

LIFE AND HEALTH SCIENCES RESEARCH INSTITUTE | ICVS

SCHOOL OF MEDICINE

UNIVERSITY OF MINHO

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1. INTRODUCTION

1.1 UNIT DESCRIPTION: 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 (School of Medicine) - 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 (School of Engineering) - 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. Additionally, two Pilot Research Lines on Community Health and on Education on Life and Health Sciences were recently created.

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.

In the context of the AL, 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 2016 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;
- start the installation of maintenance and scientific equipment in the new "Biotério" animal facility in the adjacent area of the EM/ICVS building, that has been a major bottleneck for the ICVS in the last years, and to start housing the first rodents in the new facility;
- 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;
- expand the process of certification/accreditation of procedures within the ICVS, from the animal facility activities to the overall activities of the institute;
- 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 2016:

THE MAIN ACHIEVEMENTS IN 2016 WERE:

- the 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 expansion of the network of collaborating R&D institutions, with the establishment of an active partnership with the INL – International Nanotechnology Laboratory;
- the completion of the construction of the “Biotério” animal facility and the beginning of the installation of maintenance/scientific equipment;
- 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 2016, THE ICVS WAS ABLE TO:

- Publish a total of 197 papers in international peer-reviewed journals (referenced in ISI, Scopus or in Pubmed), in addition to 7 international book chapters and 170 proceedings and communications in international congresses. Among the articles published in 2016, 178 were produced within the three research domains (Microbiology and Infection, Neurosciences and Surgical Sciences), corresponding to 79% in Q1-Q2, with 53% in Q1, with an average Impact Factor (IF) of 4.41 (including articles with IF between 3 and 5 = 66 papers; IF between 5 and 10 = 44 papers; IF between 10 and 20 = 7 papers; and IF>20 = 1 papers); and 2 additional articles in the fields of Medical Education and Public Health; 12 in the fields of Community Health and 5 in other fields;. In addition, the average IF of the 100 articles published in the journals with higher impact was 5.8.
- 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 70 clinical trials ongoing in 2016, assuming a leading position in the National context, corresponding to around 35% of the clinical trials run in Portugal. Additionally, the 2CA-Braga developed 51 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), observational studies and validation of medical devices);
- The capitation of funding from the NORTE2020 for the establishment of a collaboration with the INL and the 3B's Group, through the grant “Projeto Estruturado / Fronthera”, corresponding to a total amount of 3.8 million €.
- Operationalize of the new “Biotério”, with the installation of equipment for laboratory animal

maintenance and experimentation, since the beginning of 2016. Importantly, the first animal models were housed in the new facility starting in October 2016. The lack of an animal facility with the required capacity was been a major bottleneck for the ICVS in the last years and, therefore, this is major achievement;

- 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" (49 in total), involving the participation of an increasing number of leading scientists from foreign Institutions;
- Grant internal research projects within the ICVS/3B's AL, between members of the ICVS and the 3B's groups, to support collaborative research projects within the AL, contributing for the promotion of a strong level of complementarity between the two research groups that constitute the AL;
- Create the experimental conditions for the conclusion of 14 PhD thesis, including 3 from MDs;
- Foster collaborations between its researchers and partners from Biomedical Industries. In 2016, industry sponsored R&D was performed in areas of mutual interest with sponsors such as: TECNIMEDE; FUNDAÇÃO BIAL; BIOGEN 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 26 International and National scientific awards, including the Postdoctoral Fellowship Award, Society in Science - The Branco Weiss Fellowship 2016, Swiss Federal Institute of Technology, Germany; Postdoctoral Fellowship Award, EMBO Long-term Research Fellow 2016, European Molecular Biology Organization; 2016 NARSAD Young Investigator Grant, Brain and Behavior Research Foundation, USA; ESCMID Research Grant 2016, Switzerland; Prémio Robalo Cordeiro SPP/Novartis 2016; and Medalhas de Honra L'Oréal Portugal para as Mulheres na Ciência;
- Reinforce the level of funding obtained from competitive sources and from contracts with leading industrial partners, through 36 ongoing projects (16 from FCT; 4 from NORTE2020; 5 from other national sources; 2 from H2020; 7 from other international sources and 3 from contracts with the national industry);

- Increase the amounts of competitive funding of research grants, including a total sum of about 16 million € obtained in 2016 from calls at the international and national levels;
- Submit/register 5 patents including: “Método para determinação da posição e orientação tridimensional de implantes em imagens médicas”; “Sistema de aquisição da posição e orientação tridimensional de implantes dentários e respetivo método de utilização”; and “A radiation free guidance system for percutaneous renal access in minimally invasive interventions”;
- 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 30 Option Projects and 39 MD/PhD Laboratory Rotations;
- Maintain the offer of a high number of Advanced Post-Graduation Courses/Workshops (45 in 2016), involving 1007 participants (including 80% MDs, 14% researchers from Biological Sciences fields, 2% other Health Professionals and 4% 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 2016, the ICVS published 197 papers in international peer-reviewed journals (referenced in *ISI*, *Scopus* or in *Pubmed*).

Among the articles published in 2016, 178 were produced within the three research domains (Microbiology and Infection, Neurosciences and Surgical Sciences), corresponding to 79% in Q1-Q2, with 53% in Q1, with an average Impact Factor (IF) of 4.41 (including articles with IF between 3 and 5 = 66 papers; IF between 5 and 10 = 44 papers; IF between 10 and 20 = 7 papers; and IF>20 = 1 papers); and 2 additional articles in the fields of Medical Education and Public Health; 12 in the fields of Community Health and 5 in other fields.

In addition, the average IF of the 100 articles published in the journals with higher impact was 5.8.

SELECTED PAPERS IN PEER REVIEW JOURNALS:

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2.2.2 PhD THESES COMPLETED

- Student: MARTA SOFIA POJO SOUSA
Institution: Universidade do Minho
Date of the PhD conclusion: January 2016
PhD Program: Health Sciences
Title: HOXA9 as a key regulator in glioma initiation, aggressiveness and response to therapy
Supervisors: Bruno Costa and Nuno Sousa
- Student: SUSANA ISABEL GONÇALVES MONTEIRO
Institution: Universidade do Minho
Date of the PhD conclusion: January 2016
PhD Program: Health Sciences
Title: The role of IFN γ in higher brain function: in health and under chronic stress
Supervisors: João Cerqueira and Margarida Correia-Neves
- Student: ANA SOFIA TEIXEIRA ESTEVES
Institution: Universidade do Minho
Date of the PhD conclusion: February 2016
PhD Program: Health Sciences
Title: Preclinical trials for Machado-Joseph Disease: hypothesis-based and hypothesis-free therapeutic approaches
Supervisors: Patrícia Maciel
- Student: FILIPE MANUEL TEIXEIRA PINTO
Institution: Universidade do Minho
Date of the PhD conclusion: March 2016
PhD Program: Health Sciences
Title: From Development to Tumorigenesis: Dissecting the biological and clinical role of the T-Box transcription factor Brachyury
Supervisors: Rui M. Reis and Raquel Andrade
- Student: NUNO GONÇALO DE CARVALHO CAROÇO DOS SANTOS
Institution: Universidade do Minho
Date of the PhD conclusion: March 2016
PhD Program: Health Sciences
Title: Tuberculosis in wild ungulates in the Iberian Peninsula: applying new methods for the epidemiological analysis of intra and inter-species transmission
Supervisors: Margarida Correia-Neves and Christian Gortázar Schmidt

- Student: PATRÍCIA CARVALHO PATRÍCIO
Institution: Universidade do Minho
Date of the PhD conclusion: May 2016
PhD Program: Health Sciences
Title: Molecular regulation of the hippocampal neurogenic niche in depression and by antidepressants: Insights from an unpredictable chronic mild stress rat model
Supervisors: Luísa Pinto and Nuno Sousa
- Student: HELDER BRUNO CARVALHO FERREIRA
Institution: Universidade do Minho
Date of the PhD conclusion: July 2016
PhD Program: Medicine
Title: Contribution to minimize the aggressiveness of laparoscopic surgery in gynecology
Supervisors: Jorge Correia Pinto
- Student: ANTÓNIO MARIA RESTOLHO MATEUS PINHEIRO
Institution: Universidade do Minho
Date of the PhD conclusion: July 2016
PhD Program: Health Sciences
Title: Adult hippocampal neural plasticity: Insights into its functional relevance in the stressed and depressed brain
Supervisors: Luísa Pinto and Nuno Sousa
- Student: DINIS JOSÉ SILVA AFONSO
Institution: Universidade do Minho
Date of the PhD conclusion: July 2016
PhD Program: Medicine
Title: Regulation of sleep and circadian rhythms by TARANIS
Supervisors: Kyunghee Koh and Joana Palha
- Student: HANNA RAQUEL NEBENZAHL GUIMARÃES
Institution: Universidade do Minho
Date of the PhD conclusion: July 2016
PhD Program: Health Sciences
Title: A genomic exploration of transmissibility in Mycobacterium tuberculosis
Supervisors: Margarida Correia-Neves and Megan Murray
- Student: CARINA ISABEL SOARES DA CUNHA
Institution: Universidade do Minho

Date of the PhD conclusion: November 2016

PhD Program: Health Sciences

Title: Role of Nucleus accumbens dopamine D1- and D2-expressing neurons in reward and motivation

Supervisors: Ana João Rodrigues and Nuno Sousa

- Student: CARLOS ALBERTO PEREIRA CAPELA
Institution: Universidade do Minho
Date of the PhD conclusion: November 2016
PhD Program: Medicine
Title: Immunogenetic determinants of susceptibility/resistance to Mycobacterium ulcerans infection: a population based study – Benin biological bank on Buruli ulcer
Supervisors: Fernando Rodrigues and Jorge Pedrosa
- Student: VERA MÓNICA MIRANDA GONÇALVES
Institution: Universidade do Minho
Date of the PhD conclusion: December 2016
PhD Program: Health Sciences
Title: Monocarboxylate Transporters in gliomas: regulation and therapeutic implications
Supervisors: Fátima Baltazar and Rui M. Reis
- Student: PALMIRA DA CONCEIÇÃO DE ARAÚJO BARREIRA DA SILVA
Institution: Universidade do Minho
Date of the PhD conclusion: December 2016
PhD Program: Health Sciences
Title: T cells during mycobacterial infections: production and activation
Supervisors: Margarida Correia-Neves and Rui Lima

2.2.3 ORGANIZATION OF COURSES/WORKSHOPS

TRAINING IN CLINICAL SCIENCES

- PREMIUM CATARACT SURGERY
January 2016; 6th Edition
- MASSIVE ROTATOR CUFF TEAR: FROM BASIC SCIENCE TO CLINICS
January 2016; 3rd Edition
- MENTAL HEALTH
February 2016; 2nd Edition
- SONOANATOMY APPLIED TO PERIPHERAL NERVE BLOCK
February 2016; 8th Edition
- BASIC LAPAROSCOPY FOR RESIDENTS
April 2016; 10th Edition
- VIDEO-ASSISTED EXTRAPERITONEAL RADICAL PROSTATECTOMY
April 2016; 5th Edition
- INNOVATIONS IN MINIMALLY INVASIVE UROLOGIC SURGERY
April 2016; 1st Edition
- ADVANCED THERAPEUTIC ENDOSCOPY - EMR & ESD
April 2016; 6th Edition
- HANDS-ON SHOULDER AND ELBOW INSTABILITY
May 2016; 1st Edition
- RESEARCH METHODOLOGIES FOR MEDICAL DOCTORS
May 2016; 1st Edition
- FUNDAMENTALS IN ARTHROSCOPY
June 2016; 7th Edition
- SULCI, GYRI, VENTRICLES AND DISSECTING FIBERS
June/July 2016; 14th Edition

- FETAL AND NEONATAL ENDOSCOPIC SURGERY
September 2016; 8th Edition
- THE ROLE OF MINIMAL INVASIVE SURGERY IN MULLERIAN MALFORMATIONS
September 2016; 1st Edition
- PEDIATRIC ENDOSCOPY
September 2016; 6th Edition
- PHARMACOLOGICAL BASIS OF RATIONAL THERAPEUTICS: ANTIBIOTHERAPY
September 2016; 6th Edition
- CAPSULE ENDOSCOPY TRAINING PROGRAM
September/October 2016; 1st Edition
- MINOR SURGERY FOR PRIMARY HEALTH CARE
October 2016; 2nd Edition
- THERAPEUTIC ENDOSCOPY
October 2016; 9th Edition
- BILIARY LAPAROSCOPY
October 2016; 8th Edition
- HEPATOPANCREATIC MIS
October 2016; 2nd Edition
- GYNECOLOGICAL LAPAROSCOPIC SURGERY
October 2016; 8th Edition
- RESPIRATORY DISEASES
October/December 2016; 2nd Edition
- ARTERIAL STIFFNESS AND EARLY VASCULAR AGING
November 2016; 5th Edition
- MINIMALLY INVASIVE SPINE SURGERY
November 2016; 5th Edition
- SONOANATOMY APPLIED TO PERIPHERAL NERVE BLOCK

November 2016; 12th Edition

- BASIC LAPAROSCOPY FOR RESIDENTS
November 2016; 11th Edition
- ERCP - THE ESSENTIALS
November 2016; 2nd Edition
- MASTER CLASS SKILLS LAB FOR LIVE ANIMAL MODEL (PEDIATRIC
LAPAROSCOPY)
December 2016; 2nd Edition
- FOOT AND ANKLE SPORTS MEDICINE ADVANCED COURSE
December 2016; 3rd Edition

TRAINING IN BIOMEDICAL SCIENCES AND OTHER AREAS

- BIostatISTICS IN HEALTH SCIENCES
January 2016; 6th Edition
- LABORATORY ANIMAL SCIENCE
February 2016; 11th Edition
- STEM CELLS GET PRACTICAL
February/March 2016; 6th Edition
- INTRODUCTION TO QUALITATIVE METHODOLOGIES AND DATA
March 2016; 1st Edition
- INTRODUCTION TO COMPUTER-BASED QUALITATIVE DATA ANALYSIS
March 2016; 1st Edition
- CELL FUNCTIONAL AND PHENOTYPICAL ANALYSIS
March/April 2016; 1st Edition
- EPIGENETICS - FROM MECHANISMS TO DISEASE
April 2016; 1st Edition
- INTRODUCTION TO SYSTEMATIC REVIEW AND META-ANALYSIS
May 2016; 1st Edition

- INTRODUCTION TO STRUCTURAL EQUATION MODELING WITH AMOS
June 2016; 3rd Edition
- FUNDAMENTALS IN NEUROSCIENCE
September 2016; 9th Edition
- FUNDAMENTALS IN IMMUNOLOGY AND INFECTION
October 2016; 8th Edition
- FUNDAMENTALS IN GENETICS, DEVELOPMENT AND NEOPLASIA
October/November 2016; 8th Edition
- RESEARCH METHODOLOGIES
November 2016; 8th Edition
- INTENSIVE COMMUNICATION SKILLS COURSE
November 2016; 1st Edition
- BIOINFORMATICS IN HEALTH SCIENCES
December 2016; 8th Edition

2.2.4 INDUSTRY CONTRACT RESEARCH

In 2016, the ICVS has had the following ongoing Research Contracts:

- TECNIMEDE - SOCIEDADE TÉCNICO MEDEICINAL, SA: “Characterize the pharmacological activity of drugs in the control of pain in animals with traumatic neuropathy”.
- TECNIMEDE - SOCIEDADE TÉCNICO MEDEICINAL, 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”.
- BIOGEN IDEC: “Estudo pré-clínico do efeito do dimetilfumarato (um fármaco da BIOGEN) na capacidade cognitiva do modelo animal de esclerose múltipla”.

2.2.5 INTERNATIONALIZATION

Reflecting the high level of internationalization of the ICVS, researchers from 11 foreign countries were included in the Institute's team in 2016.

Among the ICVS papers published in international peer-reviewed journals during 2016, more than 55% 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 2016 (generating 170 communications in international congresses).

In 2016, the ICVS was involved in international networks with specific funding, including:

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

Globally, in 2016, the ongoing projects funded by international sources corresponded to a total amount of 1 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 23 International scientific awards, including the Postdoctoral Fellowship Award, Society in Science - The Branco Weiss Fellowship 2016, Swiss Federal Institute of Technology, Germany; Postdoctoral Fellowship Award, EMBO Long-term Research Fellow 2016, European Molecular Biology Organization; 2016 NARSAD Young Investigator Grant, Brain and Behavior Research Foundation, USA; and ESCMID Research Grant 2016, Switzerland.

The Post-graduation program of the ICVS/EM promoted 45 international post-graduation courses that included the participation of 94 foreign students.

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 2016, 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 outreach events in different scientific themes: the “ABC in Surgical Sciences”, the “International Brain Awareness Week”, the “International Week of Science & Technology”, the “Science Outbreak Week”, the “Prize Best Students”, the “Summer in the campus”, the “Health Olympics” and the “post-graduation EM/ICVS Open 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 also organized two visiting programs to the ICVS and School of Medicine named “Do you want to be a Medical student for one day?” and the “Open days for MSc and PhD candidates”.

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.

5.1 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 unraveling 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 members with backgrounds in biological sciences, engineering and medicine.

Research within the MIRD was supported by 7 projects from FCT, 2 from NORTE2020, 1 from other national sources and 5 from other international sources.

During the year of 2016, researchers from MIRD published 43 papers in international peer-reviewed journals, including 33 in Q1, with an average IF of 6.4, of which 5 papers were published in journals with an IF>10. Additionally, the MIRD submitted 17 communications to International Meetings/Conferences.

Researches within the MIRD were granted with 2 National and 2 International scientific awards, namely: the ESCMID Research Grant; the EFIS-EJI Travel Grants for ICI; the "Prémio Robalo

Cordeiro-SPP/Novartis”; and the “Medalha de Honra L’Oréal Portugal para as Mulheres na Ciência”.

The MIRD organized 5 post-graduation courses/workshops and graduated 4 PhD-students and 3 MSc-students. In addition, MIRD members were involved in 20 conferences and seminars in the context of international meetings outside Portugal (17 presentations/communications).

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

- Arts RJ, Carvalho A, La Rocca C, Palma C, Rodrigues F, Silvestre R, Kleinnijhuis J, Lachmandas E, Gonçalves LG, Belinha A, Cunha C, Oosting M, Joosten LA, Matarese G, van Crevel R, Netea MG. Immunometabolic Pathways in BCG-Induced Trained Immunity. *Cell Rep* 17(10):2562-2571 (2016).
- Arts RJ, Novakovic B, ter Horst R, Carvalho A, Bekkering S, Lachmandas E, Rodrigues F, Silvestre R, Cheng SC, Wang SY, Habibi E, Gonçalves LG, Mesquita I, Cunha C, van Laarhoven A, van de Veerdonk FL, Williams DL, van der Meer JW, Logie C, O'Neill LA, Dinarello CA, Riksen NP, van Crevel R, Clish C, Notebaart RA, Joosten LA, Stunnenberg HG, Xavier RJ, Netea MG. Glutaminolysis and fumarate accumulation integrate immunometabolic and epigenetic programs in trained immunity. *Cell Metab* 24(6):807-819 (2016).
- Capela C, Dossou AD, Silva-Gomes R, Sopoh GE, Makoutode M, Menino JF, Fraga AG, Cunha C, Carvalho A, Rodrigues F, Pedrosa J. “Genetic variation in autophagy-related genes influences the risk and phenotype of Buruli ulcer”. *PLoS Negl Trop Dis* 10(4):e0004671 (2016).
- Carpenter SM, Nunes-Alves C, Booty MG, Way SS, Behar SM. A Higher Activation Threshold of Memory CD8+ T Cells Has a Fitness Cost That Is Modified by TCR Affinity during Tuberculosis. *PLoS Pathog* 12(1):e1005380 (2016).
- Carvalho AL, Vale AC, Sousa MP, Barbosa AM, Torrado E, Mano JF, Alves NM. “Antibacterial bioadhesive layer-by-layer coatings for orthopedic applications”. *J Mater Chem B* 4(32):5385-5393 (2016).
- Chorny A, Casas-Recasens S, Sintes J, Shan M, Polentarutti N, García-Escudero R, Walland AC, Yeiser JR, Cassis L, Carrillo J, Puga I, Cunha C, Bastos H, Rodrigues F,

Lacerda JF, Morais A, Dieguez-Gonzalez R, Heeger PS, Salvatori G, Carvalho A, Garcia-Sastre A, Blander JM, Mantovani A, Garlanda C, Cerutti A. The soluble pattern recognition receptor PTX3 links humoral innate and adaptive immune responses by helping marginal zone B cells. *J Exp Med* 213(10):2167-2185 (2016).

- Cordeiro da Costa J, Baia L, Gaio R, Oliveira O, Correia-Neves M, Duarte R. Prevalence and factors associated to Diabetes mellitus among Tuberculosis patients – A nationwide cohort". *Eur Respir J* 48(1):264-268 (2016).
- Farhat MR, Sultana R, Iartchouk O, Bozeman S, Galagan J, Sisk P, Stolte C, Nebenzahl-Guimaraes H, Jacobson K, Sloutsky A, Kaur D, Posey J, Kreiswirth BN, Kurepina N, Rigouts L, Streicher EM, Victor TC, Warren RM, van Soolingen D, Murray M. Genetic Determinants of Drug Resistance in Mycobacterium tuberculosis and Their Diagnostic Value. *Am J Respir Crit Care Med* 194(5):621-630 (2016).
- Klionsky DJ, (...), Ludovico P, (...). Guidelines for the use and interpretation of assays for monitoring autophagy (3rd edition). *Autophagy* 12(1):1-222 (2016).
- Laforge M, Rodrigues V, Silvestre R, Gautier C, Weil R, Corti O, Estaquier J. NF- κ B pathway controls mitochondrial dynamics. *Cell Death Differ* 23(1):89-98 (2016).
- Lupiañez CB, Canet LM, Carvalho A, Alcazar-Fuoli L, Springer J, Lackner M, Segura-Catena J, Comino A, Olmedo C, Ríos R, Fernandez-Montoya A, Cuenca-Estrella M, Solano C, López-Nevot MA, Cunha C, Oliveira-Coelho A, Villaescusa T, Fianchi L, Aguado JM, Pagano L, López-Fernández E, Potenza L, Luppi M, Lass-Flörl C, Löffler J, Einsele H, Vázquez L, PCRAGA Study Group, Jurado M, Sainz J. "Polymorphisms in host immunity modulating genes and risk of invasive aspergillosis: results from the aspBIOmics consortium". *Infect Immun* 84(3):643-657 (2016).
- Mesquita I, Varela P, Belinha A, Gaifem J, Laforge M, Vergnes B, Estaquier J, Silvestre R. Exploring NAD⁺ metabolism in host-pathogen interactions. *Cell Mol Life Sci* 73(6):1225-1236 (2016).
- Pandey K, Ferreira PE, Ishikawa T, Nagai T, Kaneko O, Yahata K. Ca²⁺ monitoring in Plasmodium falciparum using the yellowameleon-Nano biosensor. *Sci Rep* 6:23454 (2016).
- Pérez-Cabezas B, Cecílio P, Robalo A, Silvestre R, Carrillo E, Moreno J, San Martín JV, Vasconcellos R and Cordeiro-da-Silva A. Interleukin-27 Early Impacts Leishmania infantum Infection in Mice and Correlates with Active Visceral Disease in Humans. *Front Immunol* 7:478 (2016).

- Silva JP, Gonçalves C, Costa C, Sousa J, Silva-Gomes R, Castro AG, Pedrosa J, Appelberg R, Gama FM. Delivery of LLKKK18 loaded into self-assembling hyaluronic acid nanogel for tuberculosis treatment. *J Control Release* 235:112-124 (2016).
- Veiga MI, Dhingra SK, Henrich PP, Straimer J, Gnädig N, Uhlemann AC, Martin RE, Lehane AM, Fidock DA. Globally prevalent PfMDR1 mutations modulate Plasmodium falciparum susceptibility to artemisinin-based combination therapies. *Nat Commun* 7:11553 (2016).
- Yruela I, Contreras-Moreira B, Magalhães C, Osório NS, Gonzalo-Asensio J. "Mycobacterium tuberculosis Complex Exhibits Lineage-Specific Variations Affecting Protein Ductility and Epitope Recognition". *Genome Biol Evol* 8(12):3751-3764 (2016)

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 neuropsychiatric 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 members with backgrounds in biological sciences, engineering and medicine.

Research within the NERD was supported by 8 projects from FCT, 4 from NORTE2020, 4 from other national sources, 2 from H2020, 2 from other international sources and 3 from contracts with the national industry.

During the year of 2016, researchers from NERD published 70 papers in international peer-reviewed journals, including 42 in Q1, with an average IF of 4.55, of which 3 papers were published in journals with an IF>10. Additionally, the NERD submitted 37 communications to International Meetings/Conferences.

Researchers within the NERD were granted with 2 National and 5 International scientific awards, including: the NARSAD Young Investigator Grant; the EMBO Long-term Research Fellow; and The Branco Weiss Fellowship.

The NERD organized 2 scientific meetings and 14 post-graduation courses/workshops and graduated 6 PhD-students and 8 MSc-students. In addition, NERD members were involved in 21 conferences and seminars in the context of international meetings outside Portugal (37 presentations/communications).

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.

6.2 RESEARCH LINE OUTPUT

6.2.1 SELECTED PUBLICATIONS IN PEER REVIEW JOURNALS

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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 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 22 PhD members with backgrounds in biological sciences, engineering and medicine.

Research within the SSRD was supported by 7 projects/grants from national (4) and international agencies (3).

During the year of 2016, researchers from SSRD published 74 papers in international peer-reviewed journals, including 27 in Q1, with an average IF of 3.09. Additionally, the SSRD submitted 85 communications to International Meetings/Conferences, and were granted with 4 National and 13 International scientific awards.

The SSRD organized 16 scientific meetings and 21 post-graduation courses/workshops and graduated 3 PhD-students and 1 MSc-student. In addition, SSRD members were involved in 45 conferences and seminars in the context of international meetings outside Portugal (85 presentations/communications).

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

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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.