

**FCT** Fundação para a Ciência e a Tecnologia

MINISTÉRIO DA CIÊNCIA, TECNOLOGIA E ENSINO SUPERIOR

Unit Name:

*Instituto de Investigação em Ciências da Vida e Saúde  
(HESC-Norte-Braga-652)*

**LIFE AND HEALTH SCIENCES RESEARCH INSTITUTE (ICVS)**  
*INSTITUTO DE INVESTIGAÇÃO EM CIÊNCIAS DA VIDA E SAÚDE*

**ANNUAL REPORT**

**2009**

**School of Health Sciences**

University of Minho, Braga

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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.

The ICVS was formally integrated into the national system of science and technology by FCT in 2003. The ICVS was ranked with the maximum grade of “Excellent”, by the FCT’s international evaluation panels that visited the Institute in 2003 and in 2008.

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

- Innovative and 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 of which with a PI. Each RD and RL is supervised by a coordinator. This flexible organization is also important for the creation of multi- and inter-disciplinary teams.
- Integrated/shared management of resources - organization of function-oriented laboratories.
- Innovative Post-graduation, organized as an International Programme that offers advanced training in biomedical and clinical sciences.

***The ICVS research activities are presently 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);

***The ICVS governing bodies are:***

- The Scientific Council (SC) - includes all ICVS PhD members, focusing its activities on the planning, development and evaluation of the research activities;
- The Director, that liaises with the SC;
- The Directive Board of ICVS (DB) – coordinated by the ICVS Director, integrates the Coordinators of the RDs, the Coordinator of the Post-graduation Programme and one representative from the ECS Direction. The DB activities are centred on monitoring the ongoing activities, establishing the operating rules, determining the sharing of resources and the planning of the ICVS funding;

- The RD Coordinators, who govern the research activities within the respective RD;
- The Boards of the RDs, composed by the respective PIs, discussing the overall planning and achievements of the different research lines;
- The RL Coordinators, who report on the ongoing RL activities to the RD Coordinator;
- The External Advisory Committee, integrating the international experts:
  - Alan Flake – Full Professor, School of Medicine, University of Pennsylvania, Philadelphia, USA.
  - Marina Bentivoglio – Full Professor, Medical Faculty, University of Verona, Italy.
  - Paulo Vieira – Chargé de Recherche, Pasteur Institute, Paris, France.

## General Objectives

In the national context, 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:

- to promote original lines of investigation, with a high scientific output and a recognized impact in the advance of the knowledge on biomedical and clinical sciences;
- to encourage an innovative interaction between research and medical undergraduate/graduate training;
- to provide international post-graduated programmes;
- to offer specialized health services to the community.

Therefore, the ICVS intends to be an institute of high profile at the international level, promoting research on biomedical and on clinical sciences, endorsing innovative interactions between research and medical training activities (under- and post-graduation).

The ICVS is, additionally, a growing institution and represents an attractive research environment, including for young researchers.

### ***The specific developmental strategies for 2009 were to:***

- promote highly competitive, multidisciplinary research projects involving scientists and health professionals;
- create formal PhD and Master Programmes in ECS/ICVS, according to the “Bologna Process”;
- pursue in the involvement of medical students and MDs within the ICVS research projects;
- support the ongoing MD/PhD 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 (including private foundations, industry and the FP7 EU programme);
- strengthen the network of shared research facilities (laboratories and scientific equipments);
- promote the public awareness on health sciences.

***Based on the above described strategies, the specific milestones for 2009 were to:***

- implement the first formal PhD Programmes in Health Sciences and in Medicine as well as Master Programmes in Health Sciences;
- increase the capacity of the provisional animal facility;
- pursue the complement of the FCT contract for ICVS's funding, namely aiming at the strengthening of the equipments for research in animal models;
- increase the number of PhD researchers, namely by recruiting post-docs and high profile fulltime PhD researchers in the context of the "*Compromisso com a Ciência*";
- expand funded collaborative research projects and diversify the funding sources, including, at least, 2 new projects at the international level;
- increase the number of independent clinical research investigators, in order to competitively apply for clinical research funding (namely in the context of the Harvard-Portugal Programme);
- continue with regular scientific seminars - "*Ciência Falada*" - and activities aiming at public awareness of science.

## **Main Achievements during the year of 2009**

- A notable increase in the quality of the scientific production, with an IF average of 4,64 including two papers in "Science";
- A complement of the contract established with the FCT, corresponding to a total amount of 1.120.000 Euros, allowing for the set up of equipments and infrastructures, reinforcing the animal facilities and equipments for animal models on Microbiology of Infection, Neurosciences and Surgical Sciences;
- The reinforcement of the clinical scope of the ICVS research, through the creation of a Clinical Academic Centre, with the partnership of the Hospital de Braga - Grupo Escala and the Minho MD Alumni Association;
- The launching by ECS/ICVS of formal PhD and Master Programmes in Medicine and in Health Sciences, according to the principles of the "Bologna Process";

- A strong increase in the capacity to attract competitive funding, including within international networks.

***Additionally, in 2009, the ICVS was able to:***

- maintain a sustained increase in staff numbers and level of differentiation: the number of PhDs increased from 38 in 2008 to 40 in 2009 (24 ECS faculty, 5 “*Compromisso com a Ciência*”, and 11 Post-Docs);
- achieve an increase in the impact of the publications: 76 papers in international journals with an average impact factor of 4.64 (including articles with an IF between 3 and 5 = 16 papers; IF between 5 and 10 = 7 papers; IF between 10 and 20 = 5 papers; IF>25 = 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 than one individual report;
- accommodate the research that led to the conclusion of 7 PhD theses;
- involve an increasing number of PhD (72) and Master (34) students, as well as 17 assistant researchers and 18 members of the non-academic staff (13 technicians and 5 administrative; financially supported by ECS);
- maintain a significant number of MD students involved in research, including 27 Option Projects and 8 MD/PhD Lab Rotations;
- get a total of 47 new fellowships granted from FCT - 11 BPD (6 allocated), 15 BD (6 allocated), 15 BI (6 allocated) and 6 BII;
- rise external/competitive funding; the ongoing projects (average duration 3 years) involve funding of about 2.2 million €, of which about 30% correspond to the activities developed in 2009. Additionally, in 2009 new projects were granted:
  - Several projects submitted to the last FCT call, corresponding to a total funding of about 1.83 million € (from 49 projects submitted, 17 were approved, corresponding to a 35% success rate).
  - In the context of European FP: 1 proposal of Consortium was approved (232 344 € granted); and 1 Research Sub-Contract extended (35 000 €); as well as 1 Marie-Curie action (budget under final negotiation).
  - An international Research Contract was established with the Industry: Bayer Schering Pharma (45 000 €).
  - Grants from Private Foundations: Fundação BIAL (37 000 €); and Hope for Depression Research Foundation (USA) (110 000 USD).

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

(for detailed information see <http://www.icvs.uminho.pt/icvs/>)



### Integrative/multidisciplinary activities during the year of 2009

At the launching of the ECS, faculty members with diverse and complementary scientific backgrounds were recruited. This was the basis for the development of strong Research Domains (RD), combining scientists able to approach scientific problems using complementary perspectives. Furthermore, an increasing number of ongoing projects are being developed transversely across the RDs. In fact, 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.

The combined teaching and research expertise of the ECS staff also contributed to the successful training of medical students, promoting the interaction between biomedical research and medical education, as, for example: (i) the Curricular Area “Option Projects” and; (ii) the MD/PhD programme (in collaboration with the Thomas Jefferson and Columbia Medical Schools). In 2009, the interplay between the research activities at ICVS and the ECS medical course is also reflected in the publication, on the field of education in Life & Health Sciences, of 5 articles (1 in press) in peer reviewed journals, as well as 7 articles in proceedings of international conferences. One researcher at ICVS was guest editor in one issue and is author of the corresponding Editorial.

Also in 2009, an important achievement corresponded to the launching of formal PhD Programmes in Health Sciences and in Medicine, as well as a Master Programme in Health Sciences. These programs fulfil the requirements of the “Bologna Process”, and are multidisciplinary in nature. The ECS/ICVS also established in 2009, in collaboration with the Faculty of Medicine of the University of Coimbra and the Faculty of Medical Sciences of the New University of Lisbon, an interactive and multi-centred Inter-University Doctoral Programme in Ageing and Degeneration of Complex Biological Systems, in which students from the PhD programs in each medical school may enrol. This programme is supported by the Gulbenkian Foundation.

Responding to the novel challenge of FCT that launched the fellowships “*grants for scientific initiation in research*” for graduation students, aiming at fostering scientific activities and developing critical reasoning skills, creativity and autonomy, the ICVS was granted with 9 fellowships. The fellowships included 7 students of Medicine, 1 from the Applied Biology course (Sciences School, UM); and 1 from the Nuclear Medicine course (*Escola Superior de Tecnologia da Saúde, Porto*).

The ICVS RDs have pursued the establishment of international collaborations with reference labs in Europe and in the USA, as well as with health institutions from developing countries, namely in Africa and Latin America. In 2009, important progresses were registered, with the successful application for competitive funding to support international networks, namely:



- In the context of European FP: 1 proposal of Consortium, 1 Research Sub-Contract, 1 Marie-Curie action;
- One research project grant from Hope for Depression Research Foundation (USA).

At the National level, following the previous networking activities involving clinicians from hospitals, the ICVS created a Clinical Academic Centre. This Centre was launched in a partnership with the Hospital de Braga - Grupo Escala and the Minho MD Alumni Association and will develop translational and clinical research projects, including clinical trials.

## **Outreach activities during the year of 2009**

The promotion of public awareness of science is an important endeavour of ICVS. Our outreach activities encompass broad interactions with the general public as well as specific groups, ranging from students from the primary and secondary schools to teachers and senior citizens. The events/activities involving Science & Society are listed below.

### **1 – ICVS Newsletter**

The Newsletter, describing the ICVS research activities, was created in 2008 and continued its regular publication during 2009.

### **2 – “Science Experimental Teaching Programme”**

The second edition of the hands-on interactive educational programme designed to support Science, Technology and Life Sciences teachers, as well as to motivate students from the secondary-level, was launched. The 2008/09 academic year involved: (i) 18 laboratory training rotations for secondary-level life sciences teachers, with 9 novel experimental protocols which are currently being tested in laboratory classes; (ii) the integration of 8 secondary-level students in research projects at ICVS during a 3-4 months period; and; (iii) 3 seminars provided by ICVS researchers at the secondary schools. The experimental protocols will be published, as well as the 8 scientific reports elaborated by the secondary-level students.

### **3 – “Community Health Teaching Programme”**

This educational programme has been designed to provide secondary-school teachers, and consequently their students, with a better knowledge on community health issues, namely diabetes, sexual education, violence within schools, etc. This programme runs throughout the 2008/09 and the 2009/10 academic years and involves the ECS Medical Students and the Community Health faculty members.

#### 4 – “Secondary School Visit Programme”

To increase the public awareness on ICVS research, we offer scientific exhibitions, presentations and guided tours in the ICVS. During 2009, several High-Schools visited our facilities (in a total of 390 students) and observed *in loco* the work of the ICVS research teams.

#### 5 - “Portas Abertas” at 2009 Science and Technology Week

During the “Science and Technology Week” (24-26Nov), open lab activities were organized involving up to 355 students from several primary and secondary schools from the Minho region. Hands-on experiments were designed for each of the three educational levels (1-6th, 7-10th and 11-12th grade students) to allow our young visitors to become “Scientists for a day”. The description of “Portas Abertas” (Open Labs, Scientists for a day) is available at <http://www.icvs.uminho.pt/icvs/domains/sct09/>.

#### 6 – “Brain Awareness Week 2009”

In the context of the “Brain Awareness Year”, dedicated activities were performed (week 10-14th March). Namely, 9 Science Sessions at Schools were attained by 640 students; Open lab activities involving 100 secondary school students and 3 Senior University sessions attained by 50 senior students (50-82 years old).

#### 7 – “Verão no campus-2009”

The second edition of this Minho University programme promotes culture and science among pre-university students. The ICVS organized 3 days of hands-on experimental activities under the designation of “Animal Models in Investigation”, directed to secondary school students (20-22<sup>nd</sup> July).

#### 8 – “ICVS a Cores”

An artistic competition of scientific images from research work produced at ICVS was organized with the support of Olympus, with the purpose of promoting the ICVS research.

## ICVS Team (PhD Researchers)

### MICROBIOLOGY AND INFECTION

#### *ECS Faculty*

António Gil Castro

Cecília Leão

Fernando Rodrigues

Jorge Pedrosa

Margarida Correia-Neves

Paula Ludovico

#### *“Compromisso Ciência”*

Margarida Saraiva

Marcus Sturme

#### *Post-Docs*

Andrea Cruz

Cláudia Nóbrega

Nuno Osório

### NEUROSCIENCES

#### *ECS Faculty*

Armando Almeida

Joana Palha

João Bessa-Peixoto

João Cerqueira

João Sousa

Jorge Cotter

José Miguel Pêgo

Manuel Lima-Rodrigues

Nuno Sousa

Patrícia Maciel

#### *“Compromisso Ciência”*

António Salgado

#### *Post-Docs*

Ana João Rodrigues

Fernanda Marques

Ioannis Sotiropoulos

Luísa Pinto

### SURGICAL SCIENCES

#### *ECS Faculty*

Adhemar Longatto-Filho

Carla Rolanda

Estevão Lima

Fátima Baltazar

Jorge Correia-Pinto

Maria João Baptista

Rui Reis

#### *“Compromisso Ciência”*

Raquel Andrade

#### *Post-Docs*

Bruno Costa

João Vilaça

Rute Moura

Sandra Costa

#### *ECS Faculty*

Manuel João Costa

#### *“Compromisso Ciência”*

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## External Advisory Committee Evaluation Report



Paulo Vieira

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Paris, 31 March, 2010

### **Report by the External Advisory Committee of the Instituto de Investigação em Ciências da Vida e Saúde**

The External Advisory Committee of the Life and Health Sciences Research Institute (ICVS) visited the Institute on December 11th 2009. On that occasion the Committee attended presentations by the Research Domain Coordinators, visited the newly opened facilities of the ICVS, and met with the Direction, research staff, post-docs and students. In this report we summarize our opinion about the accomplishments in the past two years and offer some suggestions for the future.

We note the achievements of the ICVS for scientific creativity and productivity, across a spectrum of studies covering the 3 Domains of Research. We are happy to record the high quality of the research being conducted at the Institute. It is also gratifying to register the determined and intelligent way in which all the scientist at the Institute have been able to overcome the limitations imposed on their activities by a somewhat erratic schedule in the Calls for Grant Applications by the Ministry of Research. In spite of this limitation the scientists at the ICVS have published over 170 international articles in peer-reviewed publications, some of them in very high impact journals. It is of particular notice that those very high impact publications represent for the most part research carried out, primarily or exclusively, at the Institute.

The new resources, the containment level 3 laboratory and the animal model facilities for behavioral and surgical studies, are truly impressive accomplishments. These modern laboratories, excellently equipped and fully functional, will have a very significant impact in the research at the ICVS. We encourage the Health School and the relevant authorities to maintain constant support for the operation of these outstanding facilities, including funds for their expansion, should future developments justify it.

The goal of the External Advisory Committee is to help the ICVS to realize its full potential in a highly competitive research environment. ICVS will need to develop appropriate strategies regarding the scientific areas where their efforts should be concentrated. Judging from the output, be it measured in the number of scientific publications or the number of Masters' and PhD Thesis successfully defended, the Institute has clearly followed a winning strategy. We encourage the staff to continue in this

way, always taking care to avoid dispersing their (necessarily limited) resources on too many research programs.

Another crucial issue to determine the success of any research institute is the recruitment of scientific personnel. It is of course the aim of any recruiter to hire top quality researchers and the ICVS has clearly been very successful in that endeavor. But it is also very important that the scientific staff (including PIs, Post-Docs and Students) interact easily and can devote their best efforts to fruitful collaborations. This is precisely the impression we got from our visit and the leadership of the ICVS should be commended for fostering such a pleasant and productive working environment. Praise is also due to all the PIs at the ICVS for the attitude displayed by their collaborators: the conversations with the post docs and students revealed a strong "*Esprit de Corps*", built on a firm conviction that this is an excellent centre for them to be educated and to develop as researchers.

Finally, we should like to encourage all the scientists at the ICVS to pay constant attention to three issues that can negatively influence their research activities. The solutions to these problems are not entirely on their hands, but they should permanently be aware of their existence and grab all opportunities to resolve them, or at least mitigate, their impact:

*A) The Animal Facilities*

Unfortunately it has not yet been possible to obtain sufficient funds to build animal facilities of adequate dimensions to support the research activities of all the groups at the ICVS. Although the scientists have been able to cover their present needs by keeping the old facility open and adapting some rooms in the new building, this is far from satisfactory. It is imperative that a permanent long-term solution is found to this problem, so as not to impair the continuation of research at the ICVS.

*B) Online subscriptions*

A properly functioning Institute requires a well organized Library, with online access to all major scientific journals in all areas of research at the Institute. Although the situation at the ICVS has significantly improved over the past two years it is still far from ideal. We encourage the ICVS to develop strategies, for example by negotiating matching funds from research agencies, to fund a good set of subscriptions to major scientific journals. This is very important to allow adequate training and education of students and post-docs.

*C) Teaching responsibilities*

As in all academic research institutes, there is a trade-off between the time allocated to research and the time that has to be devoted to teaching duties. A proper balance is often difficult to obtain, but the ICVS has so far managed to do so and obtained substantial benefits from the interactions with colleagues in the medical school and in the area hospitals. We recommend that the scientists at the ICVS continue to pay careful attention to this point and avoid taking on excessive duties outside of their research activities.



Paulo Vieira (for the E.A.C. of the Life and Health Sciences Research Institute)

## Research Groups

**Title / Research Domain Coordinator**

**MICROBIOLOGY AND INFECTION Research Domain**  
(Jorge Pedrosa)

**NEUROSCIENCES Research Domain**  
(Nuno Sousa)

**SURGICAL SCIENCES Research Domain**  
(Jorge Correia-Pinto)

## **a) MICROBIOLOGY AND INFECTION Research Domain**

### **Research Domain Description**

**Title of Research Group:** MICROBIOLOGY AND INFECTION

**Coordinator:** Jorge Pedrosa

**Main Scientific Domain:** Health Sciences

**Research Lines:** Immunology of Infection  
(Coordinator: António Gil Castro)  
Cellular & Molecular Microbiology  
(Coordinator: Fernando Rodrigues)

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## Objectives & Achievements

### Objectives

The Microbiology and Infection Research Domain was established in 2003 with the objective of developing biomedical research, addressing specific challenges from the prophylaxis to the treatment of infectious diseases, particularly *mycobacteriosis* and systemic fungal infections.

From the launching of this Domain, an effort has been pursued to focus the research objectives and to increase the interaction between the Domain members. As a result of this effort, no more than two lines of research were recently defined, which include the research themes described below.

#### (i) Immunology of Infection, aiming to:

- Evaluate the contribution of host genetic variations accounting for an increased risk for invasive fungal infections in immunosuppressed patients;
- Investigate the biology of infection in *mycobacteriosis* of difficult treatment: Buruli Ulcer;
- Understand the role of T cells in the immune response against mycobacteria, namely:
  - Balance between IFN-gamma and IL-17 producing cells on protection/pathology in *tuberculosis*;
  - Influence of thymic infection on the ability of T cells to mount a protective immune response;
- Develop drug delivery systems for the treatment of *mycobacteriosis*;
- Understand the molecular mechanisms of cytokine gene regulation in cells of the innate immune system in response to infections by mycobacteria.

#### (ii) Cellular & Molecular Microbiology, aiming to:

- Identify apoptotic pathway(s) in *Saccharomyces cerevisiae* by evaluating the proteomic profile and metacaspase-interactive molecules;
- Elucidate the crosstalk between yeast cell metabolism and active cell death, and the molecular determinants for entry, maintenance and exit from quiescence (G0) in yeast;
- Develop yeast models of human neurodegenerative diseases (Batten; Parkinson; Machado-Joseph; Huntington);
- Evaluate the molecular bases of dimorphism in the pathogenic fungi *Paracoccidioides brasiliensis*;
- Develop fast molecular-diagnostic procedures to identify *Candida* spp and *Aspergillus* spp infections and testing serodiagnostic techniques to improve the diagnostic of human *tuberculosis* in Portugal.

Recently, a side line was put in place with the objective to perform studies in individuals HIV+ and co-infected with either *M. tuberculosis* or *Candida* spp.

## Main Achievements

During the year of 2009, the main scientific achievements of the Domain resulted from the consolidation of the previously established cellular and animal models of infection by mycobacteria or fungi, namely those developed in fully operational BSL3 facilities.

The strategic aims for the present phase included: (i) the diversification of funding sources; (ii) the reinforcement of the translational/clinical focus of research; and (iii) the increase in the impact factor of the Domain's publications. Important advances were achieved in all areas. Indeed, 5 projects were granted from FCT and 1 from Fundação Calouste Gulbenkian. Also, we successfully participated in 2 Networks of the FP7 EU Program, one granted in 2008 for the study of *tuberculosis*, and another on the participation in a European consortium for the development of vaccines against Buruli Ulcer, to be started in 2009. The average IF of the papers increased from 4.5 to 5.9 and 2 papers were published in journals with an IF above 10.

Additionally, and following the sustained increase in the differentiation level of the Domain's PhD members, we successfully recruited a fulltime researcher in the context of the FCT program "*Compromisso com a Ciência*".

Regarding details on scientific productivity:

1. Publications
  - a. 21 publications in international peer-reviewed journals (including 6 articles in press);
  - b. 21 abstracts in international congresses;
  - c. 2 international proceedings in conferences.
2. Theses completed
  - a. 3 PhD theses;
  - b. 4 Master theses.
3. Organization of conferences
  - a. Organization of 5 international post-graduation courses;
  - b. Organization of 1 international scientific meeting.
4. Internationalization and Academic Juries
  - a. Participation in 15 PhD juries;
  - b. Participation in 6 "Agregação" juries;
  - c. Ad-hoc reviews for the journals: PNAS; Human Molecular Genetics; Journal of Medical Microbiology; Mycoses; Nature Reviews; Microbiology; PLoS Neglected Tropical Diseases;

PLos one; British Journal of Dermatology; Journal of Applied Microbiology; Cell Death Differentiation (CDD); Biochimica et Biophysica Acta-Molecular Cell Research (BBA); Apoptosis; Molecular Microbiology; FEBS Letters; FEMS Yeast Research; Gene; Free Radical Biology and Medicine (FRBM);

- d. Evaluators of funding agencies and of prizes: FCT, Wellcome Trust and Swiss Science Foundation.

## 5. Funding

- a. Diversification of funding sources and reinforcement of the translational/clinical focus of research, with 5 FCT grants and 1 FP7 consortium starting in 2009.
- b. Presently, the Domain's funding includes 9 FCT grants, 1 grant from Fundação Calouste Gulbenkian and 2 FP7 consortiums.
- c. Additionally, we have put forward a multidisciplinary proposal for the Health Cluster Portugal (QREN) in which the ICVS/Clinical Academic Centre is the Coordinator.



## Group Productivity

### Publications in peer reviewed Journals

The Microbiology and Infection Research Domain published 15 articles in 2009 (in addition, 6 other research articles were accepted for publication in 2009 and are presently *Ahead of Print* or *In Press*). The 15 published papers have a mean impact factor of 5.9 and correspond to a ratio of 1.4 papers/PhD. One article has an impact factor above 10 and 1 article above 25.

The following list of publications is divided according to the Line of Research where the publications were originated.

#### Immunology of Infection

1. Eddyani M, Fraga AG, Schmitt F, Uwizye C, Fissette C, Johnson C, Aguiar J, Sopoh G, Barrogui Y, Meyers WM, Pedrosa J, Portaels F. Fine needle aspiration, an efficient sampling technique for the bacteriological diagnosis of nonulcerative buruli ulcer lesions. *J Clin Microbiol*. 2009. 47(6):1700-4. (IF = 3.945)
2. Gonçalves C, Torrado E, Martins T, Pereira P, Pedrosa J, Gama M. Dextrin nanoparticles: Studies on the interaction with murine macrophages and blood clearance. *Colloids Surf B Biointerfaces*. 2009. [Epub ahead of print]. (IF = 2.593)
3. Huygen K, Adjei O, Affolabi D, Bretzel G, Demangel C, Fleischer B, Johnson RC, Pedrosa J, Phanzu DM, Phillips RO, Pluschke G, Siegmund V, Singh M, van der Werf TS, Wansbrough-Jones M, Portaels F. Buruli ulcer disease: prospects for a vaccine. *Med Microbiol Immunol*. 2009. 198(2): 69-77. (IF = 2.222)
4. Marques F, Sousa JC, Coppola G, Geschwind DH, Sousa N, Palha JA, Correia-Neves M. "The choroid plexus response to a repeated peripheral inflammatory stimulus" *BMC Neuroscience*. 2009. 18;10:135. (IF = 2.850)
5. Marques F, Falcão AL, Sousa JC, Coppola G, Geschwind D, Sousa N, Correia-Neves M, Palha JA. "Altered iron metabolism is part of the choroid plexus response to peripheral inflammation". *Endocrinology*. 2009. 150(6): 2822-8. (IF = 4.945)
6. Marques F, Sousa J, Coppola G, Falcão AL, Rodrigues A, Geschwind DH, Sousa N, Correia-Neves M, Palha JA. "Kinetic profile of the transcriptome changes induced in the choroid plexus by peripheral inflammation". *Journal of Cerebral Blood Flow and Metabolism*. 2009. 29(5):921-32. (IF = 5.741)
7. Nobrega C, Roque S, Nunes-Alves C, Coelho C, 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". *Journal of Immunology*. (in press). (IF = 6.000)
8. Oliveira JT, Santos TC, L. Martins, R. Picciochi, A. P. Marques, A. G. Castro, N. M. Neves, J. F. Mano, R. L. Reis. Gellan gum injectable hydrogels for cartilage tissue engineering applications: in vitro studies and preliminary in vivo evaluation. *Tissue Eng Part A*. 2009 Aug 25. Pub Ahead of print. (IF = 4.699)
9. Roque S, Correia-Neves M, Mesquita AR, Palha JA, Sousa N. "Interleukin-10: A Key Cytokine in Depression?" *Cardiovascular Psychiatry and Neurology*. 2009. Article ID 187894, doi: 10.1155/2009/187894. (IF Undetermined)
10. Santos N, Correia-Neves M, Ghebremichael S, Källénus G, Svenson SB, Almeida V. Epidemiology of *Mycobacterium bovis* infection in wild boar *Sus scrofa* from Portugal. *J Wildl Dis*. 2009 Oct;45(4):1048-61. (IF = 1.330)

11. Silva MT, Portaels F, Pedrosa J. Pathogenetic mechanisms of the intracellular parasite *Mycobacterium ulcerans* leading to Buruli ulcer. *Lancet Infect Dis*. 2009. 9:699-710. (IF = 13.165)
12. Teixeira L, Botelho AS, Mesquita SD, Correia A, Cerca F, Costa R, Sampaio P, Castro AG, and Vilanova M. Plasmacytoid and conventional dendritic cells are early producers of IL-12 in *Neospora caninum*-infected mice. *Immunol Cell Biol*. 2009 Sep 15 Epub ahead of print. (in press). (IF = 3.859)
13. Torrado E, Fraga AG, Logarinho E, Martins TM, Carmona JA, Gama JB, Carvalho MA, Proença F, Castro AG. and Pedrosa J. A protective IFN- $\gamma$ -dependent activation of macrophages induced during infection with *Mycobacterium ulcerans* is impaired by the lipid toxin mycolactone. *Journal of Immunology*. (in press). (IF = 6.000)
14. van Heijst JWJ, Gerlach C, Swart E, Sie D, Nunes-Alves C, Kerkhoven RM, Arens R, Correia-Neves M, Koen Schepers, Ton N. M. Schumacher. "Recruitment of Antigen-Specific CD8+ T Cells in Response to Infection is Markedly Efficient". *Science*. 2009. 325(5945):1265-9. (IF = 28.103)

### **Cellular & Molecular Microbiology**

1. Almeida, A.J, Cunha, C, Carmona, J.A, Sampaio-Marques, B, Carvalho, A, Malavazi, I, Steensma, H.Y, Johnson, D.I, Leão, C, Logarinho, E, Goldman, G.H, Castro, A. G, Ludovico, P, and Rodrigues, F. Cdc42p controls yeast-cell shape and virulence in *Paracoccidioides brasiliensis*. *Fungal Genet Biol*. 2009. 46:919-926. (IF = 3.005)
2. Almeida B, Ohlmeier S, Almeida AJ, Madeo F, Leão C, Rodrigues F, Ludovico P. Yeast protein expression profile during acetic acid-induced apoptosis indicates causal involvement of the TOR pathway. *Proteomics*. 2009. 9(3):720-32. (IF = 4.586)
3. Azevedo MM, Almeida B, Ludovico P, Cássio F. Metal stress induces programmed cell death in aquatic fungi. *Aquat Toxicol*. 2009 92(4):264-70. (IF = 3.517)
4. Carvalho A, Cunha C, Carotti A, Aloisi T, Guarrera O, Di Ianni M, Falzetti F, Bistoni F, Aversa F, Pitzurra L, Rodrigues F, Romani L. Polymorphisms in Toll-like receptor genes and susceptibility to infections in allogeneic stem cell transplantation. *Exp Hematol*. 2009 37(9):1022-9. (IF = 3.203)
5. Greenwood MT and Ludovico P. Expressing and functional analysis of mammalian apoptotic regulators in yeast. *Cell Death Differ*. 2009 Nov 13. [Epub ahead of print]. (IF = 7.548)
6. Mendes-Ferreira, A., C. Barbosa, V. Falco, C. Leao, and A. Mendes-Faia. 2009. The production of hydrogen sulphide and other aroma compounds by wine strains of *Saccharomyces cerevisiae* in synthetic media with different nitrogen concentrations. *J Ind Microbiol Biotechnol* 36:571-583. (IF = 1.919)
7. Osório NS, Sampaio-Marques B, Chan CH, Oliveira P, Pearce DA, Sousa N, Rodrigues F. 2009. Neurodevelopmental delay in the *Cln3*(triangle upex7/8) mouse model for Batten disease. *Genes Brain Behav*. 2009. 8(3):337-45. (IF = 3.890)

### **Other publications International**

- Book Chapters

1. Cássio F, Leão C, Baltazar F. Plasma membrane transport of monocarboxylates in yeasts. In: *Frontiers in Fungal Ecology, Diversity and Metabolites*. Ed. Sridhar, KR. IK International Publishing House Pvt. Ltd., New Delhi. pp. 248-263. (2009).

## Master and Ph.D. theses completed

- PhD theses (the research work of all theses reported was carried out at ICVS/ECS)
  1. Bruno Miguel Barroso Rodrigues Almeida. "Elucidation of molecular pathways involved in *Saccharomyces cerevisiae* apoptotic cell death". Supervised by Paula Ludovico, School of Health Sciences, University of Minho.
  2. Cláudia Nóbrega. "Thymus infection by mycobacteria: consequences for the immune response and chemotherapy". Supervised by Margarida Correia-Neves. Program in Basic and Applied Biology (GABBA), University of Porto.
  3. Nuno Osório. "Yeast models of neuronal ceroid lipofuscinosis: From different genes to common biological features". Supervised by Fernando Rodrigues, School of Health Sciences, University of Minho.
- Master theses (the research work of all theses reported was carried out at ICVS/ECS)
  1. Helena da Costa Marques (Bsc. in Clinical Laboratory Techniques) on the Master project "Aconitase as a target of fragmentation during oxidative stress induced apoptosis in *Saccharomyces cerevisiae*" in the context of the master program in Molecular Genetics from the Biology Department of Minho University. Supervised by Paula Ludovico, ICVS.
  2. Daniela Pereira (Bsc. in Clinical Laboratory Techniques) on the Master's project "Modulation of the immune response to mycobacteria: implications on protection and pathology" in the context of the masters program in Molecular Genetics from the Biology Department of Minho University. Supervised by Jorge Pedrosa, ICVS.
  3. Carol Sousa (Bsc. in Biology) on the Master's project "Characterization of the *in vitro* cytokine response of phagocytes to mycobacteria" in the context of the masters program in Molecular Genetics from the Biology Department of Minho University. Supervised by Jorge Pedrosa, ICVS.
  4. Palmira Barreira da Silva (Bsc. in Biology) on the Master project "In vitro T cell differentiation in the presence of infected cells with *Mycobacterium avium*". University of Porto. Supervised by Margarida Correia-Neves, ICVS.

## Prizes

- Bruno Almeida, Prize "Young Investigator" tribute to Prof Isabel Spencer Martins. "Elucidation of molecular pathways involved in *Saccharomyces cerevisiae* apoptotic cell death" Prize of the Portuguese Society of Microbiology (2009).
- Alexandra Silva, Prize for the best abstract "Global translation impairment during acetic acid-induced apoptosis in *Saccharomyces cerevisiae*" in the 7th International meeting on Yeast Apoptosis, Graz, Austria (2009).
- Lima-Rodrigues M, Vieira A, Lamas N, Valle-Fernandes A, Nunes R, Pedrosa J, Castro AG, Reis RM, Almeida A. Prize for best Poster for the work "Possible alternative therapies to chronic laryngitis and laryngeal cancer: the use of COX-2 specific inhibitors". 1st Meeting of the European Academy of ORL\_HNS, Mannheim-Germany (2009).
- Margarida Saraiva, Andrea Cruz, Maria Teixeira-Coelho, Jenny Carmona, Carole Sousa, Daniela Ramos-Pereira, Jorge Pedrosa, António G. Castro. Prize for best Poster, "Symposium Cellular Microbiology and Pathogenesis". "TLR2 controls IL-17 responses to *Mycobacterium tuberculosis*". "Microbiotec 09", Vilamoura, Algarve (2009).

## Organization of conferences

- Organization of Scientific Meetings and Presence in Scientific Committees
  - Cecilia Leão, Fernando Rodrigues and Paula Ludovico, Members of the organizing committee of "XVII Jornadas de Biologia de Leveduras "Professor Nicolau van Uden", Universidade do Minho, Braga, 2009.
  - Cecilia Leão, Member of the scientific committee of "Microbitec 09", Vilamoura, Algarve. 2009.
- Post-graduation courses and Workshops organized at the ICVS
  - Paula Ludovico and Elsa Logarinho. Gene silencing using RNA interference: lectures and hands-on. 1-5 June 2009.
  - Paula Ludovico and Margarida Correia-Neves. Applications of flow cytometry in biomedical research. 15-17 June 2009.
  - Magda Carlos and Margarida Correia-Neves. 5th edition Laboratory Animal Science course. November 2009.
  - António Salgado, Margarida Saraiva and Sandra Costa. Animal Cell and Tissue Culture: from basic principles to advanced techniques. 16 - 20 February 2009.
  - Margarida Correia-Neves. Immune Response to Infection (post-graduation course in the context of the GABBA program). 2-6 February 2009.
- Organization of Other Meetings

Margarida Correia-Neves, Joana Palha, Manuel João Costa. Interactive teaching and student centred learning. 26-27 November 2009. Maputo, Mozambique.

## Internationalization

- European Consortiums (funded by FP7 EU):
  - Margarida Correia-Neves. "Integrated control of neglected zoonoses: improving human health through scientific innovation and public engagement" ICONZ.
  - Jorge Pedrosa. BURULIVAC - Development of Vaccines for Buruli Ulcer.
- Collaborations:
  - Andrea Cooper, Trudeau Institute, Saranac Lake, N.Y, USA
  - Anne O'Garra, National Institute for Medical Education, London, UK.
  - Campbell Gourlay, University of Kent, UK.
  - Christophe Benoist, Section on Immunology and Immunogenetics, Joslin Diabetes Center, Brigham and Women's Hospital, Harvard University, Boston, USA.
  - David A Pearce, Center for Neural Development and Disease, University of Rochester School of Medicine and Dentistry. Rochester. USA.
  - Frank Madeo, Institute for Molecular Biosciences, Graz, Austria.
  - Fulvio Reggiori, Department of Cell Biology, University Medical Centre Utrecht Heidelberglaan, Netherlands.
  - Martin Holcik, Apoptosis Research Centre, University of Ottawa Children's Hospital of Eastern Ontario Research, Canada.
  - William C. Burhans, Dept. Molecular and Cellular Biology, Roswell Park Cancer Institute, Buffalo, NY, USA.

## Funding

### Government/Organization contract research

#### Immunology of Infection

1. 2007-2010 – Project from the Fundação para a Ciência e Tecnologia (FCT) nº PTDC/SAU-MII/70895/2006, entitled “Role of Interleukin-23 (IL-23) and IL-17 in the regulation of the immune response to the infection by *Mycobacterium tuberculosis*”, granted with 116 774 € António Gil Castro (PI);
2. 2009-2012 – Project from the Fundação para a Ciência e Tecnologia (FCT) nº PIC/IC/83313/2007. “Reconstitution and Homeostasis of the Immune System Following HIV-Infection”, granted with 140 000 €. António Gil Castro (PI);
3. 2009-2012 – Project from the Fundação Calouste Gulbenkian. “Buruli Ulcer – from the understanding of the mechanisms of host resistance to the development of new interventions against an emergent mycobacteriosis”, granted with 160 000 €. Jorge Pedrosa (PI);
4. 2010-2013 - Project from the Fundação para a Ciência e Tecnologia (FCT) nº PTDC/SAU-MII/101663/2008. “Infection of the thymus by mycobacteria: implications for the immune response, therapy and latency in tuberculosis”, granted with 130 000 €. Margarida Correia-Neves (PI);
5. 2010-2013 - Project from the Fundação para a Ciência e Tecnologia (FCT) nº PTDC PTDC/BIA-BCM/102776/2008. “Molecular mechanisms underlying regulation of IL-12 family of cytokines expression on macrophages and dendritic cells infected by *Mycobacterium tuberculosis*”, granted with 173 447 €. Margarida Saraiva (PI);
6. 2010-2013 - Project from the Fundação para a Ciência e Tecnologia (FCT) nº PTDC PTDC/SAU-MII/101977/2008. “BCG vaccination: a tool to identify new correlates of protection and pathology in experimental infection with *Mycobacterium tuberculosis*”, granted with 199 036 €. António Gil Castro (PI).

#### Cellular & Molecular Microbiology

1. 2007-2010 - Project from the Fundação para a Ciência e Tecnologia (FCT) nº PTDC/AGR-ALI/71460/2006. “Evaluation of the effects of nitrogen supply on yeast cell physiology, transcriptome, proteome and metabolome for optimizing the production of economically important odour and flavour compounds”, granted with 34 780 €. Cecília Leão (PI at ICVS);
2. 2007-2010 – Project from the Fundação para a Ciência e Tecnologia (FCT) nº PTDC/SAU-NEU/70161/2006. “Uncovering pathological mechanism underlying juvenile neuronal ceroid lipofuscinoses: from yeast to more complex model systems”, granted with 112 165 €. Fernando Rodrigues (PI);
3. 2010-2013 - Project from the Fundação para a Ciência e Tecnologia (FCT) nº NMed-SD/0076/2007. “NanoMeDiag-Nanobioanalytical platforms for improved medical diagnosis of infections caused by pathogen microorganisms”, granted with 30 000 €. Fernando Rodrigues (PI at ICVS);
4. 2010-2013 - Project from the Fundação para a Ciência e Tecnologia (FCT) nº PTDC/BIA-MIC/108309/2008. “Unraveling the specific involvement of the small Rho-like GTPase Cdc42 in the highly polymorphic nature of *Paracoccidioides brasiliensis* yeast cells”. Granted with 120 000 €. Fernando Rodrigues (PI).



## Other organization contract research

- European Consortiums (funded by FP7 EU):
  1. 2009-2014 – Margarida Correia-Neves. "Integrated control of neglected zoonoses: improving human health through scientific innovation and public engagement" ICONZ, Budget attributed to the ICVS/UMINHO: 144 181 €
  2. 2010-2015 – Jorge Pedrosa. "BURULIVAC - Development of Vaccines for Buruli Ulcer", Funding agency: Budget attributed to the ICVS/UMINHO: 232 344 €

## Future Research

### Objectives

Following the strategic plan carried until 2008, the Microbiology and Infection Research Domain is focusing its research objectives and has now reorganized its scientific interests in two lines of research: Cellular and Molecular Microbiology and Immunology of Infection. This follows the strategy pursued in the Domain, furthering the development of clearly defined objectives, increasing both the critical mass within each research line and the scientific interaction between the Domain members.

In 2009, we have improved the Domain productivity, particularly regarding the average impact factor of the published articles. It is our purpose to keep increasing the number and improving the quality of the scientific publications. Specifically, we aim at publishing more than 2 papers PhD/year and, at least, 1 article in a high profile journal.

Regarding human resources at the PhD level, following the growth registered in the two previous years, 2009 was a period of consolidation. It is our objective to start a new cycle of growth in 2010, increasing the number of PhDs 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 involve in formal PhD 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.

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 the Science Schools, as well as from the Iberian Institute of Nanotechnology, Braga, 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.

## **b) NEUROSCIENCES Research Domain**

### **Research Domain Description**

**Title of Research Group:** NEUROSCIENCES

**Coordinator:** Nuno Sousa

**Main Scientific Domain:** Health Sciences

**Research Lines:** Neurodevelopment  
(Coordinator: Patrícia Maciel)  
Neurodegeneration  
(Coordinator: Armando Almeida)  
Neuroimmunology  
(Coordinator: Joana Palha)

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## Objectives & Achievements

### Objectives

The Neurosciences Research Domain is divided in 3 research lines. The main objectives of each of these lines are:

#### 1. “Neurodevelopment” Line:

This research line addresses hormones, environmental stressors and genes as modulators of behaviour, both in animal models of disease and in patients.

- The programming effects of corticosteroids on the developing brain are studied using the rat as a model.
- The influence of thyroid hormones and iodine deficiency throughout pregnancy are assessed on human psychomotor development and in animal models of hypothyroxinemia.
- Genetic studies on Rett syndrome, non-syndromic mental retardation and schizophrenia look for associated genes and their metabolic regulators, using both human samples and rodent models of the diseases.
- Neuroimaging assessment in behaviourally- and clinically-well characterized subjects with Williams and Rett syndrome are also a focus of research.

#### 2. “Neurodegeneration” Line:

This research line views neurodegeneration not only as a process involving actual neuronal loss and gross structural lesions of the nervous system, but also the subtle 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, depression, anxiety and chronic pain syndromes) studying both patients and animal models that mimic the disorders at the molecular, cellular and system levels.
- One of our common themes is 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.

#### 3. “Neuroimmunology” Line:

This line of research studies the interaction between the nervous and the immune systems through different perspectives:

- Challenging the brain with immune stimuli including peripheral inflammation and chronic infection and evaluating the consequences in neurological disease progression;
- Studying the behavior, neuronal plasticity and neurotransmitter pathways of animal models with disruption or overexpression of immune-related molecules (e.g. interleukin 10);
- Understand the inflammatory mechanisms triggered by the choroid plexus in multiple sclerosis.

## Main Achievements

During 2009 there was a consolidation of the 3 Research Lines, namely through a significant increase in the number of researchers. In fact, and following the sustained increase in the number and differentiation level of the Domain's PhD members, we successfully recruited 7 new Post-Docs (6 with fellowships from the FCT and 1 faculty member), of which some were recruited abroad.

When compared to 2008, there was a significant increase in the number of publications in 2009, which was paralleled by an even greater increase in their impact factor (more 69%).

Of notice, in 2009, we also reinforced the translational/clinical focus of research; importantly, 4 projects were granted in a specific call on Clinical Research from FCT and we had more international grants (USA and EU).

In 2009, the main achievements of the Neurosciences Research Domain were:

1. Publications
  - a. 38 publications in international peer-reviewed journals (including 9 articles in press);
  - b. 35 abstracts in international congresses;
  - c. 29 international conferences/seminars produced by members of the Domain.
2. Theses completed
  - a. 2 PhD theses;
  - b. 5 MSc theses.
3. Organization of conferences
  - a. Organization of 9 international post-graduation courses
4. Internationalization and Academic Juries
  - a. Participation in 41 graduation (PhD/MSc) juries;
  - b. Ad-hoc reviews for the following journals in the neuroscience, endocrinology and genetics fields (American Journal Medical Genetics, Annals of Neurology, Anticancer Research, Behavioral Brain Research, Biological Psychiatry, BMC Cancer, Brain Behaviour and Immunity, Brain Research, Cancer Investigation, Cellular Oncology, Epilepsy and Behavior, European Journal of Neuroscience, European Neuropsychopharmacology, Experimental Neurology, Genes Brain and Behavior, Inflammation Research, International Journal of Cancer, International Journal of Neuropsychopharmacology, Hormones and Behavior, Learning and Memory, Journal of Clinical Pathology, Journal of Endocrinology, Journal of Neuroscience, Journal of Neuroscience Research, Journal of Neuroendocrinology, Journal of Proteomics, Journal of Psychiatry Research, Microscopy Research & Technique, Molecular Psychiatry, Neurobiology of Aging, Neurobiology of Disease, Neuroscience Letters, Neuropsychopharmacology Neurogenetics, Neuroreport,

Pain, Pediatrics, Proteomics, Psychopharmacology, Physiology and Behavior, Progress in Neuropsychopharmacology, Virchows Archives);

- c. Evaluators of funding agencies (European Science Foundation, People Marie Curie Actions, EMBO Long Term Fellowships, Wellcome Trust grant applications, Wellcome Trust Research Training Fellowships, Spanish Ministry Science and Innovation, FCT Fellowships, Chilean Foundation of Science, Israel Foundation of Science);
- d. Members of the Juries of the following prizes (Bial 2009, BES Inovação, Manuel de Mello, L'Oreal).

## 5. Funding

- a. In terms of funding, in 2009 our efforts were concentrated in widening the spectrum of funding sources; in this regard, it should be highlighted the fact that we got competitive grants internationally (2 new grants) and that we renewed the contract with an industrial partner and a sub-contract with a FP6 consortium. Currently, we have 16 funded projects in which the PIs are members of the Neurosciences Domain and 3 other in which researchers from the Neurosciences Research Domain are members of the teams;
- b. Moreover, we have integrated 3 European Consortia in the FP7 calls as work-package leaders – these proposals are under evaluation. We have also applied with several proposals for FCT grants, including one in the call of the Harvard-Portugal Consortium;
- c. We have put forward a multidisciplinary proposal for the Health Cluster Portugal (QREN) in which the ICVS/Clinical Academic Center is the Coordinator.



## Group Productivity

### Publications in peer reviewed Journals

The Neurosciences Research Domain published 29 articles in 2009 (in addition, 9 other research articles were accepted for publication in 2009 and are presently *Ahead of Print* or *In Press*). The 29 published papers have a mean impact factor of 5.8 and correspond to a ratio of 1.9 papers/PhD. Three articles have impact factor above 10 and one above 25.

The following list of publications is divided according to the Line of Research where the publications were originated.

#### Neurodevelopment

1. Baruchel S, Sharp JR, Bartels U, Hukin J, Odame I, Portwine C, Strother D, Fryer C, Halton J, Egorin MJ, Reis RM, Martinho O, Stempak D, Gammon J, Bouffet E. A Canadian paediatric brain tumour consortium (CPBTC) phase II molecularly targeted study of imatinib in recurrent and refractory paediatric Central Nervous System tumours. *Eur J Cancer*, 45:2352-9 (2009). (IF = 4.475)
2. Bax DA, Gaspar N, Little SE, Marshall L, Perryman L, Regairaz M, Viana-Pereira M, Vuononvirta R, Sharp SY, Reis-Filho JS, Stávale JN, Al-Sarraj S, Reis RM, Vassal G, Pearson AD, Hargrave D, Ellison DW, Workman P, Jones C. EGFRvIII deletion mutations in pediatric high-grade glioma and response to targeted therapy in pediatric glioma cell lines. *Clin Cancer Res*, 15:5753-61 (2009). (IF = 6.488)
3. Bax D, Little S, Gaspar G, Perryman L, Marshall L, Viana-Pereira M, Corbett-Jones T, Williams R, Vassal G, Workman P, Sheer D, Reis RM, Pearson AD, Hargrave D, Jones C. Molecular and Phenotypic Characterization of Paediatric Glioma Cell Lines as Models for Preclinical Drug Development. *PLoS One*, 4:e5209. (2009). (IF = Undetermined)
4. Costa BM, Smith JS, Chen Y, Chen J, Phillips HS, Aldape KD, Zardo G, Nigro J, James CD, Fridlyand J, Reis RM, Costello JF. Reversal of HOXA9 Oncogene Activation by Inhibition of PI3K: Epigenetic Mechanism and Prognostic Significance in Human Glioblastoma. *Cancer Research*, in press. (IF = 7.514)
5. Martinho O, Longatto-Filho A, Lambros M, Martins A, Pinheiro C, Silva A, Pardal F, Amorim J, Mackay A, Milanezi F, Tamber N, Fenwick K, Ashworth A, Reis-Filho J, Lopes JM, Reis RM. Molecular alterations of PDGFA and PDGFRA in gliomas. *Br J Cancer*, 101:973-82. (2009). (IF = 4.846)
6. Mesquita AR, Wegerich Y, Patchev AV, Oliveira M, Leão P, Sousa N, Almeida OFX. Glucocorticoids and neuro- and behavioural development. *Seminars Fetal Neonatal Medicine*. 14(3):130-5, 2009. (IF = 2.824)
7. Pinto C, Veiga I, Pinheiro M, Peixoto A, Pinto A, Lopes JM, Reis RM, Oliveira C, Baptista M, Roque L, Regateiro F, Cirnes L, Hofstra RMW, Seruca R, Castedo S, Teixeira MR. TP53 mutational spectrum and genetic modifiers of age of onset in Li-Fraumeni syndrome patients in Portugal. *Fam Cancer*, 8(4):383-90 (2009). (IF = 2.052)
8. Prior C, Nunes A, Rios M, Sequeiros J, Maciel P, Gomes L, Temudo T. Nutritional and gastrointestinal dysfunction in Rett disorder: importance of early intervention. (Spanish) *An Pediatr (Barc)*, in press. (IF Undetermined)
9. Santos M, Temudo T, Kay T, Carrilho I, Medeira A, Cabral H, Gomes R, Lourenço MT, Venâncio M, Calado E, Moreira A, Oliveira G, Maciel P. Mutations in the MECP2 gene are not a major cause of Rett-like or related neurodevelopmental phenotype in male patients. *Journal of Child Neurology*, 24(1):49-55, (2009). (IF = 1.433)



10. Sampaio A, Sousa N, Fernández M, Henriques M, Carracedo A, Gonçalves O. Cognitive Functioning in Williams Syndrome: a study in Portuguese and Spanish Patients. *European Journal of Paediatric Neurology*, 13, 337-342 (2009). (IF = 1.421)
11. Yu S, Patchev A, Wu Y, Lu J, Holsboer F, Zhang JH, Sousa N, Almeida OFX. Depletion of the neural precursor cell pool by glucocorticoids. *Annals Neurol*, in press. (IF = 9.935)
12. Temudo T, Rios M, Prior C, Carrilho I, Santos M, Maciel P, Sequeiros J, Fonseca M, Monteiro J, Cabral P, Ormazabal A, Artuch R. Evaluation of CSF neurotransmitters and folate in 25 patients with Rett disorder and effects of treatment. *Brain & Development*, 31(1):46-51, (2009). (IF = 1.401)
13. Viana-Pereira M, Almeida I, Sousa S, Mahler-Araújo B, Seruca R, Pimentel J, Reis RM. Analysis of microsatellite instability in medulloblastoma. *Neuro Oncol*, 11:458-67. (2009). (IF = 5.000)
14. Pinho T, Maciel P. Developmental disturbances associated with agenesis of the permanent maxillary lateral incisor. *British Dentistry Journal*, 207:E25 (2009). (IF = 0.916)
15. Pinho T, Silva-Fernandes A, Seada P, Bousbaa H, Maciel P. Mutational analysis of MSX1 and PAX9 genes in Portuguese families with lateral superior incisor agenesis. *European Journal of Orthodontics*, in press. (IF = 1.015)

### **Neurodegeneration**

1. Ansah OB, Gonçalves L, Almeida A, Pertovaara A. Enhanced pronociception by amygdaloid group I metabotropic glutamate receptors in nerve-injured animals. *Exp Neurol*, 216:66-74 (2009). (IF = 3.974)
2. Bessa JM, Ferreira D, Melo I, Marques F, Cerqueira JJ, Palha JA, Almeida OF, Sousa N. The mood-improving actions of antidepressants do not depend on neurogenesis but are associated with neuronal remodeling. *Mol Psychiatry*, 14:764-773 (2009). (IF = 12.537)
3. Bessa JM, Ferreira D, Melo I, Marques F, Cerqueira JJ, Palha JA, Almeida OF, Sousa N. Hippocampal neurogenesis induced by antidepressant drugs: an epiphenomenon in their mood-improving actions. *Mol Psychiatry*, 14:739 (2009). (IF = 12.537)
4. Bessa JM, Mesquita AR, Oliveira M, Pêgo JM, Cerqueira JJ, Palha JA, Almeida OF, Sousa N. A trans-dimensional approach to the behavioral aspects of depression. *Front Neurosci*, 3:1 (2009). (IF Undetermined)
5. Bettencourt MC, Santos C, Montiel R, Kay T, Vasconcelos J, Maciel P, Lima M. The (CAG)<sub>n</sub> tract of Machado-Joseph Disease gene (ATXN3): a comparison between DNA and mRNA in patients and controls. *European Journal of Human Genetics*, in press. (IF = 3.935)
6. Bettencourt C, Santos C, Montiel R, Costa MC, Simões N, Kay T, Vasconcelos V, Maciel P, Lima M. Increased transcript diversity: novel splicing variants of Machado-Joseph Disease gene (ATXN3). *Neurogenetics*, in press. (IF = 3.000)
7. Catania C, Sotiroupolos I, Silva R, Onofri C, Breen KC, Sousa N, Almeida OF. The amyloidogenic potential and behavioral correlates of stress. *Mol Psychiatry*, 14:95-105 (2009). (IF = 12.537)
8. Dias-Ferreira E, Sousa JC, Melo I, Morgado P, Mesquita AR, Cerqueira JJ, Costa RM, Sousa N. Chronic stress causes frontostriatal reorganization and affects decision-making. *Science*, 325:621-625 (2009). (IF = 28.103)
9. Leite-Almeida H, Almeida-Torres L, Mesquita AR, Pertovaara A, Sousa N, Cerqueira JJ, Almeida A. The impact of age on emotional and cognitive behaviours triggered by experimental neuropathy in the rat. *Pain*, 144:57-65 (2009). (IF = 6.030)
10. Lima E, Rolanda C, Osório L, Pêgo JM, Silva D, Henriques-Coelho T, Carvalho JL, Bergström M, Park P-O, Mosse CA, Swain P, Correia-Pinto J. Endoscopic closure of transmural bladder wall perforations. *Eur Urol*, 56:151-7 (2009). (IF = 6.512)
11. Macedo-Ribeiro S, Cortes L, Maciel P, Carvalho AL. Nucleocytoplasmic shuttling activity of Ataxin-3. *PLoS One*, 4(6):e5834 (2009). (IF Undetermined)

12. Osório NS, Sampaio-Marques B, Chan CH, Oliveira P, Pearce DA, Sousa N, Rodrigues F. Neurodevelopmental delay in the Cln3Deltaex7/8 mouse model for Batten disease. *Genes Brain Behav*, 8:337-45 (2009). (IF = 3.890)
13. Pinto-Ribeiro F, Moreira V, Pêgo JM, Leão P, Almeida A, Sousa N. Antinociception induced by chronic glucocorticoid treatment is correlated to local modulation of spinal neurotransmitter content. *Mol Pain*, 5:41 (2009). (IF = 3.705)
14. Rodrigues AJ, Neves-Carvalho A, Ferro A, Rokka A, Corthals G, Logarinho E, Maciel P. Ataxin-3, CDC-48 and UBXN-5: a new molecular complex in *C. elegans*. *Biochemical and Biophysical Research Communications*, 386(4):575-81 (2009). (IF = 2.648)
15. Rolanda C, Lima E, Silva D, Moreira I, Pêgo JM, Macedo G, Correia-Pinto J. In vivo assessment of gastrotomy closure with over-the-scope clips in an experimental model for varicocelectomy (with video). *Gastrointest Endosc*, 70:1137-45 (2009). (IF = 7.367)
16. Salgado AJ, Sousa RA, Pego JM, Fraga JS, Silva BA, Malva JO, Neves NM, Reis RL, Sousa N. Effects of Starch/Polycaprolactone Based Blends to be Used for Spinal Cord Injury Regeneration in Neurons/Glial Cells Viability and Proliferation. *J Bioact Compat Pol*, 24: 235-248 (2009). (IF = 1.896)
17. Salgado AJ, Fraga JS, Mesquita AR, Neves NM, Reis RL, Sousa N. Role of Human Umbilical Cord Mesenchymal Progenitors Conditioned Media in Neuronal/Glial Cell Densities, Viability and Proliferation. *Stem Cells Dev*, in press. (IF = 3.273)
18. Salgado AJ, Reis RL, Sousa N, Gimble JM. Adipose Tissue Derived Stem Cells Secretome: Soluble Factors and Their Roles in Regenerative Medicine. *Curr Stem Cells Res Ther*, in press. (IF Undetermined)
19. 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*, in press. (IF = 4.699)

### **Neuroimmunology**

1. Marques F, Sousa JC, Coppola G, Geschwind D, Sousa N, Palha JA, Correia-Neves M. The choroid plexus response to a repeated peripheral inflammatory stimulus. *BMC Neuroscience*, Neuroscience 10:135 (2009). (IF = 2.850)
2. Marques F, Falcao AL, Sousa JC, Coppola G, Geschwind D, Sousa N, Correia-Neves M, Palha JA. Altered iron metabolism is part of the choroid plexus response to peripheral inflammation. *Endocrinology* 150:2822-8 (2009). (IF = 4.945)
3. Marques F, Sousa JC, Coppola G, Falcao AL, Rodrigues AJ, Geschwind DH, Sousa N, Correia-Neves M, Palha JA. Kinetic profile of the transcriptome changes induced in the choroid plexus by peripheral inflammation. *J Cereb Blood Flow Metab* 29:921-32 (2009). (IF = 5.741)
4. Roque S, Correia-Neves M, Mesquita AR, Palha J, Sousa N. Interleukin-10: a key cytokine in depression?. *Cardiovascular Psychiatry and Neurology* (2009). (IF Undetermined)

### **Other publications International**

- Book Chapters

Sousa JC, Palha JA. 2009. "What have we learnt from TTR-null mice: novel functions for TTR"?, in the book *"Transferrin, the thyroid hormone distributor protein: its functions, evolution and role in human diseases"*, edited by Richardson S and Cody V., Springer.

- In Medical Education

Sousa JC, Costa MM, Palha JA. 2009. Teaching the extracellular matrix and introducing bioinformatics within a multidisciplinary course with i-cell-MATRIX: a student centered approach. *Biochem Mol Biol Educ*, in press.

Winward ML, de Champlain AF, Grabovsky I, Scoles PV, Swanson DB, Holtzman K, Pannizzo L, Sousa N, Costa MJ. Gathering evidence of external validity for the Foundations of Medicine examination: a collaboration between the National Board of Medical Examiners and the University of Minho. *Academic Medicine*, 84(10 Suppl):S116-9 (2009).

## Master and Ph.D. theses completed

- PhD theses (the research work of all theses reported was carried out at ICVS/ECS)
  1. Leonor Gonçalves - "*Plasticity of the pain control system induced by neuropathic pain: the amygdala-medulla system*". Supervised by Armando Almeida, School of Health Sciences, University of Minho.
  2. Laurinda Lemos - "*New therapeutic approaches to the treatment of trigeminal neuralgia*". Supervised by Armando Almeida, School of Health Sciences, University of Minho.
- Master theses (the research work of all theses reported was carried out at ICVS/ECS)
  1. Ashley Novais – "*Establishment and characterization of in vivo models of gliomagenesis*", in the context of the master program in Cancer from the Biology Department of Minho University. Supervised by Rui Reis, ICVS.
  2. Maria Magalhães – "*Brain Projections of the medullary ventral reticular nucleus: an anterograde and retrograde tracing study in the rat*", in the context of the master program in Biology from the Biology Department of Aveiro University. Supervised by Hugo Leite-Almeida and Armando Almeida, ICVS.
  3. Miguel Carvalho – "*Application of Stem Cell therapies and assessment of motor and non-motor changes in a rat Parkinson model*", in the context of the master program in Biology from the Biology Department of Lisbon University. Supervised by António Salgado and Nuno Sousa, ICVS.
  4. Andreia Carvalho – "*Stress Response in C. elegans in the absence of ataxin-3*", in the context of the master program in Molecular Genetics from the Biology Department of Minho University. Supervised by Ana João Rodrigues and Patricia Maciel, ICVS.
  5. Joana Fraga – "The role of conditioned media derived from adult human umbilical cord stem cells in the proliferation, survival and differentiation of neurons and glial cells", in the context of the master program in Biology from the Biology Department of Minho University. Supervised by António Salgado and Nuno Sousa, ICVS.

## Prizes

- 1st Prize for best Poster in Oncology and Molecular Biology for work of Miranda A, Amorim J, Almeida R, Alegria C, Linhares P, Vaz R, Pinheiro C, Carvalho E, Crespo I, Lopes C, Rodrigues F, Costa S, Almeida I, Reis RM. Association of Toll-like receptor 9 (TLR9) gene polymorphism with the risk of gliomas in Portuguese patients, at *YES meeting*, Porto, Portugal (2009).
- 1st Prize for best Oral Presentation for work of Martinho O, Couto R, Reis RM. Efeito citotóxico de imatinib, sunitinib e cediranib em linhas celulares de glioblastoma at *2º Congresso Nacional da Associação Portuguesa de Neuro-Oncologia*, Porto, Portugal (2009).
- 3rd Prize for Oral Presentation for work of Costa BM, Caeiro C, Guimarães I, Martinho O, Jaraquemada T, Silva A, Pardal F, Amorim J, Nabiço R, Almeida R, Alegria C, Lopes JM, Castro L, Augusto I, Osório L, Linhares P, Pires MM, Pinheiro C, Carvalho E, Honavar M, Resende M, Braga F, Costa P,

Damasceno M, Reis RM. Relevância do Estado de Metilação do Promotor do Gene MGMT como um Biomarcador de Prognóstico em Pacientes com Glioblastoma, at *Oncologia 2009, Encontros de Primavera*, Évora, Portugal (2009).

- Prize for best Poster for the work Silva NA, Salgado AJ, Sousa RA, Oliveira JT, Fraga JS, Cerqueira R, Leite-Almeida H, Almeida A, Sousa N and Reis RL. From the development to the physical and biological assessment of a novel biodegradable 3D structure for Spinal Cord Injury Repair, at the *11th Meeting of the Portuguese Society for Neurosciences*, Braga, Portugal (2009).
- Prize for best Poster for the work Silva-Fernandes A, Costa MC, Duarte-Silva S, Costa C, Maciel P. CAG-dependent motor phenotype in a transgenic mouse model of Machado-Joseph disease. V International workshop on MJD, Açores, Portugal (2009).
- Prize for best Poster for the work Lima-Rodrigues M, Vieira A, Lamas N, Valle-Fernandes A, Nunes R, Pedrosa J, Castro AG, Reis RM, Almeida A. Possible alternative therapies to chronic laryngitis and laryngeal cancer: the use of COX-2 specific inhibitors. 1<sup>st</sup> Meeting of the European Academy of ORL\_HNS, Mannheim-Germany (2009).
- Prize for the best oral communication for the work Neves-Carvalho A, Rodrigues AJ, Maciel P. "Increased thermotolerance in the absence of ataxin-3 in *C. elegans*". V International workshop on MJD, Açores, Portugal (2009).

## Organization of conferences

- Organization of Scientific Meetings and Presence in Scientific Committees
  - The Neuroscience Research Domain organized the *11<sup>st</sup> Meeting of the Portuguese Society for Neurosciences*, School of Health Sciences, University of Minho, Braga, (2009).
  - Joana Palha. Co-organized the workshop "*Drug treatment in psychiatric and neurological disorders*" of the European School of Neurosciences. Ofir (2009).
  - Patrícia Maciel, Ana João Rodrigues. Scientific and Organizing Committee, respectively, of the "*V International Workshop on Machado-Joseph disease*", S. Miguel (Açores) (2009).
- Post-graduation courses and Workshops organized at the ICVS
  - João Carlos Sousa, José Miguel Pêgo. Organized of the course *Fundamentals in Neuroscience* within the post-graduation programme of the ICVS/ECS, 2009.
  - Armando Almeida. Organization of the Module "*Anatomo-physiology and Basic Pharmacology of Pain*", integrated in the 3<sup>rd</sup> Pos-Graduation/Master Degree Course in Sciences of Pain, organized by the Faculty of Medicine of Lisbon (2009).
  - António Salgado, Margarida Saraiva, Sandra Costa. "*Animal Cell Culture: From Basic Principles to Advanced Techniques*", International Post-Graduation Program ICVS, Braga, Portugal, 2008.
  - João Carlos Sousa, José Miguel Pêgo. "*Fundamentals in Neurosciences*", Curricular Unit integrated in the Master/PhD program ICVS, Braga, Portugal, 2009.
  - Joana Palha, Nuno Sousa. "*Neuroimmune interactions*", organized within the Cost Action Neurinfnet, International Post-Graduation Program ICVS, Braga, Portugal, 2009.
- Organization of Other Meetings
  - Armando Almeida, José Miguel Pêgo. Organizing and Scientific Committee of the *Jornadas da Dor - Braga 2009*, School of health Sciences, University of Minho, Braga, (2009).
  - José Miguel Pêgo. "*Ecografia em Anestesia Loco-regional*", Workshop integrated in *Jornadas da Dor - Braga 2009*, School of health Sciences, University of Minho, Braga, (2009).

- José Miguel Pêgo. “*Bloqueios ecoguiados*”, Workshop integrated in *I Minho Medical Meeting – “Pain”*, organized by Students Association of the Medical Course from the School of Health Sciences, University of Minho, Braga (2009).

## Internationalization

In 2009 the Neuroscience Research team has been involved in several internationalization efforts. In this regard it should be highlighted that a significant number of our international peer-review publications were performed in collaboration with other research groups. This reflects the extensive network of international collaborations of the Neuroscience Research Domain (23 international long-term collaborations), as follows:

- Athens University
- Biomedicum Helsinki, Helsinki Medical School, Finland
- Bristol University, UK
- Centre for Genomic Regulation, Barcelona, Spain
- Columbia University, New York, USA
- Erasmus University, The Netherlands
- Faculdade de Medicina da Universidade Federal de São Paulo, Brazil
- Harvard Medical School, Boston, USA
- Instituto de Investigaciones Biomédicas, Madrid, Spain
- Iowa University, USA
- Max-Planck Institute for Psychiatry, Munich, Germany
- Muséum Nationale d'Histoire Naturelle, Paris, France
- National Institutes of Health, Bethesda, USA
- Northwestern University, Evanston, Illinois, USA
- Oulu University, Finland
- Paris-Descartes University
- Riken Institute, Tokyo, Japan
- Thomas Jefferson Medical School, USA
- Toronto University, Canada
- UNICAMP, Campinas, Brazil
- Universidade Federal de São Paulo, Brazil
- Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil
- U.C.L.A., USA

Members of the Neuroscience Research Domain participate in the management committee of the COST action Neurinfnet and Marie-Curie training networks consortium (it should be highlighted that a Marie-Curie Action in which we are partners of the consortium was funded in 2009).

Members of the domain have also participated in the Evaluation Panel for grants and prizes of international organizations: Austrian, and Israel Science Foundations, Foundation Jerome Le Jeune, FCT, European Commission (FP7), L’Oreal Prize for Women in Science (Portugal), Members of the domain were engaged in the establishment of the Portuguese national brain imaging network and in the Harvard Medical School - Portugal Initiative.

## Funding

### Government/Organization contract research

#### Neurodevelopment

1. 2009-2011 - Project from Fundação para a Ciência e Tecnologia (PIC/IC/83013/2007), entitled "Clinical and Genetic study of X-linked mental retardation (XLMR) in Portugal: validation of a gene panel for diagnosis", granted with 170 000 €. Patrícia Maciel (PI)
2. 2009-2011 - Project from Fundação para a Ciência e Tecnologia (PIC/IC/83026/2007), entitled "Idiopathic mental retardation: evaluation of a CGH microarray strategy for genetic diagnosis", granted with 176 000 €. Patrícia Maciel (PI)
3. 2009-2011 – Project from Fundação para a Ciência e Tecnologia (FCT) – Investigação em Projectos de Investigação Clínica – "Cognitive Training in Brain Disorders: Effectiveness of cognitive stimulation and development of a new tool for Portuguese clinicians", granted with 160 000 €. Adriana Sampaio (PI)
4. 2010-2011 – Project from Fundação para a Ciência e Tecnologia (FCT), entitled "Neudesin - characterization of a novel neurotrophic factor", granted with 36 000 €. João Carlos Sousa (PI).
5. 2010-2011 – Project from Hope for Depression Research Foundation (USA) entitled "Searching for the neurobiological targets through which prenatal corticosteroids program adult social and affective behaviors", granted with 110 000 USD. Nuno Sousa (PI)
6. 2010-2013 – Project from Fundação para a Ciência e Tecnologia (PTDC/SAU-OB/100079/2008) entitled "Role of protein kinase WNK2 as a tumour suppressor gene in malignant gliomas", granted with 109 062 €. Rui M Reis (Team Member) - ICVS budget: 44 208 €

#### Neurodegeneration

1. 2005-2009 – Project from the Fundação Calouste Gulbenkian (FCG) nº JG0495, entitled "Aged and healthy brain: a multidisciplinary neurobiological approach to the aging brain", granted with 105 000 €. Nuno Sousa (PI).
2. 2005-2009 – Project from Fundação Gulbenkian (FCG) – Investigação em Neurociências, Área do Envelhecimento – nº 74551, entitled "Identification of changes in preprotein expression in the brainstem, hippocampus and amygdala and in the emotional behaviour associated to different periods of chronic neuropathic pain along ageing", granted with 48 000 €. Armando Almeida (PI).
3. 2007-2010 – Project from the Fundação para a Ciência e Tecnologia (FCT) nº PTDC/SAU-NEU/72699/2008, entitled "New perspectives in the neurobiology of depression: beyond the "neurochemical hypothesis", granted with 96 141 €. Nuno Sousa (PI).
4. 2007-2010 – Project from the Fundação para a Ciência e Tecnologia (FCT) nº GRID/GRI/81833/2006, entitled "Brain Imaging Network Grid (BING)", granted with 3 360 €. Nuno Sousa (PI).
5. 2008-2010 - Project from the Fundação para a Ciência e Tecnologia (FCT) nº PTDC /SAU-GMG/64076/2006, entitled "Therapeutic strategies for Machado-Joseph disease: study in a mouse model", granted with 159 934 €. Patrícia Maciel (PI).
6. 2010-2012 - Project from the Fundação para a Ciência e Tecnologia (FCT) nº PTDC/SAU-GMG/101572/2008, entitled "Ataxin-3: gain and loss of function in Machado-Joseph disease", granted with 199 765 €. Patrícia Maciel (PI).
7. 2010-2012 – Project from the Fundação para a Ciência e Tecnologia (FCT) nº PTDC/SAU-NEU/108557/2008, entitled "Abnormal emotional and cognitive behaviours in chronic pain states: spatiotemporal characterization of CNS plastic correlates", granted with 56 835 Euros. Armando Almeida (PI).

8. 2010-2013 – Project from the Fundação para a Ciência e Tecnologia (FCT) nº PTDC/SAU-NEU/105180/2008, entitled “Multimodal analysis of the neurobiology of depression”, granted with 120 000 €. Nuno Sousa (PI).
9. 2010-2013 – Project from FP7-Marie Curie ITN (EU), entitled “Neuroendocrine immune networks in Aging - NINA”, budget under final negotiation. Nuno Sousa (WP Leader).
10. 2010-2012 – Project from Fundação BIAL entitled "How does cognitive enrichment impact on neuronal networks and behavioral performance?", granted with 37 000 €. João Cerqueira (PI).

### **Neuroimmunology**

1. 2007-2010 – Project from the Dana Foundation (USA), entitled “The choroid plexus as an immune-sensor for the brain: implications to neurological diseases”, granted with 145 000 USD. Joana Palha and Margarida Correia-Neves (PIs).
2. 2009-2012 – Project from the Fundação para a Ciência e Tecnologia (FCT) nº PIC/IC/83231/2007 entitled “New approaches in Multiple Sclerosis diagnosis: role of the choroid plexus”, granted with 130 000 €. João Cerqueira (PI).

### **Industry contract research**

Research contracts with Bayer-Schering Pharma; the studies are designed to characterize the behavioral and structural phenotype induced by drug compounds. Budget #1: 20 000 €, Budget #2: 25 000 €. Nuno Sousa (coordinator).

### **Other organization contract research**

Research Sub-Contract within the work-package 4 “Programmability of NRs and their Regulatory Networks”, Task 4.13 of the European Project “Crescendo – FP6-018652”. Budget: 35 000 €. Nuno Sousa (coordinator).

## Future Research

### Objectives

The main goal of any research institution should be the high quality of science and training of its research students. This is (and will certainly be) the major aim, and mission, of the Neurosciences Research Domain. In 2009, we were able to overcome all our internal goals, and we have witnessed a significant increase in the number of researchers of the Domain. In 2010, 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.

As a brief historical background, it should be noted that this Research Domain launched its activities at the ICVS in 2003 as two separate research groups, Neurosciences and Human Genetics, led by four PIs that were initially hired to teach in the new Medical School. Necessarily, at the starting point each individual had a different background, different research interests and ongoing projects. Since 2003, the group has evolved into a single larger team (merging of the two initial groups took place in 2004) with increasing internal collaborations and common research topics. This is a continuous effort, as it must foster individual interests and independence of each researcher, but by strengthening the internal collaborations and investing in the areas of common interest. Since 2009, the ECS/ICVS launched a Master and 2 Doctoral Programmes, for which the Neuroscience Research Domain is contributing significantly. More recently, and as part of a strategic reorganization of the Institute, the Neuroscience Research Domain has incorporated in the team, several researchers that have strong expertises in the neuro-oncology field; in 2010, we hope to fully explore the extra-value that this addition represents.

The quality of the science produced has been recognized internationally and we are now in a better position to attract more funding, better post-docs and PhD students and produce even better publications (on this particular parameter, we organized the team in order to have, in 2010, 2 publications in journal with IF>10) – on this particular it should be highlighted that we have exceeded our expectations in this parameter in 2009).

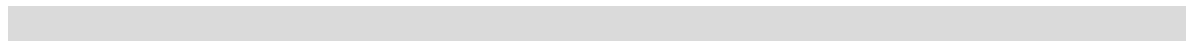
Thus, in 2010 we hope to capture more projects and in a wider spectrum of sources (including international agencies). It is also our aim to continue to recruit Post-Docs internationally in 2010 and to keep our contribution to the success of the Doctoral programmes of the ECS/ICVS, where several PhD students were and will be recruited in 2010; therefore, we hope to keep our commitment with the training and post-graduation of several students. As part, of our internationalization efforts we aimed to be involved in European training/research networks in 2009 – as this endpoint was achieved in 2009, we hope to expand our participation to another training network in 2010. A note also for the 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 2010 is to further strengthen the contracts with industrial partners. On this particular, a recent proposal in the context of the Health Cluster Portugal is expected to be instrumental. Within the same line, we have recently established an agreement with a behavioural instrument company, in order to develop novel behavioural tests. These expansions are of the utmost importance, since they may represent increased funds for exploratory or satellite projects that eventually generate the data to apply for more specific grants to then feed into the main research areas of the group.



As part of our mission, we will continue our commitment to the training and supervision of researchers. In this regard, in 2010, we aim to finish 4 PhD theses and to organize at least 6 international post-graduation courses.

A final word to our commitment to reinforce translational and clinical research in the Neuroscience Research Domain. In 2009, the creation of the Clinical Academic Center, in which members of the Domain are profoundly engaged, opened the opportunity for the design and development of several clinical research projects based on the pre-clinical data generated within the Domain. Thus, in 2010, we aim to have 4 to 6 publications in the area of clinical research but also to keep recruiting health professionals for research activities.



## c) Surgical Sciences Research Domain

### Research Domain Description

**Title of Research Group:** Surgical Sciences

**Coordinator:** Jorge Correia-Pinto

**Main Scientific Domain:** Health Sciences

**Research Lines:** Integrative Studies in Surgical Diseases  
(Coordinator: Rui Reis)

Endoscopy and Surgical Techniques  
(Coordinator: Jorge Correia-Pinto)

<b>c) Surgical Sciences Research Domain.....</b>	<b>c-1</b>
<b>Objectives &amp; Achievements.....</b>	<b>c-3</b>
Objectives .....	c-3
Main Achievements .....	c-4
<b>Group Productivity .....</b>	<b>c-5</b>
Publications in peer reviewed journals .....	c-5
Other publications International.....	c-8
Master and PhD theses completed .....	c-8
Patents/propotypes.....	c-9
Prizes .....	c-9
Organization of conferences.....	c-10
Internationalization.....	c-10
<b>Funding.....</b>	<b>c-12</b>
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Industry contract research .....	c-12
<b>Future Research.....</b>	<b>c-13</b>



## Objectives & Achievements

### Objectives

The Surgical Sciences Research Domain focus in basic, translational and clinical studies in diseases from digestive, pulmonary and urogenital systems. It is organized in two research lines: i. *Integrative Studies in Surgical Diseases*; ii. *Endoscopy and Surgical Techniques*. The main objectives of each research line are detailed herein:

- **“Integrative Studies in Surgical Diseases”**

This research line embraces studies that aim at understanding the underlying mechanisms that are in origin pathophysiology and therapeutic response of surgical diseases through studies at molecular, cellular or organ level carried out either in animal models or in Human material.

-Investigation of development mechanisms regulating time and space differentiation of cells/tissues in somites and lung growth;

-Exploration of fetal non-surgical therapeutic strategies to promote lung growth in congenital diaphragmatic hernia;

-Assessment of genetic/molecular markers as risk and prognostic factors in digestive, pulmonary and urogenital cancer.

- **“Endoscopy and Surgical Techniques”**

This research line explores new surgical techniques and equipment applicable in minimally invasive surgical treatment of benign and malignant diseases.

-Development and assessment of potential usefulness of transvesical port in Natural Orifices Transluminal Endoscopic Surgery (N.O.T.E.S.);

-Assessment of the feasibility and the reliability of transgastric port access when used either isolated or combined in N.O.T.E.S. field, envisioning Human translation;

-Exploring Human body imaging (CT scan and laser) as a surrogate to develop three-dimensional constructs to provide personalized prosthesis and surgical plans.

## Main Achievements

In 2009, the main achievements of the Surgical Sciences Research Domain were:

### 1. Publications and patents

- a. 51 publications in international peer-reviewed journals (including 11 articles in press);
- b. 48 abstracts in national and international congresses;
- c. 17 international conferences/seminars produced by members of the Domain;
- d. 1 book chapter;
- e. 1 national patent (also internationally submitted).

### 2. Theses completed

- a. 2 PhD theses;
- b. 1 Master theses.

### 3. Organization of conferences

Organization of 8 congresses/meetings and post-graduation courses: 4 national congresses/meetings and 4 international post-graduation hands-on courses.

### 4. Internationalization and Academic Juries

- a. Members of the Domain participated in 26 graduation (PhD./MSc.) juries;
- b. Ad-hoc reviewers for 26 journals in the Development, Neoplasia, Physiology and Surgical Sciences fields (Acta Paediatrica Scandinava; Acta Pharmacologica Sinica; American Journal of Physiology - Gastrointestinal and Liver Physiology; Annals of Surgery; Archives of Diseases in Childhood; Gastrointestinal Endoscopy; Journal of Cell and Molecular Medicine; Journal of Pediatric Surgery; Peptides; Journal of Endourology; Surgical Endoscopy; Proceedings of the National Academy of Sciences (PNAS); Development; Brain Research Reviews; Mechanisms of Development; Developmental Dynamics; Gene expression patterns; Anticancer Research; BMC Cancer; Cancer Investigation; Cellular Oncology; International Journal of Cancer; Journal of Clinical Pathology; Pancreas; Virchows Archives);
- c. Jorge Correia-Pinto is an associate Editor for the European Journal of Pediatric Surgery and the World Journal of Gastrointestinal Surgery; Rui Manuel Reis is a member of the Editorial Board of The Open Pathology Journal. Jorge Correia-Pinto acts as specialist medical consultant to Karl Storz in questions involving the instruments and device configurations for N.O.T.E.S. purposes;
- d. Evaluators of funding agencies and of prizes: FCT (PROTEC).

### 5. Funding

In 2009, the members of the Surgical Sciences Domain made a successful effort to get funding from FCT. Moreover, we were successful in establishing partnerships with companies of surgical equipment.

## Group Productivity

### Publications in peer reviewed journals

The Surgical Sciences Research Domain published 40 articles in 2009 (in addition, 11 other research articles were accepted for publication in 2009 and are presently *Ahead of Print* or *In Press*). The 40 published papers have a mean impact factor of 3.1 and correspond to a ratio of 3.3 papers/PhD. One article has impact factor above 10.

The following list of publications is divided according to the Research Line where the publications were originated.

#### Integrative Studies in Surgical Diseases

1. Afonso J, Santos LL, Amaro T, Lobo F, Longatto-Filho A. The aggressiveness of urothelial carcinoma largely depends on lymphovascular invasion - The prognosis contribution of related molecular markers. *Histopathology*, 55:514-24 (2009). (IF=4.131)
2. Antunes H, Afonso A, Iturriza M, Martinho I, Ribeiro C, Rocha S, Magalhães C, Carvalho L, Branca F, Gray J. G2P[4] the most prevalent rotavirus genotype in 2007 winter season in an European non-vaccinated population. *J Clin Virol*, 45:76-8 (2009). (IF=3.323)
3. Antunes H, Braga-Tavares H, Cunha I, Mendes V, Cadilhe A, Matos-Cruz J, Pereira A, Correia-Pinto J. Congenital simple hepatic cyst: a diagnostic and management challenge. *Gastroenterol Hepatol*, 32:92-6 (2009). (IF Undetermined)
4. Antunes H, Santos C, Carvalho S. Serum leptin levels in overweight children and adolescents. *Br J Nutr*, 101:1262-6 (2009). (IF=2.764)
5. Autorino R, Di Lorenzo G, Giannarini G, Cindolo L, Lima E, De Sio M, LamendolaMG, Damiano R. Looking at the prostates of our bladder cancer patients: A thoughtful exercise. *BJU Int*, 104:160-2 (2009). (IF=2.704)
6. Azevedo MM, Pinheiro C, Yaphe J, Baltazar F. Portuguese students' knowledge of antibiotics: a cross-sectional study of secondary school and university students in Braga. *BMC Public Health*, 9:359 (2009). (IF=2.029)
7. Correia-Pinto J, Henriques-Coelho T, Roncon-Albuquerque R Jr, Lourenço AP, Melo-Rocha G, Vasques-Nóvoa F, Gillebert TC, Leite-Moreira AF. Time course and mechanisms of left ventricular systolic and diastolic dysfunction in monocrotaline-induced pulmonary hypertension. *Basic Res Cardiol*, 104:535-45 (2009). (IF=5.407)
8. 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 Research*, in press. (IF=7.514)
9. Gaspar A, Nabais S, Rocha S, Torres M, Pinto J, Azevedo P, Brandão A, Pereira MA, Correia A. Smoking in acute coronary syndromes – the “smoker’s paradox” revisited. *Rev Port Cardiol*, 28:425-37 (2009). (IF Undetermined)
10. Gaspar A, Salomé N, Nabais S, Brandão A, Simões A, Portela C, Salgado A, Pereira A, Correia A. Echocardiographic assessment of a cardiac lymphoma: beyond two-dimensional imaging. *Eur J Echocardiogr*, 10:975-8 (2009). (IF=1.917)
11. Guarisi R, Sarian LO, Hammes LS, Longatto-Filho A, Derchain SF, Roteli-Martins C, Naud P, Erzen M, Branca M, Tatti S, Costa S, Syrjänen S, Bragança Jf, Syrjänen K. Smoking worsens the prognosis of mild abnormalities in cervical cytology. *Acta Obstet Gynecol Scand*, 88:514-20 (2009). (IF=1.356)

12. Longatto-Filho A, Gonçalves A, Martinho O, Schmitt C, Reis RM. Liquid based cytology in DNA-based molecular research: viability and potential application. *Anal Quant Cytol Histol*, 31:395-400 (2009). (IF = 2.940)
13. Longatto-Filho A, Malheiro L, Milanezi F, Pinheiro C, Baltazar F, Schmitt F, Montironi R. Lymphatic vessels density in the normal-looking columnar epithelium adjacent to and distant from prostatic intraepithelial neoplasia and prostate cancer assessed in whole-mount sections. *Anal Quant Cytol Histol*, 31:269-275 (2009). (IF = 2.940)
14. Longatto-Filho A, Pinheiro C, Martinho O, Moreira M, Ribeiro L, Queiroz GS, Schmitt F, Baltazar F, Reis RM. Molecular characterization of EGFR, PDGFRA and VEGFR-2 in cervical adenosquamous carcinoma. *BMC Cancer*, 9:212 (2009). (IF=3.087)
15. Longatto-Filho A. Endocervical adenocarcinoma in situ: new approaches and old concerns. *CME J Gynecol Oncol*. 2009. 14:22-29. (IF undetermined)
16. Martinho O, Gouveia A, Silva P, Pimenta A, Reis RM, Lopes JM. Absence of RKIP expression is associated with poor survival in GISTs. *Virchows Arch*, 455:277-84 (2009). (IF=2.082)
17. Martinho O, Gouveia A, Viana-Pereira M, Silva P, Pimenta A, Reis RM, Lopes JM. Low frequency of MAP kinase signalling pathway alterations in KIT & PDGFRA wild-type GISTs. *Histopathology*, 55:53-62 (2009). (IF=4.131)
18. Mauad EC, Nicolau SM, Gomes UA, Da Costa Vieira RA, De Castro Mattos JS, Longatto-Filho A, Baracat EC. Can mobile units improve the strategies for cervical cancer prevention? *Diagn Cytopathol*. In press. (IF=1.124)
19. Nabais S, Gaspar A, Costa J, Azevedo P, Rocha S, Torres M, Pereira MA, Correia A. Prognostic impact of haemoglobin drop during hospital stay in patients with acute coronary syndromes. *Rev Port Cardiol*, 28:383-95 (2009). (IF Undetermined)
20. Nabais S, Losa N, Gaspar A, Rocha S, Costa J, Azevedo P, Basto L, Pereira MA, Correia A. Association between red blood cell distribution width and outcomes at six months in patients with acute coronary syndromes. *Rev Port Cardiol*, 28:905-24 (2009). (IF Undetermined)
21. Nabais S, Salomé N, Rodrigues RA, Costa J, Costeira A, Correia A. Heart in a heart-shaped shell": a case of calcific constrictive pericarditis. *Rev Port Cardiol*, 28:1285-9 (2009). (IF Undetermined)
22. Oliveira ATT, Saad SS, Waitzberg AFL, Silva SRM, Artigiani Neto R, Longatto-Filho A, Matos D. MET is highly expressed in advanced stages of colorectal cancer and related to worse prognosis and mortality. *Anticancer Res*, 29:4807-11 (2009). (IF=1.390)
23. Oliveira PA, Arantes-Rodrigues R, Sousa-Diniz C, Colaço A, Lourenço L, De La Cruz LF, Da Silva VM, Afonso J, Lopes C, Santos L. The effects of sirolimus on urothelial lesions chemically induced in ICR mice by BBN. *Anticancer Res*, 29:3221-6 (2009). (IF=1.390)
24. Pinheiro C, Longatto-Filho A, Pereira SM, Etlinger D, Moreira MRM, Jubé LF, Queiroz GS, Schmitt FC, Baltazar F. Monocarboxylate transporters 1 and 4 are associated with CD147 in cervical carcinoma. *Dis Markers*, 26:97-103 (2009). (IF=2.303)
25. Pinheiro C, Longatto-Filho A, Simões K, Jacob C, Bresciani C, Zilberstein B, Cecconello I, Alves V, Schmitt F, Baltazar F. The prognostic value of CD147/EMMPRIN is associated with monocarboxylate transporter 1 co-expression in gastric cancer. *Eur J Cancer*, 45:2418-24 (2009). (IF=4.475)
26. Pinheiro C, Sousa B, Dufloth R, Vieira D, Schmitt F, Baltazar F. Monocarboxylate transporter 1 is upregulated in basal-like breast carcinoma. *Histopathology*, In press. (IF=4.131)
27. Pinto C, Veiga I, Pinheiro M, Peixoto A, Pinto A, Lopes JM, Reis RM, Oliveira C, Baptista M, Roque L, Regateiro F, Cirnes L, Hofstra RMW, Seruca R, Castedo S, Teixeira MR. TP53 mutational spectrum and genetic modifiers of age of onset in Li-Fraumeni syndrome patients in Portugal. *Fam Cancer*, 8:383-90 (2009). (IF=2.052)
28. Precioso J, Samorinha C, Calheiros JM, Macedo M, Antunes H, Campos H. Second hand smoke (SHS) exposure in children. An evaluation of a preventative measure. *Rev Port Pneumol*. 16:57-72 (2010). (IF Undetermined)

29. Rama CH, Villa LL, Pagliusi S, Andreoli MA, Costa MC Thomann P, Alves V, Longatto-Filho A, Eluf-Neto J. Opportunity for catch-up HPV vaccination in young women after first delivery. *J Epidemiol Community Health*. 2009 Aug 19. [Epub ahead of print]. (IF=3.186)
30. 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*. 2010;29(3):392-402. (IF=7.216)
31. Rocha S, Torres M, Nabais S, Gaspar A, Rebelo A, Magalhães S, Salgado A, Azevedo P, Pereira MA, Correia A. Síndrome coronária aguda sem elevação do segmento ST: duração do QRS e prognóstico a longo prazo. *Rev Port Cardiol*, 28:697-706 (2009). (IF Undetermined)
32. Rolanda C, Gonçalves R, Macedo G. Metamorphic lesion. *Gastroenterology*, 137:41 (2009). (IF=12.591)
33. Sarian LO, Serpa-Hammes L, Longatto-Filho A, Guaris R, Derchain SF, Roteli-Martins C, Naud P, EržEn M, Branca M, Tatti S, Matos JC, Gontijo R, Maeda M Y S, Lima TP, Costa S, Syrjänen S, Syrjänen K. Increased risk of oncogenic Human papillomavirus (HR-HPV) infections and incident high-grade cervical intraepithelial neoplasia (CIN) among smokers: Experience from the Latin American Screening (LAMS) Study. *Sex Transm Dis*, 36:241-8 (2009). (IF=2.863)
34. Shirata Nk, Sredni ST, Castelo A, Santinelli A, Mendonça B, Montironi R, Longatto-Filho A, Zerbini MC. Texture image analysis in differentiating malignant from benign adrenal cortical tumors in children and adults. *Anticancer Res*, 29:3365-8 (2009). (IF=1.390)
35. Syrjänen K, Shabalova I, Naud P, Kozachenko V, Derchain S, Zakharchenko S, Roteli-Martins C, Nerovjina R, Longatto-Filho A, Kljukina L, Tatti S, Branovskaja M, Hammes LS, Branca M, Grunjberga V, Eržen M, Sarian LO, Juschenko A, Costa S, Podistov J, Syrjänen S; the NIS and LAMS Study Research Groups. Persistent high-risk human papillomavirus infections and other End-point markers of progressive cervical disease among women prospectively followed up in the new independent states of the former Soviet Union and the Latin American screening study cohorts. *Int J Gynecol Cancer*, 19:934-42 (2009). (IF=1.932)
36. Syrjanen S, Naud P, Derchain S, Sarian L, Roteli-Martins C, Longatto-Filho A, Tatti S, Branca M, Eržen, Hammes LS, Costa S, Syrjanen K. Upregulation of plasminogen activator inhibitor-2 (PAI-2, Serpin-B2) is associated with high-risk Human Papillomavirus (HPV) and grade of cervical lesion at baseline but does not predict outcomes of HR-HPV infections or incident CIN. *Am J Clin Pathol*, 132:883-92 (2009). (IF=2.715)
37. Syrjänen S, Naud P, Sarian L, Derchain S, Roteli-Martins C, Longatto-Filho A, Tatti S, Branca M, Eržen M, Hammes LS, Costa S, Syrjänen K. Up-regulation of 14-3-3sigma (Stratifin) is associated with high-grade CIN and high-risk human papillomavirus (HPV) at baseline but does not predict outcomes of HR-HPV infections or incident CIN in the LAMS study. *Am J Clin Pathol*, in press. (IF=2.715)
38. Syrjänen S, Naud P, Sarian L, Derchain S, Roteli-Martins C, Longatto-Filho A, Tatti S, Branca M, Eržen M, Hammes LS, Costa S, Syrjänen K. Immunosuppressive cytokine Interleukin-10 (IL-10) is up-regulated in high-grade CIN but not associated with high-risk human papillomavirus (HPV) at baseline, outcomes of HR-HPV infections or incident CIN in the LAMS cohort. *Virchows Arch*, 455:505-15 (2009). (IF=2.082)
39. 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*, in press. (IF=4.734)
40. Tomita L, 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*, 2009 Jul 29. [Epub ahead of print]. (IF=4.734)
41. Tomita LY, Almeida LC, Roteli-Martins C, D'Almeida V, Cardoso MA, Cardoso MA, Tomita LY Almeida LC, Longatto-Filho A, Da Gloria Mattosinho De Castro Ferraz M, Utagawa ML, Aguiar LS Roteli-Martins C, Costa RL, Ricci MD, Alves VA, D'Almeida V, Speranca MA, Francisco-Bagnariolli AM, Villa LL, Costa MC, Andreoli MA, Sobrinho JS, Prado JC, Franco EL. Dietary predictors of serum total carotene in low-income women living in São Paulo, south-east Brazil. *Public Health Nutr*, 12:2133-42 (2009). (IF=2.123)
42. Torres M, Rocha S, Marques J, Nabais S, Rebelo A, Pereira MA, Azevedo P, Correia A. Impact of atrial fibrillation in acute coronary syndromes. *Rev Port Cardiol*, 27:1407-18 (2009). (IF Undetermined)



43. Ventura F, Antunes H, Brito C, Pardal F, Pereira T, Vieira AP. Cutaneous polyarteritis nodosa in a child following hepatitis B vaccination. *Eur J Dermatol*, 19:400-1 (2009). (IF=1.968)

### **Endoscopy and Surgical Techniques**

1. Lima E, Rolanda C, Autorino R, Correia-Pinto J. Experimental foundation for NOTES and Hybrid NOTES. *Urology*, *in press*. (IF=2.242)
2. Lima E, Rolanda C, Correia-Pinto J. NOTES performed using multiple ports of entry: current experience and potential implications for urologic applications. *J Endourol*, 23:756-64 (2009). (IF=1.930)
3. Lima E, Rolanda C, Osório L, Pêgo J, Silva D, Henriques-Coelho T, Carvalho J, Bergström M, Park PO, Mosse C, Swain P, Correia-Pinto J. Endoscopic closure of transmural bladder wall perforations. *Eur Urol*, 56:151-8 (2009). (IF=6.512)
4. Lima E. Comentário editorial sobre: Láparo-endoscopia por acesso único: Experiencia inicial. *Actas Urol Esp*, 33:110-1 (2009). (IF Undetermined)
5. Rolanda C, Lima E, Silva D, Moreira I, Pêgo JM, Macedo G, Correia-Pinto J. In vivo assessment of gastrotomy closure by over-the-scope-clips in an experimental model for varicocelectomy. *Gastrointest Endosc* 70:1137-45 (2009). (IF=7.367)
6. Vilaça JL, Fonseca JC, Pinho AC. 3D Surface Profile Machine for Characterization the Pavement Texture – TexScan. *Mechatronics*, *in press*. (IF=1.434)
7. Vilaça JL, Fonseca JC, Pinho AC. Calibration procedure for 3D measurement systems using two cameras and laser line. *Optics and Laser Technology*, 41:112-9 (2009). (IF=0.892)
8. Vilaça JL, Fonseca JC, Pinho AC. Non-contact 3D acquisition system based on stereo vision and laser triangulation. *Machine Vision and Applications*. DOI-10.1007/s00138-008-0166-7 (2009). (IF=1.485)

### **Other publications International**

- Book Chapters

Cássio F, Leão C, Baltazar F. Plasma membrane transport of monocarboxylates in yeasts. In: *Frontiers in Fungal Ecology, Diversity and Metabolites*. Ed. Sridhar, KR. IK International Publishing House Pvt. Ltd., New Delhi. pp. 248-263. (2009).

### **Master and PhD theses completed**

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

1. Sílvia Gonzaga. 'Modulation of Lung Development by in utero Gene Therapy'. Supervised by Jorge Correia-Pinto, School of Health Sciences, University of Minho (2009).
2. Carla Rolanda. 'N.O.T.E.S.: Peroral Transluminal Endoscopic Surgery'. Supervised by Jorge Correia-Pinto, School of Health Sciences, University of Minho (2009).

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

1. Sara Granja. 'Characterization of MCTs expression pattern during chick embryo development'. Supervised by Fátima Baltazar, School of Health Sciences, University of Minho (2009).

## Patents/propotypes

Vilça J, Pinho AM, Correia-Pinto J, Fonseca J, Peixinho N. System for automatic and personalized modelling/bending of surgical prosthesis for correction of pectus excavatum based on pre-surgical imaging information. PT2007010382320070913 and WO2008PT0001620080424.

## Prizes

- Grand Prize START 2009 for the best National research and inovative idea to launch a Spin-Off: *Surgical3D* by the applicants Vilça J, Fonseca J, Pinho AM, Correia-Pinto J (2009).
- Prize University of Minho to the graduated in University of Minho in 2008 with the highest classification attributed to Nogueira-Silva C (2009).
- Prize Pierre-Fabre for the best publication in the field od Pediatrics for the article Antunes *et al.* Br J Nutr, 101:1262-6 (2009), Sociedade Portuguesa de Pediatria (2009).
- Prize for the best research paper published by MDs from Hospital Geral Santo António to Lima E, Porto (2009).
- 1<sup>st</sup> prize for poster presented at the Meeting of the European Academy of ORL\_HNS by Baltazar F, Reis RM Germany (2009).
- 1<sup>st</sup> prize for the best oral communication at 5<sup>o</sup> Simpósio nacional de cancro digestivo, with the work 'A proteína RKIP é um marcador independente de sobrevivência em carcinomas gástricos' by Martinho O, Albufeira (2009).
- 1<sup>st</sup> prize for the best poster communication for the work Ramos T, Rodrigues F, Nogueira-Silva C, Abreu C, Vides B, Serrano P, Borges da Silva G, Jardim da Pena D. Cancro do colo do útero no Hospital de São Marcos, Braga – Casuística 2003 a 2007, at the 163<sup>a</sup> Reunião Científica da Sociedade Portuguesa de Ginecologia: XIII Jornadas Minhotas de Ginecologia.” Braga (2009).
- 2<sup>nd</sup> Prize for Oral presentation in Oncology and Molecular Biology for Baltazar F and Reis R at “Young European Scientist (YES) Meeting”, Porto (2009).
- 2<sup>nd</sup> Prize Award for poster presented by Baltazar F in “Encontros da Primavera – Oncologia 2009” Portugal (2009).
- FEBS Youth Travel Funds to Pinheiro C to participate in the FEBS Advanced Lecture Course “Matrix Pathobiology, Signaling and Molecular Targets”, FEBS. (2009).
- Young Researcher Scholarship to Pinheiro C attributed by the organization committee of the “JOINT 4th Eortc Pathobiology Group Annual Meeting & 1st International Multidisciplinary Cancer Research Congress” (2009).
- Awarded with Young Researcher Scholarship to Martinho O to attend the joint 4th annual meeting of the EORTC PathoBiology group & 1st International Multidisciplinary Cancer Research Congress.Turkey (2009).
- Awarded with Youth Travel Fund (YTF) by FEBS (Federation of European Biochemical Societies) to attend the: Matrix Pathobiology, Signaling and Molecular Targets FEBS Advanced Lecture Course attributed to Martinho O. Greece. (2009).

## Organization of conferences

- Organization of Scientific Meetings and Presence in Scientific Committees
  - The Surgical Sciences research domain (Jorge Correia-Pinto, Estêvão Lima, Carla Rolanda, Pedro Leão and Sandra Martins) organized the '2<sup>nd</sup> Annual Congress of the Portuguese Society of Minimally Invasive Surgery'. Braga, Portugal (2009).
  - Henedina Antunes. Organized the 'XXII Reunião anual da Secção de gastroenterologia, hepatologia e nutrição pediátrica da SPP'. Braga, Portugal (2009).
  - Henedina Antunes. Organized the 'XXXI Simpósio Minhoto-Galaico de Pediatria Extra-Hospitalar'. Ofir, Portugal (2009).
  - Jorge Correia-Pinto. Scientific Committee of the 'Annual Meeting of Portuguese Society of Pediatric Surgery'. Coimbra, Portugal (2009).
- Post-graduation courses and Workshops organized at the ICVS
  - Jorge Correia-Pinto, Tiago Henriques-Coelho, Cláudia Marques, António Alves. Organized the *Maternal-Pediatric Endoscopic Surgical Week* (included 3-days hands-on course in gynecological laparoscopy and 3-days hands-on course in Fetal and Neonatal Endoscopic Surgery), within the post-graduation programme of the ICVS/ECS (2009).
  - Jorge Correia-Pinto, Raquel Andrade, Rui M. Reis. Organized the Fundamentals of Genetics, Development and Neoplasia, School of Health Sciences, University of Minho, Portugal (2009).
  - Jorge Correia-Pinto, Carla Rolanda, Novo de Matos. Organized the 3<sup>rd</sup> *Minimally Invasive Surgical Week* (included 3-days hands-on course in digestive laparoscopy and one-day hands-on course in N.O.T.E.S.), within the post-graduation programme of the ICVS/ECS (2009).
  - Raquel Andrade. Organized the workshop in Bioinformatics for Health Sciences, School of Health Sciences, University of Minho, Portugal (2009).
  - Organization of other Meetings
  - Members of the Surgical Sciences research domain (Jorge Correia-Pinto, Estêvão Lima, Carla Rolanda, Pedro Leão and Sandra Martins) integrated the Scientific Committee of the *Minho Medical Meeting on Surgery* organized by the MD Students from School of Health Sciences, University of Minho. Braga, Portugal. (2009).
  - Martins S. Co-organization of the workshop "Curso de Suturas Manuais e Mecânicas". ECS-ICVS, 2009.

## Internationalization

The Surgical Sciences research team embraces basic, translational and clinical research related with digestive, genito-urinary and pulmonary systems, aiming to discover nature's laws of development, mechanisms of disease and minimally invasive ways to treat surgical entities. Many of these projects are in collaboration with international partners, as can be appreciated below:

Palmeirim I. and Andrade RP. - Members of the "Network of excellence "Cells into organs" EU/FP6 Cells into Organs: Functional genomics for development and disease of mesodermal organ systems ([www.cellsintoorgans.net](http://www.cellsintoorgans.net)).

Palmeirim I. and Andrade RP. - Collaborative projects with Prof. Stan Maree, John Innes Centre, UK

Reis RM. – Co-coordinator of the Marie Curie Conferences and Congresses: Genome Architecture in Relation to Disease – 2007-2009

Reis RM. – Collaborative projects with:

- Prof. George Calin, Experimental Therapeutics Department, The University of Texas, MD Anderson Cancer Center, USA
- Prof. Joseph Costello, Brain Tumor Research Center, UCSF, USA
- Prof. Bauke Ylstra, Micro Array Facility, VU University Medical Center, The Netherlands
- Prof. João Norberto Stavale, Department of Pathology, Federal University of São Paulo, Brazil
- Prof. Suely Marie, Department of Neurology, University of São Paulo (USP), São Paulo, Brazil
- Dr. Talvane Oliveira, Department of Surgery, Barretos Cancer Hospital, Brazil

Correia-Pinto J. - Collaborative projects with:

- Prof. Alan W. Flake, Department of Surgery, Children's Hospital of Philadelphia, USA

Baltazar F. - Collaborative projects with:

- Dr. Talvane Oliveira, Department of Surgery, Barretos Cancer Hospital, Brazil.
- Dr. Daniella Vieira, Federal University of Santa Catarina – UFSC, Brazil
- Dr. Venâncio Avancini Ferreira Alves, Department of Pathology, University of São Paulo, Brazil
- Dr. Marise Moreira, Department of Pathology, Federal University of Goiás, Brazil
- Dr. Luisa Villa, Luwig Institute, São Paulo branch, Brazil
- Dr. Carlos Bedrossian, Department of Pathology, Norwegian American Hospital, USA
- Dr. Rodolfo Montironi, Institute of Pathological Anatomy and Histopathology, Polytechnic University, Italy



## Funding

### Government/Organization contract research

#### Integrative Studies in Surgical Diseases

1. 2004-2009 - European Network of Excellence “Cells into Organs” ([www.cellsintoorgans.net](http://www.cellsintoorgans.net)). EU/FP6. [Raquel Andrade](#). (Team member).
2. 2009-2010 - Research Grant from Hospital S. João. ‘Markers of prognosis in newborns with CDH’; 5 000 €. [Maria J Baptista](#) (PI).
3. 2009-2010 - Grant Zeru ‘The role of growth factors of endothelial origin in fetal lung development and neonatal’; 5 000 €. [Jorge Correia-Pinto](#) (PI).
4. 2010-2012 – Project from Fundação para a Ciência e Tecnologia (FCT) with the reference PTDC/SAU-OBD/105111/2008 - O papel dos genes do relógio molecular no controlo temporal da padronização da mesoderme de embriões vertebrados, granted with 170 000 €. [Raquel Andrade](#) (PI).
5. 2010-2012 – Project from Fundação para a Ciência e Tecnologia (FCT) with the reference PTDC/SAU-FCF/104347/2008 - Monocarboxylate transporters as potential therapeutic targets in cancer: studies of inhibition in models of solid tumors, granted with 119 711 €. [Fátima Baltazar](#) (PI).
6. 2010-2012 – Project from Fundação para a Ciência e Tecnologia (FCT) with the reference PTDC/SAU-OBD/108051/2008 - Molecular mechanisms of temporal and spatial control of embryonic lung development, granted with 40 000 €. [Jorge Correia-Pinto](#) (PI).
7. 2010-2012 – Project from Fundação para a Ciência e Tecnologia (FCT) with the reference PTDC/SAU-BEB/105650/2008 – CSD-Chip - Development of a biochip for the separation and deformation of blood cells, granted with 160 000 €. [Maria J Baptista](#) (Team Member) – ICVS budget: 6.000 €.

#### Endoscopy and Surgical Techniques

1. 2010-2012 – Project from Fundação para a Ciência e Tecnologia (FCT) with the reference PTDC/SAU-BEB/103368/2008 – System pectus 3D: modeling / automatic folding and custom surgical prosthesis fixation coupled with virtual simulation and the cosmetic outcome after surgical, granted with 190 000 €. [João Vilaça](#) (PI).
2. 2010-2012 – Project from Fundação para a Ciência e Tecnologia (FCT) with the reference PTDC/SAU-OSM/105578/2008 - Preclinical Evaluation of the Effectiveness and Benefits of Transluminal Endoscopic Surgery for Natural Orifices (N.O.T.E.S.), granted with 76 471 €. [Estêvão Lima](#) (PI).

### Industry contract research

[Baptista MJ](#). Investigator of international multicentric study CLARINET (clopidogrel to lower arterial thrombotic risk in neonates and infants trial). Sanofi Aventis.

[Nabais S](#). Coordinator in the **Registo RECORD AF** (DRONED\_C\_01264).

[Nabais S](#). Co-Investigador do ensaio clínico **ENGAGE AF-TIMI**.

Research contract with Sanofi-Pasteur MSD. Studies in sexually transmitted diseases in adolescents. Budget 10 000 €. [Henedina Antunes](#) (coordinator).

## Future Research

The Surgical Sciences Research team was constituted in 2003 (formerly Development and Neoplasia Research Domain). The rationale for the change comes from the fact that we have in the Domain researchers with basic and clinical expertise in surgical diseases from digestive, urogenital and pulmonary systems. Thus, taking benefit from common research facilities and basic techniques (molecular, cell and organ level), it sounded appropriate to concentrate our efforts in studies of these systems under the same research Domain. Moreover, during the last three years and as a consequence of expertise of clinicians of the Domain in minimally invasive procedures, we successfully launched novel projects that aimed to shift the paradigm of surgical approaches making it even less invasive than the well-established laparoscopy/thoracoscopy. These projects attracted attention from international companies of surgical instruments, motivating them to provide the equipment that allowed us to install a new high definition full-equipped laboratory for research in surgical techniques.

With this strategy, and integrated within a Medical School, in 2010 we will focus in the following aspects: i. to keep and reinforce our partnership with surgical equipment companies; ii. to keep and increase the impact factor of international publications; iii. to provide a wide and well-structured hands-on international program of minimally invasive surgical courses; iv. to keep attracting motivated either basic or clinical researchers providing them the best conditions to carry out their PhD. or Post-Doc activities; v. to launch our first Spin-Off: **Surgical3D**.