ICVS

ANNUAL REPORT 2010

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

Universidade do Minho
Escola de Ciências da Saúde

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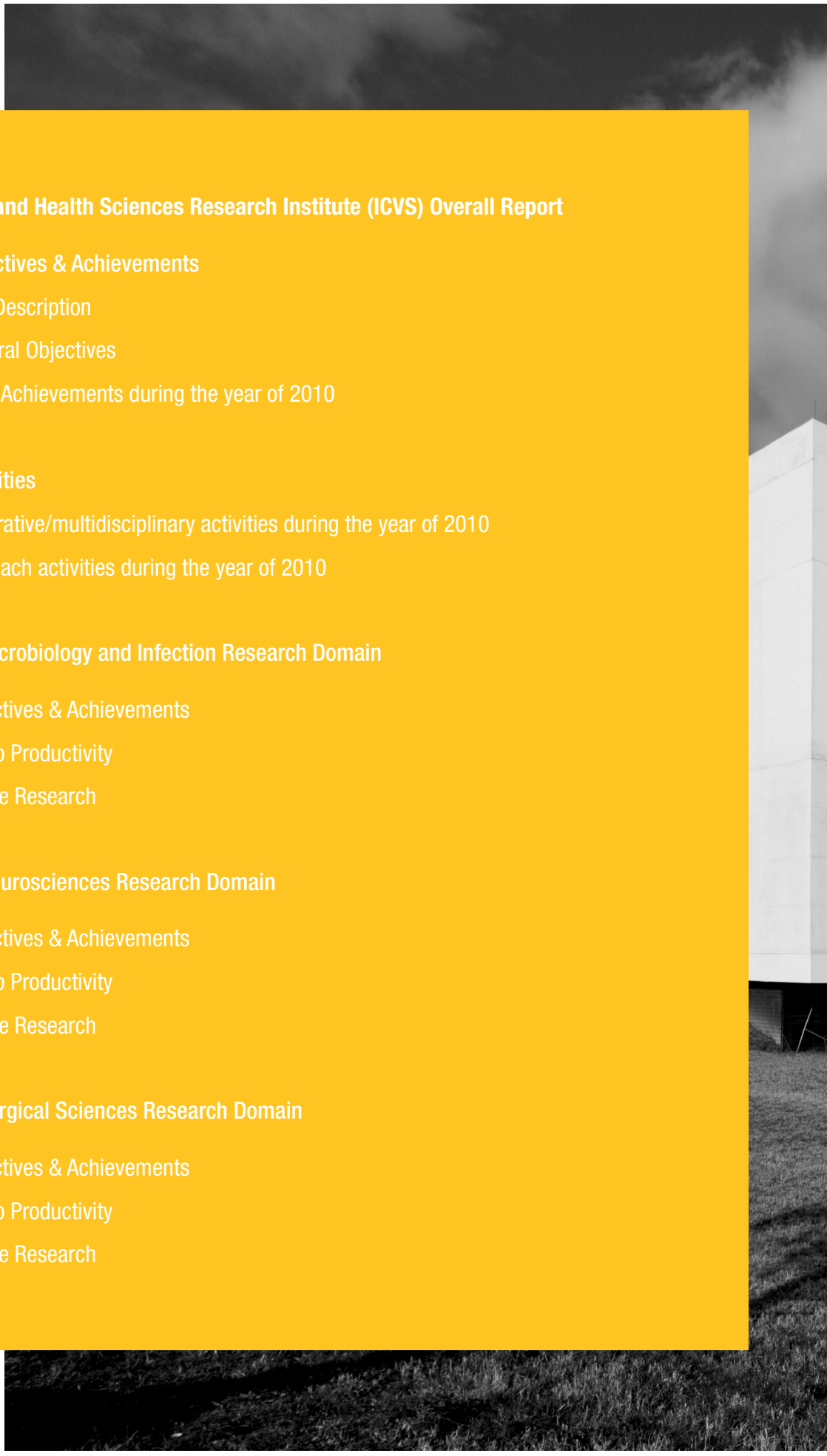

Objectives & Achievements

Unit Description

The Life and Health Sciences Research Institute (ICVS) is a fully incorporated research structure within the School of Health Sciences (ECS), University of Minho (UMinho).

The ICVS was formally integrated in the national system of science and technology in 2003 and ranked with the maximum grade of "Excellent" by the Fundação para a Ciência e a Tecnologia (FCT) international evaluation panels that evaluated the Institute in 2003 and in 2008.

The strategy for the ICVS development is based on the following principles:

• Integrated/flexible scientific structure, centred in Research Domains (RD). Each RD is composed by, at least, two Research Lines (RL) that, in turn, are composed by a minimum of two funded Research Projects (RP). The functional unit of the ICVS is, thus, the RP, each coordinated by a Principal Investigator (PI). Each RL and RD are supervised by a coordinator. This flexible organization allows, easily, the creation of multi- and inter-disciplinary teams;

• Shared management of resources - organization within function-oriented laboratories;

• Incentive to high quality scientific production (e.g. support of publication costs; award for the paper with the higher number of citations published 5 years earlier; yearly award for the paper with the highest impact factor (IF); and yearly award for the RD with higher accumulated IF);

• Advanced post-graduation, organized as an International Programme that offers advanced training in biomedical and clinical sciences.

The ICVS research activities are organized within three RDs:

- MICROBIOLOGY AND INFECTION (RLs: Cellular and Molecular Microbiology; Immunology of Infection);

- NEUROSCIENCES (RLs: Neurodevelopment; Neurodegeneration; Neuroimmunology);

- SURGICAL SCIENCES (RLs: Endoscopic and Surgical Techniques; Integrated Studies in Surgical Sciences).

General Objectives

The ICVS is a research unit within an innovative Medical School, guided by international standards of excellence. The ICVS aims to achieve the following global goals:

• promote original research, with high scientific output and recognized impact in the advance of the knowledge on biomedical, translational and clinical sciences;

• encourage an innovative interaction between research and medical undergraduate/graduate training;

• provide international advanced post-graduated programmes;

• offer specialized health services to the community;

• promote the public awareness of science.

Therefore, the ICVS's purpose is to be an institute of excellence at the international level, promoting research on biomedical and on clinical sciences, and endorsing innovative interactions between research and medical training activities (under- and post-graduate).
The ICVS is a growing institution and represents an attractive research environment for young researchers.

The specific developmental strategies for 2010 were to:

• promote highly competitive, multidisciplinary research projects involving scientists, MDs and other health professionals, with a growing focus on clinical research;

• promote an application for the FCT status of "Laboratório Associado", aiming at establishing the first Laboratório Associado centred in the UMinho;

• endorse an active policy of collaboration with the recently launched INL-International Iberian Nanotechnology Laboratory, located besides the UMinho Campus;

• pursue in the active involvement of medical students and MDs within the ICVS research projects;

• support the ongoing ECS/ICVS Ph.D. and Master Programmes, as well as the MD/Ph.D. programme in collaboration with the Thomas Jefferson and Columbia Medical Schools, USA;

• promote international post-graduate courses, fostering and strengthening existing international collaborations and developing new cooperative projects;

• diversify the funding sources at the national and international levels, namely in clinical sciences (including the Health Cluster Portugal, private foundations, industry and the FP7 EU programme);

• promote the public awareness in health sciences.

Main Achievements during the year of 2010:

• Production of an application to "Laboratório Associado";

• Increase in the number of papers and in their impact factor;

• Reinforcement of translational/clinical research;

• Increased capacity to attract competitive funding, including internationally.

Specifically, in 2010, the ICVS was able to::

• deliver and submit to the FCT a proposal for the creation of the "ICVS/3B's – Laboratório Associado", in partnership with the UMinho Research Group "3B's- Biomaterials, Biodegradables and Biomimetics";

• maintain a sustained increase in staff numbers and differentiation; Ph.D.s increasing from 40 (2009) to 50 (2010) - 28 ECS faculty, 5 "Compromisso com a Ciência", and 17 Post–Docs.
- Presently, the ICVS counts with 208 researchers [50 Ph.D.s and 158 post graduation students (87 Ph.D. students, 37 Master students and 34 associate researchers)], supported by 18 non academic staff (5 administrative and 13 in laboratories, with salaries supported by ECS);

• enhance publications impact: 89 papers in international journals with average IF of 4.9 (including articles with IF between 3 and 5 = 31 papers; IF between 5 and 10 = 15 papers; IF between 10 and 20 = 3 papers; IF>20 = 2 papers), and 3 book chapters.
NOTE: the individual Research Group Reports include all publications from each RD, some of them shared between RDs and, therefore, listed in more then one individual report.

• foster the conclusion of 9 Ph.D. theses, including 2 MDs and the first 2 students that successfully completed the ICVS/ECS MD/Ph.D. Program, an innovative initiative at the European level;

• get a total of 41 new fellowships granted by FCT: 6 BPD; 15 BD; 20 BI;

• rise competitive funding; ongoing projects (average duration 3 years) involving 4.4 million €, of which 1.2 million corresponded to the activities developed in 2010.

• fostering partnerships with the network of affiliated Hospitals in the context of *Clinical Academic Centres*; the *INL*; the *Avepark*-park of science /technology; the *3B's Research Group* and several other UMinho research units;

• involve a significant number of MD students in research, including 27 Option Projects and 8 MD/Ph.D. Lab Rotations;

• organize 20 Advanced Post-Graduation Courses/Workshops, with 424 participants (36.3% MDs, 53.2% Biological Sciences, 5.3% other Health Professionals; the remaining from other backgrounds). Some of the courses were part of training activities of European schools or within European training actions. In the ECS/ICVS International Postgraduate Programme, 86% of the participants rated courses as "Very Good" or "Excellent".

Activities

Integrative/multidisciplinary activities during the year of 2010

The ICVS is strategically located in Northern Portugal, within a growing Cluster of Biomedical Science, Technology and Healthcare institutions, creating synergies in many dimensions. Among the collaborating institutions, we highlight the network of affiliated Hospitals in which dedicated clinical research takes place in the context of *Clinical Academic Centres*, launched in partnership with the ICVS; the INL; the Avepark; the 3B's Research Group and several other UMinho research units.

At the ECS launching, faculty members with diverse scientific backgrounds were recruited. This was the basis for the development of strong Research Domains (RDs), combining scientists able to approach problems using complementary perspectives. A clear definition of an integrative policy was established in order to increase the critical mass within a setting that favoured intra- and inter-group collaborations and complementary experimental approaches.

This combined teaching and research expertise also contributed to the successful training of MD students, promoting the interaction between biomedical research and medical education. In 2010, this interplay is also reflected in the publication, on the field of education in Life & Health Sciences, of 3 articles (1 in press) in peer reviewed journals, as well as 1 article in proceedings of a national conference.

Multidisciplinary activities in Post-graduation have been also successfully pursued. In 2010, the Ph.D. Programmes in Medicine and in Health Sciences and the Master Program in Health Sciences enrolled 11, 11 and 12 students, respectively. Additionally, the ECS/ICVS is involved in a multi-centred Inter-University Doctoral Programme, supported by the Gulbenkian Foundation.

Additionally, the ICVS organized a series of post-graduation courses and work-shops, counting with 507 participants (41% MDs). It is of notice the number of participants from abroad (13%) and from national institutions outside the UMinho (43%).

In 2010, the ICVS RDs have pursued the establishment of international collaborations with reference labs in Europe, namely: INRA and CNRS – France ; LUMC – Netherlands ; LMU-MUENCHEN, UTUB-IPTC and MPG – Germany; IEM-HAS – Hungary; KI – Sweden; ISS and IRFMN – Italy; IFPAN – Poland; IMROH – Croatia; TUBITAK MAM and KSL – Turkey; INTERES – United Kingdom.

In 2010, important progresses were registered, with the successful application for competitive funding to support national and international networks, in the context of, namely:

- European FP7: 2 Consortium proposals;

- Health Cluster Portugal: 1 Consortium proposal involving several UMinho's research units, the Hospital of Viana and three private companies.

Outreach activities during the year of 2010

The program of outreach activities implemented by the ICVS/ECS represents a joint strategy to promote in the surrounding community:

• public awareness on the importance of research in life and health sciences;

• improved health education and healthier lifestyles.

The younger population is considered crucial to fulfil these goals and is, therefore, the preferential audience targeted in these initiatives. Reaching this target population is facilitated by an established contact network comprising over 80 schools dedicated to teaching activities in every level, since first year to the pre-university stage.

In 2010, the activities involved 57 ICVS researchers over 4 major events: (1) the "Science and Technology Week", 25 - 26 of November, directed to 413 primary and secondary school students; (2) the International Brain Awareness Week", 15 - 21 of March, directed to 530 secondary students and 65 senior university students; (3) the "Open Doors to High Schools" 14th of January and 4th of April, directed to 437 secondary school students; (4) the "Summer in the Campus", 19 - 23 of July, directed to 11 pre-university students. These initiatives included interactive talks in schools; experimental activities at the ICVS laboratories; exhibitions; guided tours to ICVS facilities and seminars.

These activities resulted in several articles published in national televisions (RTP, RTP-N, TVI), newspapers, radio stations and information websites ("Diário do Minho"; "Correio do Minho"; "Antena Minho"; "Radio Universitária do Minho"; "Universia.pt"; "MaisActual.pt", etc)

Research Domain Description

Designation: Microbiology and Infection

Coordinator: Jorge Pedrosa

Objectives & Achievements

Objectives

The Microbiology and Infection Research Domain addresses specific challenges in the prophylaxis and treatment of infectious diseases, including mycobacteriosis and systemic fungal infections. Research in this domain is organized in 2 research lines: *Cellular and Molecular Microbiology* and *Immunology of Infection*.

Cellular and Molecular Microbiology Research Line

The Cellular and Molecular Microbiology Research Line is devoted to the study of fundamental biological problems associated to human diseases from the integrated perspective of genetics, cell biology and biochemistry. Research within this line focuses on microbial environment sensing, transcriptional and post-transcriptional regulation, secretion, autophagy, programmed cell death and molecular aspects of pathogenicity/virulence of human related pathogens. By applying a wide range of emerging techniques in molecular genetics and cell biology, we aim at the exploration of novel targets for infectious disease therapy.

Immunology and Infection Research Line

The Immunology and Infection Research Line is concerned with the cellular and molecular mechanisms of pathogenesis and with the immune control of infectious diseases. Emphasis is given to diseases of bacterial and fungal origin, which represent a major worldwide threat to human health and against which vaccines are unavailable or inefficient. Using state of the art technology and a vast range of experimental models, the main goal in this line is to lay the basis for improved diagnostic methods and vaccination strategies for the prevention or treatment of infectious diseases.

Main Achievements

During the year of 2010, the main scientific goals proposed in 2009 were successfully achieved. The average IF of the papers increased from 5.5 to 6.3 and 4 papers were published in journals with an IF above 10.

In addition, we have greatly reinforced the translational/clinical research, on aspergillosis and mycobacteriosis, namely Tuberculosis and Buruli Ulcer, by the

establishing effective collaborations with clinicians in Portugal, Italy, United States of America, Benin and Mozambique. These new challenges have led us to engage 3 Ph.D. students in our team, 2 physicians and 1 veterinary. Following the successful grant applications we have also engaged 3 more master students.

1. Publications
   a. 28 articles, corresponding to a ratio of 2,2 papers/Ph.D..
   b. Mean impact factor of 6,3.
   c. 3 articles with impact factor above 10 and 1 article above 30.

2. Abstracts in international congresses: 8.

3. Theses completed
   d. 1 Ph.D. thesis.

4. Organization of conferences
   a. Organization of 2 international post-graduation courses.

5. Funding
   a. Presently, the Domain's funding includes 11 FCT grants, 1 grant from Fundação Calouste Gulbenkian and 2 FP7 consortiums.

6. Prizes
   a. Members of the Microbiology and Infection Research Domain were awarded 4 prizes in 2010.

Group Productivity

Publications in peer review Journals

Herein, we list representative manuscripts published in 2010 with the highest Impact factor:

1. Cunha C, Di Ianni M, Bozza S, Giovannini G, Zagarella S, Zelante T, D'Angelo C, Pierini A, Pitzurra L, Falzetti F, Carotti A, Perruccio K, Latgé JP, Rodrigues F, Velardi A, Aversa F, Romani L, Carvalho A. Dectin-1 Y238X polymorphism associates with susceptibility to invasive aspergillosis in hematopoietic transplantation through impairment of both recipient- and donor-dependent mechanisms of antifungal immunity. Blood. 2010 Dec 9;116(24):5394-402. (IF=10,555);

2. Cruz A, Fraga AG, Fountain JJ, Rangel-Moreno J, Torrado E, Saraiva M, Pereira DR, Randall TD, Pedrosa J, Cooper AM, Castro AG. Pathological role of interleukin 17 in mice subjected to repeated BCG vaccination after infection with Mycobacterium tuberculosis. J Exp Med. 2010 Aug 2;207(8):1609-16. (IF=15,463);

3. Greenwood MT and Ludovico P. Expressing and functional analysis of mammalian apoptotic regulators in yeast. Cell Death Differ. 2010 May;17(5):737-45. (IF=7,548);

4. Han KH, Chun YH, de Castro Pimentel Figueiredo B, Soriani FM, Savoldi M, Almeida A, Rodrigues F, Cairns CT, Bignell E, Tobal JM, Goldman MH, Kim JH, Bahn YS, Goldman GH, da Silva Ferreira ME. The conserved and divergent roles of carbonic anhydrases in the filamentous fungi *Aspergillus fumigatus* and *Aspergillus nidulans*. Mol Microbiol. 2010 Mar,75(6):1372-88. (IF=5,213);

5. Mesquita A, Weinberger M, Silva A, Sampaio-Marques B, Almeida B, Leão C, Costa V, Rodrigues F, Burhans WC, Ludovico P. Caloric restriction or catalase inactivation extends yeast chronological lifespan by inducing H2O2 and superoxide dismutase activity. Proc Natl Acad Sci U S A. 2010 Aug 24;107(34):15123-8. (IF=9,432);

6. Nobrega C, Roque S, Nunes-Alves C, Coelho A, Medeiros I, Castro AG, Appelberg R, Correia-Neves M. Dissemination of mycobacteria to the thymus renders newly generated T cells tolerant to the invading pathogen. J Immunol. 2010 Jan 1;184(1):351-8. (IF=6,0);

7. Robinson RT, Khader SA, Martino CA, Fountain JJ, Teixeira-Coelho M, Pearl JE, Smiley ST, Winslow GM, Woodland DL, Walter MJ, Conejo-Garcia JR, Gubler U, Cooper AM. Mycobacterium tuberculosis infection induces il12rb1 splicing to generate a novel IL-12R{beta}1 isoform that enhances DC migration. J Exp Med. 2010 Mar 15;207(3):591-605. (IF=15,463);

8. Saraiva M, O'Garra A. The regulation of IL-10 production by immune cells. Nat Rev Immunol. 2010 Mar;10(3):170-81. (IF=30,006);

9. Silva-Fernandes A, Costa MD, Duarte-Silva S, Botelho CM, Martins L, Mariz JA, Ferreira T, Pinto-Ribeiro F, Correia-Neves M, Costa C, Maciel P. Motor uncoordination and neuropathology in a transgenic mouse model of Machado-Joseph disease lacking intranuclear inclusions and ataxin-3 cleavage products. Neurobiol Dis. 2010 Oct;40(1):163-76. (IF=4,852);

10. Torrado E, Fraga AG, Logarinho E, Martins TG, Carmona JA, Gama JB, Carvalho MA, Proença F, Castro AG, Pedrosa J. IFN-{gamma}-Dependent Activation of Macrophages during Experimental Infections by Mycobacterium ulcerans Is Impaired by the Toxin Mycolactone. J Immunol. 2010 Jan 15;184(2):947-55. (IF=6,0);

Ph.D. theses completed (the research work of all theses reported was carried out at ICVS/ECS)

- Alexandra Gabriel Fraga. "Understanding Buruli ulcer: elucidation of the cellular and molecular mechanisms underlying infection with *Mycobacterium ulcerans*". Supervised by Jorge Pedrosa, School of Health Sciences, University of Minho.

Prizes

- Ciência Professor Francisco Pulido Valente 2010, with the work" Pathological role of interleukin 17 in mice subjected to repeated BCG vaccination after infection with *Mycobacterium tuberculosis*". J. Exp. Med., August 2, 2010; 207(8): 1609 – 1616".

Organization of conferences

• Organization of Scientific Meetings and Presence in Scientific Committees
- XXXVI Reunião Anual da Sociedade Portuguesa de Imunologia (SPI): "Fighting Intracellular Pathogens: from bench to bedside". 20-22, Setembro, 2010. ECS/ICVS-Universidade do Minho, Braga.

• Post-graduation courses and Workshops organized at the ICVS
- An Integrative Approach to Cell Analysis: Cell and Tissue Culture, Flow Cytometry and Microscopy. 6-16 April 2010
- Fundamentals in Immunology and Infection (2nd Edition). 27 September- 8 October 2010
- Laboratory Animal Science. 8 – 19 November 2010.
- "Host-pathogen interaction" 2010.
- "Methods of DNA analysis: state of the art". 17-28 May 2010.

• Organization of Other Meetings
- Diagnosis of Zoonotic Brucellosis, Cysticercosis and Tuberculosis. 16-27 of August 2010. Faculty of Veterinary Medicine, University Eduardo Mondlane, Maputo, Mozambique.

Future Research

Objectives

In 2010, we have increased the Domain productivity, particularly regarding the average impact factor of the published articles. It is our purpose to keep improving the quality of the scientific publications. Specifically, we aim at publishing more than two papers Ph.D./year and, at least, one article in a high profile journal.

Regarding human resources it is our objective to consolidate the new cycle of growth that we have started in 2010, by increasing the number of Ph.D.s and master students for a minimum of 20%.

Additionally, following the successful application for Clinical Research Grants on infectious diseases, with the collaboration of clinicians from Hospital Joaquim Urbano (Porto) and Hospital de Braga, we will, now, enrol in formal Ph.D. programs 2 clinicians in 2009 and, at least, one more in 2010. We are also interested in expanding our network of clinical collaborations to other Hospitals at the national and international levels, namely in Italy, Brazil and African countries.

To consolidate our collaboration within Buruli Ulcer projects, researchers from the Microbiology and Infection Domain will organize post-graduation courses in Benin.

We intend to pursue our networking efforts in the field of Nanotechnology within the University of Minho, namely with research units from the Engineering and from the Science Schools, as well as from the International Iberian Institute of Nanotechnology-Braga (INL), in order to develop applications in the area of mycobacterial and fungal infections.

One of the major challenges for the Microbiology and Infection Research Domain is to maintain the diversity of the funding sources, namely from national sources, both private and public, as well as from other sources such as NIH, European Community and International Private Foundations.

Research Domain Description

Title of Research Group: Neurosciences

Coordinator: Nuno Jorge Carvalho de Sousa

Objectives

The Neuroscience Research Domain is focused on understanding the neurobiological mechanisms implicated in several neurodevelopmental and neurodegenerative disorders, as well as in evaluating the interplay between the nervous and the immune systems. The team is composed by researchers with distinct backgrounds that create a network combining a wide spectrum of technical expertise with a diversity of research projects that aim to provide a comprehensible perspective to our major research topics. In our approach, the projects range from basic/translational to clinical research. Research in this domain is organized in 3 different research lines: *Neurodevelopment*; *Neurodegeneration* and *Neuroimmunology*.

Neurodevelopment Research Line

The Neurodevelopment Research Line addresses hormones (e.g. corticosteroids), environmental stressors (e.g. iodine insufficiency) and genes as modulators of behavior, both in animal models and in patients with various diseases (e.g. mental retardation, Rett syndrome, schizophrenia). As several cellular and molecular events occurring during normal development are recapitulated in carcinogenic processes, ongoing research also addresses brain tumors.

Neurodegeneration Research Line

The Neurodegeneration Research Line views neurodegeneration not only as a process involving actual neuronal loss and gross structural lesions of the nervous system, but also taking into account other underlying processes that include progressive axonal degeneration and dendritic dismantling. We focus on the pathogenesis of several human neuropsychiatric disorders (e.g. late-onset degenerative diseases such as dementia, depression, anxiety and chronic pain syndromes) studying both patients and animal models of the diseases. One of our common themes is the study of the impact of stress and aging on brain structure and function, and how this correlates to the increased risk of developing other aging-associated disorders.

Neuroimmunology Research Line

The Neuroimmunology Research Line investigates the interaction between the nervous and the immune systems through different perspectives: challenging the

brain with immune stimuli including peripheral inflammation or chronic infection and evaluating its consequences in neurological disease progression; studying the behavior, neuronal plasticity and neurotransmitter pathways of animal models with disruption or overexpression of immune-related molecules.

Main Achievements

During this year there was a successful integration of a significant higher number of researchers in the Neuroscience Domain. Seven new Post-Docs were incorporated, either by participation in pre-existent projects, or by launching new research projects. The present number of Ph.Ds in the Neuroscience Domain is 23.

In 2010, we have greatly reinforced the translational/clinical focus of research; importantly, we successfully applied for a EU-FP7 Grant that involves preclinical and clinical studies, a multicentered clinical consortium (HCP/QREN) and we initiated five clinical projects (some of which were granted in a specific internal call for the Clinical Academic Center). This effort was paralleled by the maintenance of high success rates in competitive funding from FCT as well as from other international agencies (USA and EU).

1. Publications
   a. 33 articles, corresponding to a ratio of 2,9 papers/Ph.D..
   b. 4,9 as mean impact factor.
   c. 1 article has impact factor above 20.

2. 46 abstracts in international congresses

3. Theses completed
   a. 6 Ph.D. theses completed
   b. 5 M.Sc. theses completed

4. Organization of conferences
   a. Organization of 8 international post-graduation courses
   b. Organization of 7 Conferences and seminars
   c. 31 international conferences/seminars produced by members of the domain

5. Funding
   a. Presently, the Domain's funding includes 2 FP7 grants, 1 Marie-Curie ITN, 24 funded projects granted by FCT, BIAL and RRR. We were also granted with a multidisciplinary proposal for the Health Cluster Portugal (QREN) in which the ICVS/Clinical Academic Center is the Coordinator.

6. Prizes
   a. Members of the Neurosciences Domain were awarded 10 prizes in 2010.

Group Productivity

Publications in peer review Journals

Herein, we list representative manuscripts published in 2010 with the highest Impact factor:

1. Bax DA, Mackay A, Little SE, Carvalho D, Viana-Pereira M, Tamber N, Grigoriadis AE, Ashworth A, Reis RM, Ellison S, Al-Sarraj S, Hargrave D, Jones C. A distinct spectrum of copy number aberrations in formalin-fixed, paraffin-embedded paediatric high grade gliomas. *Clin Cancer Res*, 16:3368-3377 (2010). IF= 6,8

2. Costa BM, Smith J, Chen Y, Phillips H, Aldape K, Zardo G, Nigro J, James D, Fridlyand J, Reis RM, Costello JF. Reversing HOXA9 Oncogene Activation by PI3K Inhibition: epigenetic mechanism and prognostic significance in human glioblastoma. *Cancer Res*, 70:453-462 (2010). IF= 6,8

3. Costa MC, Bajanca F, Rodrigues AJ, Tomé RJ, Paulson HL, Corthals G, Macedo-Ribeiro S, Logarinho E, Maciel P. The deubiquitinating enzyme ataxin-3 plays a role in myogenic differentiation through regulation of integrin subunit levels. *PLoS One*, 5(7):e11728 (2010). IF= 4,4

4. Gaspar G, Bax D, Marshall L, Viana-Pereira M, Little S, Perryman L, Vassal G, Pearson AD, Workman P, Reis RM, Hargrave D, Jones C. MGMT-independent temozolomide resistance in pediatric glioblastoma cells associated with PI3-kinase-mediateded HOX/Stem cell gene signature. *Cancer Res*, 70:1–10 (2010). IF= 7.5

5. Oliveira JM, Salgado AJ, Sousa N, Reis RL. Dendrimers and its derivatives as a potential therapeutic tool in Tissue Engineering and Regenerative Medicine strategies: a review. *Prog in Polym Sci*, 35:1163–1194 (2010). IF= 23,8

6. Oliveira TG, Chan RB, Tian H, Laredo M, Shui G, Staniszewski A, Zhang H, Wang L, Kim TW, Duff KE, Wenk MR, Arancio O, Di Paolo G. Phospholipase d2 ablation ameliorates Alzheimer's disease-linked synaptic dysfunction and cognitive deficits. *J Neurosci*, 30:16419-16428 (2010). IF= 7,2

7. Rodrigues AJ, Costa MC, Silva T, Ferreira D, Bajanca F, Logarinho E, Maciel P. Absence of ataxin-3 leads to cytoskeletal disorganization and increased cell death. *Biochim Biophys Acta*, 1803:1154-1163 (2010). IF= 4,4

8. Silva N, Salgado AJ, Sousa RA, Oliveira JT, Pedro AJ, Leite-Almeida H, Cerqueira R, Almeida A, Mastronardi F, Mano JF, Neves NM, Sousa N, Reis RL. Development and Characterization of a Novel Hybrid Tissue Engineering based Scaffolds for Spinal Cord Injury Repair. *Tissue Eng Part A*, 16:45-54 (2010). IF= 4,6

9. Silva-Fernandes A, do Carmo Costa M, Silva S, Oliveira P, Botelho C, Martins L, Mariz JA, Ferreira T, Pinto-Ribeiro F, Correia-Neves M, Costa C and Maciel P. Genetic instability, motor phenotype and neuropathology in a transgenic mouse model of Machado-Joseph disease in the absence of intranuclear inclusions and ataxin-3 cleavage products. *Neurobiol Dis*, 40:163-176 (2010). IF= 4.5

10. Yu S, Patchev AV, Wu Y, Lu J, Holsboer F, Zhang JZ, Sousa N, Almeida OF. Depletion of the neural precursor cell pool by glucocorticoids. Ann Neurol, 67:21-30 (2010). IF= 9,3

Publications in book chapters

1. Pêgo JM, Sousa JC, Almeida OFX, Sousa N. Stress and the Neuroendocrinology of Anxiety Disorders. In: "Behavioral Neurobiology of Anxiety and Its Treatment", Stein MB, Steckler T (Eds.), Springer ISBN: 978-3-642-02911-0.

We have also registered the following patent:

- Carlos Correia, Ricardo J. Machado, Marco Couto, Patrícia Pinto, Paula Monteiro, Sérgio Oliveira, Armando Almeida, Teresa McIntyre, Maribel Santos, Isabel Ramos, Carlos Oliveira. Ubiquitous Analgesia Control System for the Real-time Monitoring of Acute and Chronic Pain. Boletim da Propriedade Industrial Nº 2010/05/06, pg. 6 (2010).

Master and Ph.D. theses completed

- Ph.D. theses (the research work of all theses reported was carried out at ICVS/ECS)

1. Ana Franky Carvalho. "Modulation of limbic noradrenergic circuits by cannabinoids". Supervised by Elisabeth VanBockstaele, Thomas Jefferson University and co-supervised by Nuno Sousa, School of Health Sciences, University of Minho.

2. Anabela da Silva Fernandes. "Characterization of a transgenic mouse model of Machado-Joseph disease". Supervised by Patrícia Maciel, ICVS

3. Filipa Pinto-Ribeiro. "Interaction between Chronic Stress and Pain: the HPA axis and potential hypothalamic-medulla-spinal pathways involved. Supervised by Armando Almeida and co-supervised by Nuno Sousa, School of Health Sciences, University of Minho.

4. Maria José Costeira. “Characterization of the iodine status of Portuguese women in fertile age and its relation with the psychomotor performance of the newborn.” Supervised by Joana Palha, School of Health Sciences, University of Minho.

5. Pedro Leão. “Implications of prenatal exposure to synthethic corticosteroids in the mesolimbic reward pathway”. Supervised by Nuno Sousa, School of Health Sciences, University of Minho

6. Tiago Oliveira. “The role of phospholipase D2 in Alzheimer’s disease”. Supervised by Gilbert Di Paolo, Columbia University and co-supervised by Nuno Sousa, School of Health Sciences, University of Minho.

- M.Sc. theses (the research work of all theses reported was carried out at ICVS/ECS)

1. Daniel Pereira. “Attentional Set Shifting Task and Enrichment of the Pre-frontal Cortex”, in the context of the master program in Psychology from the Psychology department of Minho University. Supervised by João Cerqueira, ICVS.

2. Diana Amorim. “Papel do núcleo dorsomedial do hipotálamo na modulação descendente da dor”, in the context of the master program in Biochemistry from the Instituto de Ciências Biomédicas Abel Salazar, Porto University. Supervised by Armando Almeida, ICVS (2010).

3. Fábio Teixeira. “Effects of Human Umbilical Cord Perivascular Cells and their Conditioned Media on the Dentate Girus of the Rat Hippocampus”, in the context of the master program on Oncology from the Instituto de Ciências Biomédicas Abel Salazar, University of Porto. Supervised by António Salgado and Luisa Pinto, ICVS.

4. Lucília Pinto. “Efeitos do stress na distribuição dos NMDAR.2B no córtex pré-frontal”, in the context of the master program in Molecular and Cellular Biology from the Biology Department of the University of Aveiro. Supervised by João Carlos Sousa, ICVS

5. Rui Cruz. “Characterization of lipocalin 2 ontogenic expression profile”, in the context of the master program in Molecular and Cellular Biology from the biology Department of the University of Aveiro. Supervised by João Carlos Sousa, ICVS

Prizes

1. Prize from the Portuguese Society of Human Genetics. Nuno Sousa (2010).

2. Rafael Hervada Prize for Biomedical Research for the work “Modulation of the Insulin-Signaling and HSF-1 pathways rescues mutant ataxin-3-mediated proteotoxicity in C. elegans neurons”. Patrícia Maciel (2010).

3. CGC Genetics 3rd prize for the work “Clinical and genetic study of Rett syndrome in Portugal”. Patricia Maciel, Teresa Temudo, Mónica Santos (2010).

4. Prize for the best poster in the “JoCEM - XI Jornadas Científicas do Estudante de Medicina 2010” to the work, “Chronic Mycobacterium avium infection reduces depressive-like behavior and improves cognitive performance of CD1 mice”. Carlos Branco, Filipe Quintas, Susana Monteiro, Nuno Sousa, Joana Palha, Margarida Correia-Neves, Susana Roque (2010).

5. Honorable Mention to the poster “Mood Disorders in CD1 Mice Chronically Infected with Mycobacterium avium” at the V YES MEETING (Young European Scientist Meeting). Carlos Branco, Filipe Quintas, Susana Monteiro, Margarida Correia-Neves, Susana Roque (2010).

6. Prize Grünenthal PAIN 2009 – Menção honrosa”, from Fundação Grünenthal, to the work “Influence of monoarthritis in descending modulation from the paraventricular hypothalamic nucleus: electrophysiological and behaioural evaluation”, by Filipa Pinto-Ribeiro, Osei Ansah, Antti Pertovaara, Armando Almeida (2010).

7. Golden Prize at AP Society of Neurochemistry 2010 Meeting. I Sotiropoulos.

8. Prize “Programa de Investigação na Fronteira das Ciências da Vida 2010”, from Fundação Calouste Gulbenkian, Portugal, to the work “The Transcriptome of the Oncogenic HOXA9 Homeoprotein in Human Glioblastoma and Precursor Cells”. Bruno M Costa (2010).

9. Prize “Bolsa Liga Portuguesa Contra o Cancro 2010”, Portugal. Bruno M Costa (2010).

10. Prize “Envelhecimento e Demência Cerebral”, from the Portuguese Society for Neuroscience, granted by Pfizer (2010).

Organization of Conferences

• Organization of Scientific Meetings and Presence in Scientific Committees
- Symposium “The choroid plexus: a gate for signaling into the brain”, Federation of the European Neurosciences Societies. Amsterdam, Holland. 2010.
- European Commitee of the International Brain Research Organization. 2010-2012

• Post-graduation courses and Workshops organized by members of the ICVS:
- Mecanismos Fisiopatológicos e de Tratamento da Dor, integrated in the Master Degress in Physiotherapy, Escola de Tecnologias da Saúde do Porto, Instituto Politécnico do Porto (2010).
- An Integrative Approach to Cell Analysis: Cell and Tissue Culture, Flow Citometry and Microscopy, integrated in the post-graduation programme of the ICVS/ECS (2010).
- Fundamentals in Neuroscience, integrated in the post-graduation programme of the ICVS/ECS (2010).
- Drugs and the Brain:an update in psychopharmacology part of the EURON School of Neurosciences. School of Health Sciences, University of Minho (2010).
- Update on Alzheimer Research: Workshop for Ph.D. students, satellite course of the Society for Neurosciences annual meeting. San Diego, USA (2010).
- Advanced Simulation in Aneaesthesiology”, 1st Tertúlias de Anestesiologia, School of Health Sciences, University of Minho (2010).
- Methods of DNA analysis: state of the art, integrated in the post-graduation programme of the ICVS/ECS, 2010.
- Hands-on Course: Sulci, Gyri, Ventricls and Dissecting Fibers (9th Edition), integrated in the post-graduation programme of the ICVS/ECS, 2010.

Future Research

Objectives

In 2010 we have achieved most of the goals established in the 2009 report (consult future research section of the 2009 report). In 2011 we will keep our efforts to strengthen the quality of our research projects, performed by a highly-motivated multidisciplinary team that provides a multimodal technical platform to each research question. This will maintain, and hopefully strength, the appropriate environment for the highest quality of training for our research students (Ph.D. and M.Sc.s), namely through its contribution in the ECS/ICVS Master and Doctoral Programs. As part of our mission, we will continue our commitment to the training and supervision of researchers, and in 2011, we aim to finish 4 Ph.D. theses and to organize at least 6 international post-graduation courses.

In 2011 we aim to publish another set of high quality studies, and to increase the number of high-impact paper (at least 10% with IF> to Journal of Neuroscience – as a reference journal in our research field). We also aim to keep capturing more projects and in a wide spectrum of sources (including international agencies). It is also our aim to continue to recruit Post-Docs internationally in 2011 that add extra value to the Research Domain. We also aim to keep hosting a high number of medical students enrolled in research activities with the Neuroscience research domain, which is an illustration of the nice interplay with the Medical School project.

Another goal for 2011 is to further strengthen the contracts with industrial partners. On this particular, the grant obtained in the context of the Health Cluster Portugal will be instrumental, as it will allow interactions between industry and academia.

A final word to our commitment to reinforce translational and clinical research in the Neuroscience Research Domain. In 2011, the opening of the Clinical Academic Center, in which members of the Domain are profoundly engaged, will create the conditions to develop several clinical research projects based on the pre-clinical data generated within the Domain.

Research Domain Description

Title of Research Group: Surgical Sciences

Coordinator: Jorge Correia-Pinto

Objectives & Achievements

Objectives

The *Surgical Sciences Research Domain* deals with diseases from the digestive, pulmonary and urogenital systems. In surgery, repairing (for congenital disorders) and ablative/resection (for malignant disorders) are the most common procedures. Therefore, the interdisciplinary team in this domain includes basic and clinic investigators working in development biology and pathology as a way to better understand the pathophysiology towards the definition of novel therapeutic strategies for malignant and congenital diseases. From the technical point of view, the staff of this domain is composed of engineers and medical doctors devoted to 3D imaging and endoscopy as a way to minimize surgical aggression. Research in this domain is organized in 2 research lines: *Integrative Studies in Surgical Diseases* and *Endoscopy and Surgical Sciences*.

Integrative Studies in Surgical Diseases Research Line

The Integrative Studies in Surgical Diseases Research Line aims at understanding the developmental mechanisms regulating time and space differentiation of cells and tissues (e.g. somites, limb and lung growth), explores the possibility of fetal therapeutic strategies (e.g. to promote lung growth in congenital diaphragmatic hernia) and evaluates genetic/molecular markers as risk and prognostic factors in digestive, pulmonary and urogenital cancer.

Endoscopy and Surgical Sciences Research Line

In strong connection with the industry of medical devices, in this research line new techniques and equipments applicable in minimally invasive surgery are evaluated. We explore the possibility of scarless interventions through Natural Orifices Transluminal Endoscopic Surgery (N.O.T.E.S.) and on the other hand, we investigate human body imaging (CT scan and laser) as a surrogate to develop three-dimensional constructs to provide personalized prosthesis and surgical plans. As additional mission, we provide an extensive program of international hands-on courses in minimally invasive surgical techniques.

Main Achievements

Benefiting from overall facilities of ICVS and the sharing philosophy of equipment laboratory resources, with a team with different scientific background, with a strong collaboration with surgical companies (Karl Storz and Ethicon Endo-Surgery collaborations), the Surgical Sciences Research Domain got reasonable financial support for next 2-3 years with diversified sources. Moreover, we launched the basis for a postgraduate program in Surgical Sciences that is acquiring international prestige and increasing implementation. Regarding scientific metrics, in 2010 the main academics outcomes of the Surgical Sciences Research Domain can be summarized as follows:

1. Publications
   a. 32 articles, corresponding a ratio of 2,5 papers/Ph.D.
   b. Mean impact factor of 3,457
   c. Seven book chapters (2 international; 5 national).

2. Academic Degrees and Theses
   a. One Aggregation in Medicine; 2 Ph.D. theses in Health Sciences; 3 Master (M.Sc.) theses.

3. Conferences, Courses and Workshops
   a. Organization 12 international post-graduation courses;
   b. Organization 4 national congresses/meetings;
   c. 12 lectures in international congresses/conferences/seminars and 32 lectures in national scientific events;
   d. 67 posters or oral presentation either in international or national meetings.

4. Funding
   a. Presently, the Domain's funding includes 6 FCT projects with PI from ICVS, 2 FCT projects in collaboration of ICVS.
   b. Industry contract research, International multicentric study CLARINET (clopidogrel to lower arterial thrombotic risk in neonates and infants trial). Sanofi Aventis.

5. Prizes
   a. The work of the Surgical Sciences Research Domain was distinguished with 12 prizes (2 international and 10 national).

Group Productivity

Publications in peer reviewed journals in 2010

Herein, we list representative manuscripts published in 2010 with the highest Impact factor:

1. Albergaria A, Ribeiro AS, Pinho S, Milanezi F, Carneiro V, Sousa B, Sousa S, Oliveira C, Machado JC, Seruca R, Paredes J, Schmitt F. ICI 182,780 induces P-cadherin overexpression in breast cancer cells through chromatin remodelling at the promoter level: role of C/EBP in CDH3 gene activation. Hum Mol Genet, 19(13): 2554-66 (2010). (IF = 7.386)

2. Almeida MI, Reis RM, Calin GA. MYC-MicroRNA-9-Metastasis Connection in Breast Cancer. Cell Res 20(6): 603-4 (2010). (IF = 8.151)

3. Costa BM, Smith JS, Chen Y, Phillips HS, Aldape KD, Zardo G, Nigro J, James CD, Fridlyand J, Reis RM, Costello JF. Reversing HOXA9 oncogene activation by PI3K Inhibition: Epigenetic mechanism and prognostic significance in human glioblastoma. Cancer Res, 70(2): 453-62 (2010). (IF = 7.543)

4. Kibadi K, Boelaert M, Fraga AG, Kayinua M, Longatto-Filho A, Minuku JB, Mputu-Yamba JB, Muyembe-Tamfum JJ, Pedrosa J, Roux JJ, Meyers WM, Portaels F. Response to treatment in a prospective cohort of patients with large ulcerated lesions suspected to be Buruli Ulcer (Mycobacterium ulcerans disease). PLoS Negl Trop Dis, 2010 4(7):e736. (IF = 4.693)

5. Pinheiro C, Albergaria A, Paredes J, Sousa B, Dufloth R, Vieira D, Schmitt F, Baltazar F. Monocarboxylate transporter 1 is up-regulated in basal-like breast carcinoma. Histopathology, 56(7): 860-67 (2010). (IF = 3.855)

6. Rama CH, Villa LL, Pagliusi S, Andreoli MA, Costa MC, Thomann P, Alves VAF, Longatto-Filho A, Eluf-Neto J. Opportunity for catch-up HPV vaccination in young women after first delivery. J Epidemiol Community Health, 64(7): 610-5 (2010). (IF = 3.043)

7. Resende T, Ferreira M, Tavares AT, Teillet M, Andrade RP*, and Palmeirim I*. Sonic hedgehog: a new player in temporal control of somite formation. Proc Natl Acad Sci USA, 107(29): 12907-12 (2010). *These authors contributed equally to this work. (IF = 9.432)

8. Ribeiro AS, Albergaria A, Sousa B, Correia AL, Seruca R, Schmitt F, Paredes J. Extracellular cleavage of P-Cadherin is a key mechanism underlying the invasive behaviour of breast cancer cells. Oncogene, 29(3): 392-402 (2010). (IF = 7.135)

9. Termini L, Maciag PC, Soares FA, Nonogali S, Pereira SMM, Alves VAF, Longatto-Filho A, Villa LL. Analysis of Human Kallikrein 7 (hK7) expression as a Potential Biomarker in Cervical Neoplasia. Int J Cancer, 127(2): 485-90 (2010). (IF = 4.722)

10. Tomita LY, Longatto-Filho A, Costa MC, Andreoli MAA, Villa LL, Franco EL, Cardoso MA. Diet and serum micronutrients in relation to cervical neoplasia and cancer among low-income Brazilian women. Int J Cancer, 126(3): 703-14 (2010). (IF = 4.722)

Publications in book chapters

1. Lima E. The skills and training course of NOTES in Urology. In: A Course Book of Uro-laparoscopic Training. Ed. Smith A, Sun Y. Springer, In Press.

2. Oliveira RF, Teixeira S, Silva LF, Teixeira JC, Antunes H. Study of a pressurized metered-dose inhaler spray parameters in Fluent. In Lecture Notes in Engineering and Computer Science. Ed. Ao S, Gelman L, Hukins DWL, Hunter A, Korsunsky AM. International Association of Engineers (ISBN 978-988-18210-7-2). pp. 1083-1087 (2010).

3. Pinheiro C, Baltazar F. SLC16A3 (solute carrier family 16, member 3 (monocarboxylic acid transporter 4). Atlas Genet Cytogenet Oncol Haematol. March 2010. URL: http://AtlasGeneticsOncology.org/Genes/SLC16A3ID44573ch17q25.html.

4. Pinheiro C, Baltazar F. SLC16A3 (solute carrier family 16, member 3 (monocarboxylic acid transporter 1). Atlas Genet Cytogenet Oncol Haematol. March 2010. URL: http://AtlasGeneticsOncology.org/Genes/SLC16A1ID44046ch1p13.html

Master and Ph.D. theses completed

- Aggregation in Medicine

1. Jorge Correia-Pinto. Habilitation in Medicine. School of Health Sciences, University of Minho (2010).

- Ph.D. theses (the research work of all theses reported was carried out at ICVS/ECS)

1. André Albergaria. “Transcription Factors and Epigenetics in Breast Cancer: New Findings in CDH3/P-Cadherin Gene Regulation”. Ph.D. in Health Sciences, supervised by Fernando Schmitt (IPATIMUP) and Cecília Leão (ICVS), School of Health Sciences, University of Minho (2010).

2. Céline Pinheiro. ‘Role of Monocarboxylate transporters in solid tumours’. Ph.D. in Health Sciences, supervised by Fátima Baltazar, School of Health Sciences, University of Minho (2010).

- M.Sc. theses (the research work of all theses reported was carried out at ICVS/ECS)

1. Helena Pereira. 'Role of Monocarboxylate transporters colorectal carcinoma'. Supervised by Fátima Baltazar. Master Thesis in Molecular Genetics. School of Health Sciences, University of Minho (2010).

2. Ana Paula Pacheco. 'Characterization of *hairy1* and *hairy2* pattern expression during lung development of *Gallus gallus*, Master Thesis in Molecular Genetics, supervised by Jorge Correia-Pinto and Rute Moura, School of Biology, University of Minho (2010).

3. Filipe Pinto. 'Role of metastasis suppressor Raf Kinase Inhibitory Protein (RKIP) in Cervical Cancer'. Supervised by Rui M Reis. Master in Biotechnology for Health Sciences, University of Trás-os-Montes e Alto Douro (UTAD), (2010).

Prizes

1. *IPEG Research Grant Award 2010* with the work 'Experimental studies for assessing esophageal atresia repair by N.O.T.E.S.' by Henriques-Coelho T, Moreira-Pinto J, Rolanda C, Lima E, Miranda A, Correia-Pinto J. Announced in the IPEG's 19th Annual Congress, Hawai, US (2010).

2. *Gold Medal in Academic Olympics* for the work 'Renin-angiotensin system as a target to treat fetal lung hypoplasia' by Nogueira-Silva C, Dias E, Piairo P, Nunes S, Baptista MJ, Moura RS, Correia-Pinto J. Announced in the International Congress of Union of European Neonatal and Perinatal Societies (UENPS). Istanbul, Turkey (2010).

3. *Bolsa Pierre Fabre 2010*, for the work 'G2P[4] the most prevalent rotavirus genotype in 2007 winter season in an European non-vaccinated population.' by Antunes H, Afonso A, Iturriza M, Martinho I, Ribeiro C, Rocha S, Magalhães C, Carvalho L, Branca F, Gray J. and published in the J Clin Virol, 45(1):76-8 (2009). Announced by the Paediatric Portuguese Society (SPP) for the best paper published in 2009 by Portuguese Pediatricians (2010).

4. *Prize GlaxoSmithKline for best oral presentation* 'Hipertensão pulmonar na circulação de Fontan' by Neves AL, Baptista MJ in the meeting "Hipertensão arterial pulmonar: da criança ao jovem adulto. Reunião conjunta dos GECC e GEHP da SPC" (2010).

Organization of conferences

• Organization of Scientific Meetings and Presence in Scientific Committees
- 'Curso de Hemodinâmica neonatal e ecocardiografia funcional.' Porto (2010).
- 'Hipertensão arterial pulmonar: da criança ao jovem adulto. Reunião conjunta dos GECC e GEHP da SPC'. Porto (2010).
- 'IV Jornadas de Gastrenterologia do Hospital de Braga'. Braga (2010).
- 3rd Minho Medical Meeting in Perinatology organized by the MD Students from School of Health Sciences, University of Minho. Braga (2010).

• Post-graduation courses and workshops organized at the ICVS

- *Bioinformatics in Health Sciences* December 6-17, within the post-graduation program of the ICVS/ECS (2010).
- *Drug, from molecule to therapeutics* April 9-10, within the post-graduation program of the ICVS/ECS (2010).
- *How to deal with radioactive material* in May 3-5, within the post-graduation program of the ICVS/ECS (2010).
- *Fundamentals of Genetics, Development and Neoplasia* (2nd Edition) October 11-22, within the post-graduation program of the ICVS/ECS (2010).
- *Hands-on course in gynecological laparoscopy* in March 11-13, within the post-graduation program of the ICVS/ECS (2010).
- *International Hands-on Course in Fetal and Neonatal Endoscopic Surgery* in March 8-10, within the post-graduation program of the ICVS/ECS (2010).
- *Minimally invasive urological surgical week* (included 2-days hands-on course in basic urological laparoscopy and 3-days hands-on course in urological LESS and NOTES) in March 15-19, within the post-graduation program of the ICVS/ECS (2010).
- *Hands-on course in digestive laparoscopy* in October 11-13, within the post-graduation program of the ICVS/ECS (2010).
- Encontros de Oncologia, Estado da Arte - Cancro do Pâncreas. School of Health Sciences, University of Minho. Braga (2010).
- *Methods of DNA Analysis: State of the art*. School of Health Sciences, University of Minho. Braga (2010).
- *Therapeutic endoscopy hands-on course* in October 14-15, within the post-graduation program of the ICVS/ECS (2010).
- *Hands-on course in biliary laparoscopy* in October 25-27, within the post-graduation program of the ICVS/ECS (2010).

Future Research

Objectives for 2011

The Surgical Sciences Research Domain will keep its strategy of strengthen the quality of native research (with native research, we mean research protocols conceived and financed by our domain, and authored in majority by elements of our team). Thus, it is our objective that native research comes out as one 'Native paper'/year/Ph.D. with a mean IF over 4.0 on our research topics. We'll keep as priority the post-graduation activities that we planned for 2011 aiming to increase the percentage of international participants for approximately 25% of the total number of participants. Although we feel that our Domain has became credible to attract MD and even Engineers to do their academic differentiation, we feel that we need to be more pro-active to attract researchers with background in Biological Sciences. We hope that current identifiable constrains/limitations might be overcome during this year (eg, facilities for large animals; to launch the basis for a more fruitful collaboration with affiliated clinical institutions). Finally, we'll try to fight for lobbying for competitive financing in international agencies and to announce international calls for networking of surgeons/researchers proposing a couple of international research fellowships both in translation and basic sciences.

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