ICVS

ANNUAL REPORT 2012

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

Universidade do Minho
Escola de Ciências da Saúde

INDEX

1. INTRODUCTION

1.1 UNIT DESCRIPTION: ICVS/3B'S ASSOCIATE LABORATORY (AL)

The ICVS/3B's Associate Laboratory (AL) centers its activities in the Health Sciences, namely in Biomedical and Clinical Sciences, and in Engineering/Materials Science and Biomaterials. This interface Health-Sciences/Technologies fosters the generation of value through the development of innovative products and services, resulting from internationally highly competitive research.

Within the structure of the AL, the ICVS group is a R&D unit in Biomedicine and Clinical Sciences, associated with the Clinical Academic Center – Braga, Association (CCAB); while the 3B's research group is a R&D unit in Materials Science and Engineering, mainly focusing on Technologies Applied to Regenerative Medicine, including Biomaterials, Stem Cells, Tissue Engineering and Nanomedicine, being the leader of the European Institute of Excellence on Tissue Engineering and Regenerative Medicine.

The creation of the ICVS/3B's AL potentiated activities within different dimensions: (1) Scientific and technological research and development of applied research in the interface Health Sciences/Technology; (2) Advanced education and training, to provide research and training activities to undergraduate/postgraduate students and health professionals; (3) Services, consulting and technology transfer, by taking into consideration the vital importance of industrial/clinical partners; (4) Dissemination, public and scientific awareness of science.

New technologies, therapies and medical products are being developed in the ICVS/3B's AL, including in the context of vaccination, diagnosis, regenerative medicine, minimally invasive therapeutic procedures, personalized treatments and nanomedicine. Products for advanced therapies are based on genes (genetic therapy), biomolecules, cells (cellular therapies), combinations of cells and biomaterials (tissue engineering) and minimal invasive surgical approaches. Such solutions are investigated in collaboration with companies and research partners.

The ICVS/3B's AL has, therefore, the potential to cross the complete development pipeline, from the more fundamental in vitro research, testing in animal models and pre-clinical validation, to the clinical trial phase, transposing to the market innovative therapeutic solutions.

2. RESEARCH GROUP: ICVS (Life and Health Sciences Research Institute)

2.1 OBJECTIVES AND ACHIEVEMENTS:

2.1.1. OBJECTIVES

The Life and Health Sciences Research Institute (ICVS) aims at improving human health through outstanding life-science research, cutting-edge medical innovation and delivery of specialized services.

The ICVS is a R&D Unit incorporated in the School of Health Sciences (ECS) - University of Minho, strategically located in the Northern region of Portugal within a fast growing Cluster of Biomedical Science, Technology and Healthcare institutions.

The ICVS is organized around three interdisciplinary Research Domains: Microbiology and Infection, Neurosciences and Surgical Sciences. The strategy for the ICVS development has been centred in: i) establishing a research unit within an innovative Medical School guided by international standards of excellence; ii) fostering a strategic partnership with the affiliated Health Care Institutions and; iii) establishing a consortium with the research group 3B's - Biomaterials, Biodegradables and Biomimetics - a leading research group in Health Technology.

In the context of the AL, the ICVS is a growing group and represents an attractive research environment for young researchers, providing a state of the art technological platform for Cell and Tissue Culture, Electrophysiology, Biosafety Level 2 and 3, Molecular Biology, Imagiology, Microscopy Imaging, Neuroanatomy/Neuroimaging, Histology, Biological Resources, Cytometry, Endoscospy, as well as a fully equipped Centre for Animal Experimentation and a Clinical Academic Centre.

THE ICVS AIMS TO ACHIEVE THE FOLLOWING GLOBAL GOALS:

- promote original research on *Microbiology and Infection*, *Neurosciences* and *Surgical Sciences*, with high scientific output and recognized impact in the advance of knowledge on the biomedical, translational and clinical scopes;
- boost the development of new diagnostic systems and new therapies, with added potential value;
- encourage an innovative interaction between research and medical undergraduate/graduate training, in partnership with the affiliated network of Health Care Institutions;
- provide international advanced post-graduated programmes;
- provide specialized clinical and scientific services to the community, including medical diagnosis and clinical trials, particularly in the context of the Clinical Academic Center – Braga, Association (CCAB);
- promote the registration of Patents and the creation of Spin-Offs on innovative medical products;
- promote the public awareness of science;
- impact the society, as a nucleus to support the development of a national policy for scientific research in Biomedicine and Clinical Sciences.

THEREFORE, THE SPECIFIC DEVELOPMENTAL STRATEGIES FOR 2012 WERE TO:

- formalize the creation of the CCAB, for developing clinical research, including clinical trials;
- to foster the creation of one Spin-Off;
- promote highly competitive, multidisciplinary research projects involving scientists, MDs and other health professionals, with a growing focus on clinical research;

- increase the staff differentiation, including the nº of PhD researchers by a minimum of 10%;
- pursue in the active involvement of medical students and MDs within the ICVS research projects;
- support the ongoing ECS/ICVS PhD and Master Programmes, as well as the 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, namely in clinical sciences;
- promote the public awareness in health sciences.

2.1.2. MAIN ACHIEVEMENTS DURING THE YEAR OF 2012:

- a major increase in the scientific outputs, reflected in a very important increase in the number of publications, as well as in their average impact factor;
- the formalization of the Clinical Academic Centre – Braga, Association (CCAB) and reinforcement of translational/clinical research;
- the launching of the Spin-off "Bn´ML- Behavioral & Molecular Lab";
- the increase in the number of Advanced Post-Graduation Courses;
- the sustained increase in staff numbers/differentiation;
- the involvement of a high number of MD students in research activities.

SPECIFICALLY, IN 2012, THE ICVS WAS ABLE TO:

- Formally establish the Clinical Academic Centre – Braga, Association (CCAB), in January 2012, resulting from a partnership with the Hospital of Braga, with infrastructures located at both the Hospital and the ICVS, and beneficiating from specific staff devoted to the development of clinical research, including clinical trials. The CCAB achieved the following goals in 2012 (ongoing or under analyses): 5 clinical research projects (funded by FP7 and FCT); 23 clinical trials; 6 observational studies; and 2 validation studies of medical devices;

- Develop and expand the ICVS/3B's-PT Government Associate Laboratory's activities, resulting in an increasing recognition of the AL, namely by international funding agencies and by leading scientific journals. In 2012, the activities of the AL resulted in the publication of 227 articles in ISI journals - 45% in journals of the first quartile (Q) and 90% of Q1 + Q2;

- Pursue a sustained increase in staff numbers/differentiation:
PhDs increasing from 60 (2011) to 66 (2012): 37 ECS faculty, 4 Assistant Researchers, 1 Marie Currie and 24 Post–Docs;
PhDs students increasing from 100 (2011) to 114 (2012);
Masters students reaching 36 in 2012;
Presently, the ICVS counts with 281 researchers [66 PhDs and 197 post-graduation students (114 PhD students, 36 Master students and 47 research assistant)], supported by 18 non-academic staff (5 administrative and 13 in laboratories, with salaries supported by the ECS);

- Achieve a major increase in scientific publications. The ICVS published 136 papers in

international journals, in the context of the three Research Domains, with 59% in Q1 and 86% in Q1 + Q2, corresponding to an average IF of 4.5 (including articles with IF between 3 and 5 = 44 papers; IF between 5 and 10 = 16 papers; IF between 10 and 20 = 8 papers; IF>20 = 1 paper); plus 8 additional articles in medical education and Public Health.

- Create the experimental conditions for the conclusion of 10 PhD theses, including from 2 MDs;

- Launch the Spin-off "Bn´ML- Behavioral & Molecular Lab", providing customized services for pre-clinical assessment of the therapeutic potential of new compounds, using pre-validated and reliable animal models of disease;

- Foster collaborations between its researchers at the forefront of Biomedical advances and partners from Biomedical Industries, in areas of mutual interest. In 2012, industry sponsored R&D involved the following companies: TECNIMEDE; F. BIAL; NOVARTIS FARMA; New Textiles; BEBÉ VIDA; and BOEHRINGER;

- Provide molecular diagnostics services, by providing the genetic diagnostics of intellectual disability related disorders, with a CGH microarrays service for the screening of microdeletions and duplications of chromosome regions;

- Obtain 9 International awards;

- Get a total of 22 new fellowships granted by FCT: 3 BPD; 19 BD;

- Increase the competitive funding with new projects granted, including:
6 FCT projects;
1 FP7-Marie Curie Action;
Projects from private foundations and industry: ATAXIA UK; TECNIMEDE;

- Involve a high number of MD students in research, including 35 MD/PhD Lab Rotations (from 17 in 2011) and 46 Option Projects (from 50 in 2011);

- Organize an increasing number of Advanced Post-Graduation Courses/Workshops (from 26 in 2011 to 37 in 2012), with 752 participants (including 59 % MDs, 38 % Biological Sciences, 8 % other Health Professionals). Importantly, 92 % of the participants rated the attended courses as "Very Good" or "Excellent" and some of the courses were part of training activities of European schools or within European training actions.

2.2 GROUP PRODUCTIVITY:

2.2.1 PUBLICATIONS IN PEER REVIEW JOURNALS

In 2012, the ICVS published 136 papers in international peer-reviewed journals (plus eight papers in Medical Education/Public Health), with an average IF of 4.5, including: articles with IF between 3 and 5 = 44 papers; IF between 5 and 10 = 16 papers; IF between 10 and 20 = 8 papers; IF>20 = 1 paper.

20 SELECTED PAPERS IN PEER REVIEW JOURNALS

1. Ferreira I, Domingues VS. Acro-osteolysis. *Lancet*, 380(9845):916 (2012) (IF=38,3)

2. Sousa N, Almeida OFX. Disconnection and reconnection: the morphological basis of (mal)adaptation to stress. *Trends in Neurosciences* 35:742-751 (2012). (IF=14,235)

3. Rodrigues AJ, Leão P, Pêgo JM, Cardona D, Carvalho MM, Oliveira M, Costa BM, Carvalho AF, Morgado P, Araújo D, Palha JA, Almeida OF, Sousa N. Mechanisms of initiation and reversal of drug-seeking behavior induced by prenatal exposure to glucocorticoids. *Mol Psychiatry*, 17:1295-1305 (2012). (IF= 13,668)

4. Martin CJ, Booty MG, Rosebrock TR, Nunes-Alves C, Desjardins DM, Keren I, Fortune SM, Remold HG, Behar SM. Efferocytosis Is an Innate Antibacterial Mechanism. *Cell Host & Microbe.* 12(3): 289–300 (2012). (IF=13,5)

5. Luca AD, Iannitti RG, Bozza S, Beau R, Casagrande A, D'Angelo C, Moretti S, Cunha C, Giovannini G, Massi-Benedetti C, Carvalho A, Boon L, Latgé JP, Romani L. CD4+ T cell vaccination overcomes defective cross-presentation of fungal antigens in a mouse model of chronic granulomatous disease. *J Clin Invest.* 1;122(5):1816-31 (2012). (IF=14,152)

6. Almeida MI, Nicoloso M, Zeng L, Ivan C, Spizzo R, Gafà R, Xiao L, Bondaruk J, Fabbri M, Czerniak B, Lanza G, Reis RM, Zweidler-McKay P, Calin GA. Disjunction on Biological Effects of Hairpin Strand Specific miR-28-5p and miR-28-3p in colon cancer. *Gastroenterology* 142:886-896 (2012). (IF=11,675)

7. Ferreira A, Gonçalves R, Rolanda C. A different kind of colon polyps. *Gastroenterology* 143(6):1693-4 (2012). (IF=11,675)

8. Ferreira A, Pereira P, Rolanda C. Diffuse hepatic metastasis - or not? *Gastroenterology* 142:1070-25 (2012). (IF=11,675)

9. Iannitti RG, Carvalho A, Romani L. From memory to antifungal vaccine design. *Trends Immunol.* 33(9):467-74 (2012). (IF= 10,403)

10. Carvalho A, De Luca A, Bozza S, Cunha C, D'Angelo C, Moretti S, Perruccio K, Iannitti RG, Fallarino F, Pierini A, Latgé JP, Velardi A, Aversa F, Romani L. TLR3 essentially promotes protective class I-restricted memory CD8+ T-cell responses to Aspergillus fumigatus in hematopoietic transplanted patients. *Blood* 26;119(4):967-77 (2012). (IF=9,898)

11. Martino A, Campa D, Buda G, Sainz J, García Sanz R, Jamroziak K, Reis RM, Weinhold N,

Jurado M, Ríos R, Szemraj-Rogucka Z, Marques H, Stein A, Kumar R, Orciuolo E, Gemignani F, Landi S, Goldschmidt H, Petrini M, Dumontet C, Canzian F, Rossi AM. Polymorphisms in xenobiotic transporters ABCB1, ABCG2, ABCC2, ABCC1, ABCC3 and Multiple Myeloma Risk: a case-control study in the context of the IMMEnSE (International Multiple Myeloma rESEarch) consortium. *Leukemia* 26:1419-22 (2012). (IF=9,561)

12. Franco NH, Correia-Neves M, Olsson IA. How "humane" is your endpoint?-Refining the science-driven approach for termination of animal studies of chronic infection. *PLoS Pathog.* 8(1):e1002399 (2012). (IF= 9,127)

13. Pinheiro C, Longatto-Filho A, Schmitt FC, Baltazar F. Lactate-Induced IL-8 Pathway in Endothelial Cells – Letter. *Cancer Res.*72: 1901-2 (2012). (IF=7,856)

14. Sampaio-Marques B, Felgueiras C, Silva A, Rodrigues M, Tenreiro S, Franssens V, Reichert AS, Outeiro TF, Winderickx J, Ludovico P.SNCA (α-synuclein)-induced toxicity in yeast cells is dependent on sirtuin 2 (Sir2)-mediated mitophagy. *Autophagy* 8(10):1494-509 (2012). (IF=7,453)

15. Silva NA, Cooke MJ, Tam RY, Sousa N, Salgado AJ, Reis RL, Shoichet MS. The Effects of Peptide Modified Gellan Gum and Olfactory Ensheathing Glia Cells on Neural Stem/Progenitor Cell Fate. *Biomaterials* 33:6345-6354 (2012). (IF=7,404)

16. Baptista M, Duarte C and Maciel P. "Role of the ubiquitin-proteasome system in nervous system function and disease: using *C. elegans* as a dissecting tool". *Cell Mol Life Sci* 69(16):2691-2715 (2012). (IF=6,57)

17. Spizzo R, Almeida MI, Colombatti A, Calin GA. Long non-coding RNAs and cancer: a new frontier of translational research? *Oncogene* 31(43):4577-87 (2012). (IF=6,373)

18. Leite-Almeida H, Cerqueira JJ, Wei H, Ribeiro-Costa N, Anjos-Martins H, Sousa N, Pertovaara A, Almeida A. Differential effects of left/right neuropathy on rats' anxiety and cognitive behavior. *Pain* 153:2218-2225 (2012). (IF=5,777)

19. Pinto PR, McIntyre T, Almeida A, Araújo-Soares V. The mediating role of pain catastrophizing in the relationship between presurgical anxiety and acute postsurgical pain after hysterectomy. *Pain* 153:218-226 (2012). (IF=5,777)

20. Pinto PR, McIntyre T, Almeida A, Araújo-Soares V. Understanding pre-surgical predictors of acute pain experience following hysterectomy for benign causes: conceptual and methodological issues. *Pain* 153:1974-1976 (2012). (IF=5,777)

2.2.3 PhD THESIS COMPLETED

1.
Student: Ana Luísa Mendanha Falcão
Title: Novel perspectives on the subependymal zone complexity and modulation
Supervisor: João Carlos Sousa
Institution: School of Health Sciences, University of Minho

2.
Student: Ana Paula Ventura da Silva

Title: Molecular and Functional Correlates of Stress-Related Anxiety
Supervisor: José Miguel Pêgo
Institution: School of Health Sciences, University of Minho

3.
Student: Cristina Isabel Nogueira da Silva
Title: Looking for Novel Physiological Regulators of Lung Development
Supervisor: Jorge Correia Pinto
Institution: School of Health Sciences, University of Minho

4.
Student: Júlia Margarida Raposo Monteiro dos Santos
Title: Ammonium toxicity in aging yeast cells reduces chronological life span: cell death mechanisms and nutriente sensing pathways
Supervisor: Cecília Leão
Institution: School of Health Sciences, University of Minho

5.
Student: Maria Alexandra Oliveira da Silva
Title: New insight into translation during yeast programmed cell death
Supervisor: Paula Ludovico
Institution: School of Health Sciences, University of Minho

6.
Student: Maria de Belém de Sousa Sampaio Marques.
Title: The emerging role of autophagy/mitophagy in a-synuclein-induced toxicity: studies on the yeast chronological aging model
Supervisor: Paula Ludovico
Institution: School of Health Sciences, University of Minho

7.
Student: Maria Inês da Cunha Doutel Almeida
Title: MicroRNas in Cancer: Biological Effects of microRNas in Colorectal Cancer
Supervisor: Rui Reis
Institution: School of Health Sciences, University of Minho

8.
Student: Maria Rosinda Teixeira Coelho
Title: Impact of mycobacterial recognition by toll like receptors in the regulation of IL-10 and T helper type of responses
Supervisor: Gil Castro
Institution: School of Health Sciences, University of Minho

9.
Student: Sandra de Fátima Fernandes Martins
Title: Expression of Colorectal Cancer Metabolic and Angiogenic Markers: Association with Clinicopathological Characteristics and Impact on Prognosis
Supervisor: Adhemar Longatto
Institution: School of Health Sciences, University of Minho

10.
Student: Teresa Maria Gonçalves Martins
Title: Host-pathogen interactions in *Mycobacterium ulcerans* infections: implications for the

development of new control strategies
Supervisor: Jorge Pedrosa
Institution: School of Health Sciences, University of Minho

2.2.4 PATENTS/PROPOTYPES

Di Paolo G, Oliveira TG, Kim T-W. Modulation of Phospholipase D for the treatment of neurodegenerative disorders. WIPO Patent WO/2010/138869A1. US Patent Application No: 2012/0178,719 (2012).

2.2.5 ORGANIZATION OF COURSES/WORKSHOPS

1. Baltazar F, Andrade RP, Reis RM. “Fundamentals of Genetics, Development and Neoplasia (3rd Edition)”. Jan 9-20;

2. Salgado AJ, Saraiva M, Correia-Neves M, Ludovico P. “An integrative approach to cell analysis: cell and tissue culture, flow cytometry and microscopy (3rd Edition)”. Feb 27 - Mar 9;

3. Costa P. “Methods for grouping variables: data reduction using the Principal Component Analysis (PCA)”. Mar 8-9;

4. Salgado AJ, Pinto L. “Stem Cells Get Practical: Approaches on Stem Cell Isolation, Characterization and Differentiation”. Mar 12-16;

5. Saraiva M, Castro AG, Pedrosa J. “Host Pathogen Interaction”. Mar 19-23;

6. Henriques-Coelho T, Correia-Pinto J. “Fetal and Neonatal Endoscopic Surgery (4th Edition)”. Mar 22-24;

7. Moreira-Pinto J, Carvalho-Dias E, Nogueira-Silva C, Correia-Pinto J. “Basic Laparoscopy for Residents (2nd Edition)”. Mar 26-27;

8. Lima E, Teixeira de Sousa, Correia-Pinto J. “Extraperitoneal Laparoscopic Radical Prostatectomy”. Apr 11-12;

9. Lima E, Autorino R, Calais Silva, Rassweiler J, Correia-Pinto J. “3rd Minimally Invasive Urological Surgical Week”. Apr 13-14;

10. Palha JA, Steinbusch HW, Leonard B. “Drugs and the Brain: an update in psychopharmacology”. Apr 15-20;

11. Alves A, Ferreira H, Fradique A, Correia-Pinto J. “Gynecological Laparoscopy (4th Edition)”. Apr 19-21;

12. Duarte R, Ferreira N, Fidalgo R, da Silva MV, Correia-Pinto J. “Fundamentals in Arthroscopy (3rd Edition)”. Apr 26-27;

13. Costa P. “Methods for grouping subjects: subjects classification using the Cluster Analysis”. May 3-4;

14. Costa MJ. “Identifying and working with the health sciences student in difficulty”. May 8;

15. Costa MJ. “M-Learning in Health Sciences Education”. May 9;

16. Bastos H, Baltazar F, Carvalho A. “Pharmacological Basis of Rational Therapeutics: Antibiotherapy (2nd edition)”. May 11-12;

17. Costa P. “Topics of Regression: introduction to linear and logistic regression models”. Jun 14-15;

18. Fernandes F, Silva FM, Correia-Pinto J. “Around the Nose: Endoscopic Sinus Surgery”. Jun 28;

19. Fernandes F, Silva FM, Correia-Pinto J. “Around the Nose: Fundamentals in Rhinoseptoplasty”. Jun 29;

20. Fernandes F, Matos C, Correia-Pinto J. “Around the Nose: Surgery for Snoring and OSAS”. Jun 30;

21. Almeida A, Encarnação A, Pinto H, Antunes F. “Medical Acupuncture”. Sep 14 - Mar 10 2013;

22. Sousa JC, Cerqueira JJ, Pêgo JM. “Fundamentals in Neurosciences (5th Edition)”. Sep 17-28;

23. Antunes H, Rolanda C, Correia-Pinto J. “Pediatric Endoscopy (2nd Edition)”. Sep 20-21;

24. Castro AG. “Fundamentals in immunology and infection (4th Edition)”. Oct 1-12;

25. Matos Nd, Leão P, Correia-Pinto J. “Digestive Laparoscopy and LESS Surgery (6th Edition)”. Oct 8-10;

26. Rolanda C, Correia-Pinto J. “Therapeutic Endoscopy (5th Edition)”. Oct 11-12;

27. Vilaça J, Leão DS, Correia-Pinto J. “Biliary Laparoscopy (4th Edition)”. Oct 15-17;

28. Andrade RP. “Bioinformatics in health sciences (4th Edition)”. Oct 15-26;

29. Sousa N, Alegria C. “Hands-on Course: Sulci, Gyri, Ventricles and Dissecting Fibers (10th Edition)”. Oct 20-24;

30. Sevivas N, Oliveira M, Leão P. “Microsurgical Anastomosis (4th Edition)”. Oct 25-27;

31. MJ Costa. “Research methodologies (4th Edition)”. Oct 29 - Nov 9;

32. Moreira-Pinto J, Carvalho-Dias E, Nogueira-Silva C, Correia-Pinto J. “Basic Laparoscopy for Residents (3rd Edition)”. Nov 9-10;

33. Sousa N, Cunha P, Cotter J. “Arterial Stiffness and Early Vascular Aging (2nd Edition)”. Nov 12-13;

34. Varanda P, Coutinho PC, da Silva MV, Correia-Pinto J. “Minimally Invasive Spine Surgery”. Nov 16-17;

35. Costa P. “Biostatistics in health sciences (3rd Edition)”. Nov 19-30;

36. Sousa N, Cunha P, Cotter J. “Patient Education for Health and Clinical Research”. Nov 22-

23;

37. Castelhano-Carlos M, Correia-Neves M. “Laboratory Animal Science (8th Edition)”. Dec 3-14.

2.2.6 INDUSTRY CONTRACT RESEARCH

In 2012, the ICVS established Research Contracts with:

1. Boehringer Engelheim; the studies are designed to characterize the behavioral phenotype and structural changes induced by drug compounds. Luisa Pinto (coordinator).

2. Tecnimede; the studies are designed to characterize the behavioral phenotype and structural changes induced by drug compounds. João Bessa (coordinator).

3. Tecnimede; the studies are designed to characterize the pharmacological screening of drugs for the control of experimental neurophatic pain. Armando Almeida (coordinator).

4. New Textiles, Lda; the studies are designed to testing the efficacy of repellents encapsulated in the malaria insect. Cecília Leão (coordinator).

5. NOVARTIS FARMA, SA; the studies are designed to characterize the effects of iron chelation on autophagy and its impact on haematopoiesis in myelodysplastic syndrome patients. Paula Ludovico (coordinator).

6. Ethicon Endo-Surgery; to promote activities designed to provide training of surgeons (Gynecologists; General Surgeons) in minimally invasive surgical techniques. Jorge Correia-Pinto (coordinator).

7. BEBÉ VIDA, SA; Processing and cryopreservation of tissue of the umbilical cord. António Salgado (coordinator).

2.2.7 INTERNATIONALIZATION

- Reflecting the high level of the ICVS internationalization, researchers from 14 foreign countries were members of the Institute team in 2012;

- Among the ICVS papers published in international peer-reviewed journals during 2012, 73 (corresponding to 54% of the overall production) resulted from partnerships involving research teams from leading research institutions outside Portugal. In addition, ICVS members were involved in 24 conferences and seminars in the context of international meetings outside Portugal (49 participations/presentations);

- In 2012, the ICVS was involved in international networks with specific funding, including:
6 European FP7 research projects (4 Cooperation grants and 2 Marie Curie); 1 Industry research contract; 3 grants funded by other international institutions.
These collaborative networks involved the participation of institutions from the following countries: Belgium, Benin, Congo, Denmark, France, Germany, Ghana, Hungary, Israel, Italy, Mali, Morocco, Mozambique, Netherlands, Nigeria, Norway, South Africa, Spain, Sweden, Switzerland, Tanzania, Uganda, United Kingdom and Zambia;

- The international recognition of the ICVS research activities is also reflected by the granting of 9 International awards, including the Excellence in Paediatrics Award, granted by the

Excellence In Paediatrics Institute (EiP);

- The Post-graduation program of the ICVS/ECS promoted 37 international post-graduation courses that included the participation of 121 foreign students and 85 foreign Professors;

3. ACTIVITIES

3.1 OUTREACH ACTIVITIES

The program of outreach activities implemented by the ICVS and the School of Health Sciences represents a joint strategy to promote scientific awareness in the surrounding community on:

- the importance of research on life and health sciences;
- health education and healthier lifestyles.
- advanced technologies in biomedicine.

In 2012, the younger population was a crucial target in the context of a network comprising over 80 schools, since first year to the pre-university stage. The activities were organized in 6 major events: the “Open Doors to high schools”, the “International Brain Awareness Week”, the “Science Outbreak Week”, the visiting program to the School of Health Sciences the “Summer in the Campus”, the “ABCs of Surgery” and the “Science and Technology Week”. These initiatives included interactive talks in schools, experimental activities at the ICVS laboratories, exhibitions, guided tours to the ICVS facilities and seminars. Overall, these activities counted with more than 3500 participants and their organization and implementation involved up to 60 ICVS researchers.

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

4. OTHER ACTIVITIES

4.1 INTERNAL SERVICES AND RESOURCES

At the ICVS facilities, all the scientific equipment from the installed technological platform is shared amongst Research Lines (Research Domains/teams). Indeed, the ICVS has promoted an active policy of equipment purchase based on the perspective of shared usage, to obtain higher efficiency at lower costs. In addition, this equipment is also available under request to the other research units of the University of Minho and to the Portuguese scientific community in general.

A laboratory management organizational plot has been setup, including both Functional Core facilities (equipment with a team of dedicated technical staff that provides services for researchers in the ICVS) and Shared Technical facilities (equipment and infrastructures organized into dedicated spaces on the basis of a particular usage/technique).

A web platform has been developed in-house and it constitutes the basis of all Quality Management System. The purpose of this platform is the on-line management of all information regarding equipment, labs and consumables. Moreover, this platform has information, available to all researchers, related with SOPs and other procedures related with materials and biological research methods.

Specifically, the ICVS provides: fully operational Functional Cores for Animal Housing, Microscopy, Histology and Molecular Biology, and Shared Technical Facilities for Cytometry, Cell and Tissue Culture, Bio Banking, Electrophysiology and Biosafety Level 2 and 3. Some of this Functional Cores, such as histology, microscopy and animal housing also provide external services.

4.2 EXTERNAL SERVICES AND RESOURCES

The ICVS provides services to the general and the clinical communities. This external services were born from the knowledge developed by the researchers and were recently expanded in the context of the ICVS activities, with the formal establishment of a Molecular Diagnostics Service (SDM). The SDM includes a head-technician and a diagnostics technician amongst the dedicated staff and occupies a space in a reserved area of the ICVS facilities and is fully equipped for molecular diagnostics.

During the last years, the ICVS has been providing, to public and private Health services, genetic diagnostics of intellectual disability related disorders (a panel of genes from chromosome X including Fragile X syndrome genes) and Rett Syndrome (screening of mutations in the MECP2, CSDKL5 and FOXG1 genes), as well as a microarrays service for the screening of microdeletions and duplication of chromosome regions.

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

5. RESEARCH LINE: MICROBIOLOGY AND INFECTION

5.1 OBJECTIVES AND ACHIEVEMENTS

5.1.1 GENERAL OBJECTIVES

The Research Line "Microbiology and Infection Research Domain (MIRD)" addresses specific challenges in the prophylaxis and treatment of infectious diseases, including mycobacteriosis and systemic fungal infections. The MIRD is organized in two topics of research:
I - "Cellular and Molecular Microbiology"
Devoted to the study of biological problems associated to human diseases from the integrated perspective of genetics, cell biology and biochemistry. The research focuses on microbial environmental sensing, transcriptional and posttranscriptional regulation, secretion, autophagy, programmed cell death and molecular aspects of pathogenicity/virulence of human related pathogens.
I – "Immunology and Infection"
Devoted to the study of the cellular/molecular mechanisms of immune control/pathogenesis associated to infectious diseases. Emphasis is given to those of bacterial and fungal origin, which represent a major threat to human health and against which vaccines are unavailable or inefficient.

5.1.2 MAIN ACHIEVEMENTS

The MIRD has followed a policy of staff recruitment/differentiation, counting presently more than 40 members with multidisciplinary backgrounds, including biological sciences, engineering and MDs.
Research within the MIRD was supported by 7 projects funded by FCT, 2 FP7 grants and 2 contracts with industry.
During the year of 2012, researchers from MIRD published 36 papers in international peer-reviewed journals, including 26 in Q1, with an average IF of 5.2, of which 3 papers in a journal with an IF>10. Additionally, the MIRD submitted 16 abstracts to International Meetings.
Researches within the MIRD were granted with 3 National awards (Prémio Robalo Cordeiro SPP/GSK 2012, Bolsa Jovens Especialistas de Pneumologia and SPP-AstraZeneca 2012).
The MIRD organized 1 scientific meeting and 3 post-graduation courses/workshops and graduated 5 PhD-students and 13 MSc-students.
In line with the previous year, we kept reinforcing the translational/clinical research, on aspergillosis and mycobacteriosis, namely Tuberculosis and Buruli Ulcer, by fortifying our effective collaborations with clinicians in Portugal, Italy, United States of America, Benin and Mozambique.

5.2 RESEARCH LINE OUTPUT

5.2.1 FIFTEEN SELECTED PUBLICATIONS IN PEER REVIEW JOURNALS

1. Martin CJ, Booty MG, Rosebrock TR, Nunes-Alves C, Desjardins DM, Keren I, Fortune SM, Remold HG, Behar SM. Efferocytosis Is an Innate Antibacterial Mechanism. *Cell Host & Microbe.* 12(3): 289–300 (2012). (IF=13,5)

2. Luca AD, Iannitti RG, Bozza S, Beau R, Casagrande A, D'Angelo C, Moretti S, Cunha C,

Giovannini G, Massi-Benedetti C, Carvalho A, Boon L, Latgé JP, Romani L. CD4+ T cell vaccination overcomes defective cross-presentation of fungal antigens in a mouse model of chronic granulomatous disease. *J Clin Invest.* 122(5):1816-31 (2012). (IF=13,069)

3. Iannitti RG, Carvalho A, Romani L. From memory to antifungal vaccine design. *Trends Immunol.* 3(9):467-74 (2012). (IF=10,403)

4. Carvalho A, De Luca A, Bozza S, Cunha C, D'Angelo C, Moretti S, Perruccio K, Iannitti RG, Fallarino F, Pierini A, Latgé JP, Velardi A, Aversa F, Romani L. TLR3 essentially promotes protective class I-restricted memory CD8+ T-cell responses to Aspergillus fumigatus in hematopoietic transplanted patients. *Blood* 119(4):967-77 (2012). (IF=9,898)

5. Franco NH, Correia-Neves M, Olsson IA. How "humane" is your endpoint?-Refining the science-driven approach for termination of animal studies of chronic infection. *PLoS Pathog.* 8(1):e1002399 (2012). (IF=9,127)

6. Sampaio-Marques B, Felgueiras C, Silva A, Rodrigues M, Tenreiro S, Franssens V, Reichert AS, Outeiro TF, Winderickx J, Ludovico P.SNCA (α-synuclein)-induced toxicity in yeast cells is dependent on sirtuin 2 (Sir2)-mediated mitophagy. *Autophagy* 8(10):1494-509 (2012). (IF=7,453)

7. Borges M, Barreira-Silva P, Flórido M, Jordan MB, Correia-Neves M, Appelberg R. Molecular and Cellular Mechanisms of Mycobacterium avium-Induced Thymic Atrophy. *J Immunol.* 189(7):3600-8 (2012). (IF=5,788)

8. Costa V, Ludovico P. Yeast as a platform to uncover ceramide-induced ancient cell death routines. *Cell Cycle* 11(1):14-5 (2012). (IF= 5,359)

9. Veiga MI, Ferreira PE, Malmberg M, Jörnhagen L, Björkman A, Nosten F, Gil JP. pfmdr1 amplification is related to increased Plasmodium falciparum in vitro sensitivity to the bisquinoline piperaquine. *Antimicrob Agents Chemother.* 56(7):3615-9 (2012). (IF= 4,841)

10. Mishra AK, Alves JE, Krumbach K, Nigou J, Castro AG, Geurtsen J, Eggeling L, Saraiva M, Besra GS. Differential arabinan capping of lipoarabinomannan modulates innate immune responses and impacts T helper cell differentiation. *J Biol Chem.* 287(53):44173-83 (2012). (IF=4,773)

11. Martins TG, Trigo G, Fraga AG, Gama JB, Longatto-Filho A, Saraiva M, Silva MT, Castro AG, Pedrosa J. Corticosteroid-Induced Immunosuppression Ultimately Does Not Compromise the Efficacy of Antibiotherapy in Murine Mycobacterium ulcerans Infection. *PLoS Negl Trop Dis*. 6(11):e1925 (2012). (IF=4,716)

12. Carvalho A, Cunha C, Bistoni F, Romani L. Immunotherapy of aspergillosis. *Clin Microbiol Infect.* 18(2):120-5 (2012). (IF=4,54)

13. Marques F, Mesquita SD, Sousa JC, Coppola G, Gao F, Geschwind DH, Columba-Cabezas S, Aloisi F, Degn M, Cerqueira JJ, Sousa N, Correia-Neves M, Palha JA. Lipocalin 2 is present in the EAE brain and is modulated by natalizumab. *Front Cell Neurosci.* 6:33 (2012) (IF=4,171)

14. Mesquita SD, Ferreira AC, Sousa JC, Santos NC, Correia-Neves M, Sousa N, Palha JA, Marques F. Modulation of iron metabolism in aging and in Alzheimer's disease: relevance of the choroid plexus. *Front Cell Neurosci.* 6:25 (2012) (IF=4,171)

15. Fraga AG, Martins TG, Torrado E, Huygen K, Portaels F, Silva MT, Castro AG, Pedrosa J. Cellular Immunity Confers Transient Protection in Experimental Buruli Ulcer following BCG or Mycolactone-Negative Mycobacterium ulcerans Vaccination. *PLoS One* 7(3):e33406 (2012).

(IF=4.092)

5.2.3 PHD THESIS COMPLETED

1.
Student: Maria Alexandra Oliveira da Silva
Title: New insight into translation during yeast programmed cell death
Supervisor: Paula Ludovico
Institution: School of Health Sciences, University of Minho

2.
Student: Teresa Maria Gonçalves Martins
Title: Host-pathogen interactions in Mycobacterium ulcerans infections: implications for the development of new control strategies
Supervisor: Jorge Pedrosa
Institution: School of Health Sciences, University of Minho

3.
Student: Maria de Belém de Sousa Sampaio Marques.
Title: The emerging role of autophagy/mitophagy in a-synuclein-induced toxicity: studies on the yeast chronological aging model.
Supervisor: Paula Ludovico
Institution: School of Health Sciences, University of Minho

4.
Student: Júlia Margarida Raposo Monteiro dos Santos
Title: Ammonium toxicity in aging yeast cells reduces chronological life span: cell death mechanisms and nutriente sensing pathways
Supervisor: Cecília Leão
Institution: School of Health Sciences, University of Minho

5.
Student: Maria Rosinda Teixeira Coelho
Title: Impact of mycobacterial recognition by toll like receptors in the regulation of IL-10 and T helper type of responses
Supervisor: Gil Castro
Institution: School of Health Sciences, University of Minho

6. RESEARCH LINE: NEUROSCIENCES

6.1 OBJECTIVES AND ACHIEVEMENTS

6.1.1 GENERAL OBJECTIVES

The Research Line "Neurosciences Research Domain (NERD)" launched its activities at the ICVS in 2003 as two separate research teams, Neurosciences and Human Genetics. Since 2003, the NERD evolved into a single team with increasing internal collaborations and common research topics, profiting from the varied backgrounds of its members.
The NERD is devoted to the study of the Central Nervous System with emphasis in three main research topics: Neurodevelopment, Neurodegeneration and Neuroimmunology. Studies at the molecular, cellular and system levels are performed in physiological conditions covering from neurodevelopment to senescence, as well as in several human neuropsychiatric disorders, such as early- and late-onset degenerative diseases, neuroimmune disorders, depression, anxiety and chronic pain syndromes. In line with the multimodal approaches of research questions, the team is composed by members with a wide spectrum of backgrounds (MDs from neurology, neuroradiology, psychiatry, internal medicine, endocrinology, urology, surgery, neonatology, pediatrics, medical genetics; biochemists; molecular biologists, statisticians, mathematicians, biomedical and electronic engineers, psychologists, veterinaries, pharmacists).
The NERD benefits from an extensive technical platform, conducting studies in parallel in humans and animal models, covering fundamental, translational and clinical research.

6.1.2 MAIN ACHIEVEMENTS

Research within the NERD was supported by 24 projects funded by FCT, 4 FP7 grants and 8 contracts with industry.
During the year of 2012, researchers from NERD published 36 papers in international peer-reviewed journals, including 23 in Q1, with an average IF of 5,5. Additionally, the NERD submitted 40 abstracts to International Meetings.
In 2012, the NERD produced 1 patent and 1 computer application and launched the Spin-off "Bn´ML- Behavioral & Molecular Lab".
Researchers within the NERD were granted with 7 awards (including the JANSSEN Neuroscience Award and the Grünenthal Pain Award).
The NERD organized 16 post-graduation courses/workshops and graduated 2 PhD-students and 6 MSc-students.

6.2 RESEARCH LINE OUTPUT

6.2.1 FIFTEEN SELECTED PUBLICATIONS IN PEER REVIEW JOURNALS

1. Sousa N, Almeida OFX. Disconnection and reconnection: the morphological basis of (mal)adaptation to stress. *Trends in Neurosciences* 35:742-751 (2012). (IF=14,235)

2. Rodrigues AJ, Leão P, Pêgo JM, Cardona D, Carvalho MM, Oliveira M, Costa BM, Carvalho AF, Morgado P, Araújo D, Palha JA, Almeida OF, Sousa N. Mechanisms of initiation and reversal of drug-seeking behavior induced by prenatal exposure to glucocorticoids. *Mol Psychiatry*17:1295-1305 (2012). (IF=13,668)

3. Silva NA, Cooke MJ, Tam RY, Sousa N, Salgado AJ, Reis RL, Shoichet MS. The Effects of Peptide Modified Gellan Gum and Olfactory Ensheathing Glia Cells on Neural Stem/Progenitor Cell Fate. *Biomaterials*, 33:6345-6354 (2012). (IF=7,404)

4. Baptista M, Duarte C and Maciel P. "Role of the ubiquitin-proteasome system in nervous system function and disease: using *C. elegans* as a dissecting tool". *Cell Mol Life Sci* 69(16):2691-2715 (2012). (IF=6,57)

5. Leite-Almeida H, Cerqueira JJ, Wei H, Ribeiro-Costa N, Anjos-Martins H, Sousa N, Pertovaara A, Almeida A. Differential effects of left/right neuropathy on rats' anxiety and cognitive behavior. *Pain* 153:2218-2225 (2012). (IF=5,777)

6. Pinto PR, McIntyre T, Almeida A, Araújo-Soares V. The mediating role of pain catastrophizing in the relationship between presurgical anxiety and acute postsurgical pain after hysterectomy. *Pain* 153:218-226 (2012). (IF=5,777)

7. Pinto PR, McIntyre T, Almeida A, Araújo-Soares V. Understanding pre-surgical predictors of acute pain experience following hysterectomy for benign causes: conceptual and methodological issues. *Pain*, 153:1974-1976 (2012). (IF=5,777)

8. Pinto PR, McIntyre T, Nogueira-Silva C, Almeida A, Araújo-Soares V. Risk factors for persistent postsurgical pain in women undergoing hysterectomy due to benign causes: a prospective predictive study. *J Pain* 13(11):1045-57 (2012). (IF=4,926)

9. Chan RB, Oliveira TG, Cortes EP, Honig LS, Duff KE, Small SA, Wenk MR, Shui G, Di Paolo G. Comparative lipidomic analysis of mouse and human brain with Alzheimer's disease. *J Biol Chem* 287:2678-2688 (2012). (IF=4,773)

10. Falcao AM, Marques F, Novais A, Sousa N, Palha JA, Sousa JC. The path from the choroid plexus to the subventricular zone: go with the flow! *Front Cell Neurosci* 6:34 (2012). (IF=4,171)

11. Palha JA, Santos NC, Marques F, Sousa JC, Bessa JM, Miguelote RF, Sousa N, Belmonte de Abreu P. Do genes and environment meet to regulate cerebrospinal fluid dynamics? Relevance for schizophrenia. *Front Cell Neurosci* 6:31 (2012). (IF=4,171)

12. Marques F, Mesquita SD, Sousa JC, Coppola G, Gao F, Geschwind DH, Columba-Cabezas S, Aloisi F, Degn M, Cerqueira JJ, Sousa N, Correia-Neves M, Palha JA. Lipocalin 2 is present in the EAE brain and is modulated by natalizumab. Front Cell Neurosci. 6:33 (2012). (IF=4,171)

13. Mesquita SD, Ferreira AC, Sousa JC, Santos NC, Correia-Neves M, Sousa N, Palha JA, Marques F. Modulation of iron metabolism in aging and in Alzheimer's disease: relevance of the choroid plexus.Front Cell Neurosci. 6:25 (2012). (IF=4,171)

14. Falcão AM, Palha JA, Ferreira AC, Marques F, Sousa N, Sousa JC. Topographical analysis of the subependymal zone neurogenic niche. *PLoS One* 7:e38647 (2012). (IF=4,092)

15. Martinho O, Granja S, Jaraquemada T, Caeiro C, Miranda-Gonçalves V, Honavar M, Costa P, Damasceno M, Rosner MR, Lopes JM, Reis RM. (2012) Downregulation of RKIP is associated with poor outcome and malignant progression in gliomas. Plos One 7:e30769-e30769 (2012) (IF=4,092)

6.2.3 PHD THESIS COMPLETED

1.
Student: Ana Luísa Mendanha Falcão
Title: Novel perspectives on the subependymal zone complexity and modulation
Supervisor: João Carlos Sousa
Institution: School of Health Sciences, University of Minho

2.
Student: Ana Paula Ventura da Silva
Title: Molecular and Functional Correlates of Stress-Related Anxiety
Supervisor: José Miguel Pêgo
Institution: School of Health Sciences, University of Minho

7. RESEARCH LINE: SURGICAL SCIENCES

7.1 OBJECTIVES AND ACHIEVEMENTS

7.1.1 GENERAL OBJECTIVES

The Research Line "Surgical Sciences Research Domain (SSRD)" deals with diseases from digestive, pulmonary and urogenital systems. An interdisciplinary team including biologists, engineers and MDs work together aiming to understand the development mechanisms regulating time and space differentiation of cells/tissues (eg. somites, limb and lung growth); evaluate genetic/molecular markers as risk and prognostic factors as well as therapeutic strategies (eg. congenital malformations and oncological diseases). As surgery has a strong technical dimension, in connection with industry: we explore the possibility of scarless interventions through Natural Orifices Transluminal Endoscopic Surgery (N.O.T.E.S.); using human body imaging (CT scan and laser), as a surrogate to develop three-dimensional constructs, we provide personalized prosthesis and surgical plans. As additional mission, we provide an extensive international hands-on program with courses in minimally invasive techniques.

7.1.2 MAIN ACHIEVEMENTS

Research within the SSRD was supported by 6 projects funded by FCT and 1 contract with industry.
During the year of 2012, researchers from SSRD published 65 papers in international peer-reviewed journals, including 24 in Q1, with an average IF of 3,5. Additionally, the SSRD submitted 94 abstracts to International Meetings.
Researchers within the SSRD were granted with 5 International and 13 National awards (including the Excellence in Paediatrics Award and the ESPGHAN Award).
The SSRD organized 3 scientific meetings and 19 post-graduation courses/workshops and graduated 3 PhD-students and 3 MSc-students.

7.2 RESEARCH LINE OUTPUT

7.2.1 FIFTEEN SELECTED PUBLICATIONS IN PEER REVIEW JOURNALS

1. Almeida MI, Nicoloso M, Zeng L, Ivan C, Spizzo R, Gafà R, Xiao L, Bondaruk J, Fabbri M, Czerniak B, Lanza G, Reis RM, Zweidler-McKay P, Calin GA. Disjunction on Biological Effects of Hairpin Strand Specific miR-28-5p and miR-28-3p in colon cancer. *Gastroenterology* 142:886-896 (2012). (IF=11,675)

2. Ferreira A, Gonçalves R, Rolanda C. A different kind of colon polyps. *Gastroenterology* 143(6):1693-4 (2012). (IF=11,675)

3. Ferreira A, Pereira P, Rolanda C. Diffuse hepatic metastasis - or not? *Gastroenterology* 142:1070-25 (2012). (IF=11,675)

4. Martino A, Campa D, Buda G, Sainz J, García Sanz R, Jamroziak K, Reis RM, Weinhold N, Jurado M, Ríos R, Szemraj-Rogucka Z, Marques H, Stein A, Kumar R, Orciuolo E, Gemignani

F, Landi S, Goldschmidt H, Petrini M, Dumontet C, Canzian F, Rossi AM. Polymorphisms in xenobiotic transporters ABCB1, ABCG2, ABCC2, ABCC1, ABCC3 and Multiple Myeloma Risk: a case-control study in the context of the IMMEnSE (International Multiple Myeloma rESEarch) consortium. *Leukemia* 26:1419-22 (2012). (IF=9,561)

5. Pinheiro C, Longatto-Filho A, Schmitt FC, Baltazar F. Lactate-Induced IL-8 Pathway in Endothelial Cells – Letter. *Cancer Res.*72: 1901-2 (2012). (IF=7,856)

6. Spizzo R, Almeida MI, Colombatti A, Calin GA. Long non-coding RNAs and cancer: a new frontier of translational research? *Oncogene* 31(43):4577-87 (2012). (IF=6,373)

7. Moreira-Pinto J, Ferreira A, Miranda A, Rolanda C, Correia-Pinto J. Transesophageal pulmonary lobectomy with single transthoracic port assistance: study with survival assessment in porcine model. *Endoscopy* 44:1-8 (2012). (IF=5,21)

8. Pimentel-Nunes P, Dinis-Ribeiro M, Soares JB, Marcos-Pinto R, Santos C, Rolanda C, Areia M, Afonso L, Bergman J, Sharma P, Gotoda T, Henrique R, Moreira-Dias L. A multicenter validation of an endoscopic classification with narrow band imaging for gastric precancerous and cancerous lesions. *Endoscopy* 44: 236-46 (2012). (IF=5,21)

9. Campa D, Martino A, Sainz J, Buda G, García Jamroziak K, Weinhold N, Reis RM, García-Sanz R, Jurado M, Ríos R, Szemraj-Rogucka Z, Marques H, Lesuer F, Bugert P, Moreno V, Szemraj J, Orciuolo E, Gemignani F, Rossi AM, Dumontet C, Petrini M, Goldschmidt H, Landi S, Canzian F. Comprehensive investigation of genetic variation in the 8q24 region and multiple myeloma risk in the IMMEnSE (International Multiple Myeloma rESEarch) consortium. *Br J Haematol.* 157:331-8 (2012). (IF=4,941)

10. Martino A, Campa D, Jamroziak K, Reis RM, Sainz J, Buda G, García-Sanz R, Lesueur F, Marques H, Moreno V, Jurado M, Ríos R, Szemraj-Rogucka Z, Szemraj J, Tjønneland A, Overvad K, Vangsted AJ, Vogel U, Mikala G, Kádár K, Szombath G, Varkonyi J, Orciuolo E, Dumontet C, Gemignani F, Rossi AM, Landi S, Petrini M, Houlston RS, Hemminki K, Canzian F. Impact of polymorphic variation at 7p15.3, 3p22.1 and 2p23.3 loci on risk of multiple myeloma. *Br J Haematol*. 158(6):805-9 (2012). (IF=4,941)

11. Moreira-Pinto J, Ferreira A, Miranda A, Rolanda C, Correia-Pinto J. Left atrial appendage ligation with single transthoracic port assistance: a study of survival assessment in a porcine model (with videos). *Gastrointest Endosc.* 75: 1055-61 (2012). (IF=4,878)

12. Amorim R, Vilaça N, Martinho O, Reis RM, Sardo M, Rocha J, Fonseca AM, Baltazar F, Neves IC. Zeolite Structures Loading with an Anticancer Compound As Drug Delivery Systems. *J. Phys. Chem.* 116(48):25642–25650 (2012). (IF=4,805)

13. Cardeal LB, Boccardo E, Termini L, Rabachini T, Andreoli MA, di Loreto C, Longatto-Filho A, Villa LL, Maria-Engler SS. HPV16 oncoproteins induce MMPs/RECK-TIMP-2 imbalance in primary keratinocytes: possible implications in cervical carcinogenesis. *PLoS One.* 7(3):e33585 (2012). (IF=4,092)

14. Le XF, Almeida MI, Mao W, Spizzo R, Rossi S, Nicoloso MS, Zhang S, Wu Y, Calin GA, Bast RC Jr. Modulation of MicroRNA-194 and Cell Migration by HER2-Targeting Trastuzumab in Breast Cancer. *PLoS One.* 7(7):e41170 (2012). (IF=4,092)

15. Nogueira-Silva C, Piairo P, Carvalho-Dias E, Peixoto FO, Moura RS, Correia-Pinto J. Leukemia Inhibitory Factor in Rat Fetal Lung Development: Expression and Functional Studies.

PLoS One. 7:e30517 (2012). (IF=4,092)

7.2.3 PHD THESIS COMPLETED

1.
Student: Cristina Isabel Nogueira da Silva
Title: Looking for Novel Physiological Regulators of Lung Development
Supervisor: Jorge Correia Pinto
Institution: School of Health Sciences, University of Minho

2.
Student: Maria Inês da Cunha Doutel Almeida
Title: MicroRNas in Cancer: Biological Effects of microRNas in Colorectal Cancer
Supervisor: Rui Reis
Institution: School of Health Sciences, University of Minho

3.
Student: Sandra de Fátima Fernandes Martins
Title: Expression of Colorectal Cancer Metabolic and Angiogenic Markers: Association with Clinicopathological Characteristics and Impact on Prognosis
Supervisor: Adhemar Longatto
Institution: School of Health Sciences, University of Minho