDENTS
May 2017; 12th Edition
- FUNDAMENTALS IN ARTHROSCOPY
May 2017; 8th Edition

- SONOANATOMY APPLIED TO PERIPHERAL NERVE BLOCK
June 2017; 11th Edition
- PEDIATRIC ENDOSCOPY
June 2017; 7th Edition
- FETAL AND NEONATAL ENDOSCOPIC SURGERY
September 2017; 9th Edition
- HYPOSPADIAS REPAIR
September 2017; 1st Edition
- GYNECOLOGICAL LAPAROSCOPIC SURGERY
September 2017; 9th Edition
- CAPSULE ENDOSCOPY TRAINING PROGRAM
September 2017; 2nd Edition
- ADVANCED EMR AND ESD WORKSHOP
September 2017; 2nd Edition
- BILIARY LAPAROSCOPY
October 2017; 9th Edition
- THERAPEUTIC ENDOSCOPY
October 2017; 10th Edition
- EVALUATION AND TREATMENT OF INFERTILE COUPLE
November 2017; 1st Edition
- MASTER CLASS SKILLS LAB FOR LIVE ANIMAL MODEL (PEDIATRIC
LAPAROSCOPY)
November 2017; 2nd Edition
- BASIC LAPAROSCOPY FOR RESIDENTS
November 2017; 13th Edition
- ARTERIAL STIFFNESS AND EARLY VASCULAR AGING
November 2017; 6th Edition

- MINIMALLY INVASIVE SPINE SURGERY
November 2017; 6th Edition
- SONOANATOMY APPLIED TO PERIPHERAL NERVE BLOCK
November 2017; 12th Edition
- FOOT AND ANKLE SPORTS MEDICINE
December 2017; 4th Edition

TRAINING IN BIOMEDICAL SCIENCES AND OTHER AREAS

- BIOSTATISTICS IN HEALTH SCIENCES
January 2017; 7th Edition
- LABORATORY ANIMAL SCIENCE
January/March 2017; 12th Edition
- STANDARDIZED PATIENTS: FROM THEORY TO PRACTICE
February 2017; 1st Edition
- TRANSFORMATIONAL HEALTH LEADERSHIP
February 2017; 1st Edition
- CELL FUNCTIONAL AND PHENOTYPICAL ANALYSIS
March 2017; 2nd Edition
- PATHOGENESIS OF NEURODEGENERATIVE DISEASES
March 2017; 2nd Edition
- HANDS-ON THE RODENT BRAIN
April/May 2017; 1st Edition
- MOLECULAR AND CELLULAR ANALYSIS
May/June 2017; 7th Edition
- BEING A RESEARCH INNOVATOR
June 2017; 3rd Edition

- **FUNDAMENTALS IN NEUROSCIENCE**
September 2017; 10th Edition
- **FUNDAMENTALS IN IMMUNOLOGY AND INFECTION**
October 2017; 9th Edition
- **FUNDAMENTALS IN GENETICS, DEVELOPMENT AND NEOPLASIA**
October 2017; 9th Edition
- **RESEARCH METHODOLOGIES**
November 2017; 9th Edition
- **BIOINFORMATICS IN HEALTH SCIENCES**
December 2017; 9th Edition

2.2.3 INDUSTRY CONTRACT RESEARCH

In 2017, the ICVS has 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: “The impact of lipid signalling modulation in cognition”.
- FUNDAÇÃO BIAL: “Exploring the neural basis of motivation”
- FUNDAÇÃO BIAL: “Developing a neurofunctional intervention for emotion regulation under stress”

2.2.4 INTERNATIONALIZATION

Reflecting the high level of internationalization of the ICVS, researchers from 11 foreign countries were included in the Institute's team in 2017.

Among the ICVS papers published in international peer-reviewed journals during 2017, over 51% 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 2017 (generating 220 communications in international meetings).

In 2017, the ICVS was involved in international networks with specific funding, including:

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

Globally, in 2017, the ongoing projects funded by international sources corresponded to a total amount of 1.4 million €. These collaborative networks involved the participation of institutions from the following countries: Belgium, Benin, Congo, Denmark, France, Germany, Ghana, Hungary, Israel, Italy, Mali, Morocco, Mozambique, Netherlands, Nigeria, Norway, South Africa, Spain, Sweden, Switzerland, Tanzania, Uganda, United Kingdom and Zambia.

The international recognition of the ICVS research activities is also reflected by the granting of 34 International scientific awards, including the "Prémio Thomé Villar", awarded by Boehringer Ingelheim.

The Post-graduation program of the ICVS/EM promoted 42 international post-graduation courses that included the participation of 148 foreign students.

Finally, the ICVS strategy of internationalization was also fostered by the digitization 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, in the last 12 months, the ICVS website and its social networks 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 2017, the ICVS continued its strong activity in disseminating scientific awareness and public perception of science and technology. The activities were organized in 9 major events, involving more than 1750 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 outreach events in different scientific themes: the “International Brain Awareness Week”; the “ABC in Surgical Sciences”; the “Science Epidemic Week”; the “UMinho Open Week; the “Post-graduation Open Day”; the “Prize Best Student”, the “Health Olympics”; the “Summer in the campus” and the “Do you want to be a Medical student for one day?”. 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 and different TV programs.

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 the last 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. Specific cellular mechanisms, common to microorganisms and mammals, are studied transversally in various cellular and animal models and in patients; these include autophagy and programmed cell death and molecular mechanisms underlying immune responses. The MIRD takes an all-inclusive view on host-pathogen interactions and encompasses a multidisciplinary team dedicated to projects involving a diverse set of pathogens: bacteria (mycobacteria), virus (HIV), fungi (*Paracoccidioides spp*; *Aspergillus spp*) and parasites (*Plasmodium spp*).

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 unravel 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 20 PhD integrated members with backgrounds in biological sciences, engineering and medicine.

Research within the MIRD was supported by 11 projects from FCT, 2 from NORTE2020, 1 from other national sources and 8 from other international sources.

During the year of 2017, researchers from MIRD published 38 papers in international peer-reviewed journals, including 24 in Q1, with an average IF of 5.9, of which 5 papers were published in journals with an IF>10.

Researches within the MIRD were granted with 3 international and 5 national scientific awards, including: the “Medalha de Honra L’Oréal Portugal para as Mulheres na

Ciência”, awarded by *L’Oréal Portugal*, the *Comissão Nacional da UNESCO* and the *Fundação para a Ciência e a Tecnologia (FCT)*; and the “Prémio Thomé Villar” awarded by Boehringer Ingelheim.

The MIRD organized 1 post-graduation course/workshop and graduated 4 PhD-students and 5 MSc-students. In addition, MIRD members were involved in 8 lectures/seminars in the context of international meetings and submitted 41 communications to International Conferences/Meetings.

In line with the previous year, we kept reinforcing the translational/clinical research by fortifying our effective collaborations with clinicians in Portugal, Belgium, Italy, United Kingdom, Spain, Netherlands, United States of America, Benin and Mozambique.

5.2 RESEARCH LINE OUTPUT

5.2.1 SELECTED PUBLICATIONS IN PEER REVIEW JOURNALS

- Babo PS, Pires RL, Santos L, Franco A, Rodrigues F, Leonor I, Reis RL, Gomes ME. Platelet Lysate-Loaded Photocrosslinkable Hyaluronic Acid Hydrogels for Periodontal Endogenous Regenerative Technology. *ACS Biomaterials Science and Engineering* 3(7):1359-1369 (2017)
- Carvalho A, Goldman GH. Editorial: An Omics Perspective on Fungal Infection: Toward Next-Generation Diagnosis and Therapy. *Frontiers in Microbiology* 8(JAN):85 (2017)
- Castela A, Gomes P, Silvestre R, Guardão L, Leite L, Chilro R, Rodrigues I, Vendeira P, Virag R, Costa C. Vasculogenesis and Diabetic Erectile Dysfunction: How Relevant Is Glycemic Control? *Journal of Cellular Biochemistry* 118(1):82-91 (2017)
- Correia CR, Gaifem J, Oliveira MB, Silvestre R, Mano JF. The influence of surface modified poly(l-lactic acid) films on the differentiation of human monocytes into macrophages. *Biomaterials Science* 5(3):551-560 (2017)
- Costa M, Cerqueira MT, Santos TC, Sampaio-Marques B, Ludovico P, Marques AP, Pirraco RP, Reis RL. Cell sheet engineering using the stromal vascular fraction of adipose tissue as a vascularization strategy. *Acta Biomaterialia* 55:131-143 (2017)
- Cunha C, Gonçalves SM, Duarte-Oliveira C, Leite L, Lagrou K, Marques A, Lupiañez CB, Mesquita I, Gaifem J, Barbosa AM, Pinho Vaz C, Branca R, Campilho F, Freitas F, Ligeiro D, Lass-Flörl C, Löffler J, Jurado M, Saraiva M, Kurzai O, Rodrigues F, Castro AG, Silvestre R, Sainz J, Maertens JA, Torrado E, Jacobsen ID, Lacerda JF, Campos Jr A,

Carvalho A. IL-10 overexpression predisposes to invasive aspergillosis by suppressing antifungal immunity. *Journal of Allergy and Clinical Immunology* 140(3):867-870.e9 (2017)

- De Trizio A, Srisuk P, Costa RR, Fraga AG, Modena T, Genta I, Dorati R, Pedrosa J, Conti B, Correlo VM, Reis RL. Natural based eumelanin nanoparticles functionalization and preliminary evaluation as carrier for gentamicin. *Reactive and Functional Polymers* 114:38-48 (2017)
- Duarte-Oliveira C, Rodrigues F, Gonçalves SM, Goldman GH, Carvalho A, Cunha C. The Cell Biology of the Trichosporon-Host Interaction. *Frontiers in Cellular and Infection Microbiology* 7(APR):118 (2017)
- Fernandes FF, Oliveira AF, Landgraf TN, Cunha C, Carvalho A, Vendruscolo PE, Gonçalves RA, Almeida F, da Silva TA, Rodrigues F, Roque-Barreira MC. Impact of Paracoccin Gene Silencing on Paracoccidioides brasiliensis Virulence. *mBio* 8(4)e00537-17 (2017)
- Gonçalves SM, Lagrou K, Duarte-Oliveira C, Maertens JA, Cunha C, Carvalho A. The microbiome-metabolome crosstalk in the pathogenesis of respiratory fungal diseases. *Virulence* 8(6):673-684 (2017)
- Gonçalves SM, Lagrou K, Rodrigues CS, Campos CF, Bernal-Martínez L, Rodrigues F, Silvestre R, Alcazar-Fuoli L, Maertens JA, Cunha C, Carvalho A. Evaluation of bronchoalveolar lavage fluid cytokines as biomarkers for invasive pulmonary aspergillosis in at-risk patients. *Frontiers in Microbiology* 8:2362 (2017)
- Gresnigt MS, Jaeger M, Subbarao Malireddi RK, Rasid O, Jouvion G, Fitting C, Melchers W, Kanneganti TD, Carvalho A, Ibrahim-Granet O, van de Veerdonk FL. The absence of NOD1 enhances killing of Aspergillus fumigatus through modulation of dectin-1 expression. *Frontiers in Immunology* 8:1777 (2017).
- Guedes A, Ludovico P, Sampaio-Marques B. Caloric restriction alleviates alpha-synuclein toxicity in aged yeast cells by controlling the opposite roles of Tor1 and Sir2 on autophagy. *Mechanisms of Ageing and Development* 161:270-276 (2017)
- Lind AL, Wisecaver JH, Lameiras C, Wiemann P, Palmer JM, Keller NP, Rodrigues F, Goldman GH, Rokas A. Drivers of genetic diversity in secondary metabolic gene clusters within a fungal species. *PLoS Biology* 15(11):e2003583 (2017)
- Ludovico P, Côrte-Real M. Yeast on the corner of life and death decisions. *Mechanisms of Ageing and Development* 161:199-200 (2017)

- Moukambi F, Rodrigues V, Fortier Y, Rabezanahary H, Borde C, Krust B, Andreani G, Silvestre R, Petrovas C, Laforge M, Estaquier J. CD4 T Follicular Helper Cells and HIV Infection: Friends or Enemies? *Frontiers in Immunology* 8(FEB):135 (2017)
- Resende M, Cardoso MS, Ribeiro AR, Flórido M, Borges M, Castro AG, Alves NL, Cooper AM, Appelberg R. Innate IFN- γ -Producing cells developing in the absence of IL-2 receptor common γ -chain. *Journal of Immunology* 199(4):1429-1439 (2017)
- Silva EM, Mariano VS, Pastrez PRA, Pinto MC, Castro AG, Syrjanen KJ, Longatto-Filho A. High systemic IL-6 is associated with worse prognosis in patients with non-small cell lung cancer. *PLoS One* 12(7):e0181125 (2017)
- Vanaerschot M, Lucantoni L, Li T, Combrinck J, Ruecker A, Kumar TR, Rubiano K, Ferreira PE, Siciliano G, Gulati S, Henrich P, Ng C, Murithi J, Corey V, Duffy S, Lieberman O, Veiga MI, Sinden R, Alano P, Delves M, Sim KL, Winzeler E, Egan T, Hoffman SL, Avery V, Fidock D. Hexahydroquinolines are Antimalarial Candidates with Potent Blood Stage and Transmission-Blocking Activity. *Nature Microbiology* 2(10):1403-1414 (2017)
- Vriens K, Kumar PT, Struyfs C, Cool TL, Spincemaille P, Kokalj T, Sampaio-Marques B, Ludovico P, Lammertyn J, Cammue BPA, Thevissen K. Increasing the Fungicidal Action of Amphotericin B by Inhibiting the Nitric Oxide-Dependent Tolerance Pathway. *Oxidative Medicine and Cellular Longevity* 4064628 (2017)

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 us 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 43 PhD integrated members with backgrounds in biological sciences, engineering and medicine.

Research within the NERD was supported by 8 projects from FCT, 3 from NORTE2020, 2 from other national sources, 2 from H2020, 5 from other international sources and 7 from contracts with the national industry.

During the year of 2017, researchers from NERD published 101 papers in international peer-reviewed journals, including 64 in Q1, with an average IF of 6.5, of which 11 papers were published in journals with an IF>10.

Researchers within the NERD were granted with 16 international and 5 national scientific awards, including: the “Prémio Santa Casa Neurociências – Melo e Castro” awarded by *Santa Casa da Misericórdia de Lisboa*.

In addition, the NERD organized 11 post-graduation courses/workshops and graduated 13 PhD-students.

In line with the previous year, we kept reinforcing the translational/clinical research by fortifying our effective collaborations with clinicians in Portugal, Belgium, Brasil, Denmark, France, Germany, Hungary, Italy, Netherlands, Norway, Spain, Sweden, Switzerland, United Kingdom and United States of America.

6.2 RESEARCH LINE OUTPUT

6.2.1 SELECTED PUBLICATIONS IN PEER REVIEW JOURNALS

- Batista AFR, Martinez JC, Hengst U. Intra-axonal Synthesis of SNAP25 Is Required for the Formation of Presynaptic Terminals. *Cell Reports* 20(13):3085-3098 (2017)
- Caetano L, Pinheiro H, Patrício P, Mateus-Pinheiro A, Alves ND, Coimbra B, Baptista FI, Henriques SN, Cunha C, Santos AR, Ferreira SG, Sardinha VM, Oliveira JF, Ambrósio AF, Sousa N, Cunha RA, Rodrigues AJ, Pinto L, Gomes CA. Adenosine A2A receptor regulation of microglia morphological remodeling-gender bias in physiology and in a model of chronic anxiety. *Molecular Psychiatry* 22(7):1035-1043 (2017)
- Coimbra B, Soares-Cunha C, Borges S, Vasconcelos NAP, Sousa N, Rodrigues AJ. Impairments in laterodorsal tegmentum to VTA projections underlie glucocorticoid triggered reward deficits. *eLIFE* 6:e25843 (2017)
- Dioli C, Patrício P, Trindade R, Pinto LG, Silva JM, Morais M, Ferreiro E, Borges S, Mateus-Pinheiro A, Rodrigues AJ, Sousa N, Bessa JM, Pinto L, Sotiropoulos I. Tau-dependent suppression of adult neurogenesis in the stressed hippocampus. *Molecular Psychiatry* 22(8):1110-1118 (2017)
- Esteves M, Marques P, Magalhães R, Castanho TC, Soares JM, Almeida A, Santos NC, Sousa N, Leite-Almeida H. Structural laterality is associated with cognitive and mood outcomes: An assessment of 105 healthy aged volunteers. *Neuroimage* 153:86-96 (2017)
- Esteves S, Duarte-Silva S, Maciel P. Discovery of Therapeutic Approaches for Polyglutamine Diseases: A Summary of Recent Efforts. *Medicinal Research Reviews* 37(4):860-906 (2017)

- Leroy F, Brann DH, Meira T, Siegelbaum SA. Input-Timing-Dependent Plasticity in the Hippocampal CA2 Region and Its Potential Role in Social Memory. *Neuron* 95(5):1089-1102.e5 (2017)
- Lopes S, Teplytska L, Vaz-Silva J, Dioli C, Trindade R, Morais M, Webhofer C, Maccarrone G, Almeida OFX, Turck CW, Sousa N, Sotiropoulos I, Filiou MD. Tau Deletion Prevents Stress-Induced Dendritic Atrophy in Prefrontal Cortex: Role of Synaptic Mitochondria. *Cerebral Cortex* 27(4):2580-2591 (2017)
- Machado DR, Afonso DJ, Kenny AR, Öztu Rk-Çolak A, Moscato EH, Mainwaring B, Kayser M, Koh K. Identification of octopaminergic neurons that modulate sleep suppression by male sex drive. *eLIFE* 6:e23130 (2017)
- Mackay A, Burford A, (...) Reis RM, (...) Resnick A, Jones C. Integrated Molecular Meta-Analysis of 1,000 Pediatric High-Grade and Diffuse Intrinsic Pontine Glioma. *Cancer Cell* 32(4):520-537.e5 (2017)
- Mateus-Pinheiro A, Alves ND, Patricio P, Machado-Santos AR, Campos E, Silva J, Sardinha V, Reis, J, Schorle H, Oliveira JF, Ninkovic J, Sousa N, Pinto L. AP2γ controls adult hippocampal neurogenesis and modulates cognitive, but not anxiety or depressive-like behavior. *Molecular Psychiatry*, 22(12):1725-1734 (2017)
- Monteiro P, Feng G. SHANK proteins: roles at the synapse and in autism spectrum disorder. *Nature Reviews Neuroscience* 18(3):147-157 (2017)
- Monteiro S, Roque S, Marques F, Correia-Neves M, Cerqueira JJ. Brain interference: Revisiting the role of IFNγ in the central nervous system. *Progress in Neurobiology* 156:149-163 (2017)
- Pinto V, Sousa P, Catarino SO, Correia-Neves M, Minas G. Microfluidic immunosensor for rapid and highly-sensitive salivary cortisol quantification. *Biosensors & Bioelectronics* 90:308-313 (2017)
- Pires AO, Teixeira FG, Mendes-Pinheiro B, Serra SC, Sousa N, Salgado AJ. Old and new challenges in Parkinson's disease therapeutics. *Progress in Neurobiology* 156:69-89 (2017)
- Santos CR, Duarte AC, Quintela T, Tomás J, Albuquerque T, Marques E, Palha JA, Gonçalves I. The choroid plexus as a sex hormone target: Functional implications. *Frontiers in Neuroendocrinology* 44:103-121 (2017)
- Sardinha VM, Guerra-Gomes S, Caetano I, Tavares G, Martins M, Reis JS, Correia JS, Teixeira-Castro A, Pinto L, Sousa N, Oliveira JF. Astrocytic signaling supports

hippocampal–prefrontal theta synchronization and cognitive function. *Glia* 65(12):1944-1960 (2017)

- Sevivas N, Teixeira FG, Portugal R, Araújo L, Carriço LF, Ferreira N, Vieira da Silva M, Espregueira-Mendes J, Anjo S, Manadas B, Sousa N, Salgado AJ. Mesenchymal Stem Cell Secretome: A Potential Tool for the Prevention of Muscle Degenerative Changes Associated With Chronic Rotator Cuff Tears. *American Journal of Sports Medicine* 45(1): 179-188 (2017)
- Silva A, Almeida B, Fraga JS, Taboada P, Martins PM, Macedo-Ribeiro S. Distribution of amyloid-like and oligomeric species from protein aggregation kinetics. *Angewandte Chemie - International Edition* 56(45):14042-14045 (2017)
- Zemel BM, Muqem T, Brown EV, Goulão M, Urban MW, Tymanskyj SR, Lepore AC, Covarrubias M. Calcineurin Dysregulation Underlies Spinal Cord Injury-Induced K⁺ Channel Dysfunction in DRG Neurons. *Journal of Neuroscience* 37(34):8256-8272 (2017)

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 we 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, we provide personalized prosthesis and surgical plans. As additional mission, we provide 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 18 PhD integrated members with backgrounds in biological sciences, engineering and medicine.

Research within the SSRD was supported by 1 project from FCT, 2 from NORTE2020 and 1 from other international sources.

During the year of 2017, researchers from SSRD published 97 papers in international peer-reviewed journals, including 27 in Q1, with an average IF of 4.8, of which 7 papers were published in journals with an IF>10. Additionally, researchers within the SSRD were granted with 15 International and 4 National scientific awards.

The SSRD organized 17 post-graduation courses/workshops, participated in the organization of 10 external meetings and graduated 4 PhD-students and 3 MSc-students. In addition, SSRD members were involved by invitation in 47 lectures/seminars in the context of international meetings and submitted 94 communications to International Conferences/Meetings.

In line with the previous year, we kept reinforcing the translational/clinical research by fortifying our effective collaborations with clinicians in Portugal, Belgium, Denmark,

France, Germany, Hungary, Italy, Netherlands, Norway, Spain, Sweden, Switzerland, United Kingdom and United States of America.

7.2 RESEARCH LINE OUTPUT

7.2.1 SELECTED PUBLICATIONS IN PEER REVIEW JOURNALS

- Bogaert J, Curione D, Morais P, Barreiro-Perez M, Tilborghs S, Maes F, Dresselaers T. Imaging Ischemic and Reperfusion Injury in Acute Myocardial Infarction: Putting the Pieces Together With CMR. *JACC: Cardiovascular Imaging* 10(12):1520-1523 (2017)
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8. PILOT RESEARCH LINES

8.1 COMMUNITY HEALTH

The pilot research line on Community Health was established with the objective of developing research on the management of chronic diseases in the community, with a focus on chronic respiratory diseases, including asthma, allergic rhinitis and chronic obstructive pulmonary disease (COPD).

This research field was chosen as a natural evolution of previous successful projects involving EM Professors and Researchers from the ICVS-Community Health area, in collaboration with the Primary Care Respiratory Group of the Portuguese Association of General and Family Medicine (GRESF / APMGF) and the International Primary Care Respiratory Group (IPCRG).

8.2 EDUCATION ON LIFE AND HEALTH SCIENCES

The pilot research line on Education on Life and Health Sciences was established with the objective of developing a program of research with the goal of addressing international contemporary questions on health sciences education. This program has a particular focus on the medical degree of the University of Minho and aims at consolidating and expanding the research projects already under development by the medical education unit of the EM.

The main areas of activity are student development and the evaluation of innovations in teaching and learning in health sciences education. The research is developed in collaboration with students and faculty from the EM, national researchers in educational and social sciences and international research groups in medical education. The research benefits from an extensive database originating from the Longitudinal Study of School of Medicine of the University of Minho (ELECSUM) that was initiated in 2001.