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# ICVS

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ANNUAL REPORT 2014

**ICVS**  
Life and Health Sciences Research Institute  
Instituto de Investigação em Ciências da Vida e Saúde



Universidade do Minho  
Escola de Ciências da Saúde



**ICVS/3B's**  
Associate  
Laboratory

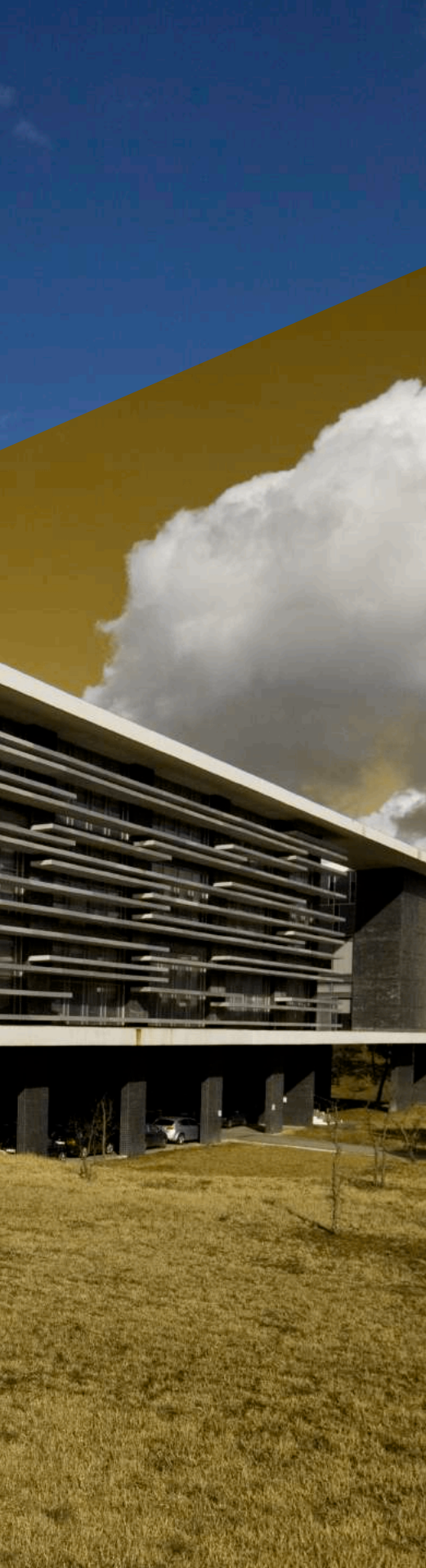
# ICVS



ANNUAL REPORT 2014







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## INTRODUCTION

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ICVS/3B'S – ASSOCIATE LABORATORY

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## ICVS

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OBJECTIVES AND ACHIEVEMENTS

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GROUP PRODUCTIVITY

Publications in peer review journals

PhD theses completed

Organization of courses/workshops

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## ACTIVITIES

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OBJECTIVES AND ACHIEVEMENTS

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PhD theses completed

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OBJECTIVES AND ACHIEVEMENTS

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RESEARCH LINE OUTPUTS

Selected publications in peer review journals

PhD theses completed

46

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OBJECTIVES AND ACHIEVEMENTS

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RESEARCH LINE OUTPUT

Selected publications in peer review journals

PhD theses completed

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# INTRODUCTION



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 (2CABraga), 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 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.



# ICVS

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## OBJECTIVES & ACHIEVEMENTS

### Objectives

The Life and Health Sciences Research Institute (ICVS) 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 fast 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, 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 2014 WERE TO:

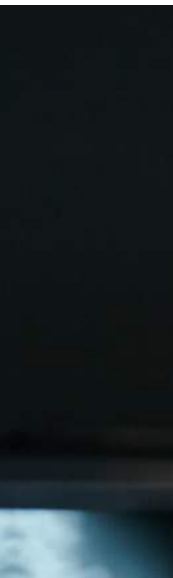
- develop flexible and integrated functional models that endorse multidisciplinary R&D projects, actively promoting the interplay Health-Sciences/Technologies
- involving the ICVS's researchers, health professionals from the 2CA-Braga, as well as researchers from the 3B's research group, on: i) the Research 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 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 and foster the creation of a new Spin-Off;
- 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 (e.g. Health Cluster Portugal and EU FP7);
- apply to the second FCT call of Doctoral Programs and obtain funding for, at least, one of the ECS/ICVS programs;
- expand the process of certification/accreditation of procedures within the ICVS, from the animal facility activities to the overall activities of the institute;
- implement a specific Program of International Seminars, with leading scientists from foreign Institutions, to complement the existing 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 2014

### MAIN ACHIEVEMENTS IN 2014 WERE:

- the increase in the impact of the ICVS scientific outputs, reflected in the average impact factor of the publications in international peer-reviewed journals;
- the increase in the number and in the impact of the clinical studies developed in the 2CABraga, including clinical trials;
- the approval of the project for the construction of the “Biotério” animal facility;
- the approval of two applications in the context of the call “FCT Doctoral Programs”;
- the launching of the Spin-off “Enlightenment”;
- the implementation of the Program of International Seminars “ICVS Seminar Series”;
- the establishment of joint research grants within the ICVS/3B’s AL;
- the involvement of a high number of MD students in the ICVS research activities;
- the increase in the number of Advanced Post-Graduation Courses;

### SPECIFICALLY, IN 2014, THE ICVS WAS ABLE TO:

- Significantly increase the Impact Factor (IF) of the ICVS publications, corresponding to an average IF of 5.1 among the 122 publications produced by the three Research Domains;
- Publish a total of 139 papers in international peer-reviewed journals (referenced in ISI, Scopus or in Pubmed). In addition, 6 international book chapters were published. Among the articles published in 2014, 122 were produced within the three research domains (Microbiology and Infection, Neurosciences and Surgical Sciences), corresponding to 75% in Q1-Q2 and to 50% in Q1, with an average IF of 5.1. Additionally, 17 articles were published in the fields of Education on Life and Health Sciences and on Community Health, as well as other related areas. Furthermore, globally, the activities of the ICVS/3B’s AL resulted in the publication of 222 articles (referenced in ISI, Scopus or in Pubmed);

- Develop clinical research with a growing impact, through the 2CA-Braga, in partnership with the Hospital of Braga and the ReferenceProfile, including clinical trials in collaboration with international industrial leading partners. This strategy potentiated the capacity of the ICVS to provide specialized services in the testing of new therapies, with 24 clinical trials ongoing in 2014, assuming a leading position in the National context, with more than 30% of the clinical trials run in Portugal. Additionally, the 2CA-Braga achieved the following goals: 23 clinical research projects in partnership with the ICVS and other research institutions from the UMinho (with projects funded by the European Commission - FP7 - or nationally, by the FCT); 30 observational studies; and 1 validation study of medical devices;

- Trigger the construction of the “Biotério” animal facility, a major accomplishment in 2014. 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 being solved with the beginning of the construction of the “Biotério” in the adjacent area of the ECS/ICVS building;

- Achieve the granting of specific funding for two FCT Doctoral Programs: the PhD Program in Advanced Therapies for Health (a joint PhD Program between the ICVS and the 3B’s) and the Doctoral Program in Health Sciences (a partnership with leading companies in the Biotech/Health fields in Portugal);

- Launch the spin-off “Enlightenment”, devoted to the development of portable medical devices for diagnosis and monitoring of vital parameters;

- Implement a specific and structured Program of International Seminars that complemented the existing Seminars “Ciência Falada”, involving the participation of leading scientists from foreign Institutions. A working group has been created to implement this specific Program of International Seminars and to prepare the program-type for the Seminar Series;

- Establish research grants 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 these two research groups that constitute the AL;
- Keep actively involved in R&D activities a differentiated research team of 276 members, including 93 PhDs and 183 post-graduation students (99 PhD students, 32 Master students and 52 research assistants), supported by 22 non-academic staff (7 administrative and 15 specialized technicians, with salaries supported by the ECS);
- Create the experimental conditions for the conclusion of 14 PhD theses, including 5 from MDs, and obtained 11 new fellowships granted in the FCT National call (7 BPD and 4 BD), in addition to PhD fellowships associated with the 4 ECS/ICVS Doctoral Programs funded by the FCT;
- Foster collaborations between its researchers and partners from Biomedical Industries. In 2014, 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 11 National and 17 International scientific awards, including: the Early Career Award, granted by the Education and Training Committee - International Society of Behavioral Medicine; the Newton Freire-Maia Award in genetics and human evolution and medical genetics; the SpinUM Award – Concurso de Ideias, TecMinho; the Research Grant ESCMID/ FEMS 2014, granted by the Executive Board of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the Executive Council of the Federation of European Microbiological Societies (FEMS); and the Young Investigator Award, granted by the American Association of Immunologists;
- Increase the competitive funding of ongoing projects (3 years average): 11.9 million € (from 11.2 million € in 2013), of which 2.7 million € corresponded to 2014 activities;
- Increase the competitive funding with new research projects granted, including: 5 projects submitted to the last FCT call (0.36 million €); 1 project in the context of QREN Integrated Program (2.5 million €); Private Foundations and Industry (0.06 million €); 3 projects from other international sources (0.07 million €); 1 project from other national sources (0.2 million €);
- Pursue its policy of fostering an active involvement of medical students and MDs within the ICVS research projects, involving a high number of MD students in research, including 48 Option Projects and 32 MD/PhD Lab Rotations;
- Organize an increasing number of Advanced Post-Graduation Courses/Workshops (from 40 in 2013 to 46 in 2014), involving 1021 participants (including 74% MDs, 17% of researchers from Biological Sciences fields and 4% of other Health Professionals). Importantly, 44% of the participants rated the attended courses as “Excellent” and 43% rated as “Very Good” and some of the courses were part of training activities of European schools or within 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 2990 participants and involved up to 60 ICVS researchers.

# GROUP PRODUCTIVITY

## Publications in peer review journals

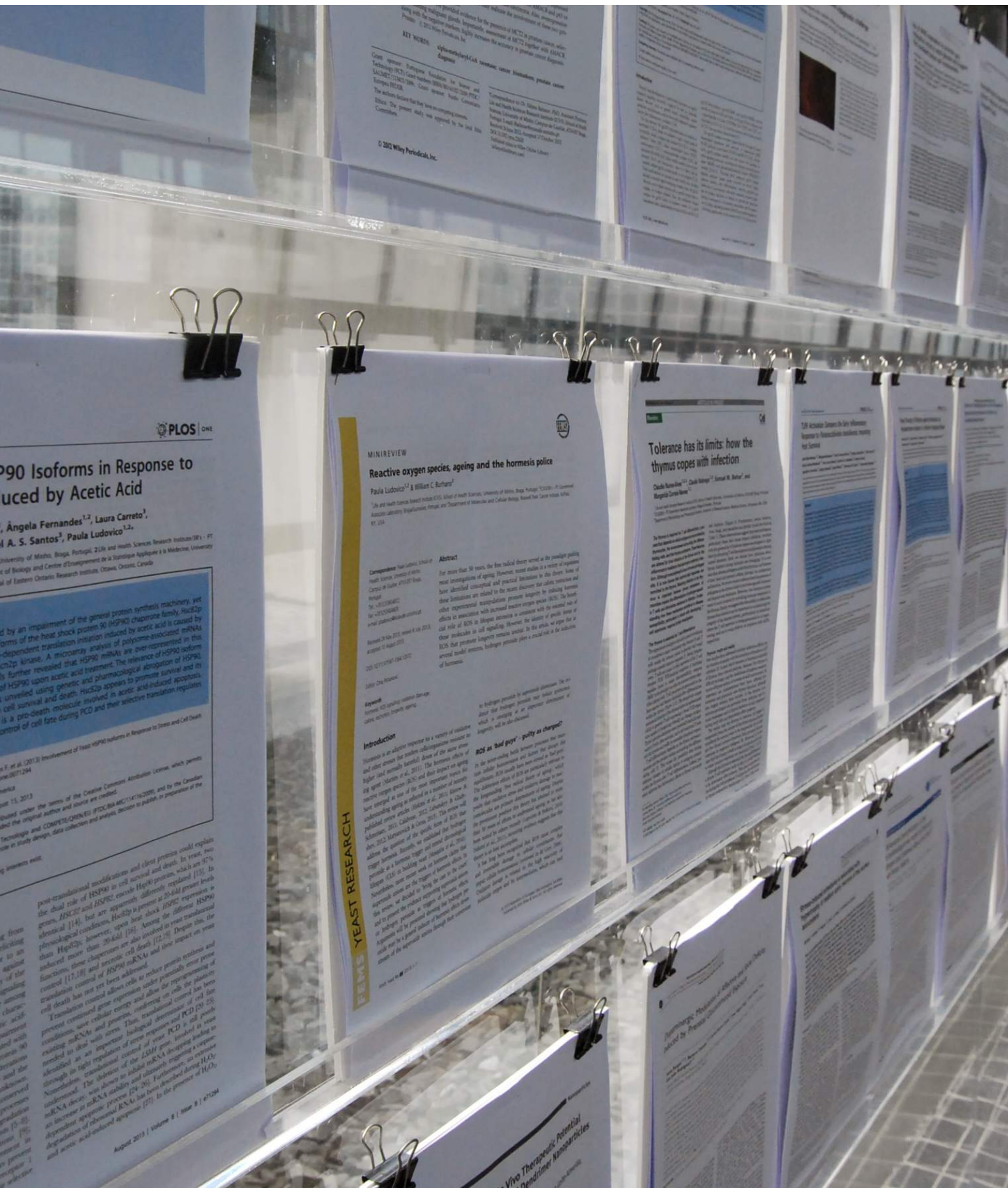
In 2014, the ICVS published 139 papers in international peer-reviewed journals (referenced in ISI, Scopus or in Pubmed). In addition, 6 international book chapters were published.

Among the articles published in 2014, 122 were produced within the three research domains, corresponding to 75% in Q1-Q2 and to 50% in Q1, with an average Impact Factor (IF) of 5.1 (including articles with IF between 3 and 5 = 48 papers; IF between 5 and 10 = 13 papers; IF between 10 and 20 = 5 papers; and IF>20 = 3 papers). Additionally, 17 articles were published in the fields of Education on Life and Health Sciences and on Community Health and other related areas.

### 30 SELECTED PAPERS IN PEER REVIEW JOURNALS

1. Cunha C, Aversa F, Lacerda JF, Busca A, Kurzai O, Grube M, Loffler J, Maertens JÁ, Bell AS, Inforzato A, Barbati E, Almeida B, Sousa PSE, Barbui A, Potenza L, Caira M, Rodrigues F, Salvatori G, Pagano L, Luppi M, Mantovani A, Velardi A, Romani L, Carvalho A. Genetic PTX3 Deficiency and Aspergillosis in Stem-Cell Transplantation. *The New England Journal of Medicine*; 370(5):421-432 (2014) (IF=54.42)
2. Nunes-Alves C, Booty MG, Carpenter SM, Jayaraman P, Rothchild AC, Behar SM. In search of a new paradigm for protective immunity to TB. *Nature Reviews Microbiology*. 12(4):289-299 (2014) (IF=23.317)
3. Lima A, Sardinha VM, Oliveira AF, Reis M, Mota C, Silva MA, Marques F, Cerqueira JJ, Pinto L, Sousa N, Oliveira JF. Astrocyte pathology in the prefrontal cortex impairs the cognitive function of rats. *Molecular Psychiatry*. 19(7): 834-841 (2014) (IF=15.147)
4. Opal MD, Klenotich SC, Morais M, Bessa J, Winkle J, Doukas D, Kay LJ, Sousa N, Dulawa SM. Serotonin 2C receptor antagonists induce fast-onset antidepressant effects. *Molecular Psychiatry*. 19(10):1106-1114 (2014) (IF=15.147)
5. Herbert A, Cruickshank JK, Laurent S, Boutouyrie P, Reference Values for Arterial Measurements Collaboration. Establishing reference values for central blood pressure and its amplification in a general healthy population and according to cardiovascular risk factors. *European Heart Journal*. 35(44):3122-33 (2014). (IF = 14,723)





# HSP90 Isoforms in Response to Acetic Acid

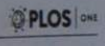
Angela Fernandes<sup>1,2</sup>, Laura Carreto<sup>3</sup>, A. S. Santos<sup>2</sup>, Paula Ludovico<sup>1,2,4</sup>

University of Minho, Braga, Portugal, 2Life and Health Sciences Research Institute (I3S) - PT, 3Centre of Biology and Centre of Environment and Statistical Application in Medicine, University of Eastern Ontario Research Institute, Ottawa, Ontario, Canada

...ed by an impairment of the general protein synthesis machinery, yet forms of the heat shock protein 90 (HSP90) chaperone class, Hsc27p dependent translation initiation induced by acetic acid is caused by HSP90 isoforms. A microarray analysis of polyome-associated mRNAs further revealed that HSP90 mRNAs are over-represented in this HSP90 upon acetic acid treatment. The relevance of HSP90 to cell survival and death. Hsc27p appears to promote survival and its is a pro-death molecule involved in acetic acid-induced apoptosis control of cell fate during PCD and their selective translation regulates

...F. et al. (2013) Involvement of Heat Shock Protein 90 Isoforms in Response to Stress and Cell Death

...post-translational modifications and client proteins could explain the dual role of HSP90 in cell survival and death. In yeast, two genes, *HSC27* and *HSC28*, encode Hsp90 proteins, which are 97% identical [14], but are differently regulated [15]. In physiological conditions, Hsc27p is present at 20-fold greater level than Hsc28p; however, upon heat shock HSP90 expression is transcriptionally repressed and also involved in yeast translational control [17,18] and necrotic cell death [12,9]. Despite this, the translation control of HSP90 mRNAs and their impact on yeast cell death has not yet been addressed. Translation control allows cells to reduce protein error prone proteins, save cellular energy and allow the reprogramming of existing mRNAs and proteins, conferring on cells the plasticity needed to deal with stress. Thus, translational control has been identified as an important biological phenomenon and PCD [20-23] through its tight regulation of stress responses and cell fate. Nevertheless, translational control of stress PCD is still poorly understood. The inhibition of the *ASH1* gene, involved in yeast mRNA decay, was shown to inhibit mRNA degrading leading to an increase in mRNA stability and ultimately resulting in a competitive response process [24-26]. Furthermore, an extensive degradation of ribosomal RNAs has been described during H<sub>2</sub>O<sub>2</sub> and acetic acid-induced apoptosis [27]. In the presence of H<sub>2</sub>O<sub>2</sub>



**MINIREVIEW**

## Reactive oxygen species, ageing and the hormesis police

Paula Ludovico<sup>1,2</sup> & William C. Burkhardt<sup>3</sup>

<sup>1</sup>Life and Health Sciences Research Institute (I3S), School of Health Sciences, University of Minho, Braga, Portugal, <sup>2</sup>IC3S - I3S, University of Eastern Ontario Research Institute, Ottawa, Ontario, Canada, <sup>3</sup>Department of Molecular and Cellular Biology, Rosalind Franklin Cancer Institute, Ry, USA

**Abstract**

For more than 50 years, the free radical theory served as the paradigm guiding most investigations of aging. However, recent studies in a variety of organisms have identified conceptual and practical limitations in this theory. Some of these limitations are related to the recent discovery that caloric restriction and other interventions with increased longevity present analogous to inducing hormesis effects in association with increased massive organismal stress. The hormesis effects in association with increased massive organismal stress are of central role in cell survival. However, the identity of specific genes or molecules that mediate this cell survival remains unclear. In this article, we argue that ROS that promote longevity remain unclear. In this article, we argue that ROS that promote longevity remain unclear. In this article, we argue that ROS that promote longevity remain unclear.

**Introduction**

Hormesis is an adaptive response to a variety of oxidative stressors and other stressors that produce deleterious effects. The hormesis effect is higher than normally harmful. Some of the most striking examples of hormesis are seen in the response to oxidative stress. Oxidative stress is a major cause of aging and its effects are mediated by reactive oxygen species (ROS) and their impact on aging have been extensively studied in a variety of organisms. In this review, we will discuss the role of ROS in aging and the hormesis effect. We will also discuss the role of ROS in aging and the hormesis effect.

**ROS as 'bad guys' - guilty as charged?**

In the 1950s, the free radical theory of aging was proposed. It suggested that ROS were the main cause of aging and that antioxidants would be beneficial. However, recent studies have shown that ROS are not always 'bad guys' and that they can have beneficial effects. In this review, we will discuss the role of ROS in aging and the hormesis effect.

## Tolerance has its limits: how the thymus copes with infection


Cláudia Ferreira<sup>1,2</sup>, Cláudia Sáez<sup>1,2</sup>, Samuel M. Barata<sup>1,2</sup>, and Margarida Carneiro<sup>1,2</sup>

**Abstract**

The thymus is a primary lymphoid organ that is essential for the development of the adaptive immune system. It is a site of high cellular turnover and is highly sensitive to infection. In this review, we will discuss the role of the thymus in the immune system and how it copes with infection.

**Introduction**

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6. Zecchini V, Madhu B, Russell R, Pértega-Gomes N, Warren A, Gaude E, Borlido J, Stark R, Ireland-Zecchini H, Rao R, Scott H, Boren J, Massie C, Asim M, Brindle K, Griffiths J, Frezza C, Neal DE, Mills IG. Nuclear ARRB1 induces pseudohypoxia and cellular metabolism reprogramming in prostate cancer. *EMBO Journal*. 33(12): 1365-1382 (2014) (IF=10.748)
  7. Silva NA, Sousa N, Reis RL, Salgado AJ. From basics to clinical: A comprehensive review on spinal cord injury. *Progress in Neurobiology*. 114:25-57. (2014) (IF= 10.301)
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  9. Mesquita SD, Ferreira AC, Falcao AM, Sousa JC, Oliveira TG, Correia-Neves M, Sousa N, Marques F, Palha JA. Lipocalin 2 modulates the cellular response to amyloid beta. *Cell Death and Differentiation*. 21(10):1588-1599 (2014) (IF= 8.385)
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25. Sotiropoulos I, Lopes AT, Pinto V, Lopes S, Carlos S, Duarte-Silva S, Neves-Carvalho A, Pinto-Ribeiro F, Pinheiro S, Fernandes R, Almeida A, Sousa N, Leite-Almeida H. Selective impact of Tau loss on nociceptive primary afferents and pain sensation. *Experimental Neurology*. 261:486-493 (2014) (IF= 4.617)
26. Sampaio A, Soares JM, Coutinho J, Sousa N, Gonçalves ÓF. The Big Five default brain: functional evidence. *Brain Structure & Function*. 219(6):1913-1922. (2014) (IF=4.567)
27. Teixeira-Coelho M, Guedes J, Ferreirinha P, Howes A, Pedrosa J, Rodrigues F, Lai WS, Blackshear PJ, O'Garra A, Castro AG, Saraiva M. Differential post-transcriptional regulation of IL-10 by TLR2 and TLR4-activated macrophages. *European Journal of Immunology*. 44(3):856-866. (2014) (IF= 4.518)





28. Gama JB, Ohlmeier S, Martins TG, Fraga AG, Sampaio-Marques B, Carvalho MA, Proença F, Silva MT, Pedrosa J, Ludovico P. Proteomic Analysis of the Action of the Mycobacterium ulcerans Toxin Mycolactone: Targeting Host Cells Cytoskeleton and Collagen. *Plos Neglected Tropical Diseases*. 8(8):e3066. (2014) (IF= 4.489)

29. Silva-Carvalho R, Miranda-Goncalves V, Ferreira AM, Cardoso SM, Sobral AJFN, Almeida-Aguiar C, Baltazar F. Antitumoural and antiangiogenic activity of Portuguese propolis in in vitro and in vivo models. *Journal of Functional Foods*. 11:160-171. (2014) (IF= 4.480)

30. Veiga MI, Osório NS, Ferreira PE, Franzén O, Dahlstrom S, Lum JK, Nosten F, Gil JP. Complex Polymorphisms in the Plasmodium falciparum Multidrug Resistance Protein 2 Gene and Its Contribution to Antimalarial Response. *Antimicrobial Agents and Chemotherapy*. 58(12):7390-7397. (2014) (IF= 4.451)



## PhD thesis completed

1.

Student: Ana Horta

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

PhD Program: Medicine

Title: Regulatory CD4+Tcells in the immune reconstitution

HIV-infected individuals

Supervisors: Margarida Correia-Neves and Rui Sarmento e Castro

2.

Student: Andreia Carvalho

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

PhD Program: Health Sciences

Title: When gaining is losing: insights into the function of

ataxin-3 in neurons and its perturbation in the context of

Machado-Joseph disease

Supervisor: Patrícia Maciel

3.

Student: Diana Alexandra da Silva Amorim

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

PhD Program: Health Sciences

Title: Pronociception in experimental monoarthritis: the role

of galanin in descending pathways

Supervisors: Armando Almeida and Isaura Tavares

4.

Student: Herlander Marques

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

PhD Program: Medicine

Title: Herpes-Y virus and polymorphisms of antigen processing

systems: importance in the oncogenesis and in the prognosis

of B-cell lymphomas

Supervisors: Adhemar Longatto and Rui Medeiros

5.

Student: João Moreira Pinto

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

PhD Program: Medicine

Title: Hybrid Thoracic NOTES: a translational research project

Supervisors: Jorge Correia-Pinto and Carla Rolanda

6.

Student: José Bernardo Gama

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

PhD Program: Health Sciences

Title: Molecular cytopathogenesis induced by Mycobacterium

ulcerans toxin, mycolactone

Supervisors: Jorge Pedrosa and Paula Ludovico

7.

Student: José Miguel Soares

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

PhD Program: Health Sciences

Title: A multimodal neuroimaging approach to the interplay between stress and aging

Supervisor: Nuno Sousa

8.

Student: Luís Miguel Lopes

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

PhD Program: Medicine

Title: Needle-knife fistulotomy in deep biliary cannulation

Supervisors: Carla Rolanda and Mário Jorge Dinis-Ribeiro



9.

Student: Mazen Harb

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

PhD Program: Health Sciences

Title: Biobehavioural mechanisms of feeding behaviour: associative learning, hedonic preference and motivation

Supervisors: Nuno Sousa and Osborne Almeida

10.

Student: Miguel Carvalho

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

PhD Program: Health Sciences

Title: From Parkinson's disease to Dopamine Dysregulation Syndrome and Impulse Control Disorders: the balance of dopamine in brain function and behaviour

Supervisors: António Salgado and Nuno Sousa

11.

Student: Nelma Gomes

Institution: Universidade do Porto

Year of the PhD conclusion: 2014

PhD Program: Pathology and Molecular Genetics

Title: Role of monocarboxylate transporters in prostate carcinoma

Supervisors: Fátima Baltazar

12.

Student: Rui Quinta

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

PhD Program: Health Sciences

Title: Fabry disease: novel insights into secondary lipid alterations and invariant Natural Killer T cell deficiency

Supervisors: Rui Reis and Maria Clara Miranda

13.

Student: Shilan Aslani

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

PhD Program: Health Sciences

Title: Dissecting the crosstalk between stress, depression and obesity

Supervisors: Joana Palha and Nuno Sousa

14.

Student: Vítor Hugo Pereira

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

PhD Program: Medicine

Title: The impact of chronic stress on the cardiovascular system

Supervisors: João Cerqueira and Nuno Sousa



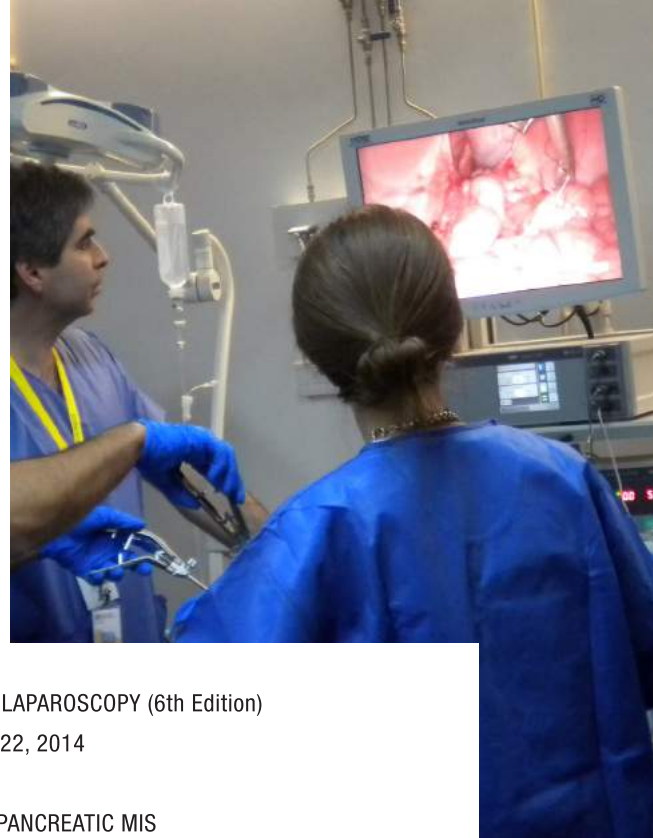




## Organization of courses/workshops

### CLINICAL TRAINING

- |   |   |
|---|---|
| <p>1. MEDICAL ACUPUNCTURE (2nd Edition)<br/>January 17 - June 29, 2014</p> <p>2. PREMIUM CATARACT SURGERY:<br/>ALL THAT YOU WANT TO KNOW<br/>January 18, 2014</p> <p>3. ONCOLOGY MEETINGS:<br/>GASTRIC CANCER - STATE OF ART<br/>March 27-28, 2014</p> <p>4. BASIC LAPAROSCOPY FOR RESIDENTS (6th Edition)<br/>March 28-29, 2014</p> <p>5. ADVANCED THERAPEUTIC ENDOSCOPY<br/>live porcine model hands-on EMR, RFA and ESD workshop<br/>March 31 - April 1, 2014</p> <p>6. ARTERIAL STIFFNESS AND EARLY VASCULAR AGING<br/>(3rd Edition)<br/>April 3-4, 2014</p> <p>FETAL AND NEONATAL ENDOSCOPIC SURGERY<br/>(6th Edition)<br/>April 7-9, 2014</p> | <p>7. WOUNDS AND MINOR SURGERY<br/>Pedro Leão, André Goulart, Hugo Rios, Mesquita Rodrigues<br/>April 28, 2014</p> <p>8. GYNECOLOGICAL LAPAROSCOPY (6th Edition)<br/>hands-on course with live porcine models<br/>May 8-10, 2014</p> <p>9. 2nd UPDATE IN SURGERY FOR FAMILY MEDICINE<br/>RESIDENTS<br/>May 10 - June 21, 2014</p> <p>10. SULCI, GYRI, VENTRICLES AND DISSECTING FIBERS<br/>(12th Edition)<br/>May 19-23, 2014</p> <p>11. SLEEP - SNORING AND OSAS: CLINICAL CONCEPTS<br/>June 3-4, 2014</p> <p>12. AROUND THE NOSE:<br/>ENDOSCOPIC SINUS SURGERY (3rd Edition)<br/>June 5, 2014</p> <p>13. AROUND THE NOSE:<br/>FUNDAMENTALS IN RHINOSEPTOPLASTY (3rd Edition)<br/>June 6, 2014</p> |
|---|---|



14. AROUND THE NOSE: SURGERY FOR SNORING AND OSAS (3rd Edition)  
June 7, 2014

15. FUNDAMENTALS IN ARTHROSCOPY (5th Edition)  
June 12-13, 2014

16. MASTERCLASS IN LAPAROSCOPIC RADICAL CYSTECTOMY (2nd Edition)  
July 8, 2014

17. MASTERCLASS IN LAPAROSCOPIC RADICAL PROSTATECTOMY (3rd Edition)  
July 9-10, 2014

18. MASTERCLASS IN ADVANCED 3D-VIDEO-ASSISTED UROLOGICAL SURGERY (5th Edition)  
July 11-12, 2014

19. PEDIATRIC ENDOSCOPY (4th Edition)  
September 16-17, 2014

20. PHARMACOLOGICAL BASIS OF RATIONAL THERAPEUTICS: ANTIBIOTHERAPY (4th Edition)  
September 26-27, 2014

21. THERAPEUTIC ENDOSCOPY (7th Edition)  
October 2-3, 2014

22. MICROSURGICAL ANASTOMOSIS (6th Edition)  
October 9-11, 2014

23. BILIARY LAPAROSCOPY (6th Edition)  
October 20-22, 2014

24. HEPATOPANCREATIC MIS  
October 23-24, 2014

25. MINIMALLY INVASIVE SPINE SURGERY (3rd Edition)  
November 14-15, 2014

26. BASIC LAPAROSCOPY FOR RESIDENTS (7th Edition)  
November 17-18, 2014

27. MASSIVE ROTATOR CUFF TEAR: FROM BASIC SCIENCE TO CLINICS (2nd Edition)  
November 21-22, 2014

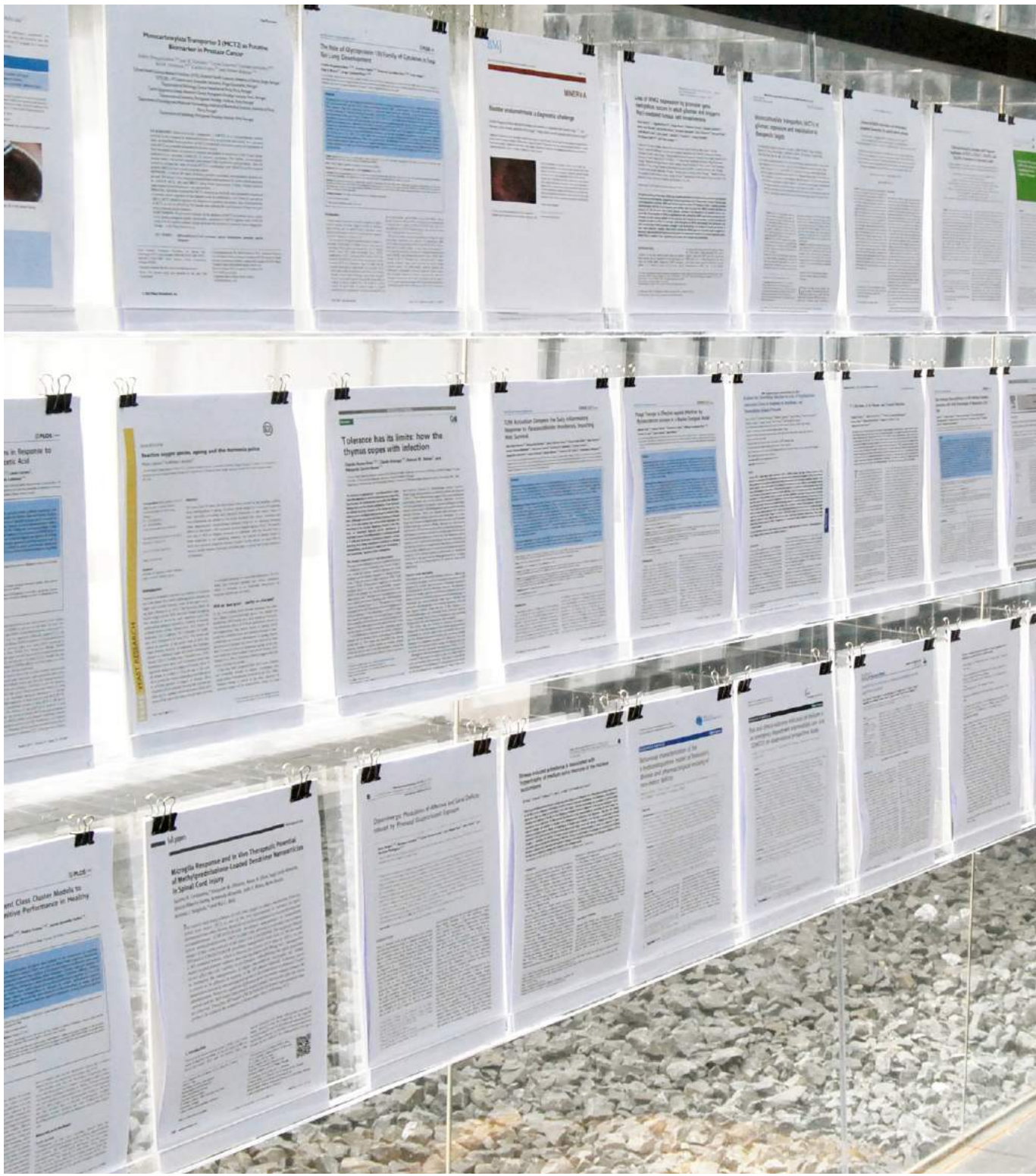
28. WOUNDS AND MINOR SURGERY (2nd Edition)  
November 24, 2014

#### BIOMEDICAL SCIENCES

29. BIostatISTICS IN HEALTH SCIENCES (4th Edition)  
January 6-17, 2014

30. A HANDS-ON APPROACH TO CELL AND TISSUE CULTURE from cell isolation, manipulation and characterization to advanced microscopy  
February 10-21, 2014









31. STEM CELLS GET PRACTICAL (4th Edition)  
approaches on stem cell isolation, characterization and  
differentiation  
March 10-14, 2014

32. NEW TARGETS IN NEURODEGENERATIVE DISEASES  
emphasis on advances in Alzheimer's disease research  
September 1-5, 2014

33. FUNDAMENTALS IN NEUROSCIENCE (7th Edition)  
September 15-27, 2014

34. FUNDAMENTALS IN IMMUNOLOGY AND INFECTION  
(6th Edition)  
September 29 - October 10, 2014

35. FUNDAMENTALS IN GENETICS, DEVELOPMENT AND  
NEOPLASIA (6th Edition)  
October 13-24, 2014

36. RESEARCH METHODOLOGIES (6th Edition)  
October 27 - November 7, 2014

37. BIOINFORMATICS IN HEALTH SCIENCES (6th Edition)  
November 10-21, 2014

38. LABORATORY ANIMAL SCIENCE (10th Edition)  
December 1-12, 2014

#### **TEACHING AND EDUCATION**

39. HOW TO TEACH 50, 100 OR MORE STUDENTS:  
WORKING WITH LARGE CLASSES  
February 17, 2014

40. HOW TO TEACH 50, 100 OR MORE STUDENTS:  
WORKING WITH LARGE CLASSES  
May 16, 2014

41. HANDS-ON INTRODUCTION TO THE SCIENTIFIC LITERATURE  
AND SEARCHING WITH PUBMED  
May 15, 2014

42. WRITING MULTIPLE CHOICE QUESTIONS FOR THE  
NATURAL AND CLINICAL SCIENCES  
May 15, 2014

43. CURRENT DEVELOPMENTS IN EMPATHY TEACHING  
AND RESEARCH IN THE HEALTH  
PROFESSIONS  
July 1, 2014

#### **BIostatISTICS**

44. METHODS FOR GROUPING VARIABLES WITH IBM SPSS  
STATISTICS (3rd Edition)  
April 3-4, 2014

45. TOPICS OF REGRESSION WITH IBM SPSS STATISTICS  
AND MATLAB (3rd Edition)  
May 7-9, 2014

46. TOPICS OF REGRESSION WITH IBM SPSS STATISTICS  
AND MATLAB (3rd Edition)  
June 11-12, 2014



## Industry contract research

In 2014, 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. 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. Biogen Idec Portugal: the studies are designed to develop a pre-clinical research study.

João Cerqueira (coordinator).

## Internationalization

Reflecting the high level of internationalization of the ICVS, researchers from 17 foreign countries were included in the Institute's team in 2014.

Among the ICVS papers published in international peer-reviewed journals during 2014, more than 45% 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 2014 (generating 166 communications in international congresses).

In 2014, the ICVS was involved in international networks with specific funding, including: 4 European FP7 research projects (3 Cooperation grants and 1 Marie Curie); 4 grants funded by other international institutions.

Globally, in 2014, the ongoing projects funded by international sources corresponded to a total amount of 1.8 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 17 International awards, including the Early Career Award, granted by the Education and Training Committee - International Society of Behavioral Medicine; the Newton Freire-Maia

Award in genetics and human evolution and medical genetics; the Research Grant

ESCMID/FEMS 2014, granted by the Executive Board of the European Society of Clinical

Microbiology and Infectious Diseases (ESCMID) and the Executive Council of the Federation of

the European Microbiological Societies (FEMS); and the Young Investigator Award, granted by

the American Association of Immunologists.

The Post-graduation program of the ICVS/ECS promoted 46 international post-graduation

courses that included the participation of 115 foreign students and 86 foreign Professors.



# 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 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 2014, the activities were organized in 8 major events: the “International Brain Awareness Week”, the “Science Outbreak Week”, the initiative “Science in School”, the visiting program to the ECS “Do you want to be an ECS student for a day”, the visiting program to the ECS “Summer in the Campus”, the “ABC in Surgical Sciences”, the initiative “Neurosciences in the Municipality of Barcelos” and the “Science and Technology Week”. These initiatives included interactive talks in schools, experimental activities at the ICVS laboratories, exhibitions, guided tours to the

ICVS facilities and seminars. Overall, these activities counted with more than 2990 participants and their organization and implementation involved up to 60 ICVS researchers.

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.

# OTHER ACTIVITIES

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## 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 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 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.







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## EXTERNAL SERVICES AND RESOURCES

The ICVS provides services to the general and the clinical communities. These external services were born from the knowledge developed by the ICVS researchers, with emphasis to the Molecular Diagnostics Service (SDM). The SDM includes a head-technician and a diagnostics technician amongst the dedicated staff and is fully equipped for molecular diagnostics. During the last years, the ICVS has been providing, to public and private Health services, genetic diagnostics of intellectual disability related disorders.

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

Additionally, through the 2CA-Braga - in partnership with the Hospital of Braga and the ReferenceProfile – 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 that ensure a professional management structure.

# RESEARCH DOMAIN: MICROBIOLOGY AND INFECTION

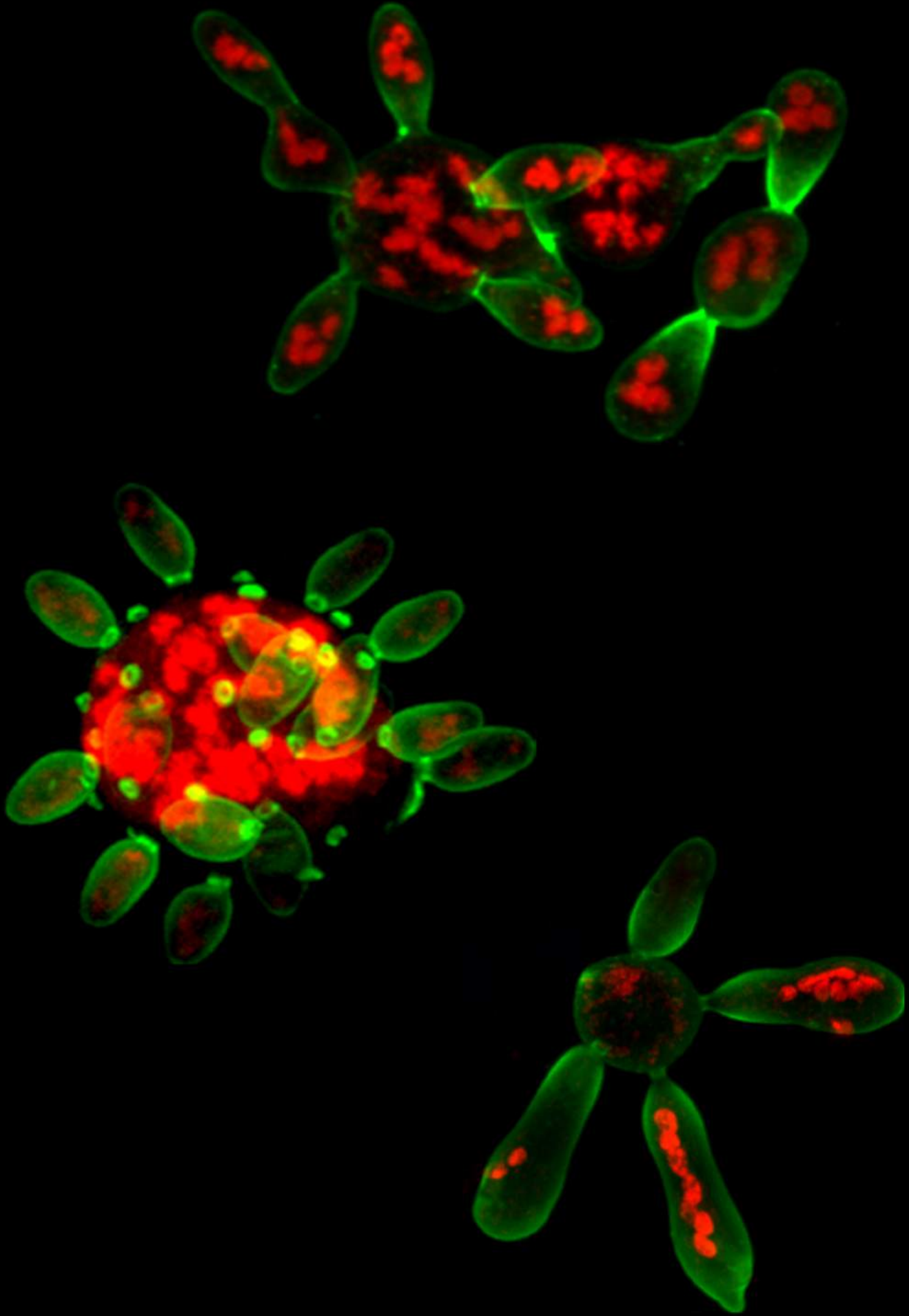
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## OBJECTIVES & ACHIEVEMENTS

### 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 more than 50 members with multidisciplinary backgrounds, including biological sciences, engineering and medicine.

Research within the MIRD was supported by 3 projects funded by FCT, 1 QREN Integrated Program, 1 FP7 grant and 1 additional International project.

During the year of 2014, researchers from MIRD published 21 papers in international peerreviewed journals, including 15 in Q1, with an average IF of 8.3, of which 2 papers were published in journals with an IF>10

Additionally, the MIRD submitted 11 abstracts to International Meetings.

Researchers within the MIRD were granted with 2 National and 4 International scientific awards, including: the Research Grant ESCMID/FEMS 2014, granted by the Executive Board of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the Executive Council of the Federation of European Microbiological Societies (FEMS); and the Young Investigator Award, granted by the American Association of Immunologists.

The MIRD organized 1 scientific meeting and 3 post-graduation courses/workshops and graduated 2 PhD-students and 5 MSc-students. In addition, MIRD members were involved in 11 conferences and seminars in the context of international meetings outside Portugal (11 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,



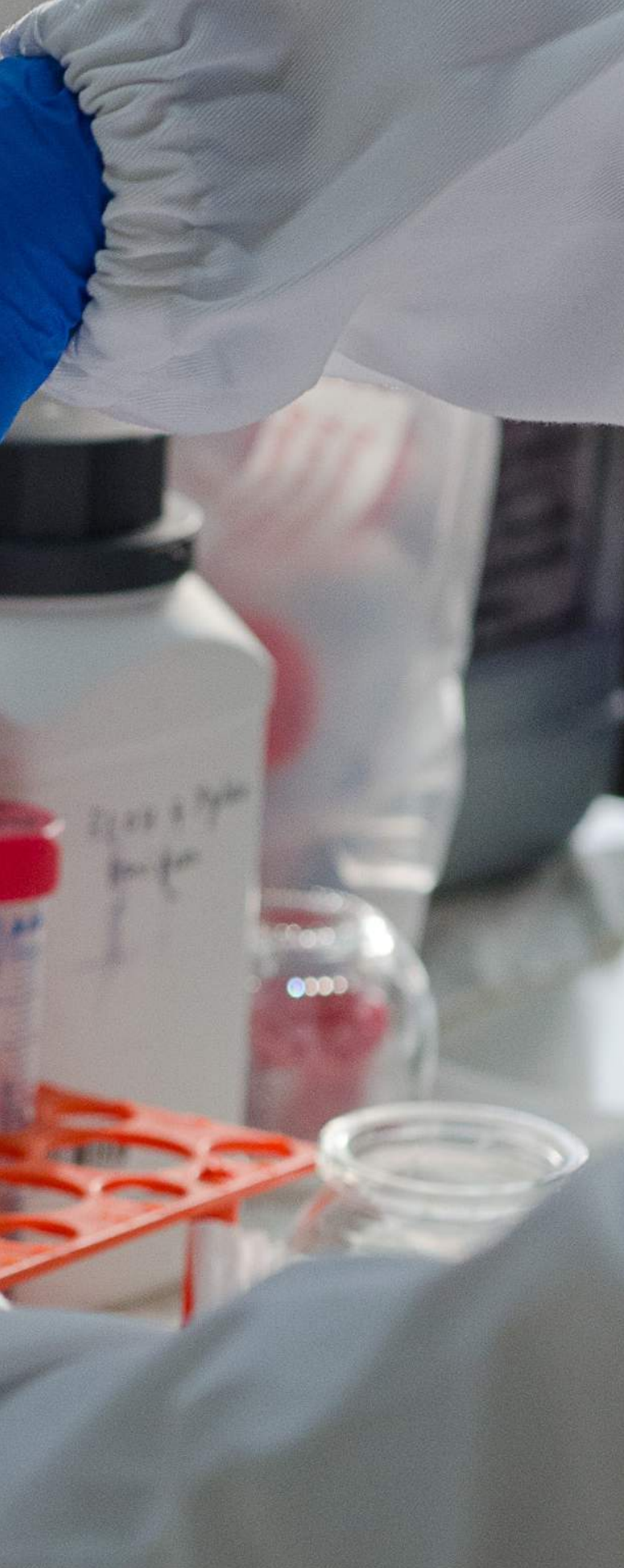


## Research line outputs

Selected publications in peer review journals:

1. Cunha C, Aversa F, Lacerda JF, Busca A, Kurzai O, Grube M, Loffler J, Maertens JA, Bell AS, Inforzato A, Barbati E, Almeida B, Sousa PSE, Barbui A, Potenza L, Caira M, Rodrigues F, Salvatori G, Pagano L, Luppi M, Mantovani A, Velardi A, Romani L, Carvalho A. Genetic PTX3 Deficiency and Aspergillosis in Stem-Cell Transplantation. *The New England Journal of Medicine*. 370:421-32 (2014). (IF = 54,42)
2. Nunes-Alves C, Booty MG, Carpenter SM, Jayaraman P, Rothchild AC, Behar SM. In search of a new paradigm for protective immunity to TB. *Nature Reviews Microbiology*. 12(4):289-99 (2014). (IF = 23,317)
3. Rothchild AC, Jayaraman P, Nunes-Alves C, Behar SM. INKT Cell Production of GM-CSF Controls Mycobacterium tuberculosis. *PLoS Pathogens*. 10(1):e1003805 (2014). (IF = 8,057)
4. Mesquita SD, Ferreira AC, Falcao AM, Sousa JC, Oliveira TG, Correia-Neves M, Sousa N, Marques F, Palha JA. "Lipocalin 2 modulates the cellular response to amyloid beta". *Cell Death Differ*. 21(10):1588-99 (2014). (IF = 8.385)
5. Fernandes E, Martins VC, Nóbrega C, Carvalho CM, Cardoso FA, Cardoso S, Dias J, Deng D, Kluskens LD, Freitas PP, Azeredo J. A bacteriophage detection tool for viability assessment of Salmonella cells. *Biosensors and Bioelectronics*. 52:239-46 (2014). (IF = 6,451)
6. Colabardini AC, Ries LN, Brown NA, Dos Reis TF, Savoldi M, Goldman MH, Menino JF, Rodrigues F, Goldman GH. Functional characterization of a xylose transporter in *Aspergillus nidulans*. *Biotechnology of Biofuels*. 7:46 (2014). (IF = 6,221)





7. Nebenzahl-Guimaraes H, Jacobson KR, Farhat MR, Murray MB. Systematic review of allelic exchange experiments aimed at identifying mutations that confer drug resistance in *Mycobacterium tuberculosis*. *Journal of Antimicrobial Chemotherapy*. 69(2):331-342 (2014). (IF = 5,439)

8. McNab FW, Ewbank J, Howes A, Moreira-Teixeira L, Martirosyan A, Ghilardi N, Saraiva M, O'Garra A. Type I IFN Induces IL-10 Production in an IL-27– Independent Manner and Blocks Responsiveness to IFN-g for Production of IL-12 and Bacterial Killing in *Mycobacterium tuberculosis*–Infected Macrophages. *The Journal of Immunology*. 193(7):3600-12 (2014). (IF = 5,362)

9. Mira NP, Münsterkötter M, Dias-Valada F, Santos J, Palma M, Roque FC, Guerreiro JF, Rodrigues F, Sousa MJ, Leão C, Güldener U, Sá-Correia I. The Genome Sequence of the Highly Acetic Acid-Tolerant *Zygosaccharomyces bailii*-Derived Interspecies Hybrid Strain ISA1307, Isolated From a Sparkling Wine Plant. *DNA Research*. 21(3):299-313 (2014). (IF = 4,975)

10. Teixeira-Coelho M, Guedes J, Ferreirinha P, Howes A, Pedrosa J, Rodrigues F, Lai WS, Blackshear PJ, O'Garra A, Castro AG, Saraiva M. Differential posttranscriptional regulation of IL-10 by TLR2 and TLR4-activated macrophages *European Journal of Immunology*. 44(3):856-66 (2014). (IF = 4,518)

11. Gama JB, Ohlmeier S, Martins TG, Fraga AG, Sampaio-Marques B, Carvalho MA, Proenca F, Silva MT, Pedrosa J, Ludovico P. Proteomic Analysis of the Action of the *Mycobacterium ulcerans* Toxin Mycolactone: Targeting Host Cells Cytoskeleton and Collagen. *PLoS Neglected Tropical Diseases*. 8(8):e3066 (2014). (IF = 4,489)

12. Veiga MI, Osório NS, Ferreira PE, Franzén O, Dahlstrom S, Lum JK, Nosten F, Gil JP. Complex Polymorphisms in the *Plasmodium falciparum* Multidrug Resistance Protein 2 Gene and Its Contribution to Antimalarial Response. *Antimicrobial Agents and Chemotherapy*. 58(12):7390-7 (2014). (IF = 4,451)



13. Roque S, Mesquita AR, Palha JA, Sousa N, Correia-Neves M. "The behavioral and immunological impact of maternal separation: a matter of timing". *Front Behav Neurosci.* 22;8:192. (2014). (IF = 4.16)

14. Moiane I, Machado A, Santos N, Nhambir A, Inlamea O, Hattendorf J, Kallenius G, Zinsstag J, Correia-Neves M. Prevalence of Bovine Tuberculosis and Risk Factor Assessment in Cattle in Rural Livestock Areas of Govuro District in the Southeast of Mozambique. *PLoS One.* 9(3):e91527 (2014). (IF = 3,534)

15. Nebenzahl-Guimaraes H, Borgdorff MW, Murray MB, van Soolingen D. A Novel Approach - The Propensity to Propagate (PTP) Method for Controlling for Host Factors in Studying the Transmission of Mycobacterium Tuberculosis. *PLoS One.* 9(5):e97816 (2014). (IF = 3,534)

16. Gabryšová L, Howes A, Saraiva M, O'Garra A. The Regulation of IL-10 Expression. *Current Topics in Microbiology and Immunology.* 380:157-90 (2014). (IF = 3,471)

17. Jovel IT, Ferreira PE, Veiga MI, Malmberg M, Mårtensson A, Kaneko A, Zakeri S, Murillo C, Nosten F, Björkman A, Ursing J. Single nucleotide polymorphisms in Plasmodium falciparum V type H+ pyrophosphatase gene (pfvp2) and their associations with pfprt and pfmdr1 polymorphisms. *Infection, Genetics and Evolution.* 24:111-5 (2014). (IF = 3,264)

18. Ludovico P, Burhans WC. Reactive oxygen species, ageing and the hormesis police. *FEMS Yeast Research.* 14(1):33-9 (2014). (IF = 2,436)

19. Cunha C, Kurzai O, Löffler J, Aversa F, Romani L, Carvalho A. "Neutrophil responses to aspergillosis: new roles for old players". *Mycopathologia.* 178(5-6):387-93. (2014). (IF = 1.545)

## Phd thesis completed

1.

Student: Ana Horta

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

Scientific Area: Medicine

Title: Regulatory CD4+Tcells in the immune reconstitution HIV-infected individuals

Supervisors: Margarida Correia-Neves and Rui Sarmento e Castro

2.

Student: José Bernardo Gama

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

Scientific Area: Health Sciences

Title: Molecular cytopathogenesis induced by Mycobacterium ulcerans toxin, mycolactone

Supervisors: Jorge Pedrosa and Paula Ludovico

# RESEARCH DOMAIN: NEUROSCIENCES

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## OBJECTIVES & ACHIEVEMENTS

### General objectives

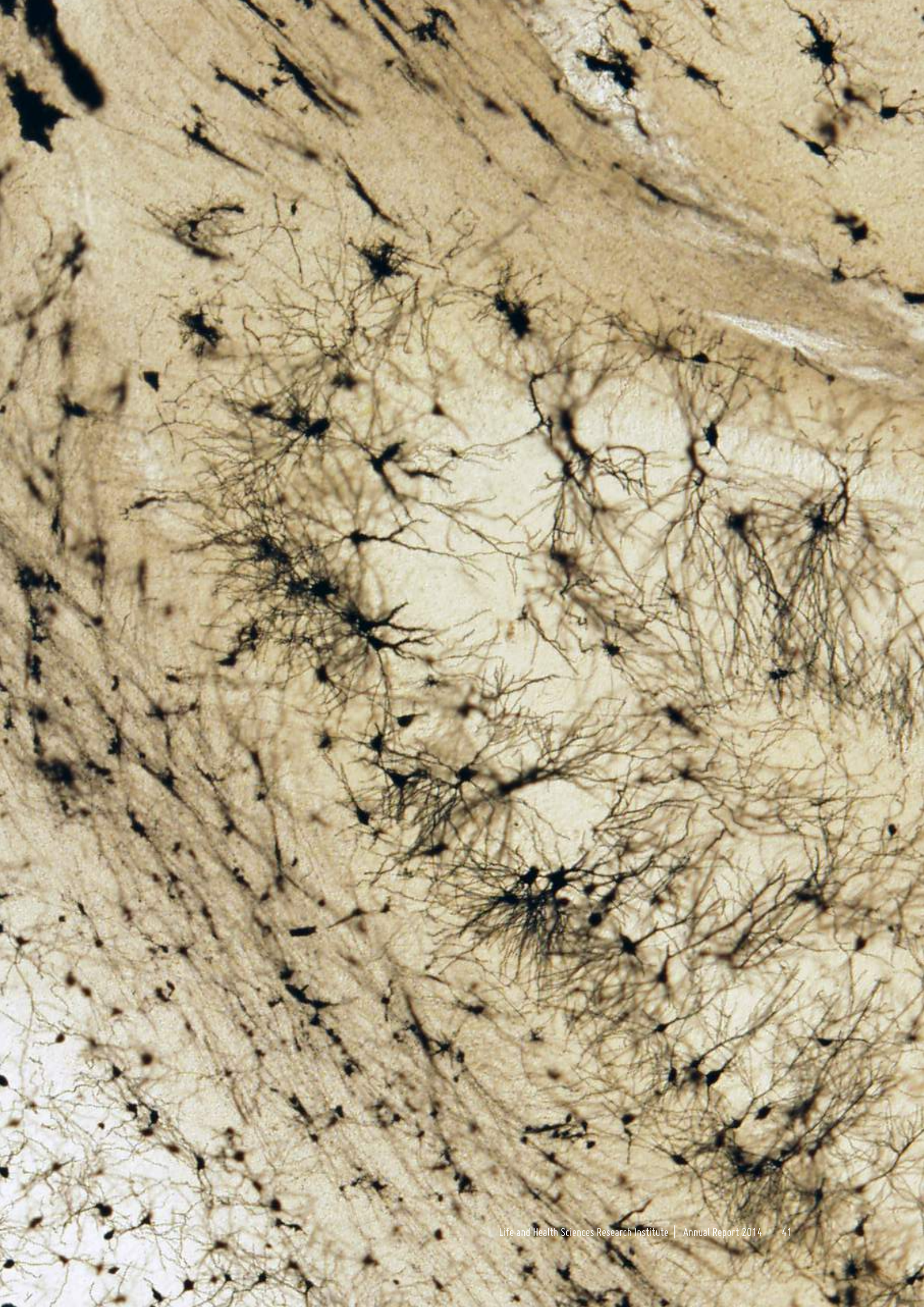
The Neurosciences Research Domain (NERD) launched its activities at the ICVS in 2003 as two separate research teams, Neurosciences and Human Genetics. Since 2003, the NERD evolved into a single team with increasing internal collaborations and common research topics, profiting from the varied backgrounds of its members.

The NERD is devoted 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. In line with the multimodal approaches of research questions, the team is composed by

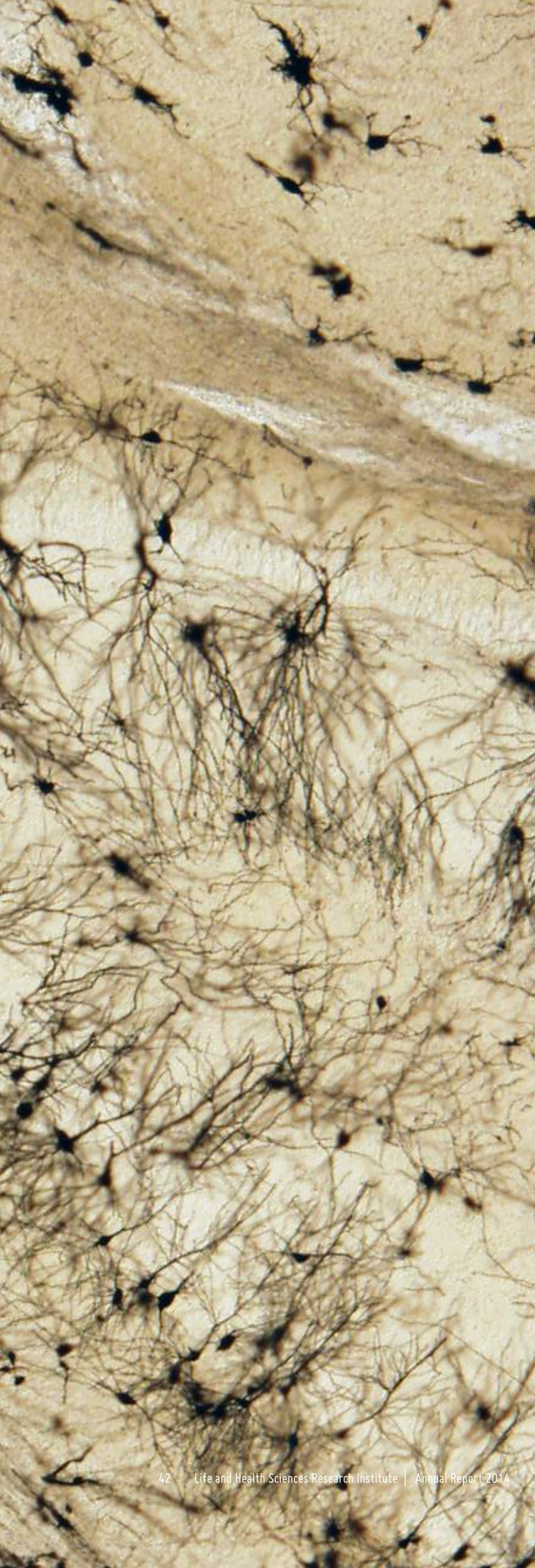
members with a wide spectrum of backgrounds (MDs from neurology, neuroradiology, psychiatry, internal medicine, endocrinology, urology, surgery, neonatology, paediatrics, medical genetics, biochemists, molecular biologists, statisticians, mathematicians, biomedical and electronic engineers, psychologists, veterinaries, pharmacists).

The NERD benefits from an extensive technical platform, conducting studies in parallel in humans and animal models, covering fundamental, translational and clinical research.









## Main achievements

Research within the NERD was supported by 19 projects funded by FCT, 1 project funded by QREN, 1 QREN Integrated Program, 3 FP7 grants and 4 contracts with industry, 2 additional International projects and 1 National project.

During the year of 2014, researchers from NERD published 57 papers in international peer reviewed journals, including 36 in Q1, with an average IF of 4.6, of which 4 papers were published in journals with an IF>10.

Additionally, the NERD submitted 100 abstracts to International Meetings.

Researchers within the NERD were granted with 6 National and 9 International scientific awards, including: the Early Career Award, granted by the Education and Training Committee - International Society of Behavioral Medicine; the Newton Freire-Maia Award in genetics and human evolution and medical genetics; the SpinUM Award – Concurso de Ideias, TecMinho.

The NERD organized 6 scientific meetings and 13 post graduation courses/workshops and graduated 7 PhD-students and 10 MSc-students. In addition, NERD members were involved in 14 conferences and seminars in the context of international meetings outside Portugal (approximately 130 presentations/communications).

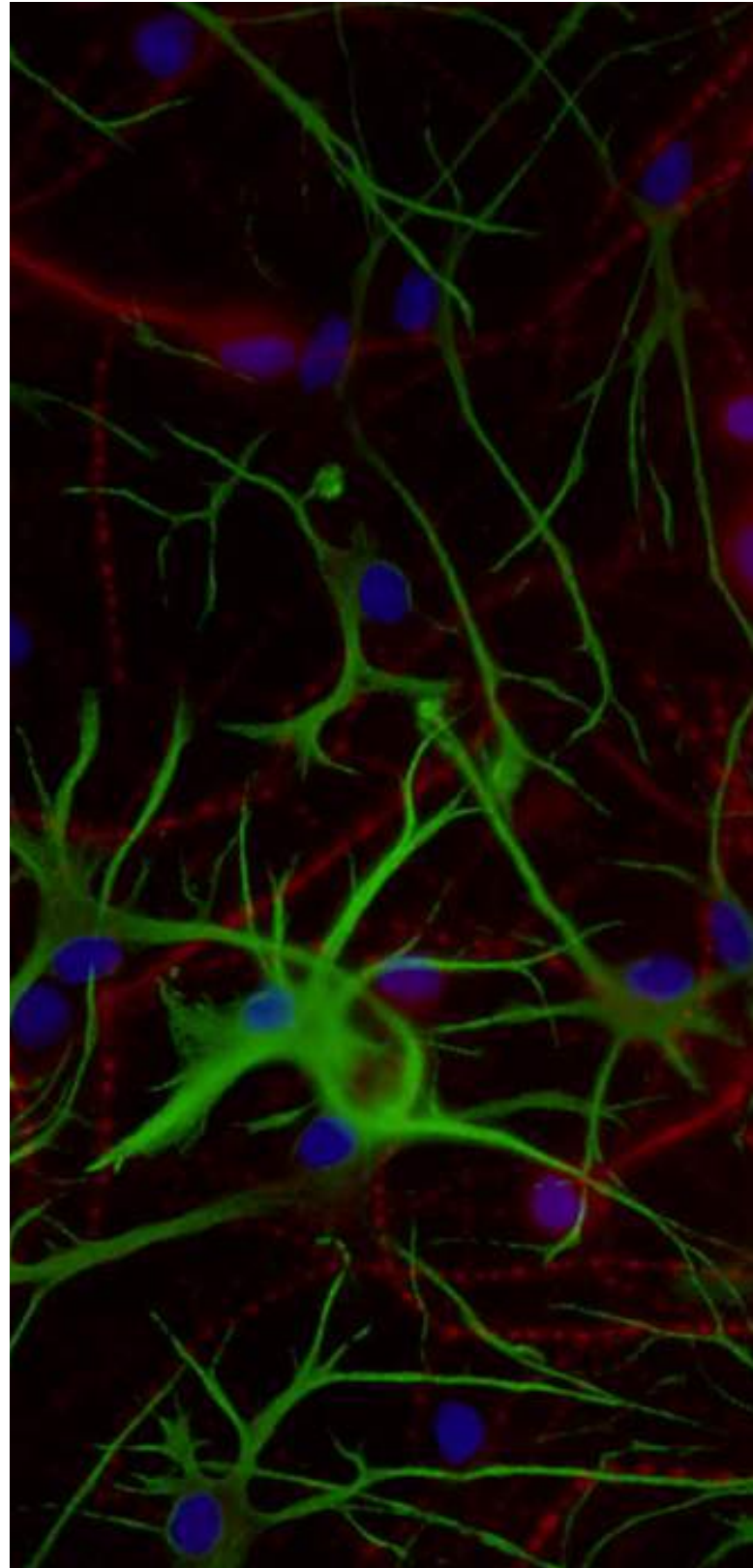
## Research line outputs

### Selected publications in peer review journals

1. Lima A, Sardinha VM, Oliveira AF, Reis M, Mota C, Silva MA, Marques F, Cerqueira JJ, Pinto L, Sousa N, Oliveira JF. Astrocyte pathology in the prefrontal cortex impairs the cognitive function of rats. *Molecular Psychiatry*. 19(7):834-41. (2014). (IF = 15,147)
2. Opal MD, Klenotich SC, Morais M, Bessa J, Winkle J, Doukas D, Kay LJ, Sousa N, Dulawa SM. Serotonin 2C receptor antagonists induce fast-onset antidepressant effects. *Molecular Psychiatry*. 19(10):1106-14 (2014). (IF = 15,147)
3. Herbert A, Cruickshank JK, Laurent S, Boutouyrie P, Reference Values for Arterial Measurements Collaboration. Establishing reference values for central blood pressure and its amplification in a general healthy population and according to cardiovascular risk factors. *European Heart Journal*. 35(44):3122-33 (2014). (IF = 14,723)
4. Silva NA, Sousa N, Reis RL, Salgado AJ. From basics to clinical: A comprehensive review on spinal cord injury. *Progress in Neurobiology*. 114:25-57 (2014). (IF = 10,301)
5. Lucassen PJ, Pruessner J, Sousa N, Almeida OF, Van Dam AM, Rajkowska G, Swaab DF, Czeh B. Neuropathology of stress. *Acta Neuropathologica*. 127(1):109-135 (2014). (IF = 9,777)
6. Mesquita SD, Ferreira AC, Falcao AM, Sousa JC, Oliveira TG, Correia-Neves M, Sousa N, Marques F, Palha JA. Lipocalin 2 modulates the cellular response to amyloid beta. *Cell Death and Differentiation*. 21(10):1588-99 (2014). (IF = 8,385)
7. Segura-Puimedon M, Sahún I, Velot E, Dubus P, Borralleras C, Rodrigues AJ, Valero MC, Valverde O, Sousa N, Herault Y, Dierssen M, Pérez-Jurado LA, Campuzano V. Heterozygous deletion of the Williams-Beuren syndrome critical interval in mice recapitulates most features of the human disorder. *Human Molecular Genetics*. 23(24):6481-94 (2014). (IF = 6,677)
8. Kimura T, Whitcomb DJ, Jo J, Regan P, Piers T, Heo S, Brown C, Hashikawa T, Murayama M, Seok H, Sotiropoulos I, Kim E, Collingridge GL, Takashima A, Cho K. Microtubule-associated protein tau is essential for long-term depression in the hippocampus. *Philosophical Transactions of the Royal Society B-Biological Sciences*. 369(1633):20130144 (2014). (IF = 6,314)
9. Pandey JP, Kaur N, Costa S, Amorim J, Nabico R, Linhares P, Vaz R, Viana-Pereira M, Reis RM. Immunoglobulin genes implicated in glioma risk. *Oncotarget*. 3:e28609 (2014). (IF = 6,283)
10. da Glória VG, Martins de Araújo M, Mafalda Santos A, Leal R, de Almeida SF, Carmo AM, Moreira A. T Cell Activation Regulates CD6 Alternative Splicing by Transcription Dynamics and SRSF. *Journal of Immunology*. 193(1):391-9 (2014). (IF = 5,362)
11. Pinto P, McIntyre T, Araujo-Soares V, Ferro R, Almeida A. The role of pain catastrophizing in the provision of rescue analgesia by health care providers following major joint arthroplasty. *Pain Physician*. 17(6):515-24 (2014). (IF = 4,766)
12. Sotiropoulos I, Lopes AT, Pinto V, Lopes S, Carlos S, Duarte-Silva S, Neves-Carvalho A, Pinto-Ribeiro F, Pinheiro S, Fernandes R, Almeida A, Sousa N, Leite-Almeida H. Selective impact of Tau loss on nociceptive primary afferents and pain sensation. *Experimental Neurology*. 261:486-93 (2014). (IF = 4,617)



13. Sampaio A, Soares JM, Coutinho J, Sousa N, Gonçalves ÓF. The Big Five default brain: functional evidence. *Brain Structure and Function*. 219(6):1913-22 (2014). (IF = 4,567)
14. Castelhana-Carlos M, Costa PS, Russig H, Sousa N. PhenoWorld: a new paradigm to screen rodent behavior. *Translational Psychiatry*. 4:e399 (2014). (IF = 4,36)
15. Harb MR, Almeida OF. Pavlovian conditioning and cross-sensitization studies raise challenges to the hypothesis that overeating is an addictive behavior. *Translational psychiatry*. 4:e387 (2014). (IF = 4,36)
16. Soares-Cunha C, Coimbra B, Borges S, Carvalho MM, Rodrigues AJ, Sousa N. The motivational drive to natural rewards is modulated by prenatal glucocorticoid exposure. *Translational Psychiatry*. 4:e397 (2014). (IF = 4,36)
17. Wrobel S, Serra SC, Ribeiro-Samy S, Sousa N, Heimann C, Barwig C, Grothe C, Salgado AJ, Haastert-Talini K. In Vitro Evaluation of Cell-Seeded Chitosan Films for Peripheral Nerve Tissue Engineering. *Tissue Engineering, PART A*. 20(17-18):2339–2349 (2014). (IF = 4,254)
18. Patchev AV, Rodrigues AJ, Sousa N, Spengler D, Almeida OF. The future is now: early life events preset adult behavior. *Acta Physiologica*. 210(1):46-57 (2014). (IF = 4,251)
19. Campanella NC, Berardinelli GR, Scapulatempo-Neto C, Viana D, Palmero E, Pereira R, Reis RM. Optimization of a Pentaplex Panel for MicroSatellite Instability (MSI) Analysis Without Control DNA in a Brazilian Population: Correlation with Ancestry Markers. *European Journal of Human Genetics*. 22(7):875-80 (2014). (IF = 4,225)
20. Mateus-Pinheiro A, Patrício P, Alves ND, Machado-Santos AR, Morais M, Bessa JM, Sousa N, Pinto L. The Sweet Drive Test: refining phenotypic characterization of anhedonic behavior in rodents. *Frontiers in Behavioral Neuroscience*. 8:74 (2014). (IF = 4,16)





## Phd thesis completed

1.

Student: Andreia Carvalho

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

Scientific Area: Health Sciences

Title: When gaining is losing: insights into the function of ataxin-3 in neurons and its perturbation in the context of Machado-Joseph disease

Supervisor: Patrícia Maciel

2.

Student: Diana Alexandra da Silva Amorim

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

Scientific Area: Health Sciences

Title: Pronociception in experimental monoarthritis: the role of galanin in descending pathways

Supervisors: Armando Almeida and Isaura Tavares

3.

Student: José Miguel Soares

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

Scientific Area: Health Sciences

Title: A multimodal neuroimaging approach to the interplay between stress and aging

Supervisor: Nuno Sousa

4.

Student: Mazen Harb

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

Scientific Area: Health Sciences

Title: Biobehavioural mechanisms of feeding behaviour: associative learning, hedonic preference and motivation

Supervisors: Nuno Sousa and Osborne Almeida

5.

Student: Miguel Carvalho

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

Scientific Area: Health Sciences

Title: From Parkinson's disease to Dopamine Dysregulation Syndrome and Impulse Control Disorders: the balance of dopamine in brain function and behaviour

Supervisors: António Salgado and Nuno Sousa

6.

Student: Shilan Aslani

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

Scientific Area: Health Sciences

Title: Dissecting the crosstalk between stress, depression and obesity

Supervisors: Joana Palha and Nuno Sousa

7.

Student: Vítor Hugo Pereira

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

Scientific Area: Medicine

Title: The impact of chronic stress on the cardiovascular system

Supervisors: João Cerqueira and Nuno Sousa

# RESEARCH DOMAIN: SURGICAL SCIENCES

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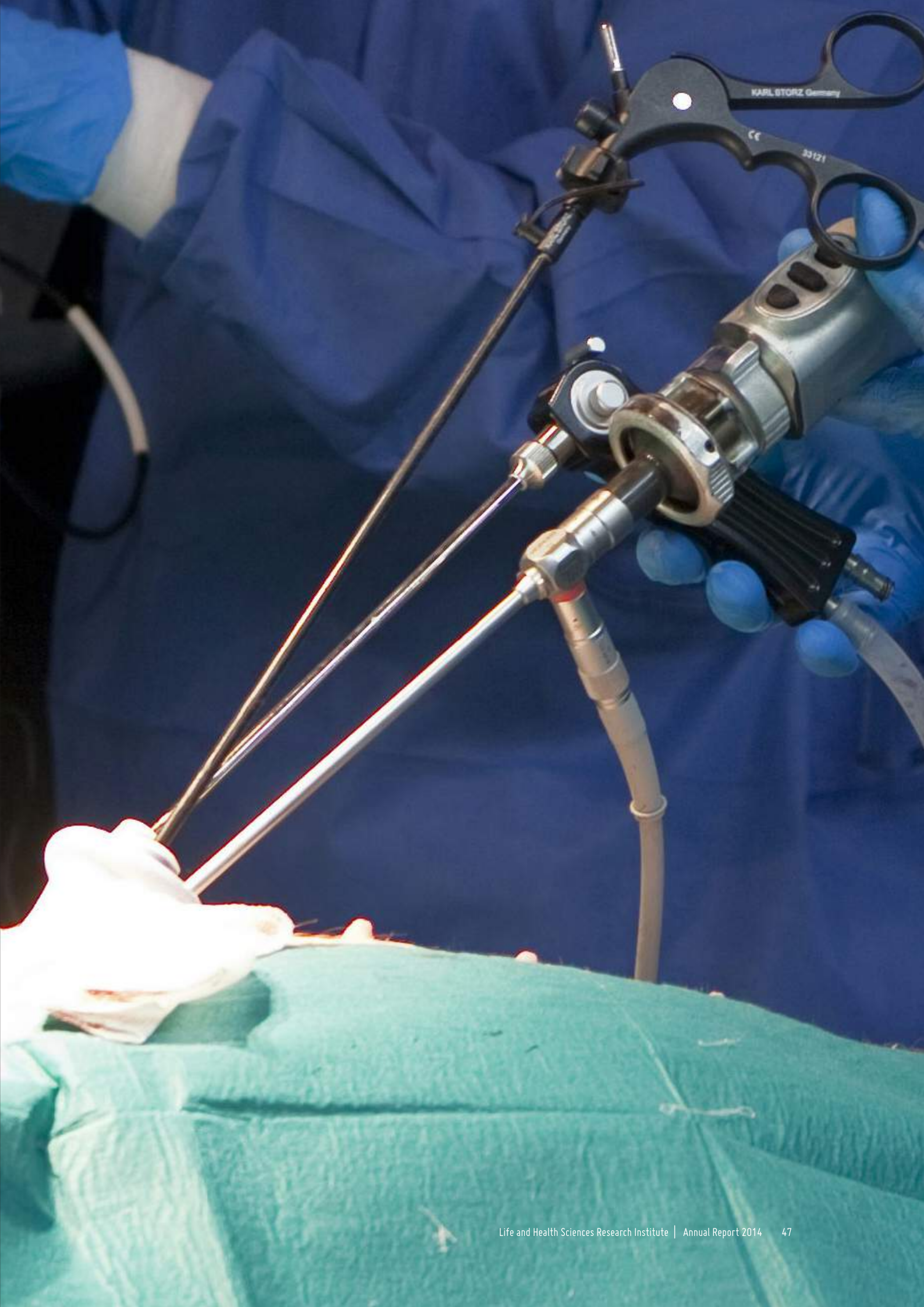
## OBJECTIVES & ACHIEVEMENTS

### General objectives

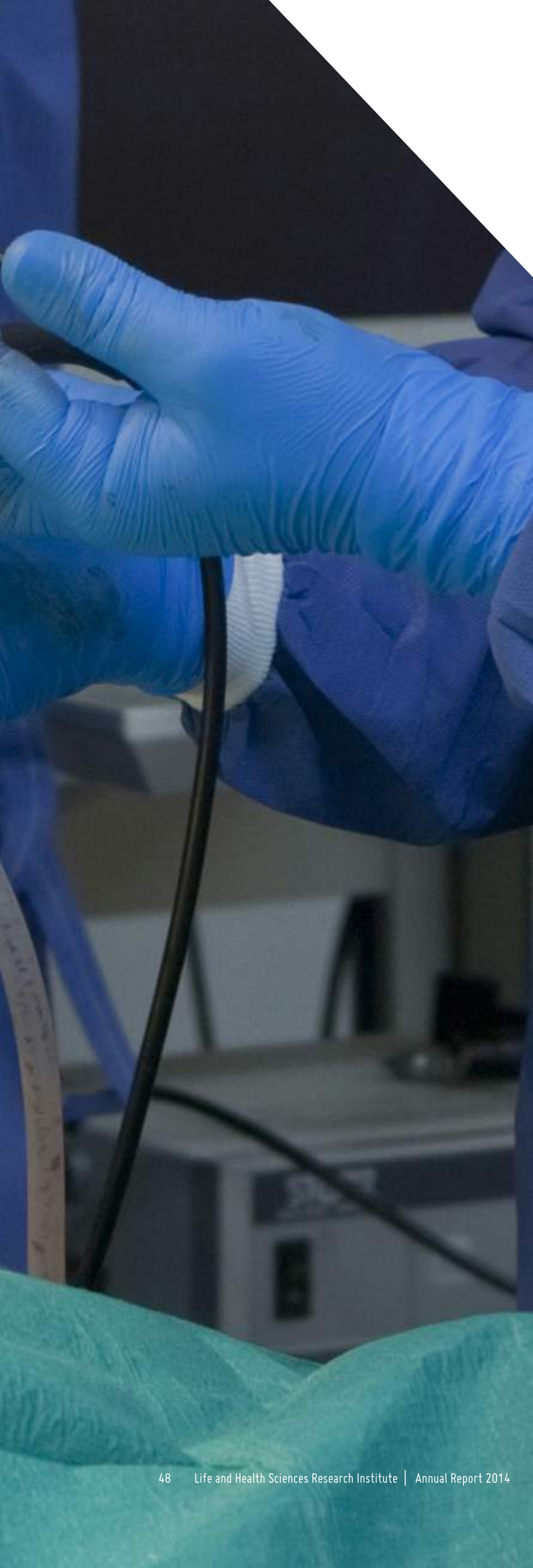
The Surgical Sciences Research Domain (SSRD) deals with diseases from the digestive, pulmonary and urogenital systems.

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 5 projects funded by FCT, 1 QREN Integrated Program and 1 additional International project.

During the year of 2014, researchers from SSRD published 50 papers in international peer reviewed journals, including 17 in Q1, with an average IF of 4.6, of which 4 papers were published in journals with an IF>10, with 3 of them published in journals ranked as 1st in their scientific category.

The SSRD organized 1 scientific meeting and 22 post-graduation courses/workshops and graduated 5 PhD-students. In addition, SSRD members were involved in 20 conferences and seminars in the context of international meetings outside Portugal (25 presentations/communications).

## Research line outputs

### Selected publications in peer review journals

1. Correia-Pinto J, Ribeiro A. Congenital duodenal obstruction and double-bubble sign. *The New England Journal of Medicine*. 371:e16 (2014). (IF = 54,42)
2. Autorino R, Cicione A, Rassweiler J, Lima E. Re: Willem M. Brinkman, Irene M. Tjiam, Barbara M. A. Schout, et al. Results of the European Basic Laparoscopic Urological Skills Examination. *Eur Urol* 2014;65:490-6. *European Urology*. 65(3):e38-9 (2014). (IF = 12,48)
3. Zecchini V, Madhu B, Russell R, Pértega-Gomes N, Warren A, Gaude E, Borlido J, Stark R, Ireland-Zecchini H, Rao R, Scott H, Boren J, Massie C, Asim M, Brindle K, Griffiths J, Frezza C, Neal DE, Mills IG. Nuclear ARRB1 induces pseudohypoxia and cellular metabolism reprogramming in prostate cancer. *The EMBO Journal*. 33(12):1365-82 (2014). (IF = 10,748)
4. Pinto F, Pértega-Gomes N, Pereira MS, Vizcaíno JR, Monteiro P, Henrique RM, Baltazar F, Andrade RP, Reis RM. T-box transcription factor Brachyury is associated with prostate cancer progression and aggressiveness. *Clinical Cancer Research*. 20(18):4949 (2014). (IF = 8,193)
5. Lopes L, Dinis-Ribeiro M, Rolanda C. Early precut fistulotomy for biliary access: time to change the paradigm of “the later the better”? *Gastrointestinal Endoscopy*. 80(4):634-41 (2014). (IF = 4,9)
6. Silva-Carvalho R, Miranda-Goncalves V, Ferreira AM, Cardoso SM, Sobral AJFN, Almeida-Aguiar C, Baltazar F. Antitumoural and antiangiogenic activity of Portuguese propolis in in vitro and in vivo models. *Journal of Functional Foods*. 11; 160-171 (2014). (IF = 4,48)
7. Martino A, Campa D, Jurczyszyn A, Martínez-López, la Fuente, Varkonyi J, Dumontet C, García-Sanz R, Gemignani F, Jamroziak K, Jurado M, Landi S, Rossi AM, Lesueur F, Marques H, Dudziński M, Wóitek M, Moreno V, Orciuolo E, Petrini M, Reis RM, Ríos R, Sainz J, Vogel U, Buda G, Vangsted A, Canzian F. Genetic variants and multiple myeloma risk: IMMEnSE validation of the best reported associations -An Extensive Replication of the Associations from the Candidate Gene Era. *Cancer Epidemiology Biomarkers and Prevention*. 23(4):670-4 (2014). (IF = 4,324)
8. Pinheiro C, Penna V, Morais-Santos F, Abrahão-Machado L, Ribeiro G, Curcelli EC, Olivieri MV, Morini S, Valença I, Ribeiro D, Schmitt FC, Reis RM, Baltazar F. Characterization of monocarboxylate transporters (MCTs) expression in soft tissue sarcomas: Distinct prognostic impact of MCT1 sub-cellular localization. *Journal of Translational Medicine*. 12:118 (2014). (IF = 3,991)
9. Sheeba CJ, Andrade RP, Palmeirim I. Limb patterning: from signalling gradients to molecular oscillations. *Journal of Molecular Biology*. 426(4):780-784 (2014). (IF = 3,959)
10. Queirós S, Barbosa D, Heyde B, Morais P, Vilaça JL, Friboulet D, Bernard O, D'hooge J. Fast Automatic Myocardial Segmentation in 4D cine CMR datasets. *Journal of Medical Image Analysis*. 18(7):1115-1131 (2014). (IF = 3,681)
11. Moura R, Carvalho-Correia E, da Mota P, Correia-Pinto J. Canonical Wnt Signaling Activity in Early Stages of Chick Lung Development. *PlosOne*. 9(12):e112388 (2014). (IF = 3,534)
12. Marino AL, Evangelista AF, Vieira RA, Macedo T, Kerr LM, Abrahão-Machado LF, Longatto-Filho A, Silveira HC, Marques MM. MicroRNA expression as risk biomarker of breast cancer metastasis: a pilot retrospective case-cohort study. *BMC Cancer*. 14:739 (2014). (IF = 3,319)

13. Pérttega-Gomes N, Vizcaíno JR, Attig J, Jurmeister S, Lopes C, Baltazar F. A lactate shuttle system between tumour and stromal cells is associated with poor prognosis in prostate cancer. *BMC Cancer*. 14:352 (2014). (IF = 3,319)

14. Pinheiro C, Garcia EA, Morais-Santos F, Scapulatempo Neto C, Mafra A, Stenbergen R, Boccardo E, Villa LL, Baltazar F, Longatto-Filho A. Lactate transporters and vascular factors in HPV-induced squamous cell carcinoma of the uterine cervix. *BMC Cancer*. 14:751 (2014). (IF = 3,319)

15. Sousa B, Ribeiro AS, Nobre AR, Lopes N, Martins D, Pinheiro C, Vieira AF, Albergaria A, Gerhard R, Schmitt F, Baltazar F, Paredes J. The basal epithelial marker P-cadherin associates with breast cancer cell populations harboring a glycolytic and acid-resistant phenotype. *BMC Cancer*. 14:734 (2014). (IF = 3,319)

16. Moreira-Pinto J, Ferreira A, Miranda A, Rolanda C, Correia Pinto J. Hybrid Endoscopic Thymectomy: combined transesophageal and transthoracic approach in a survival porcine model with cadaver assessment. *Surgical Endoscopy*. 28(9):2671-2678 (2014). (IF = 3,313)



## Phd thesis completed

1.

Student: Herlander Marques

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

Scientific Area: Medicine

Title: Herpes-Y virus and polymorphisms of antigen processing systems: importance in the oncogenesis and in the prognosis of B-cell lymphomas

Supervisors: Adhemar Longatto and Rui Medeiros

2.

Student: João Moreira Pinto

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

Scientific Area: Medicine

Title: Hybrid Thoracic NOTES: a translational research project

Supervisors: Jorge Correia-Pinto and Carla Rolanda

3.

Student: Luís Miguel Lopes

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

Scientific Area: Medicine

Title: Needle-knife fistulotomy in deep biliary cannulation

Supervisors: Carla Rolanda and Mário Jorge Dinis Ribeiro

4.

Student: Nelma Gomes

Institution: Universidade do Porto

Year of the PhD conclusion: 2014

Scientific Area: Patologia e Genética Molecular

Title: Role of monocarboxylate transporters in prostate carcinoma

Supervisors: Fátima Baltazar

5.

Student: Rui Quinta

Institution: Universidade do Minho

Year of the PhD conclusion: 2014

Scientific Area: Health Sciences

Title: Fabry disease: novel insights into secondary lipid alterations and invariant Natural Killer T cell deficiency

Supervisors: Rui Reis and Maria Clara Miranda

# 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 (GRESF / APMGF) and the International Primary Care Respiratory Group (IPCRG).



## Selected Publications

- Linhares DVBR, da Fonseca JAL, Borrego LM, Matos Á, Pereira AM, Sá-Sousa A, Gaspar Â, Mendes C, Moreira C, Gomes E, Rebelo FF, Cidrais Rodrigues JC, Onofre JM, Azevedo LF, Alfaro M, Calix MJ, Amaral R, Rodrigues-Alves R, Correia de Sousa J, Morais-Almeida M. Validation of Control of Allergic Rhinitis and Asthma Test for Children (CARATKids) – a prospective multicenter study. *Pediatr Allergy Immunol* 2014; 25: 173–179. DOI:10.1111/pai.12218

- Basto-Pereira M, Furtado SI, Silva RJ, Fachado González F, Vara Fernandes TM, Correia de Sousa J, Yaphe J. Performance indicators for clinical practice management in primary care in Portugal: Consensus from a Delphi study. *Eur J Gen Pract.* 2014; Early Online: 1–6

- McDonnell J, Correia de Sousa J, Baxter N, Pinnock H, Roman-Rodriguez M, van der Molen T, Williams S. Building capacity to improve respiratory care: the education strategy of the International Primary CareRespiratory Group 2014-2020. *NPJ Prim Care Respir Med.* 2014 Sep 25;24:14072. doi: 10.1038/npjpcrm.2014.72.



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# 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 Health Sciences of the University of Minho (ELECSUM) that was initiated in 2001. NPJ Prim Care Respir Med. 2014 Sep 25;24:14072. doi: 10.1038/npjpcrm.2014.72.

## Selected Publications

- Costa P, Alves R, Neto I, Marvão P, Portela M, Costa MJ. Associations between medical student empathy and personality: a multi-institutional study. PLoS One. 2014 Mar 17;9(3):e89254. doi: 10.1371/journal.pone.0089254. eCollection 2014. PubMed PMID: 24637613; PubMed Central PMCID: PMC3956603.

- Lemos AR, Sandars JE, Alves P, Costa MJ. The evaluation of student-centredness of teaching and learning: a new mixed-methods approach. Int J Med Educ. 2014 Aug 14;5:157-64. doi: 10.5116/ijme.53cb.8f87. PubMed PMID: 25341225; PubMed Central PMCID: PMC4212413.

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