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

INSTITUTO DE INVESTIGAÇÃO EM CIÊNCIAS DA VIDA E SAÚDE

ANNUAL REPORT
2008

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 and ranked as "Excellent" by a FCT's international evaluation panel.

The second evaluation of ICVS took place in 2008, on two separate occasions (February and March), and was undertaken by two distinct panels of experts: one specialized in "Neurosciences" and the other in "Molecular Genetics, Cellular and Molecular Biology, Experimental Pathology, Development and Oncobiology". The final rank given to the ICVS was "Very Good". Given the effective and sustained progresses recorded in all indicators of scientific productivity during the four-year period under evaluation, the ICVS Direction prepared a rebuttal appealing for a re-evaluation, which is still under consideration by FCT.

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

• Implementation of multi- and inter-disciplinary research groups, designated as Research Domains (RDs). Each RD is composed by at least two Research Lines (RL) that, in turn, are composed for at least two funded Research Projects. The functional cell of the ICVS is thus the Research Project (each of which has a PI). Each RD and RL also has a coordinator.

• Integrated/shared management of resources - organization of function-oriented laboratories.

• Incentive to high quality scientific production (e.g. support of publication costs; annual awards for the paper published within the previous 5 years with the higher number of citations, for the paper of the current year with the highest IF, as well as for the RD with higher accumulated IF).

• Innovative Post-graduation, organized as an International Post-graduation Program that offers advanced training in biomedical and clinical sciences. An innovative MD/PhD program has also been set up in collaboration with the Thomas Jefferson and Columbia Medical Schools, USA.

The ICVS research activities are presently organized within three RDs:

- MICROBIOLOGY AND INFECTION (RLs: Clinical Microbiology; Immunology of Infection and Unicellular Eukaryotic Modeling systems);

- DEVELOPMENT AND NEOPLASIA (RLs: Chronobiology in Development; Cancer Biomarkers; Lymphangiogenesis and Angiogenesis; Fetal and Neonatal Physiology and a new emerging one 3rd Generation Surgery);

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

The ICVS governing bodies are:

• The Scientific Council (SC) - includes all PhD members of the ICVS, 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 each RD, the Coordinator of the Post-graduation Program and one representative from the ECS Direction. The DB activities are centered on monitoring the ongoing activities, establishing the operating rules, determining the sharing of resources and the planning the ICVS funding.

• The Coordinators of each RD, who govern the research within the respective RD.

• The Boards of the RDs, composed by all PIs of each RD.

• The Coordinator of each RL.

• The External Advisory Committee that integrates three international experts:

- Marina Bentivoglio – Full Professor, Medical Faculty, University of Verona, Italy.

- Alan Flake – Full Professor, School of Medicine, University of Pennsylvania, Philadelphia, USA.

- Paulo Vieira – Chargé de Recherche, Pasteur Institute, Paris, France.

General Objectives

In the national context, the ICVS is a novel 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 recognized impact in biomedical and clinical sciences, with high scientific output;

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

• to develop international post-graduated programs;

• to provide specialized health services to the community (this objective was set out at the beginning of 2008, following the relocation of ICVS to the new building – see below).

In accordance, the ICVS intends to be a research institute of high profile in biomedical and clinical sciences, governed with originality by high profile international standards, endorsing innovative interaction between research and medical training (under- and post-graduation). As a result, we hope to build a growing institution with an attractive research environment for young researchers.

The specific developmental strategies for 2008 were to:

• scale up the network of shared research facilities (laboratories and scientific equipments) for a total area of 6000 m2, in an independent wing of the new ECS building, to establish the grounds for a new cycle of development of the Institute.

• promote flexible and integrated functional models that identify local needs and promote multidisciplinary projects involving health professionals of all levels;

• enroll medical students and MDs within ICVS research projects;

• support the ongoing MD/PhD program in collaboration with the Thomas Jefferson and Columbia Medical Schools, USA;

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

• diversify the funding sources at the national and international levels, including private foundations, industry and the FP7 EU program;

• promote the public awareness of science in the biomedical field.

Therefore, the specific aims for 2008 were to:

• install the ICVS in the new ECS building without compromising the scientific production;

• increase the number of PhD researchers for at least 20%, namely by recruiting high profile fulltime PhD researchers in the context of the "Ciência 2007";

• expand funded collaborative research projects and diversify the funding sources, including, at least, 1 project at the international level;

• increase the number of independent clinical research investigators, in order to competitively apply for clinical research funding in the context of specific programs from private foundations and FCT;

• actively pursue the complement of the contract established with the FCT for the ICVS's funding;

• keep the "internal" and "external" communities informed about the ICVS activities through, respectively, the "Ciência Falada" seminar cycle and the promotion of activities aiming the public awareness of science.

Main Achievements during the year of 2008

The strategy designed for the development of ICVS as a high profile research unit has reached a crucial stage in 2008, with the relocation to a 6000 m2 area of the new ECS building. The new facilities were equipped with different scientific equipment of transversal use (e.g. microscopy and cellular imaging, cell/tissue culture, microbiology, molecular biology, animal experimentation, biological resources).

Regarding the more relevant scientific findings in 2008:

• Our previous research studies in the Neurosciences RD have unravelled the dysfunction of the hippocampal-to-prefrontal cortex link after stress exposure; this year we decided to explore the impact of stress in the reorganization of the corticostriatal networks and in decision making processes. These studies showed that stress bias subjects to habits due to a preferential activation of the sensiromotor network in detriment of the activity of the associative network – this study has recently been accepted in Science.

• Following the studies of the polymorphisms in toll-like receptors and susceptibility to immune diseases, developed in the Microbiology and Infection RD, we identified a polymorphism in the TLR-9 gene that

associates with increased risk to develop Non-Hodgkin lymphoma. This study has involved the establishment of an extensive network of hospitals and clinicians and is currently under revision in a high profile journal.

• From the research activities of the Development and Neoplasia RD, we would highlight the contribution to clarify the underlying mechanisms of lung malformation. By inducing FGF10 overexpression *in vivo*, we induced lung malformations that closely recapitulate the morphology and histology of the spectrum of human congenital cystic adenomatoid malformation (CCAM). These findings support a role for FGF10 in the induction of human CCAM, providing further mechanistic insights into its participation in normal and abnormal lung development.

Additionally, in 2008, the ICVS achieved:

• a sustained increase in both staff numbers and level of differentiation; the number of PhDs increasing from 31 in 2007 to 38 in 2008 (25 ECS faculty, 4 "Ciência 2007", and 9 Post–Docs);

• to maintain its scientific productivity (in spite of the constrains associated the relocation of the ICVS): 84 papers in international journals (IF<2 = 34 papers; IF between 2 and 4 = 32; IF between 4 and 6 = 11; IF between 6 and 10 = 6; IF>10 = 1 paper) plus 25 in press, and 6 book chapters (2 in press);

• to accommodate the research work that led to the conclusion of 13 PhD thesis;

• to attract an increasing number (52) of PhD students, in addition to 18 Master students, 23 assistant researchers and 18 members of the non-academic staff (14 technicians and 4 administrative, financially supported by ECS);

• to increase the number of MD students involved in research (26 Option Projects; 12 MD/PhD Lab Rotations);

• to obtain a total of 29 fellowships from FCT (3 BPD, 8 BD, 9 BI and 9 BII);

• to raise the external/competitive funding. The ongoing projects (average duration: 3 years) attracted funding of about 2 million €, of which about a quarter correspond to the activities developed in 2008;

• to organize 20 Advanced Post-Graduation Courses and Workshops with 446 participants (form which 39% were MDs, 44% Biological Sciences, 11% other Health Professionals) in the context of the ECS International Post-graduation Program; Overall, 79% of the participants rated the courses as "Very Good" or "Excellent";

• to extend the collaborative activities within the MD/PhD program with the Thomas Jefferson (1 student) and the Columbia Medical Schools (2 students).

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

Activities

Integrative/multidisciplinary activities during the year of 2008

At the launching of the ECS, professors with diverse and complementary scientific backgrounds were recruited and committed to research within the ICVS. This lead to the development of strong Research Domains (RDs), combining scientists able to approach common scientific problems using complementary perspectives. Furthermore, some of the ongoing projects are being developed transversely across the three RDs. In fact, a clear definition of an integrative policy was established in order to increase the critical mass within a setting that favored intra- and inter-group collaborations and complementary experimental approaches.

Overall, the scientific background of the ICVS PhD researchers includes MDs, Biochemists, Engineers, Biologists, Pharmaceutics, Mathematicians, Microbiologists and Veterinarians. As such, the ICVS's methodological approaches to each scientific question in biomedicine, using cell/tissue cultures, animal models or human samples, include functional and genetic studies, fulfilled with, among others, imagiology, cytometry, cellular and molecular biochemistry, and mathematical modeling.

The combined teaching and research expertise of the ECS PhD staff also contributed to the successful training of medical students, promoting the interaction between different fields of biomedical research and medical education, as, for example, in the context of: (i) the Curricular Area "Option Projects" and; (ii) the MD/PhD program, in collaboration with the Thomas Jefferson and Columbia Medical Schools, in which medical students perform several Lab Rotations.

The interplay between the research activities at ICVS and the ECS medical course is also reflected in the publication, in 2008, of research articles on education in the Life & Health Sciences field: 3 papers in peer reviewed journals (1 in press) a and 1 book chapter (in press).

The ICVS RDs have been establishing international collaborations with reference labs in Europe and the USA, as well as participating in a network involving health institutions from developing countries, namely in Africa and Latin America. These interactions resulted not only in important scientific achievements but is also expressed by successful applications for competitive funding, namely one Dana Foundation, one EU FP7 project granted (involving research groups from the USA, UK, Belgium, Denmark, France, Germany, Portugal, Spain, Sweden, Switzerland, as well as from Mali, Morocco, Mozambique, Nigeria, Uganda, South Africa, Tanzania, and Zambia) and one Marie-Curie action in the context of the FP7.

In what regards network activities, the ICVS intra-network of Shared Facilities, besides supporting the different ICVS RDs, has also hosted several researchers from other national and international Research Units. On the other hand, at the National level, the ICVS RDs were also able to establish a network of clinicians involved in collaborative research activities (e.g.from H. S.Marcos, Braga, H. S. Oliveira, Guimarães, H. J. Urbano, Porto). This policy resulted in the ability to attract specific funding for translational and clinical research, obtained in competitive calls from FCT (5 projects – 3 years Budgets ranging form 130.000 € to 176.000 € in the total amount of 776.000 €) and FCG (1 project – 4 years Budget of 160.000 €).

Collaborations at the National level are also increasing: from 49 projects submitted to the last FCT call, 27 included collaborations with other National research units.

Outreach activities during the year of 2008

The promotion of public awareness of science is also an important endeavor of the 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, teachers and senior citizens. Accordingly, in 2008, several events/activities involving Science & Society were promoted and are listed below:

1 – ICVS Newsletter

For the first time, a bi-annual publication describing the ICVS research, directed to the general public, was launched on-line. The first number came out in July 2008 (http://www.ecsaude.uminho.pt/uploads/Newsletter1_ICVS.pdf) and the second in February 2009 (http://www.ecsaude.uminho.pt/uploads/Newsletter2_ICVS.pdf).

2 – "Science Experimental Teaching Program"

A hands-on and highly interactive educational program designed to support Science, Technology and Live Sciences teachers, as well as to inspire secondary-level school students to develop their study on these subjects, has been organized. This program is running during the 2008/09 academic year and involves: (i) laboratory training of secondary-level life sciences teachers; (ii) admission of secondary-level students in research projects at ICVS; and (iii) seminars provided by ICVS researchers at the participating secondary schools. At the end, a congress will be organized at ICVS, allowing students, teachers and ICVS/ECS members to share their experience.

3 – "Community Health Teaching Program"

Another educational program has been designed to provide secondary-school teachers, and consequently their students, with a better knowledge on community health problems, namely regarding diabetes, sexual education, violence within schools, etc. This program also runs throughout the 2008/09 academic year.

4 – "Secondary School Visit Programme"

To increase the public awareness on our research, we offer scientific exhibitions, presentations and guided tours of the ICVS. During 2008, several High-Schools visited our facilities (in a total of 274 students) and observed in loco the work of the ICVS research teams.

5 - "Portas Abertas" at 2008 Science and Technology Week

During the "Science and Technology week" (24-28Nov), open lab activities were organized involving up to 620 students from several primary and secondary schools from the Minho region. Hands-on experiments were designed for each of the three educational levels (4th, 7th and 10-12th grade students) to allow our young visitors to become "Scientists for a day". A full report of "Portas Abertas" (Open Labs, Scientists for a day) is available at http://www.icvs.uminho.pt/icvs/icvs/index.htm.

6 – “Brain Awareness Week 2008”

In the context of the Brain Awareness Year, dedicated activities were performed during the week of 10-14th March. Namely, Science Sessions at Schools; Open lab activities and General Public open sessions “Around the Brain 2008” at FNAC, Braga.

7 - “ICVS a cores”

An artistic competition of scientific images from research work produced at ICVS was organized with the purpose of promoting the ICVS research and selecting a set of images to put up as a continuous display along the ICVS corridors.

8 – Others

Members of ICVS have been participating in other public activities, such as TV and radio programs, interviews to newspapers and conference cycles promoted by different external institutions.

ICVS Team (PhD Researchers)

ICVS members (PhD Researchers) at 31 December 2008

DEVELOPMENT AND NEOPLASIA

ECS Faculty

Adhemar Longatto-Filho

Fátima Baltazar

Isabel Palmeirim

Jorge Correia-Pinto

Rui Reis

Estevão Lima

Maria João Baptista

"Compromisso Ciência"

Raquel Andrade

Post-Docs

Fernanda Bajanca

Rute Moura

Sandra Costa

MICROBIOLOGY AND INFECTION

ECS Faculty

António Gil Castro

Cecília Leão

Elsa Logarinho

Fernando Rodrigues

Jorge Pedrosa

Margarida Correia-Neves

Paula Ludovico

"Compromisso Ciência"

Margarida Saraiva

Post-Docs

Agostinho Almeida

Andrea Cruz

NEUROSCIENCES

ECS Faculty

Armando Almeida

Joana Palha

João Sousa

João Cerqueira

Nuno Sousa

Patrícia Maciel

João Bessa-Peixoto

José Miguel Pêgo

Manuel Lima-Rodrigues

Ana Raquel Mesquita

"Compromisso Ciência"

António Salgado

Post-Docs

Ana João Rodrigues

Cláudia Botelho

Fernanda Marques

Ioannis Sotiropoulos

ECS Faculty

Manuel João Costa

"Compromisso Ciência"

Ana Cristina Paulo

Research Groups

Title / Research Domain Coordinator

DEVELOPMENT AND NEOPLASIA Research Domain
(Jorge Correia-Pinto)

MICROBIOLOGY AND INFECTION Research Domain
(Jorge Pedrosa)

NEUROSCIENCES Research Domain
(Nuno Sousa)

a) DEVELOPMENT AND NEOPLASIA Research Domain

Research Domain Description

Title of Research Group: DEVELOPMENT AND NEOPLASIA

Coordinator: Jorge Correia-Pinto

Main Scientific Domain: Health Sciences

Objectives & Achievements

Objectives

- Chronobiology and Development

Developmental biology considers that embryo development comprises proliferation, differentiation, morphogenesis and growth. We draw our attention to a fifth issue: How is time controlled during embryonic development? We pioneered the identification of a molecular clock underlying chick somite formation and providing positional information during development. Later on, we showed that this mechanism is also an early link for left-right patterning. Recently, we reported the existence of a limb molecular clock.

- Fetal and Neonatal Physiology

The understanding of fetal lung growth mechanisms has clinical relevance since it can open new perspectives in the treatment of lung hypoplasia as well as in the modulation of lung repair. Our main achievements were: To discover the role of mechanical and molecular mechanisms regulating fetal lung growth; by this way, we expect to find the most appropriate strategy to promote fetal lung growth.

- Angiogenesis and Lymphoangiogenesis

Our efforts have been to investigate the principal molecules related to neoplastic neovascularization since they can determine prognosis parameters and also represent potential targets for cancer therapy. Most of our projects focused the role of VEGF family, ligands and receptors, and lymphangiogenic markers, such as D2-40, Prox-1 and Lyve-1, in benign and malignant cellular proliferative conditions.

- Cancer Biomarkers

Carcinogenesis is a highly complex process, characterized by the interaction between genetic and environmental factors. In the last years, we have been concentrated in the study of several genetic players involved in cancer susceptibility, behavior and therapeutic response. We focused this analysis in several primary human tumors, namely breast, gastric, colorectal, GISTs, cervix and brain neoplasms. In addition, tumor cell lines models are used to perform functional and therapeutic assays.

Main Achievements

In 2008, the main achievements of the Development and Neoplasia Research Domain were:

1. Publications and patents
    a. 54 publications in international peer-reviewed journals, the selected 24 listed below.
    b. 30 abstracts in international congresses
    c. 26 international conferences/seminars produced by members of the domain.
    d. 3 book chapters
    e. 1 patent

2. Theses

    a. 5 PhD theses completed

    b. 2 Master and 4 undergraduate theses completed

3. Organization of conferences

    a. Organization of 5 international post-graduation courses

4. Internalization and academic juries

    a. Members of the Domain participated in 16 graduation (PhD/Master) juries and were Ad-hoc reviewers for 25 journals in the Development, Neoplasia, Physiology and Surgical Sciences (Acta Paediatrica Scandinava; Acta Pharmacologica Sinica; American Journal of Physiology - Gastrointestinal and Liver Physiology; 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 Archive).

    b. Jorge Correia-Pinto is associate Editor for European Journal of Pediatric Surgery and World Journal of Gastrointestinal Surgery; Isabel Palmeirim worked as reviewer for Fondation Recherche Médicale (France), National Science Foundation (EUA), Wellcome Trust (UK) and is currently associate Editor for The International journal of Developmental Biology; Rui M Reis is member of the Editorial Board of the 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.

5. 5. Funding

    a. Since 2008, the members of Development and Neoplasia Reseach Domain are making efforts to get funding other than FCT, namely in partnership with companies of surgical equipment.

Group Productivity

Publications in peer review Journals

- 24 papers selected from 54:

1. Baptista MJ, Clemente F, Rocha G, Areias JC, Guimaraes H, Correia-Pinto J. NT-proBNP as useful tool to evaluate pulmonary hypertension and cardiac function in CDH infants. Neonatology 94:22-30 (2008). (IF - 1.920)

2. Baptista MJ, Nogueira-Silva C, Areias JC, Correia-Pinto J. Perinatal Profile of Ventricular Overload Markers in Congenital Diaphragmatic Hernia. J Pediatr Surg 43:627-633 (2008). (IF - 1.557)

3. Box G, Averch T, Cadeddu J, Cherullo E, Clayman R, Desai M, Frank I, Gettman M, Gill I, Gupta M, Haber GP, Kaouk J, Landman J, Lima E, Ponsky L, Rane A, Sawyer M, Humphreys M; Urologic NOTES Working Group. Nomenclature of natural orifice translumenal endoscopic surgery (NOTES) and laparoendoscopic single-site surgery (LESS) procedures in urology. J Endourol 22:2575-81 (2008). (IF - 1.930)

4. Costa S, Pinto D, Pereira D, Rodrigues H, Cameselle-Teijeiro J, Medeiros R and Schmitt F. Importance of TP53 codon 72 and intron 3 duplication 16bp polymorphisms in prediction of susceptibility on breast cancer. BMC Cancer 8:32 (2008). (IF - 3.087)

5. Costa S, Pinto D, Pereira D, Rodrigues H, Cameselle-Teijeiro J, Medeiros R and Schmitt F. XRCC1 Arg399Gln and RAD51 5'UTR G135C polymorphisms and their outcome in tumor aggressiveness and survival of Portuguese breast cancer patients. Breast Cancer Res Treat 109:183-185 (2008). (IF - 5.684)

6. Derchain S.F., Sarian L O, Naud P, Roteli-Martins C, Longatto-Filho A, Tatti S, Branca M, Erzen M, Serpa-Hammes L, Gontijo R C, Bragança J F, Lima T P, Maeda M Y S, Lörincz A, Dores G B, Costa S, Syrjänen S, Syrjänen K. Safety of screening with Human papillomavirus (HPV) testing for cervical cancer at 3-year intervals in a high-risk population: Experience from the LAMS study. J Med Screen 15:97-104 (2008). (IF - 1.802)

7. Gama A, Paredes J, Gärtner F, Alves A, Schmitt F. Expression pattern of adhesion molecules (E-cadherin, P-cadherin and β-catenin) and their relationship with clinicopathological parameters, proliferation and survival in canine mammary malignant tumours. Vet J 177: 45-53 (2008). (IF - 1.802)

8. Gaspar MM, Cruz A, Penha AF, Reymão J, Sousa AC, Eleutério CV Domingues SA, Fraga AG, Longatto Filho A, Cruz ME, Pedrosa J. Rifabutin encapsulated in liposomes exhibits increased therapeutic activity in a model of disseminated tuberculosis. Int J Antimicrob Ag 31:37-45 (2008). (IF - 3.067)

9. Gettman MT, Box G, Averch T, Cadeddu JA, Cherullo E, Clayman RV, Desai M, Frank I, Gill I, Gupta M, Haber G-P, Humphreys M, Kaouk J, Landman J, Lima E, Ponsky L. Consensus Statement on Natural Orifice Transluminal Endoscopic Surgery and Single-Incision Laparoscopic Surgery: Heralding a New Era in Urology? Eur Urol 53:1117-1120 (2008). (IF - 6.512)

10. Gomes AL, Gouveia A, Capelinha AF, Cruz D, Silva P, Reis RM, Pimenta A, Lopes JM. Molecular alterations of c-Kit and PDGFRA in GISTs. A evaluation study of a Portuguese series. J Clin Pathol 61:203-8 (2008). (IF - 2.342)

11. Gonzaga S, Henriques-Coelho T, Davey M, Zoltick PW, Leite-Moreira AF, Correia-Pinto J, Flake AW. Cystic Adenomatoid Malformations are Induced by Localized FGF10 Overexpression in Fetal Rat Lung. Am J Respir Cell Mol Biol 39:346-55 (2008). (IF - 4.477)

12. Goto T, Takano M, Albergaria A, Briese J, Pomeranz KM, Cloke B, Fusi L, Feroze-Zaidi F, Maywald N, Sajin M, Dina RE, Ishihara O, Takeda S, Lam EW, Bamberger AM, Ghaem-Maghami S, Brosens JJ. Mechanism and functional consequences of loss of FOXO1 expression in endometrioid endometrial cancer cells. Oncogene 27:9-19 (2008). (IF - 7.216)

13. Henriques-Coelho T, Oliveira SM, Moura RS, Roncon-Albuquerque R Jr, Neves AL, Santos M, Nogueira-Silva C, La Fuente Carvalho F, Brandão-Nogueira A, Correia-Pinto J, Leite-Moreira AF. Thymulin inhibits monocrotaline-induced pulmonary hypertension modulating interleukin-6 expression and suppressing p38 pathway. Endocrinology 149:4367-4373 (2008). (IF - 4.945)

14. Lima-Rodrigues M, Valle-Fernandes A, Lamas N, Cruz A, Baltazar F, Milanezi F, Nunes R, Pedrosa J, Reis RM, Castro AG, Almeida A. A New Model of Laryngitis: neuropeptide, COX and cytokine profile. Laryngoscope 118:78-86 (2008). (IF - 1.877)

15. Longatto-Filho A, Pinheiro C, Ferreira L, Scapulatempo C, Alves VAF, Baltazar F, Schmitt F. Peritumoral, but not intratumoral, lymphatic vessel density and invasion correlate with colorectal carcinoma poor outcome markers. Virchows Arch 452:133-8 (2008). (IF - 2.082)

16. Macedo FYB, Baltazar F, Almeida PRC, Távora F, Ferreira FV, Schmitt F, Ribeiro RA. Cyclooxygenase expression on ifosfamide-induced hemorrhagic cystitis in rats. J Cancer Res Clin 134:19-27 (2008). (IF - 2.217)

17. Martinho O, Gonçalves A, Moreira M, Ribeiro L, Queiroz G, Schmitt FC, Reis RM, Longatto-Filho A. KIT activation in uterine cervix adenosquamous carcinomas by KIT/SCF autocrine/paracrine stimulation loops. Gynecol Oncol 111:350-5 (2008). (IF - 2.919)

18. Nabais S, Salomé N, Brandão A, Simões A, Marques J, Costa J, Basto L, Costeira A, Correia A. Coexistence of coronary cameral fistulae and cortriatriatum sinister in an elderly patient. Eur J Echocardiogr 9:712-715 (2008). (IF - 1.917)

19. Nogueira-Silva C, Moura RS, Esteves N, Gonzaga S, Correia-Pinto J. Intrinsic catch-up growth of hypoplasic fetal lungs is mediated by interleukin-6. Pediatr Pulmonol 43:680-689 (2008). (IF - 1.883)

20. Nunes S, Nogueira-Silva C, Dias E, Moura RS, Correia-Pinto J. "Ghrelin and obestatin: different role in fetal lung development?". Peptides 29:2150-2158 (2008). (IF - 2.565)

21. Paredes J, Correia AL, Ribeiro AS, Milanezi F, Cameselle-Teijeiro J, Schmitt FC. Breast carcinomas that co-express E- and P-cadherin are associated with p120-catenin cytoplasmic localization and poor patient survival. J Clin Pathol 61:856-62 (2008). (IF - 2.342)

22. Pinheiro C, Longatto-Filho A, Ferreira L, Pereira SMM, Etlinger D, Moreira MA, Jubé LF, Queiroz GS, Schmitt F, Baltazar F. Increasing Expression of Monocarboxylate Transporters 1 and 4 Along Progression to Invasive Cervical Carcinoma. Int J Gynecol Pathol 27:568-74 (2008). (IF - 1.766)

23. Pinheiro C, Longatto-Filho A, Scapulatempo C, Ferreira L, Martins S, Pellerin L, Mesquita Rodrigues, Alves VAF, Schmitt F, Baltazar F. Increased expression of monocarboxylate transporters 1, 2 and 4 in colorectal carcinomas. Virchows Arch 452:139-46 (2008). (IF - 2.082)

24. Schmitt FC, Longatto-Filho A, Valent A, Vielh O. Molecular cytopathology: opportunities and challenges. J Clin Pathol 61:258-67 (2008). (IF - 2.342)

Other publications International

Book Chapters

1. Longatto Filho A. Screening del cáncer de cuello uterino: nuevas tecnologías. IN: Tatti S, Colposcopia y patologías del tracto genital inferior en la era de la vacunación. Editorial Panamericana, Buenos Aires, pp115-120 (2008).

2. Longatto Filho A, Syrjanen KJ. Citologia cervical. IN: Câncer do colo do útero. Coelho FRG et al, Editores, Tecmedd, São Paulo, Brasil, pp 128-140 (2008).

3. Palmeirim I, Rodrigues S, Dale JK, and Maroto M. Development on time. In: "Cellular oscillatory mechanisms", Landes Bioscience Publishers, Adv Exp Med Biol. 2008; 641: 62-71. (2008)

Other publications National

1. 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 (2008).

2. Brandão A, Nabais S, Salomé N, Gaspar A, Simões A, Costeira A, Correia A. Thrombosed aneurysm of the left sinus of Valsalva. Rev Port Cardiol 27:485-491 (2008).

3. Henriques-Coelho T, Brandão-Nogueira A, Moreira-Gonçalves D, Correia-Pinto J, Leite-Moreira AF. Effects of TNF-alpha blockade in monocrotaline-induced pulmonary hypertension. Rev Port Cardiol 27:341-348 (2008).

4. Nabais S, Rocha S, João C, Marques J, Torres M, Magalhães S, Pereira MA, Correia A. Prognostic impact of moderate renal dysfunction in acute coronary syndromes. Rev Port Cardiol 27:303-312 (2008).

- Book Chapters

1. Baptista MJ, Sampaio MA. O coração do recém nascido prétermo. Capítulo de livro dirigido aos pais de recém nascidos prétermo, implementado nas Unidades de Neonatologia nacionais. (2008).

Master and Ph.D. theses completed

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

1. PhD of Maria João Baptista, MD. Perinatal Cardiac Function in Congenital Diaphragmatic. Supervised by Jorge Correia-Pinto - February 2008.

2. PhD of Leonor Silva. Development of the caudal-most neural crest in the chick embryo. Supervised by Isabel Palmeirim and co-supervision by Martin Catala - April 2008.

3. PhD of Tiago Henriques-Coelho, MD. Celular and neurohumoral regulation of pulmonary growth and hypertension: Pathophysiological implications Supervised by Adelino Leite-Moreira and co-supervised by Jorge Correia-Pinto - July 2008 (at Faculty of Medicine, University of Porto).

4. PhD of Estêvão Lima, MD. Development of Novel techniques for Intra-abdminal Scarless Surgery' Supervised by Jorge Correia-Pinto - September 2008.

5. PhD of Bruno Costa. Molecular determinants of Glioma Risk and Patient Outcome. Supervised by Rui Manuel Reis and co-supervision by Joseph Costello - December 2008.

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

1. MSc of Isis Alonso. Evaluation of the effect of somatostatin analogs in the inhibition of angiogenesis". Supervised by Fátima Baltazar - December (2008).

2. MSc of Marta Tibúrcio. Characterization of par1 and fgfr1 expression in invasive breast carcinomas. Supervised by Adhemar Longatto-Filho and co-supervision by Fernando Schmitt November (2008).

Patents/propotypes

1. VILACA J, MARQUES-PINHO A, CORREIA-PINTO J, CRUZ FONSECA JF, PEIXINHO N. Surgical prosthesis i.e. thoracic prosthesis, modeling/bending system for correction of pectus excavatum, inserts and positions bar for manufacture of prosthesis in automatic bending machine. WO2009035358-A1; PT103823-A1.

Organization of conferences

- Post-graduation courses and Workshops organized by the ICVS

1. Bajanca F. Co-organization of "Animal Cell and Tissue Culture: From Basic Principles to Advanced Techniques" Feb (2008).

2. Bajanca F. Co-organization of "Confocal Microscopy in Cell Biology" June (2008)

3. Correia-Pinto J, Lima E, Carvalho JL, Macedo G. Hands-on course in Laparoscopy and N.O.T.E.S. April 16-18 (2008).

4. Correia-Pinto J, Lima E, Carvalho JL, Macedo G. Minimally Invasive Surgical Week: Laparoscopy, Endoscopy and 3rd Generation Surgery (N.O.T.E.S.). October 6-10 (2008).

5. Baltazar F, Teixeira T, Sarmento A. Pharmacological Basis of Rational Therapeutics, School of Health Sciences, University of Minho, 5-6th December, (2008).

Industry contract research

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

2. Correia-Pinto J acts as specialist medical consultant to Karl Storz in questions involving the instruments and device configurations for N.O.T.E.S. purposes.

3. Lima E. Open study to evaluate the efficacy and tolerance of sildenafil administered as required to male patients with erectile dysfunction: protocolo nº SDN-P-98-001.

4. Lima E. T-IPSS: "Tadenan International Prostate Symptoms StCAudy"

5. Lima E. TREND: "Transuretral Entry Drug Study"

6. Nabais S. Investigador do Registo RECORD-AF: estudo global da abordagem de doentes com fibrilhação auricular diagnosticada há menos de um ano.

Internationalization

1. Palmeirim I. - Member 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). Coordinator of the "Workpackage: Vertebrate somitogenesis" from this European Network of Excelence.

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

3. Reis RM – Member of the Anglo-Portuguese Joint Research Programme - Treaty of Windsor – 2008, in collaboration with Dr. Chris Jones from Institute of Cancer Research, London, UK, with the project entitled "Study of Molecular Targets for Paediatric Brain Tumours Therapy".

Future Research

Objectives

The Development and Neoplasia research team was constituted in 2003. This team was initially composed by 4 PhD researchers coming from different National and International Institutes and with different researchs interests, namely in breast and central nervous system tumors, vertebrate embryonic development, heart physiology and development. Although we were not working in the same organic system, we realized that we could benefit from joining efforts in an attempt to exchange knowledge between our two fundamental areas: Development and Neoplasia.

Currently, specific circumstances in staff re-organization, the 2008 evaluation by the FCT panel and supported by internal discussion the Domain realized it would profit from a re-organization taking into account the major strengths of the current staff/projects. Therefore, as the main internationally recognized research topics address Surgical Diseases and Techniques, it was decided to change the name of the Domain into 'Surgical Sciences'. In this perspective two research lines frame the current research projects: i. Integrative Studies in Surgical Diseases; ii. Endoscopy and Surgical Techniques.

The rationale for this change comes from the fact that we have in the Domain researchers with basic and clinical expertise in surgical diseases from digestive, urogenital and lung 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 2009 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.

b) MICROBIOLOGY AND INFECTION Research Domain

Research Domain Description

Title of Research Group: MICROBIOLOGY AND INFECTION

Coordinator: Jorge Pedrosa

Main Scientific Domain: Health Sciences

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 their members. As a result of this effort, three lines of research were defined along the 2003-2008 period, including the research themes described below.

(i) Immunology of Infection:

• Evaluate the contribution of host genetic variations that account for an increased risk for invasive fungal infections in immunossupressed 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:
  - Balance between IFN-gamma and IL-17 producing cells in the 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.

(ii) Clinical Microbiology:

• 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;

• Investigate the usefulness of serodiagnostic techniques to improve the diagnostic of human tuberculosis in Portugal;

• Evaluate the prevalence of tuberculosis in the wild-life in Portugal as a potential source of disease to humans.

(iii) Unicellular Eukaryotic Modelling Systems:

• 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;

• Evaluate the molecular determinants for entry, maintenance and exit from quiescence (G0) in yeast: implications for aging research;

• Develop yeast models of human neurodegenerative diseases (Batten; Parkinson; Machado-Joseph; Huntington).

Main Achievements

During the year of 2008, the main scientific achievements of the Domain resulted from the consolidation of 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 the diversification of funding sources and the reinforcement of the translational/clinical focus of research. Important advances were achieved in both areas. Indeed, one project was granted in a specific call on Clinical Research from FCT and we successfully participated in 2 Networks of the FP7 EU Program, one of which granted in 2008 for the study of tuberculosis. The other, a participation in a European consortium on the development of vaccines for Buruli ulcer, is to be reviewed in 2009.

Additionally, and following the sustained increase in the number and differentiation level of the Domain's PhD members, we successfully recruited a fulltime, high profile researcher in the context of the FCT program "Ciência 2007". Furthermore, one additional position was announced, resulting in the selection of a candidate to start activities in 2009.

Regarding details on scientific productivity:

1. Publications and patents
    a. 21 publications in international peer-reviewed journals (of which 3 in press), with a mean impact factor of 4.5 and a ratio of 1.9 papers/PhD;
    b. 2 book chapters at the international level;
    c. 17 abstracts in international congresses;
    d. 2 international proceedings in conferences.
2. Theses completed
    a. 1 PhD thesis;
    b. 4 Master theses.
3. Organization of conferences
    a. Organization of 6 international post-graduation courses.
4. Internationalization and Academic Juries
    a. Participation in 19 PhD juries;
    b. Participation in 5 "Agregação" juries;
    c. Ad-hoc reviews for 10 different journals: PNAS; Human Molecular Genetics; Journal of Medical Microbiology; Mycoses; Nature Reviews; Microbiology; PLos Neglected Tropical Diseases; PLos one; British Journal of Dermathology; Journal of Applied Microbiology.
    d. Evaluators of funding agencies and of prizes: Welcome Trust.
5. Funding
    a. Diversification of funding sources and reinforcement of the translational/clinical focus of research, as specified above.

Group Productivity

Publications in peer review Journals

1. Almeida B, Silva A, Mesquita A, Sampaio-Marques B, Rodrigues F, Ludovico P. Drug-induced apoptosis in yeast. Biochim Biophys Acta. 2008.1783 (7):1436-48. Review. (IF – 4.374)

2. Almeida T, Marques M, Mojzita D, Amorim MA, Silva RD, Almeida B, Rodrigues P, Ludovico P, Hohmann S, Moradas-Ferreira P, Côrte-Real M, Costa V. Isc1p Plays a Key Role in Hydrogen Peroxide Resistance and Chronological Lifespan through Modulation of Iron Levels and Apoptosis. Mol Biol Cell. 2008.19(3):865-76. (IF – 6.028)

3. Carvalho A, Pasqualotto AC, Pitzurra L, Romani L, Denning DW, Rodrigues F. Polymorphisms in Toll-like receptor genes and susceptibility to pulmonary aspergillosis. J Infect Dis. 2008. 197(4):618-21. (IF – 6.035)

4. Carvalho A, Santos M, Maciel P, Rodrigues F. (2008) The T-1237C polymorphism of TLR9 gene is not associated with multiple sclerosis in the Portuguese population. Mult Scler. 2008.14(4):550-2. (IF – 3.26)

5. Gaspar MM, Cruz A, Fraga AG, Castro AG, Cruz MEM, Pedrosa J. 2008. Developments on drug delivery systems for the treatment of mycobacterial infections. Curr Topics Med Chem. 2008. 8:579-91. (IF – 4.3)

6. Gaspar MM, Cruz A, Penha AF, Reymão J, Sousa AC, Eleutério CV, Domingues SA, Fraga AG, Longatto Filho A, Cruz MEM, Pedrosa J. Rifabutin encapsulated in liposomes exhibits increased therapeutic activity in a model of disseminated tuberculosis. Int J Antimicrob Agents. 2008. 1:37-45. (IF – 2.3)

7. Kibadi K, Panda M, Tamfum JM, Fraga AG, Longatto-Filho A, Anyo G, Pedrosa J, Nakazawa Y, Suykerbuyk P, Meyers WM, Portaels F. New foci of Buruli Ulcer, Angola and Democratic Republic of Congo. Emerg Infect Dis. 2008. 14:1790-2. (IF – 5.8)

8. Kibadi K, P. Stragier, J.J. Muyembe-Tamfum, Pedrosa J, Portaels F. Follow-up of the first case of Mycobacterium ulcerans infection documented by PCR, genotyping and culture in the Republic of Congo-Brazzaville. Med Trop. 2008. 68:137-43. (IF – NA)

9. Logarinho E, Bousbaa H. Kinetochore-microtubule interactions "in check" by Bub1, Bub3 and BubR1: The dual task of attaching and signalling. Cell Cycle. 2008. 7:1763-8. (IF – 3.314)

10. Logarinho E, Resende T, Torres C, Bousbaa H. The human spindle assembly checkpoint protein Bub3 is required for the establishment of efficient kinetochore-microtubule attachments. Mol Biol Cell. 2008. 19(4):1798-813. (IF – 6.028)

11. Lima-Rodrigues M, Valle-Fernandes A, Lamas N, Cruz A, Baltazar F, Milanezi F, Nunes R, Reis RM, Pedrosa J, Castro AG, Almeida A. A new model of laryngitis: neuropeptide, cyclooxygenase, and cytokine profile. Laryngoscope. 2008. 118:78-86. (IF – 1.80)

12. Lyashchenko KP, Greenwald R, Esfandiari J, Chambers MA, Vicente J, Gortazar C, Santos N, Correia-Neves M, Buddle BM, Jackson R, O'Brien DJ, Schmitt S, Palmer MV, Delahay RJ, Waters WR. Animal-side serologic assay for rapid detection of Mycobacterium bovis infection in multiple species of free-ranging wildlife. Veterinary Microbiology. 2008. 132:283-92. (IF – 2.01)

13. Marques F, Rodrigues AJ, Sousa JC, Coppola G, Geschwind DH, Sousa N, Correia-Neves M, Palha JA. Lipocalin 2 is a choroid plexus acute-phase protein. J Cereb Blood Flow Metab. 2008. 28(3):450-5. (IF – 5.147)

14. 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 (in press). (IF – 4.945)

15. Marques F, Sousa J, Coppola G, Falcao 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. J Cereb Blood Flow Metab (in press). (IF – 5.147)

16. Mesquita AR, Correia-Neves M, Roque S, Castro AG, Vieira P, Pedrosa J, Palha J, Sousa N. IL-10 modulates depressive-like behavior. J Psychiatr Res. 2008. 43:89-97. (IF – 3.71)

17. O'Garra A, Barrat F, Castro AG, Vicari A, Hawrylowicz C. Strategies for use of IL-10 or its antagonists in human disease. 2008. Immunol Rev. 2008. 223:114-31. (IF – 10.758)

18. Portaels F, Meyers WM, Ablordey A, Castro AG, Chemlal K, De Rijk P, Elsen P, Fissette K, Fraga AG, Lee R, Mahrous E, Small PLC, Stragier P, Torrado E, Van Aerde A, Silva MT, Pedrosa J. First Cultivation and Characterization of Mycobacterium ulcerans from the Environment. PLoS Negle Trop Dis. 2008. 26;2(3):e178. (IF – 4.172)

19. Santos J, Sousa MJ, Cardoso H, Inácio J, Silva S, Spencer-Martins I, Leão C. Ethanol tolerance of sugar transport, and the rectification of stuck wine fermentations. Microbiology-SGM. 2008. 154(Pt 2):422-30. (IF – 3.11)

20. Santos N, Correia-Neves M, Ghebremichael S, Källenius G, Svenson S, Almeida A. Epidemiology of Mycobacterium bovis infection in wild boar Susscrofa from Portugal. J Wildlife Diseases (in press). (IF – NA)

21. Thevissen K, Madeo F, Ludovico P, Cammue B, Winderickx J. Joined in death: highlights of the Sixth International Meeting on Yeast Apoptosis in Leuven, Belgium, 30 April-4 May 2008. Yeast. 2008.25(12):927-34. (IF – 2.62)

Other publications International

- Book Chapters

1. Alcami A and Saraiva M. 2008. Chemokine binding proteins encoded by pathogens. In Pathogen-derived Immunomodulatory Molecules (P. Fallon, ed.). Landes. In press.

2. Sampaio-Marques B, Almeida B, Maciel P and LudovicoP. 2008. Protein misfolding and cell death. In Protein Misfolding in Biology and Disease, Editor Tiago Outeiro. Published by Transworld Research Network, India.

Master and Ph.D. theses completed

- PhD thesis

1. Agostinho Albérico Carvalho. "Susceptibility of immunosuppressed patients to invasive fungal infections: analysis of molecular factors". Supervised by Prof. 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. Matilde de Oliveira Barbosa (Bsc. in Clinical Laboratory Techniques) on the Master project "Estudo dos mecanismos de resistência ao stress oxidativo em Candida krusei". in the context of the master program in microbiology from the University of Aveiro. Supervised by Prof. Paula Ludovico, ICVS.

2. Carina Ferreira (Bsc. in Clinical Laboratory Techniques) on the Master project "Search of mycobacterial DNA in different human tissues" in the context of the master program in microbiology from the University of Aveiro. Supervised by Prof. Margarida Correia Neves, ICVS.

3. Andrea Costa (Bsc. in Biology) on the Master project "Environmental enrichment and the immune response in mice chronically infected with Mycobacterium avium" in the context of the master program in biology from the University of Porto. Supervised by Prof. Margarida Correia Neves, ICVS.

4. Andrea Afonso (Bsc. in Clinical Laboratory Techniques) on the Master project "The use of serum diagnostics as a complement for the diagnosis of tuberculosis in Portugal" in the context of the master program in clinical immunology from the University of Beira Interior. Supervised by Prof. Margarida Correia Neves, ICVS.

Organization of conferences

- Post-graduation courses and Workshops organized by the ICVS

1. Margarida Saraiva, António Salgado and Fernanda Bajanca. Animal Cell and Tissue Culture: from basic principles to advanced techniques – 18-22 February 2008.

2. Elsa Logarinho e Paula Ludovico. Gene Silencing using RNA interference – Lecture and hands-on. International Posgraduate Programme ECS/ICVS. 2-6 June 2008.

3. Elsa Logarinho, Fernanda Bajanca. Confocal Microscopy in Cell Biology. International Posgraduate Programme ECS/ICVS. 16-20 June 2008.

4. Magda Carlos, Patrícia Maciel, Jorge Pedrosa. Laboratory Animal Science – 4th Edition. International Posgraduate Programme ECS/ICVS. 1-12 September 2008.

5. Jorge Pedrosa and António G. Castro. Immunoregulation in Infectious Diseases: From Immunity to Bugs and Back – 16-18 October 2008.

- External Programs with modules developed at ICVS:

1. Margarida Correia-Neves. Immune response to infection. GABBA Program, University of Porto – 7-8 February 2008.

Internationalization

- European Consortiums (funded by FP7 EU):

- Integrated control of neglected zoonoses: improving human health and animal production through scientific innovation and public engagement (Large collaborative project - SICA).

- BURULIVAC - Development of Vaccines for Buruli Ulcer (under evaluation).

- 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.

- Gustavo Henrique Goldman. Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo, São Paulo, Brazil.

- Gunilla Källenius, Department of Microbiology, Tumor and Cell Biology, Karolinska Institute, Stockholm, Sweden.

- Joris Winderickx, Katholieke Universiteit Leuven, Belgium.

- Martin Holcik, Apoptosis Research Center, CHEO Research Institute, Ottawa, Canada.

- Neil A.R. Gow School of Medical Sciences, Institute of Medical Sciences, University of Aberdeen. UK.

- Samuel Behar, Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Harvard University, Boston, USA.

- Steffen Ohlmeier, Proteomics Core Facility, Biocenter Oulu, Department of Biochemistry, University of Oulu, Oulu, Finland.

Future Research

Objectives

As a result of the strategic plan carried until 2008, the Microbiology and Infection Research Domain has now reorganized its scientific interests in two lines of research: Cellular and Molecular Microbiology and Immunology of Infection. This follows the strategy of improving the focus of research, previously 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.

It is our purpose to keep improving the number and the quality of the scientific publications. Specifically, we aim at publishing two papers PhD/year and, at least, one article in a high profile journal per year.

Following the successful application for Clinical Research Grants on infectious diseases, with the collaboration of clinicians from H. Joaquim Urbano (Porto) and H. S. Marcos (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 level.

One of the major challenges defined for the Microbiology and Infection Research Domain is to increase and to expand the sources of funding. Therefore, it will be a priority to reinforce the fundraising efforts from national sources, both private and public, as well as from other sources such as NIH, European Community and International Private Foundations.

c) NEUROSCIENCES Research Domain

Research Domain Description

Title of Research Group: NEUROSCIENCES

Coordinator: Nuno Sousa

Main Scientific Domain: Health Sciences

Objectives & Achievements

Objectives

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

- "Neurodevelopment" Line:

This research line addresses hormones, environmental stressors and genes as modulators of behavior, 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 behaviorally- and clinically-well characterized subjects with Williams and Rett syndrome are also focus of research.

- "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, multiple sclerosis, 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.

- "Neuroimmunology" Line:

This line of research studies the interaction between the nervous and the immune systems through two 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).

Main Achievements

During 2008 there was a consolidation of the 3 Research Lines, namely through an 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 a fulltime, high profile researcher in the context of the FCT program "Ciência 2007". Of notice, in 2008, we also reinforced the translational/clinical focus of research; importantly, four projects were granted in a specific call on Clinical Research from FCT.

In 2008, the main achievements of the Neuroscience Research Domain were:

1. Publications and patents
    a. 26 publications in international peer-reviewed journals, with a mean impact factor of 3,43
    b. 24 abstracts in international congresses
    c. 14 international conferences/seminars produced by members of the domain
    d. 1 patent
2. Theses
    a. 8 PhD theses completed
    b. 1 Master and 4 undergraduate theses completed
3. Organization of conferences
    a. Organization of 5 international post-graduation courses
4. Internalization and academic juries
    a. Participation in 4 grant/prize juries; Participation in 19 graduation (PhD/Master) juries; Ad-hoc reviews for 26 different journals in the neuroscience, endocrinolgy and genetics fields (American Journal Medical Genetics, Annals of Neurology, Hormones and Behavior, Journal of Endocrinology, Journal of Neuroendocrinology, Neuroscience Letters, Neuropshychopharmacology, Brain Research, European Journal of Neuroscience, Learning and Memory, Journal of Psychiatry Research, Epilepsy and Behavior, Behavioral Brain Research, Experimental Neurology, Neurobiology of Aging, Neurogenetics, Neuroreport, Microscopy Research & Technique, Pediatrics, Proteomics, Psychopharmacology, European Neuropsychopharmacology, Journal of Neuroscience Research, Physiology and Behavior, Molecular Psychiatry, Progress in Neuropsychopharmacology and Biological Psychiatry)
    b. Evaluators of funding agencies and of prizes
5. Funding
    a. In terms of funding, in 2008 our efforts were concentrated in widening the spectrum of funding sources; in this regard, it should be highlighted the establishment of a contract with an industrial partner and a sub-contract with a FP6 consortium.

Group Productivity

Publications in peer review Journals

1. Alonso I, Marques JM, Sousa N, Sequeiros J, Olsson AS, Silveira I. Motor and cognitive deficits in the heterozygous leaner mouse, a Cav2.1 voltage-gated Ca2+ channel mutant. Neurobiol Aging, 29:1733-1743 (2008). IF: 5.61

2. Bettencourt C, Nunes-Fialho R, Santos C, Montiel R, Bruges-Armas J, Maciel P, Lima M. Segregation distortion of wild-type alleles at the Machado-Joseph disease locus: a study in normal families from the Azores islands (Portugal). J. Hum Genet, 53:333-339 (2008). IF: 2.28

3. Carvalho A, Santos M, Maciel P, Rodrigues F. The T-1237C polymorphism of TLR9 gene is not associated with multiple sclerosis in the Portuguese population. Multiple sclerosis, 14:550-552 (2008). IF: 3.26

4. Cerqueira JJ, Almeida OFX, Sousa N. The stressed prefrontal cortex. Left? Right. Brain Behav Immun, 22:630-638 (2008). IF: 4.66

5. Ferro A, Castro MJ, Lemos C, Santos M, Sousa A, Pereira-Monteiro J, Sequeiros J, Maciel P. The C677T polymorphism in MTHFR is not associated with migraine in Portugal. Disease Markers, 25:107-113 (2008). IF: 1.80

6. Gonçalves L, Silva R, Pinto-Ribeiro F, Pêgo JM, Bessa JM, Pertovaara A, Sousa N, Almeida A. Neuropathic pain is associated with depressive behaviour and induces neuroplasticity in the amygdala of the rat. Exp Neurol, 213:48-56 (2008). IF: 3.98

7. Lemos L, Flores S, Oliveira P, Almeida A. Gabapentin supplemented with Ropivacain block of trigger-points improves pain control and quality of life in Trigeminal Neuralgia patients when compared with gabapentin alone. Clin J Pain, 24:64-75 (2008). IF: 2.55

8. Lima-Rodrigues M, Valle-Fernandes A, Lamas N, Cruz A, Baltazar F, Milanezi F, Nunes R, Pedrosa J, Reis RM, Castro AG, Almeida A. A New Model of Laryngitis: neuropeptide, COX and cytokine profile. Laryngoscope, 118:78-86 (2008). IF: 1.80

9. Marques F, Rodrigues AJ, Sousa JC, Coppola G, Geschwind DH, Correia-Neves M, Sousa N, Palha JA. Lipocalin 2 is a choroid plexus acute phase protein. J Cereb Blood Flow Metab, 28:450-455 (2008). IF: 5.15

10. Mesquita AR, Correia-Neves M, Roque S, Castro AG, Vieira P, Pedrosa J, Palha JA, Sousa N. IL-10 modulates depressive-like behavior. J Psychiatr Res, 43:89-97 (2008). IF: 3.71

11. Morgado C, Pinto-Ribeiro F, Tavares I. Diabetes affects the expression of GABA and potassium chloride cotransporter in the spinal cord: a study in streptozotocin diabetic rats. Neurosci. Lett, 438:102-106 (2008). IF: 2.09

12. Pêgo JM, Morgado P, Pinto LG, Cerqueira JJ, Almeida OFX, Sousa N. Dissociation of the morphological correlates of stress-induced anxiety and fear. Eur J Neurosci, 27:1503-17 (2008). IF: 3.67

13. Pickering C, Hägglund M, Szmydynger-Chodobska J, Palha JA, Marques F, Waller L, Chodobski A, Fredriksson R, Lagerström MC, Schiöth HB. The Adhesion GPCR GPR125 is specifically expressed in the choroid plexus and is upregulated following brain injury. BMC Neuroscience, 9:97 (2008). IF: 2.99

14. Pinto-Ribeiro F, Ansah OB, Almeida A, Pertovaara A. Influence of arthritis on descending modulation of nociception from the paraventricular nucleus of the hypothalamus. Brain Res, 1197:63-75 (2008). IF: 2.22

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26. Vargas HE, Gama CS, Andreazza AC, Medeiros D, Stertz L, Fries G, Palha JA, Cereser KM, Berk M, Kapczinski F, Belmonte-de-Abreu P. Decreased serum neurotrophin 3 in chronically medicated schizophrenic males. Neuroscience Lett, 440:197-201 (2008). IF: 2.09

Other publications International

Book Chapters

1. Salgado AJ, Silva N, Neves NM, Reis RL, Sousa N. Hydrogel Based Systems for Spinal Cord Injury Regeneration, in Handbook of Natural-based Polymers for Biomedical Applications, ed: Rui L. Reis, Woodhead Publishing, Cambridge United Kingdom, (2008), 570-594.

Master and Ph.D. theses completed

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

1. Ana João Rodrigues. "C. elegans ATX-3: function, loss of function and molecular partners". Supervisor: Patrícia Maciel. Escola de Ciências da Saúde, Universidade do Minho, 2008.

2. Ana Raquel Mesquita. "Study of the programming effects of early life stress in the limbic system". Supervisor: Nuno Sousa. Escola de Ciências da Saúde, Universidade do Minho, 2008.

3. Fernanda Marques. "The Choroid Plexus as a sensor of peripheral inflammation". Supervisor: Joana Palha. Escola de Ciências da Saúde, Universidade do Minho, 2008.

4. João Bessa. "Interaction between anxiety and depression in animal models of behaviour: insights on neuroplasticity and cognitive function". Supervisor: Nuno Sousa. Escola de Ciências da Saúde, Universidade do Minho, 2008.

5. Jorge Cotter. "Longitudinal follow-up of the relation between hypertension, renal function and urinary excrescent rate of proteins in a Portuguese cohort". Supervisor: Nuno Sousa (in collaboration with Jorge Polónia, Porto Medical School, University of Porto). Escola de Ciências da Saúde, Universidade do Minho, 2008.

6. José Miguel Pêgo. "Influence of stress in the structure and function of the amygdala". Supervisor: Nuno Sousa. Escola de Ciências da Saúde, Universidade do Minho, 2008.

7. Manuel Lima-Rodrigues. "Nerve terminals in the larynx: morphology, pathological aspects and therapeutic perspectives". Supervisor: Armando Almeida. Escola de Ciências da Saúde, Universidade do Minho, 2008.

8. Maria do Carmo Costa. "Molecular genetic analysis of the Mus musculus homologue of the Machado-Joseph disease gene". Supervisor: Patrícia Maciel. Escola de Ciências da Saúde, Universidade do Minho, 2008.

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

1. Cassandra Sampaio. Behavioural and cognitive effects of environmental enrichment and isolation in animal models of depression. Institute of Education and Psychology, University of Minho.

Patents/propotypes

1. Santos JD, Lopes MA, Botelho CM. Inventors. "Substitute based on hydroxyapatite, biocompatible glass and silicon and its production and applications".

Organization of conferences

- Organization of Scientific Meetings and Presence in Scientific Committees

In order to increase the public awareness members of the Neuroscience team, we took part in the following events:

a) Meetings on Tuesday, organized by the Psychology students association with the seminar "Cognitive enrichment";

b) "À volta do cérebro" FNAC in 2008: "The impact of stress for neuropsychiatric disorders",; "Genes, Ambiente e Esquizofrenia,; Neurodegenerative disorders", Forensic Sciences" c) Café scientific – "How does our brain keep memories and forgets", May 2008.

c) Brain Awareness Week – with several visits to High Schools and other institutions in the Minho Region and through activities organized at the ICVS for distinct publics, March 2008.

d) Monthly high school visits to ICVS to learn how we "make science".

- Post-graduation courses and Workshops organized at the ICVS

1. Psychomotor Development Evaluation of Newborns (2nd edition)
   Maria José Costeira, Joana Palha
   28-29 January

2. Animal Cell and Tissue Culture: From Basic Principles to Advanced Techniques
   António Salgado, Fernanda Bajanca, Margarida Saraiva
   18-22 February

3. Microarray: theory and practicals. From RNA extraction to functional data analysis
   Joana Palha
   19-21 May

4. From Acute to Chronic Pain: Basic and Clinical Approaches (3rd edition)
   José Correia, Armando Almeida
   26-28 May

5. Hands-on Course: Sulci, Gyri and Ventricles (2nd edition)
   Carlos Alegria, Evandro de Oliveira, Nuno Sousa
   29-31 May

6. Hands-on Course: Sulci, Gyri, Ventricles and Dissecting Fibers (6th Edition)
   Nuno Sousa, Carlos Alegria, Evandro de Oliveira
   17-21 November

- Organization of Other Meetings

A member of the Research Domain was involved in the organizing committee of the Annual Meeting of the Tissue Engineering and Regenerative Medicine Society – European Chapter, June 2008 (TERMIS-EU 2008) and in the Symposyum on "Tissue Engineering and Cell Based Therapies in Spinal Cord Injury Regeneration" at the TERMIS-EU-2008, June 2008.

Industry contract research

In 2008 the Neuroscience Research Domain established its first scientific contract with an industrial partner (Bayer-Schering Pharma). The study is designed to characterize the behavioral phenotype after treatment with a novel compound; and to perform a structural analysis of specific brain regions of animals treated with the compound.

The success of this first contract has opened the possibility to establish a new contract in 2009.

Internationalization

In 2008 the Neuroscience Research team has been involved in several internationalization efforts.

In this regard, it should be highlighted that 20 (out of 26) 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 (19 international long-term collaborations), as follows:

- Athens University

- Biomedicum Helsinki, Helsinki Medical School, Finland

- Centre for Genomic Regulation, Barcelona, Spain

- Columbia University, New York, USA

- Erasmus University, The Netherlands

- Faculdade de Medicina da Universidade de São Paulo, Brazil

- Faculdade de Medicina da Universidade Federal de São Paulo, Brazil

- Harvard Medical School, Boston, USA

- Instituto de Investigaciones Biomédicas, Madrid, Spain

- Iowa University, USA

- Neuroadaptation Group, Max-Planck Institute for Psychiatry, Munich, Germany

- Northwestern University, Evanston, Illinois, USA

- Oulu University, Finland

- Paris Descartes University

- 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 Neurosciences Research Domain participated 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 Portugal Initiative.

Future Research

Objectives

The Neurosciences Domain launched its activities at the ICVS in 2003 as two separate research groups, Neurosciences and Human Genetics, led by four PI's 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. This effort endowed the Neurosciences Research Domain with the ability to perform a multidisciplinary and integrative approach to each research question.

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 2009, 2 publications in journal with IF>10. One, totally performed at the ICVS has been accepted, in June, for publication in Science). More specifically, in 2009 we hope to capture more projects and in a wider spectrum of sources (including international agencies). It is also our aim to attract Post-Docs internationally in 2009 and to contribute to the success of the Doctoral programmes of the ICVS, where several PhD students are expected to be recruited; therefore, we hope to keep our commitment with the training and post-graduation of several students. As part of our internationalization efforts, we aim to be involved in European training/research networks in 2009.

Another goal for 2009 is to further strengthen the contracts with industrial partners. These contracts are of the utmost importance, since they raise the funds for exploratory or satellite projects that eventually generate the data to apply for more specific grants that will 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 2009, we aim to finish 3 PhD theses and to organize at least 5 international post-graduation courses.