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2015











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ASSOCIATE LABORATORY

LIFE AND HEALTH SCIENCES RESEARCH INSTITUTE: ICVS

OBJECTIVES AND ACHIEVEMENTS

GROUP PRODUCTIVITY
Publications in peer-review journals
PhD theses completed
Organization of courses/workshops
Industry contract research
Internationalization

28 ACTIVITIES

OUTREACH ACTIVITIES

30 OTHER ACTIVITIES

INTERNAL SERVICES AND RESOURCES

EXTERNAL SERVICES AND RESOURCES

RESEARCH LINE: MICROBIOLOGY AND INFECTION

OBJECTIVES AND ACHIEVEMENTS

RESEARCH LINE OUTPUTS
Selected publications in peer-review journals

38

RESEARCH LINE: NEUROSCIENCES

OBJECTIVES AND ACHIEVEMENTS

RESEARCH LINE OUTPUTS
Selected publications in peer-review journals

44

RESEARCH LINE: SURGICAL SCIENCES

OBJECTIVES AND ACHIEVEMENTS

RESEARCH LINE OUTPUT
Selected publications in peer review journals

50

PILOT RESEARCH LINE

COMMUNITY HEALTH

EDUCATION ON LIFE AND HEALTH SCIENCES



ICVS/3B'S

ASSOCIATE LABORATORY

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 Health Sciences) a group on Biomedicine and Clinical Sciences, focusing its activities on Microbiology and Infection, Neurosciences and Surgical Sciences, member of the Clinical Academic Center - 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) 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 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.

LIFE AND HEALTH SCIENCES RESEARCH INSTITUTE: ICVS

OBJECTIVES & ACHIEVEMENTS

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 Health Sciences (ECS) – 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, the ICVS has recently launched 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.

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, Endoscospy and Minimally Invasive Surgery, as well as a fully equipped Centre for Animal Experimentation and a Clinical Academic Centre (2CA-Braga).

THE ICVS AIMS TO ACHIEVE THE FOLLOWING GLOBAL GOALS:

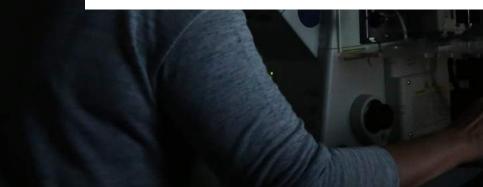
- promote original research on health sciences with high scientific outputs and recognized impact

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 on biomedicine and 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.

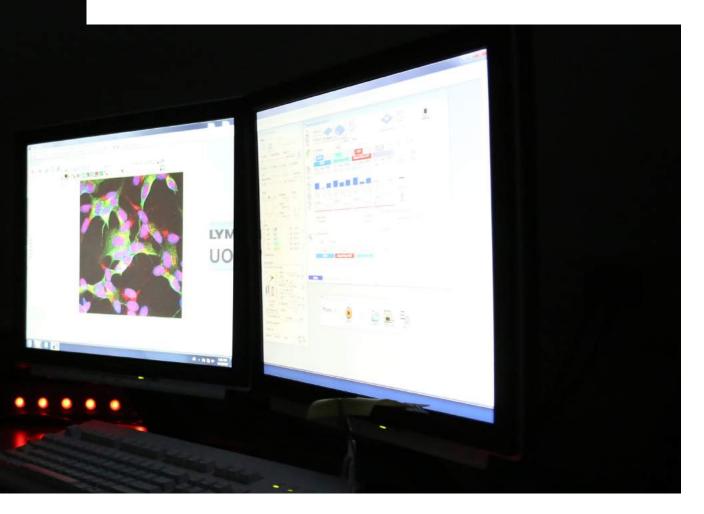
THEREFORE, THE SPECIFIC DEVELOPMENTAL STRATEGIES FOR 2015 WERE TO:

- 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;

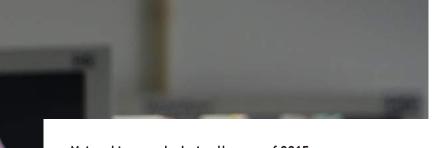


- complete the construction of the new "Biotério" animal facility in the adjacent area of the ECS/ICVS building, once the lack of an animal facility with the required capacity has been a major bottleneck of the ICVS in the last years;
- expand the activities of the 2CA-Braga, namely the development of clinical research, particularly with the capacity to accommodate clinical trials;
- 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 ECS graduates;
- support the ongoing ECS/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 developed in the ICVS;
- reinforce the specific Program of the ICVS Seminars Series, with leading scientists from foreign Institutions, to complement 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.







Main achievements during the year of 2015

MAIN ACHIEVEMENTS IN 2015 WERE:

- the increase in the number of peer-reviewed international publications;
- the increase of the scientific productivity per PhD member:
- the increase in the number and in the impact of the clinical studies developed in the 2CA-Braga;
- the completion of the construction of the "Biotério" animal facility;
- the involvement of an increasing number of MD students in the ICVS research activities;
- the increase in the number and impact of the Advanced Post-Graduation Courses:

SPECIFICALLY, IN 2015, THE ICVS WAS ABLE TO:

- Publish a total of 172 papers in international peer-reviewed journals (referenced in *ISI, Scopus* or in *Pubmed*), in addition to 16 international book chapters and 162 communications and proceedings in international congresses. Among the articles published in 2015, 168 were produced within the three research domains (Microbiology and Infection, Neurosciences and Surgical Sciences), corresponding to 79.2% in Q1-Q2, with 56% in Q1 and average Impact Factor (IF) of 4.53 (including articles with IF between 3 and 5=67 papers; IF between 5 and 10=36 papers; IF between 10 and 20=3 papers; and IF>20=1 paper); and 4 additional articles in the fields of Medical Education and Public Health. In addition, the average IF of the 100 articles published in the journals with higher impact was 5.6.
- 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 in testing new therapies, with 35 clinical trials ongoing in 2015, assuming a leading position in the national context, with around 30% of the clinical trials run in Portugal. Additionally, the 2CA-Braga developed 42 clinical studies,

including research projects in partnership with the ICVS and other research units from the UMinho (with projects funded by the European Commission - FP7 - or nationally, by the FCT), observational studies and validation of medical devices.

- Kept actively involved in R&D activities a differentiated and productive research team. The ICVS pursued a strategy of reinforcing the productivity of the body of PhD members (the actual number was reduced to 79). The total number of ICVS members is 267, including 79 PhDs (36 ECS Faculty, 2 Faculty from collaborating institutions, 13 Assistant Researchers and 28 Post–Docs) and 188 post-graduation students (96 PhD students, 32 Master students and 60 research assistants), supported by 24 non-academic staff (8 administrative and 16 specialized technicians, with salaries supported by the ECS).
- Finish the construction of the "Biotério" animal facility. The lack of an animal facility with the required capacity has been a major bottleneck of the ICVS in past years. This constraint is now solved with the construction of the "Biotério" in the adjacent area of the ECS/ICVS building;
- Pursue supporting the ECS's Master Program in Health Sciences, as well as the four PhD Programs that have been granted with specific funding from the FCT;
- Reinforce the program of international ICVS Seminars Series that complement the Seminars "Ciência Falada", 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;
- Create the experimental conditions for the conclusion of 13 PhD theses, including 3 from MDs;

- Foster collaborations with partners from Biomedical Industries: in 2015, industry sponsored R&D was performed in areas of mutual interest with sponsors such as: TECNIMEDE; F. BIAL; and BIOGEN;
- 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 13 National and 12 International scientific awards, including the "Prémio Novo Banco" – Prémio Nacional de Inovação 2015: Stent biodegradável;
- Keep a high level of competitive funding: the ongoing projects (3 years average) represent 9.3 million €, of which 2 million € corresponded to activities developed in 2015;
- Keep a high level of funding from competitive sources and contracts with leading industrial partners, through 39 ongoing projects (16 from FCT; 5 from QREN/COMPETE; 4 from other national sources; 2 from FP7; 6 from other international sources; and 6 from contracts with the national industry);

- Pursue a policy of fostering an active involvement of medical students and MDs in the ICVS research projects, involving an increasing number of MD students in research, including 61 Option Projects (from 48 in 2014) and 62 Master's, PhD and MD/PhD Programs Lab Rotations;
- Organize an increasing number of Advanced Post-Graduation Courses/Workshops (from 46 in 2014 to 51 in 2015), involving 1357 participants (including 86% MDs, 9% of researchers from Biological Sciences fields and 5% of other Health Professionals). Importantly, 45% of the participants rated the attended courses as "Excellent" and 43% as "Very Good" and some of the courses were part of training activities of European schools or European training actions;
- 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 1800 participants and involved the interaction with over 60 external institutions.

GROUP PRODUCTIVITY

Publications in peer- review journals

In 2015, the ICVS published 172 papers in international peer-reviewed journals (referenced in *ISI*, *Scopus* or in *Pubmed*).

Among the articles published in 2015, 168 were produced within the three research domains (Microbiology and Infection, Neurosciences and Surgical Sciences), corresponding to 79.2% in Q1-Q2, with 56% in Q1, and an average Impact Factor (IF) of 4.53 (including articles with IF between 3 and 5=67 papers; IF between 5 and 10=36 papers; IF between 10 and 20=3 papers; and IF>20=1 paper); and 4 additional articles in the fields of Medical Education and Public Health.

In addition, the average IF of the 100 articles published in the journals with higher impact was 5.6.

50 SELECTED PAPERS IN PEER REVIEW JOURNALS

- Afonso DJS, Liu D, Machado DR, Pan H, Jepson JEC, Rogulja D, Koh K. TARANIS Functions with Cyclin A and Cdk1 in a Novel Arousal Center to Control Sleep in Drosophila. Current Biology. 25(13), 1717-1726 (2015).
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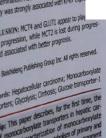
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Student: Alexandre Manuel Câmara Carvalho

Institution: Universidade Católica Year of the PhD conclusion: 2015

PhD Program: Health Sciences - Medicine

Title: Determining the immune response in human

immunodeficiency virus infection

Supervisors: Henrique Lecour and Jorge Pedrosa

Student: Ana Pires Marques

Institution: Universidade do Minho Year of the PhD conclusion: 2015 PhD Program: Health Sciences

Title: Exploring the secretome of mesenchymal like stem cells for central nervous system regenerative medicine: a

focus on Parkinson's disease

Supervisors: António Salgado and Nuno Sousa

Student: Ana Sofia Lopes

Institution: Universidade do Minho Year of the PhD conclusion: 2015 PhD Program: Health Sciences

Title: Stress-triggered synaptic malfunction: a gate along

the path from depression to dementia

Supervisors: Ioannis Sotiropoulos and Nuno Sousa

Student: Fábio Teixeira

Institution: Universidade do Minho Year of the PhD conclusion: 2015 PhD Program: Health Sciences

Title: Modulation of the secretome of mesenchymal stem cells for central nervous system regenerative medicine

applications

Supervisors: António Salgado and Nuno Sousa

Student: Filipa Campos

Institution: Universidade do Minho Year of the PhD conclusion: 2015 PhD Program: Health Sciences

Title: Rat models of Parkinson's disease: insights into the

treatment of refractory symptoms

Supervisor: Nuno Sousa

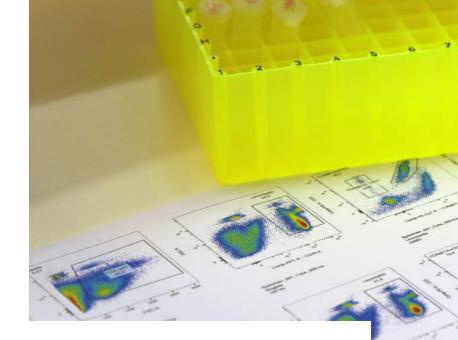
Student: José de Almeida Cotter Institution: Universidade do Minho Year of the PhD conclusion: 2015

PhD Program: Medicine

Title: Enteroscopia por cápsula e doença de Crohn:

Caminhos para a otimização

Supervisors: Nuno Sousa and Miguel Mascarenhas Saraiva



Student: Magda João Carlos Institution: Universidade do Minho Year of the PhD conclusion: 2015 PhD Program: Health Sciences

Title: "PhenoWorld": a new multidimensional strategy for

studying behaviour in rodents

Supervisors: Nuno Sousa and Vera Baumans

Student: Nuno Lamas

Institution: Universidade do Minho Year of the PhD conclusion: 2015

PhD Program: MD/PhD

Title: Harnessing the potential of pluripotent stem cells to develop novel platforms to study human motor neurons

in vitro

Supervisors: Chistopher Henderson; Hynek Wichterle and

Nuno Sousa

Student: Patrícia Terra

Institution: Universidade do Minho Year of the PhD conclusion: 2015 PhD Program: Health Sciences

Title: Looking for mechanisms regulating lung growth in

CDH: rat and human studies

Supervisors: Jorge Correia Pinto and Alan W. Flake

Student: Paulo César Marques Institution: Universidade do Minho Year of the PhD conclusion: 2015 PhD Program: Health Sciences Title: A network approach to brain aging through

multimodal neuroimaging Supervisor: Nuno Sousa Student: Pedro Miguel Cunha Institution: Universidade do Minho Year of the PhD conclusion: 2015

PhD Program: Medicine

Title: Study to determine the cardiovascular risk of the population of Guimarães/Vizela, including the prevalence of arterial stiffness and early vascular aging syndrome

Supervisor: Jorge Cotte

Student: Sandro Mesquita

Institution: Universidade do Minho Year of the PhD conclusion: 2015 PhD Program: Health Sciences

Title: Aging and Alzheimer's disease: Searching for novel

molecular cues

Supervisors: Fernanda Marques and Joana Palha

Student: Sara Duarte Silva

Institution: Universidade do Minho Year of the PhD conclusion: 2015 PhD Program: Health Sciences

Title: Searching for therapeutic strategies in a mouse model of Machado-Joseph disease: targeting

proteostases

Supervisor: Patrícia Maciel



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Industry contract research

In 2015, the ICVS has had the following ongoing Research Contracts:

- 1. TECNIMEDE Sociedade Técnico Medicinal, SA: the studies are designed to characterize the pharmacological activity of drugs in the control of pain in animals with traumatic neuropathy. Armando Almeida (coordinator);
- 2. TECNIMEDE Sociedade Técnico Medicinal, SA: Study of Antidepressant properties of pirlindol an animal model Chronic Mild stress. João Bessa (coordinator);
- 2. FUNDAÇÃO BIAL: the studies are designed to analyze the neuro-glia interactions in complex cognitive functions. João Oliveira (coordinator);
- 3. FUNDAÇÃO BIAL: the studies are designed to analyze the temporal modulation of the subventricular zone neural stem cell niche by choroid plexus-cerebrospinal fluid derived factors. João Sousa (coordinator);
- 4. FUNDAÇÃO BIAL: the studies are designed to analyze the temporal modulation of the subventricular zone neural stem cell niche by choroid plexus-cerebrospinal fluid derived factors. João Sousa (coordinator);
- 5. FUNDAÇÃO BIAL: Gliogenesis control of brain plasticity, neurophysiology and cognitive function. Luísa Pinto (coordinator);
- 6. FUNDAÇÃO BIAL: The impact of lipid signalling modulation in cognition. Tiago Oliveira (coordinator).

Internationalization

Reflecting the high level of internationalization of the ICVS, researchers from around 20 foreign countries were included in the Institute's team in 2015.

Among the ICVS papers published in international peer-reviewed journals in 2015, more than 50% 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 (generating 162 communications in international congresses in 2015).

In 2015, the ICVS was involved in international networks with specific funding, including:

2 European FP7 research projects;

4 grants funded by other international institutions.

Globally, in 2015, the ongoing projects funded by international sources corresponded to a total amount of 1.6 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.

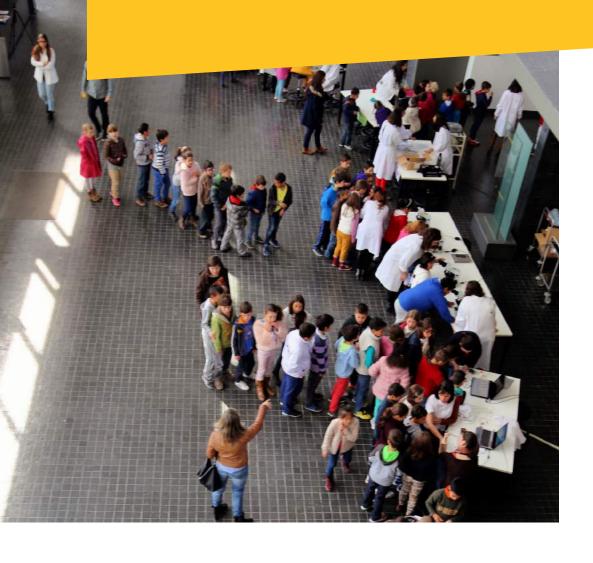
The international recognition of the ICVS research activities is also reflected by the granting of 12 International awards, including: ECNP Junior Scientists Symposia Invited Speaker, Amsterdam; Grant for the ECNP Workshop of Neuropsychopharmacology for Junior Scientists in Europe, Amsterdam; SPIE Medical Imaging 2015, Orlando, USA - Best poster Prize; SPIE Medical Imaging 2015, Orlando, USA - Honorable mention; 47th Annual Meeting of Canadian Association of Paediatric Surgeons, Niagara Falls, Canada - First Prize Winner for podium presentations; and COST Mye-Uniter - Best Poster Award.

The Post-graduation program of the ICVS/ECS promoted 51 international post-graduation courses that included the participation of 162 foreign students.



ACTIVITIES

OUTREACH ACTIVITIES



The program of outreach activities implemented by the ICVS and the ECS represents a joint strategy to promote scientific awareness in the surrounding community, namely 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 48 schools, since first year to the pre-university stage.

In 2015, the ICVS continued pursuing a strong activity in disseminating scientific awareness and public perception of science and technology. The activities were organized in 7 major events, involving more than 1800 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 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" and the "Summer in the campus". 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 the ECS named "Do you want to be a Medical student for one day?" and the "Open days for MSc and PhD candidates".

Overall, the ICVS activities were vastly publicized in a variety of media vehicles, including the main Portuguese journals, radio stations, information websites, several magazines with high circulation and different TV programs.

OTHER ACTIVITIES

INTERNAL SERVICES AND RESOURCES

At the ICVS facilities, all the scientific equipment from the installed technological platform is shared amongst the 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.

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 on the basis of 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 Core Facilities 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 Core Facilities, such as Histology, Microscopy and Animal Housing also provide external services.



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.

RESEARCH DOMAIN: MICROBIOLOGY AND INFECTION

OBJECTIVES & ACHIEVEMENTS

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.



Main achievements

The MIRD has followed a policy of staff recruitment/ differentiation, counting presently with more than 60 members (including 18 PhDs) with multidisciplinary backgrounds, including biological sciences, engineering and medicine.

Research within the MIRD was supported by 2 projects funded by FCT, 1 QREN Integrated Program and 3 International projects.

During the year of 2015, researchers from MIRD published 37 papers in international peer-reviewed journals, including 24 in Q1, with an average IF of 4.88.

Researches within the MIRD were granted with 4 National and 1 International scientific awards, including: the COST Mye-Uniter - Best Poster Award; and the "Prémio Robalo Cordeiro-SPP/Novartis" for the work Validating Evolving Mycobacterium tuberculosis T Cell Antigens for Vaccine Development.

The MIRD organized 2 scientific meetings [11th IMYA (International Meeting on Yeast Apoptosis), XLI meeting da Sociedade Portuguesa de Imunologia] and 3 post-graduation courses/workshops (Autophagy in Health and Disease; Fundamentals in Immunology and Infection;

Bioinformatics in Health Sciences) and graduated 1 PhD-student and 6 MSc-students. In addition, MIRD members were involved in 22 conferences and seminars in the context of international meetings outside Portugal (35 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 States of America, Benin, Mozambique and Dominican Republic.







Research line outputs

Selected publications in peer review journals:

- Appelberg R, Moreira D, Barreira-Silva P, Borges M, Silva L, Dinis-Oliveira RJ, Resende M, Correia-Neves M, Jordan M, Ferreira N, Abrunhosa A, Silvestre R. "The Warburg effect in mycobacterial granulomas is dependent on the recruitment and activation of macrophages by gamma interferon". Immunology. Aug;145(4):498-507 (2015).
- Bruchfeld J, Correia-Neves M, Källenius G. "Tuberculosis and HIV coinfection". Cold Spring Harb Perspect Med. Feb 26;5(7) (2015).
- Capela C, Sopoh GE, Houezo JG, Fiodessihoué R, Dossou AD, Costa P, Fraga AG, Menino JF, Silva-Gomes R, Ouendo EM, Rodrigues F, Pedrosa J. "Clinical epidemiology of Buruli ulcer from Benin (2005-2013): effect of time-delay to diagnosis on clinical forms and severe phenotypes". PLoS Negl Trop Dis. Sep 10;9(9):e0004005 (2015).
- Cardoso F, Castro F, Moreira-Teixeira L, Sousa J, Torrado E, Silvestre R, Castro AG, Saraiva M, Pais TF. Myeloid Sirtuin
 Expression Does Not Impact Long-Term Mycobacterium tuberculosis Control. PLoS One. Jul 2;10(7):e0131904 (2015).
- Cardoso MS, Silva TM, Resende M, Appelberg R, Borges M. "Lack of the transcription factor hypoxia-inducible factor (HIF)-1⊠ in macrophages accelerates the necrosis of Mycobacterium avium-induced granulomas". Infect Immun. Sep;83(9):3534-44 (2015).
- Carvalho A, Costa P, Triunfante V, Branca F, Rodrigues F, Santos CL, Correia-Neves M, Saraiva M, Lecour H, Castro AG, Pedrosa J, Osório NS. "Analysis of a local HIV-1 epidemic in Portugal highlights established transmission of non-B and non-G subtypes". J Clin Microbiol. May;53(5):1506-14 (2015).
- Costa I, Carvalho F, Magalhães T, Pinho PG, Silvestre R, Dinis-Oliveira RJ. "Promising blood-derived biomarkers for estimation of the postmortem interval". Toxicol Res. 4(6):1443-1452 (2015).

- Cruz A, Torrado E, Carmona J, Fraga AG, Costa P, Rodrigues F, Appelberg R, Correia-Neves M, Cooper AM, Saraiva M, Pedrosa J, Castro AG. "BCG vaccination-induced long-lasting control of Mycobacterium tuberculosis correlates with the accumulation of a novel population of CD4+IL-17+TNF+IL-2+ T cells". Vaccine. Jan 1;33(1):85-91 (2015).
- Cunha C, Monteiro AA, Oliveira-Coelho A, Kühne J, Rodrigues F, Sasaki SD, Schio SM, Camargo JJ, Mantovani A, Carvalho A, Pasqualotto AC. "PTX3-based genetic testing for risk of aspergillosis after lung transplant". Clin Infect Dis. Dec 15;61(12):1893-4 (2015).
- Fernandes Â, Azevedo MM, Pereira O, Sampaio-Marques B, Paiva A, Correia-Neves M, Castro I, Ludovico P. "Proteolytic systems and AMP-activated protein kinase are critical targets of acute myeloid leukemia therapeutic approaches". Oncotarget. Oct 13:6(31):31428-40 (2015).
- Garcia J, Costa VM, Carvalho AT, Silvestre R, Duarte JA, Dourado DF, Arbo MD, Baltazar T, Dinis-Oliveira RJ, Baptista P, de Lourdes Bastos M, Carvalho F. "A breakthrough on Amanita phalloides poisoning: an effective antidotal effect by polymyxin B". Arch Toxicol. Dec;89(12):2305-23 (2015).
- Gomes V, Pala M, Salas A, Álvarez-Iglesias V, Amorim A, Gómez-Carballa A, Carracedo Á, Clarke DJ, Hill C, Mormina M, Shaw MA, Dunne DW, Pereira R, Pereira V, Prata MJ, Sánchez-Diz P, Rito T, Soares P, Gusmão L, Richards MB. "Mosaic maternal ancestry in the Great Lakes region of East Africa". Hum Genet. Sep;134(9):1013-27 (2015).
- Janganan TK, Chen G, Chen D, Menino JF, Rodrigues F, Borges-Walmsley MI, Walmsley AR. "A G⊠ protein and the TupA Co-Regulator Bind to Protein Kinase A Tpk2 to Act as Antagonistic Molecular Switches of Fungal Morphological Changes". PLoS One. Sep 3;10(9):e0136866 (2015).

- Lopes Santos C, Nebenzahl-Guimaraes H, Mendes MV, van Soolingen D, Correia-Neves M. To Be or Not to Be a Pseudogene: A Molecular Epidemiological Approach to the mclx Genes and Its Impact in Tuberculosis. PLoS One. 10(6):e0128983 (2015).
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RESEARCH DOMAIN: **NEUROSCIENCES**

OBJECTIVES & ACHIEVEMENTS

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.





Main achievements

The NERD has followed a policy of staff recruitment/ differentiation that combines the balance of keeping the very best researchers for its research goals and renewing its members. Presently, the team is composed by 36 PhDs and a total of 138 members with multidisciplinary backgrounds, including biological sciences, engineering and medicine.

Research within the NERD was supported by 11 projects funded by FCT, 1 QREN Integrated Program, 2 FP7 grants, 6 contracts with industry, 2 International projects and 4 National projects.

During the year of 2015, researchers from NERD published 83 papers in international peer-reviewed journals, including 49 in Q1, with an average IF of 4.49, of which 2 papers were published in journals with an IF≥10.

Researchers within the NERD were granted with 3 National and 3 International scientific awards, including: the ECNP Junior Scientists Symposia Invited Speaker, Amsterdam; and the Grant for the ECNP Workshop of Neuropsychopharmacology for Junior Scientists in Europe, Amsterdam.

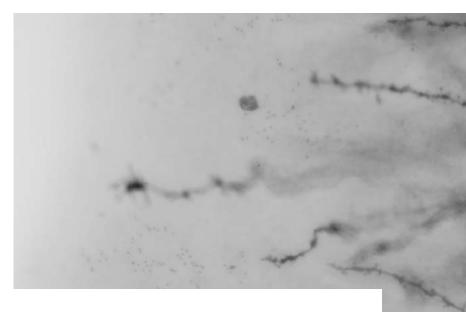
The NERD organised 2 scientific meetings and 12 postgraduation courses/workshops and graduated 8 PhDstudents and 7 MSc-students. In addition, NERD members were involved in 25 conferences and seminars in the context of international meetings outside Portugal (56 presentations/communications).

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

Research line outputs

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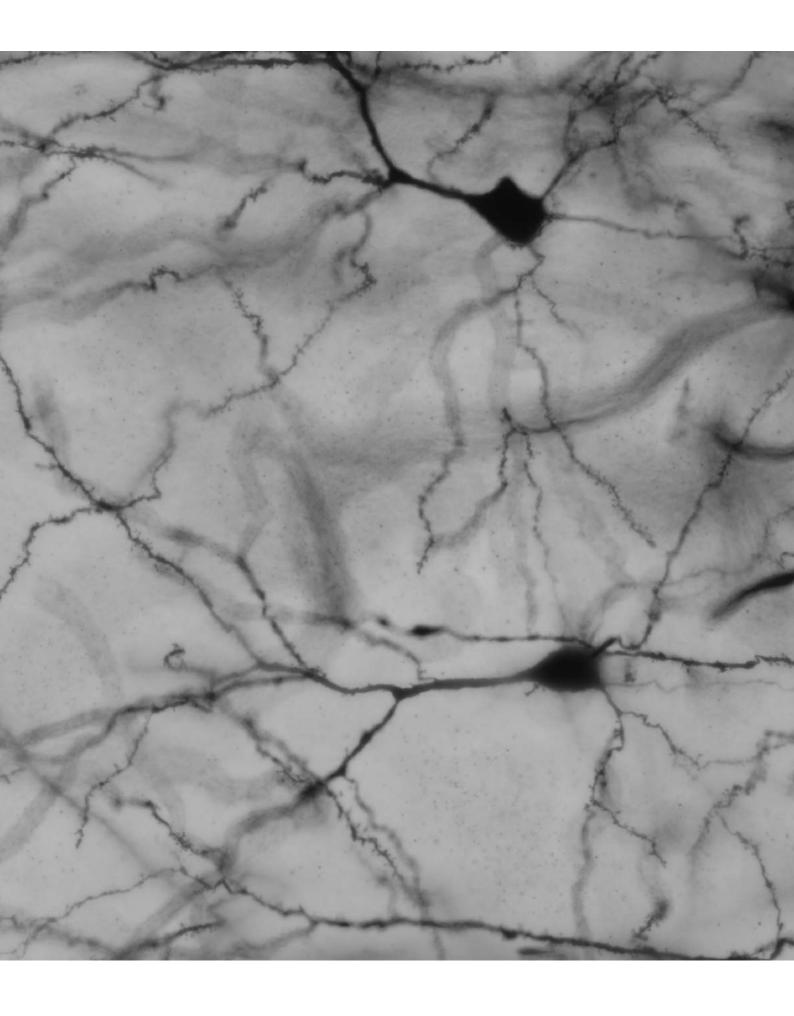
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RESEARCH DOMAIN: SURGICAL SCIENCES

OBJECTIVES & ACHIEVEMENTS

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.





Main achievements

Research within the SSRD was supported by 3 projects funded by FCT, 1 QREN Integrated Program and 1 International project

During the year of 2015, researchers from SSRD published 70 papers in international peer-reviewed journals, including 35 in Q1, with an average IF of 4.57.

Researchers within the SSRD were granted with 6 National and 8 International scientific awards, including: the SPIE Medical Imaging 2015, Orlando, USA - Best poster Prize; the SPIE Medical Imaging 2015, Orlando, USA - Honorable mention; the 47th Annual Meeting of the Canadian Association of Paediatric Surgeons, Niagara Falls, Canada - First Prize Winner for podium presentations; and the "Prémio Novo Banco" - Prémio Nacional de Inovação 2015: Stent biodegradável.

The SSRD organized 24 scientific meetings and 30 post-graduation courses/workshops and graduated 1 PhD-student. In addition, SSRD members were involved in 60 conferences and seminars in the context of international meetings outside Portugal (71 presentations/communications).

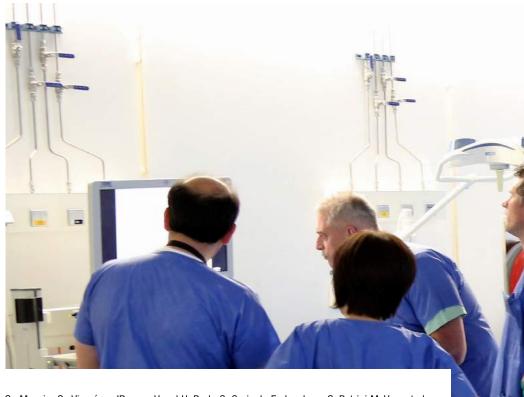
In line with the previous year, we kept reinforcing the translational/clinical research by fortifying our effective collaborations with clinicians in Portugal, France, Belgium, Germany, Hungary, Italy, Spain, Sweden, Switzerland, United Kingdom, Canada and United States of America.

Research line outputs

Selected publications in peer review journals

- Afonso J, Santos LL, Miranda-Gonçalves V, Morais A, Amaro T, Longatto-Filho A, Baltazar F. CD147 and MCT1 Potential partners in bladder cancer aggressiveness and cisplatin resistance. Molecular Carcinogenesis. 54:1451—66 (2015).
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PILOT RESEARCH LINES

COMMUNITY HEALTH

Objectives and Achievements

The pilot research line on Community Health was established in 2014.

The current objectives of the team are to develop 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 ECS 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 (GRESP / APMGF) and the International Primary Care Respiratory Group (IPCRG).



EDUCATION ON LIFE AND HEALTH SCIENCES

Objectives and Achievements

The pilot research line on Education on Life and Health Sciences was established in 2014.

The current objectives of the team are to develop a program of research to address international contemporary questions on health sciences education with a particular focus on the medical degree of the University of Minho and to consolidate and expand the research projects already being developed by the medical education unit of the ECS.

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 ECS, 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 Heath Sciences of the University of Minho (ELECSUM) that was initiated in 2001.



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