

# ICVS

ANNUAL REPORT 2011

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



Universidade do Minho  
Escola de Ciências da Saúde





# ICVS

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ANNUAL REPORT 2011

6	<b>Introduction</b>
6	Unit Description
8	<b>ICVS (Life And Health Sciences Research Institute)</b>
8	Objectives and Achievements
	Objectives
	Main achievements during the year of 2011
11	Group Productivity
	Publications in peer reviewed journals
	Other international publications
	PhD thesis completed
	Patents/Propotypes
	Organization of conferences
	Industry contract research
	Internationalization
19	<b>Activities</b>
19	Outreach activities
20	<b>Other activities</b>
20	Internal services and resources
21	External services and resources



22      **Line: Microbiology and Infection**

24      Objectives & Achievements

General objectives

Main achievements

25      Research Line output

Ten selected publications in peer reviewed journals

Collaborative publications within the Associate Laboratory in peer reviewed journals

PHD thesis completed

28      **Line: Neurosciences**

30      Objectives & Achievements

General objectives

Main achievements

32      Research Line output

Ten selected publications in peer reviewed journals

Collaborative publications within the Associate Laboratory in peer reviewed journals

PHD thesis completed

36      **Line: Surgical Sciences**

38      Objectives & Achievements

General objectives

Main achievements

39      Research Line output

Ten selected publications in peer reviewed journals

Collaborative publications within the Associate Laboratory in peer reviewed journals

PHD thesis completed

# Unit description

## **ICVS (Life and Health Sciences Research Institute)**

### **ICVS/3B'S ASSOCIATE LABORATORY (AL)**

#### **Introduction**

The ICVS/3B's Associate Laboratory (AL) centers its activities in the Health Sciences, namely in Biomedical and Clinical Sciences, and in Biomedical Science & Engineering/Materials Science & Engineering (Biomaterials). This interface Health-Sciences/Technologies pursues the goal of generating 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, incorporating Clinical Academic Centers in partnership with the affiliated network of Health Care Institutions; 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 between Health Sciences/Technology; (2) Advanced education and training in order to provide research and training activities to undergraduate and postgraduate students and health professionals; (3) Services, consulting and technology transfer by taking into consideration the vital importance of the industrial/clinical partners; (4) Dissemination, scientific awareness and public perception especially through International scientific journals and conferences.

New technologies, therapies and medical products are emerging 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 have been investigated in collaboration with companies and other research groups, using competitive financial support.

These developments have the potential to cross the complete development pipeline, from the more fundamental in vitro research, testing in animal models and pre-clinical validation, to clinical trials, that can transpose to the market innovative therapeutic solutions.

## **ICVS (Life and Health Sciences Research Institute)**

**ICVS Director:** Jorge Pedrosa

### **8 Objectives and Achievements**

Objectives

Main achievements during the year of 2011

### **11 Group Productivity**

Publications in peer reviewed journals

Other international publications

PhD thesis completed

Patents/Propotypes

Organization of conferences

Industry contract research

Internationalization

### **19 Activities**

#### **19 Outreach activities**

#### **20 Other activities**

#### **20 Internal services and resources**

#### **21 External services and resources**





# Objectives & Achievements

## ICVS (Life and Health Sciences Research Institute)

### Objectives

The strategy for the ICVS development of has been centred in two main aspects: i) establishment of a research unit within an innovative Medical School (School of Health Sciences - ECS), guided by international standards of excellence and involving a network of health care institutions; ii) fostering a strategic partnership with the group 3B's - Biomaterials, Biodegradables and Biomimetics (School of Engineering), aiming at develop a strong interface between Health Sciences and Technologies.

This strategy resulted in the implementation of biomedical, translational and clinical research of international impact that resulted in the creation of the ICVS/3B's- Associate Laboratory (AL) in 2011, in the context of the Portuguese R&D network. The AL maximizes the development of innovative biomaterials, diagnostic strategies, regenerative approaches and therapeutic products, with a strong link to spin-off companies, a clinical academic centre and health care providers.

Within the AL, the ICVS is a growing group and represents an attractive research environment for young researchers, providing a state of the art technological platform for Cell and Tissue Culture, Electrophysiology, Biosafety Level 2 and 3, Molecular Biology, Imagiology, Microscopy Imaging, Neuroanatomy/Neuroimaging, Histology, Biological Resources, Cytometry, Endoscopy 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;
- 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 Clinical Academic Centers, in partnership with the affiliated network of Health Care Institutions;
- 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 2011 WERE TO:

- proceed in the negotiation process with the PT Government to obtain the status of Associate Laboratory in partnership with the 3B's Group;
- formalize the creation of a Clinical Academic Centre with the Hospital of Braga, to develop clinical research, including clinical trials;
- 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 n° 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 (Health Cluster Portugal; private foundations, industry and the FP7 EU programme), including at least 2 new projects;
- promote the public awareness in health sciences.

#### **Main achievements during the year of 2011:**

- Success in the application for the status of Associate Laboratory;
- Creation of the Clinical Academic Centre CCAB and reinforcement of translational/clinical research;
- Major increase in the capacity to attract competitive funding, including internationally;
- Increase the number of Advanced Post-Graduation Courses;
- Sustained increase in staff numbers/differentiation;
- Increase the number of MD students involved in research.

SPECIFICALLY, IN 2011, THE ICVS WAS ABLE TO:

- Create the ICVS/3B's-PT Government Associate Laboratory in March 2011, the first AL centred in the University of Minho, representing a historic achievement for the ICVS and the 3B's. The AL focuses its research in the interface Health Sciences/ Technologies, pursuing the goal of expanding the boundaries of current knowledge and developing translational activities on innovative prophylactic, diagnostic and therapeutic solutions;

- Formally establish a Clinical Academic Centre in partnership with the Hospital of Braga, with infrastructures located at both the Hospital and the ICVS, and specific staff devoted to the development of clinical research, including clinical trials;
  - Formally establish a Molecular Diagnostics Service (SDM), following the ICVS efforts to provide services to the general and the clinical communities. The SDM includes technicians and a dedicated laboratorial space fully equipped for molecular diagnostics. In addition to providing the genetic diagnostics of intellectual disability related disorders, in 2011 the SDM started a CGH microarrays service for the screening of microdeletions and duplications of chromosome regions;
  - Pursue a sustained increase in staff numbers/differentiation:  
PhDs increasing from 50 (2010) to 60 (2011); 36 ECS faculty, 4 “Compromisso com a Ciência”, and 20 Post-Docs;  
PhDs students increasing from 87 (2010) to 100 (2011);  
Masters students increasing from 37 (2010) to 53 (2011);  
Presently, the ICVS counts with 238 researchers [60 PhDs and 178 post graduation students (100 PhD students, 53 Master students and 25 associate researchers)], supported by 18 non-academic staff (5 administrative and 13 in laboratories, with salaries supported by the ECS);
  - Publish 78 papers in international journals: 74 within the three Lines, with 40% in Q1 and an average IF of 3.9 (including articles with IF between 3 and 5 = 25 papers; IF between 5 and 10 = 8 papers; IF>35 = 1 paper); and four additional articles in medical education and Public Health.
- NOTE: the individual reports from the Research Lines include all publications from each Line, some of them resulting from shared projects and, therefore, listed by more than one Line.
- Foster the conclusion of 10 PhD theses, including 2 MDs;
  - Obtain 5 International and 7 National awards;
  - Get a total of 33 new fellowships granted by FCT: 8 BPD; 12 BD; 13 BI;
  - Achieve a major increase in competitive funding.
  - Additionally, new projects were granted, including:  
6 projects submitted to the last FCT call;  
2 Consortium proposals in the European FP7;  
Private Foundations and Industry: BOEHRINGER; FC Gulbenkian; F BIAL; TECNIMEDE; Bébe Vida;
  - Involve an increasing number of MD students in research, including 50 Option Projects (from 27 in 2010) and 17 MD/PhD Lab Rotations (from 13 in 2010);
  - Organize an increasing number of Advanced Post-Graduation Courses/Workshops (from 20 in 2010 to 26 in 2011), with 473 participants (including 60 % MDs, 34 % Biological Sciences, 4 % other Health Professionals); 91 % of the participants rated courses as “Very Good” or “Excellent” and some of the courses were part of training activities of European schools or within European training actions.

# Group productivity

## Publications in peer reviewed journals

In 2011, the ICVS published 78 papers in international peer-reviewed journals (plus four papers in Medical Education/Public Health), with an average IF of 3.9, including: articles with IF between 3 and 5 = 25 papers; IF between 5 and 10 = 8 papers; IF>35 = 1 paper.

In addition, more 14 papers were accepted for publication and are in press.

## 20 SELECTED PAPERS IN PEER REVIEW JOURNALS

Takeda Y, Costa S, Delamarre E, Roncal C, Leite De Oliveira R, Squadrito ML, Finisguerra V, Deschoemaeker S, Bruyère F, Wenes M, Hamm A, Serneels J, Magat J, Bhattacharyya T, Anisimov A, Jordan BF, Alitalo K, Maxwell P, Gallez B, Zhuang ZW, Saito Y, Simons M, De Palma M, Mazzone M. A switch in macrophage polarization induced by PHD2 haplodeficiency prevents ischemic damage by inducing arteriogenesis. *Nature*. 479:122-26 (2011). (IF=36,1)

Madureira P, Andrade EB, Gama B, Oliveira L, Moreira S, Ribeiro A, Correia-Neves M, Trieu-Cuot P, Vilanova M, Ferreira P. Inhibition of IL-10 Production by Maternal Antibodies against Group B Streptococcus GAPDH Confers Immunity to Offspring by Favoring Neutrophil Recruitment. *PLoS Pathog*. 7(11):e1002363 (2011). (IF=9,1)

Autorino R, Cadeddu JA, Desai MM, Gettman M, Gill IS, Kavoussi LR, Lima E, Montorsi F, Richstone L, Stolzenburg JU, Kaouk JH. Laparoendoscopic single-site and natural orifice transluminal endoscopic surgery in urology: a critical analysis of the literature. *Eur Urol*. 59:26-45 (2011). (IF=8,8)

Gettman MT, White WM, Aron M, Autorino R, Averch T, Box G, Cadeddu JA, Canes D, Cherullo E, Desai MM, Frank I, Gill IS, Gupta M, Haber GP, Humphreys MR, Irwin BH, Kaouk JH, Kavoussi LR, Landman J, Liatsikos EN, Lima E, Ponsky LE, Rane A, Ribal M, Rabenhalt R, Rao P, Richstone L, Sawyer MD, Sotelo R, Stolzenburg JU, Tracy CR, Stein RJ; Endourological Society NOTES and LESS Working Group; European Society of Urotechnology NOTES and LESS Working Group. Where Do We Really Stand With LESS and NOTES? *Eur Urol*. 59:231-4 (2011). (IF=8,8)

Teixeira-Castro A, Ailion M, Jalles A, Brignull HR, Vilaça JL, Dias N, Rodrigues P, Oliveira JF, Neves-Carvalho A, Morimoto RI, Maciel P. Neuron-specific proteotoxicity of mutant ataxin-3 in *C. elegans*: rescue by the DAF-16 and HSF1 pathways, *Hum Mol Genet*. 20:2996-3009 (2011). (IF=8,1)

Sotiropoulos I, Catania C, Pinto LG, Silva R, Pollerberg GE, Takashima A, Sousa N, Almeida O.F.X. Stress acts cumulatively to precipitate Alzheimer's disease-like TAU pathology and cognitive deficits. *J Neuroscience*, 31:7840-7847 (2011). (IF=7,3)

Bettencourt C, Raposo M, Kazachkova N, Cymbron T, Santos C, Kay T, Vasconcelos J, Maciel P, Jardim L, Sequeiros J & Lima M. The  $\epsilon 2$  allele of APOE increases the risk of earlier age-at-onset in Machado-Joseph Disease (MJD/SCA3). *Arch Neurol*, 68:1580-1583 (2011). (IF=7,1)

Rolanda C, Silva D, Branco C, Moreira I, Macedo G, Correia-Pinto J. Peroral esophageal segmentectomy and anastomosis with single transthoracic trocar: a step forward in thoracic NOTES. *Endoscopy*. 43:14-20 (2011). (IF=6,1)

Butowski N, Chang S, Lamborn KR, Polley MY, Pieper R, Costa BM, Reis RM, Costello J, Vandenberg S, Parvataneni R, Nicole A, Kazmierski MH, Nicol S, Thornton DE, Prados MD. Phase II and Pharmacogenomics Study of Enzastaurin Plus Temozolomide During and Following Radiation Therapy in Patients With Newly Diagnosed Glioblastoma Multiforme and Gliosarcoma. *Neuro Oncology*, 12:1331-1338 (2011). (IF=5,5)

Almeida MI, Reis RM, Calin GA. BRCA1, microRNAs and cancer predisposition: Challenging the dogma. *Cell Cycle*. 10:377 (2011). (IF=5.0)

Pereira DR, Silva-Correia J, Caridade SG, Oliveira JT, Sousa RA, Salgado AJ, Oliveira JM, Mano JF, Sousa N, Reis RL. Development of Gellan-Gum based Microparticles/Hydrogel Matrices for Application in the Intervertebral Disc Regeneration. *Tissue Eng Part C Methods*, 17:961-972. (2011). (IF=4,6)

Paulo AC, Sampaio A, Santos NC, Costa PS, Cunha P, Zihl J, Cerqueira JJ, Palha JA, Sousa N. Patterns of Cognitive Performance in Healthy Ageing in Northern Portugal: A Cross-Sectional Analysis. *PLoS ONE*, 6(9):e24553. (2011). (IF=4,4)

Rodrigues AJ, Neves-Carvalho A, Teixeira-Castro A, Rokka A, Logarinho E, Maciel P. Absence of ataxin-3 leads to enhanced stress response in *C. elegans*. *PLoS One*, 6(4):e18512 (2011). (IF=4,4)

Viana-Pereira M, Lee A, Popov S, Bax DA, Al-Sarraj S, Bridges L, Stávale JN, Hargrave D, Jones C, Reis RM. Microsatellite instability in paediatric high grade glioma is associated with genomic profile and differential target gene inactivation. *PlosOne*, 6(5): e20588 (2011). (IF=4,4)

Yu S, Yang S, Holsboer F, Sousa N, Almeida OF. Glucocorticoid regulation of astrocytic fate and function. *PLoS One*, 6(7):e22419 (2011). (IF=4,4)

Carvalho A, Osório NS, Saraiva M, Cunha C, Almeida AJ, Teixeira-Coelho M, Ludovico P, Pedrosa J, Pitzurra L, Aversa F, Romani L, Castro AG and Rodrigues F The C Allele of rs5743836 Polymorphism in the Human TLR9 Promoter Links IL-6 and TLR9 Up-Regulation and Confers Increased B-Cell Proliferation. *PLoS One*. 6(11):e28256 (2011). (IF=4,4)

Cunha C, Giovannini G, Pierini A, Bell AS, Sorci G, Riuzzi F, Donato R, Rodrigues F, Velardi A, Aversa F, Romani L, Carvalho A. Genetically-Determined Hyperfunction of the S100B/RAGE Axis Is a Risk Factor for Aspergillosis in Stem Cell Transplant Recipients. *PLoS One*. 2011;6(11):e27962 (2011). (IF=4,4)



Moura RS, Coutinho-Borges JP, Pacheco AP, daMota PO, Correia-Pinto J. 2011. FGF signaling pathway in the developing chick lung: expression and inhibition studies. PLoS ONE. 6:e17660 (2011). (IF=4,4)

Silva A, Almeida B, Sampaio-Marques B, Reis MI, Ohlmeier S, Rodrigues F, Vale AD, Ludovico P. Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) is a specific substrate of yeast metacaspase. Biochim Biophys Acta. 1813(12):2044-9 (2011). (IF=4,4)

Fraga AG, Cruz A, Martins TG, Torrado E, Saraiva M, Pereira DR, Meyers WM, Portaels F, Silva MT, Castro AG, Pedrosa J. Mycobacterium ulcerans triggers T cell immunity followed by local and regional but not systemic immunosuppression. Infect Immun. 79(1):421-30 (2011). (IF=4,2)

#### **Other international publications**

1. Queirós S, Vilaça JL, Rodrigues N, Neves S, Teixeira PM, Correia-Pinto J. A serious game for laparoscopic surgery training, IEEE SEGAH – Serious Games and Applications for health. 12 - 17 November 2011, Braga, Portugal.

2. Rodrigues N, Vilaça JL. A Health Care Mobile Rule-Based System, ENTERprise Information Systems Communications in Computer and Information Science, Volume 221, Part 6, 371-383, 2011, DOI: 10.1007/978-3-642-24352-3\_39; [http://dx.doi.org/10.1007/978-3-642-24352-3\\_39](http://dx.doi.org/10.1007/978-3-642-24352-3_39)

3. Vilaça JL, Moreira AHJ, Rodrigues P, Rodrigues N, Fonseca JC, Pinho ACM, Correia-Pinto J. Virtual simulation of the postsurgical cosmetic outcome in patients with Pectus Excavatum, Proc. SPIE 7964, 79642L, 2011; <http://dx.doi.org/10.1117/12.878328>.

4. Rodrigues P, Vilaça JL, Fonseca JC. An image processing application for liver tumour segmentation, Bioengineering (ENBENG). 1-4 March 2011, DOI: 10.1109/ENBENG.2011.6026097; <http://ieeexplore.ieee.org/stamp/stamp.jsp?tp=&arnumber=6026097&isnumber=6026034>.

5. Castro A, Rodrigues P, Oliveira J, Rodrigues N, Dias N, Vilaça JL. An image processing application for quantification of protein aggregates in Caenorhabditis elegans, 5th International Conference on Practical Applications of Computational Biology & Bioinformatics (PACBB 2011), Advances in Intelligent and Soft Computing, Volume 93/2011, 31-38, 2011, DOI: 10.1007/978-3-642-19914-1\_5; <http://www.springerlink.com/content/7070687356x0g015>.

#### **PhD thesis completed**

1.

Student: Ana Mesquita

Title: New insights into the effects of caloric restriction on *Saccharomyces cerevisiae* chronological lifespan

Supervisor: Paula Ludovico

Institution: School of Health Sciences, University of Minho

2.

Student: Andreia Castro

Title: Identification of modulators of ataxin-3 proteotoxicity in animal models of Machado Joseph disease

Supervisor: Patrícia Maciel

Co-supervisor: Richard Morimoto

Institution: School of Health Sciences, University of Minho

3.

Student: António Jaime Botelho Correia de Sousa

Title: Patient enablement and management of asthma: a study in family practice

Supervisor: Constantino Sakellarides

Institution: School of Health Sciences, University of Minho

4.

Student: Caroline Sheeba

Title: Molecular parallelism between vertebrate limb development and somitogenesis

Supervisor: Isabel Palmeirim

Co-supervisor: Jorge Correia-Pinto

Institution: School of Health Sciences, University of Minho

5.

Student: Hugo Almeida

Title: Impact of chronic pain in emotional and cognitive behaviour in the rat: the effects of age and lateralization

Supervisor: Armando Almeida

Co-supervisor: Nuno Sousa

Institution: School of Health Sciences, University of Minho

6.

Student: Mário Oliveira

Title: The programming effects of antenatal exposure to corticosteroids in the brain

Supervisor: Nuno Sousa

Institution: School of Health Sciences, University of Minho

7.

Student: Marta Viana Pereira

Title: Molecular Genetics of Paediatric versus Adult Brain Tumours

Supervisor: Rui Manuel Vieira Reis

Institution: School of Health Sciences, University of Minho

8.

Student: Olga Martinho

Title: RTKs and MAPK pathway alterations in solid tumors: dissecting prognostic and therapeutic biomarkers

Supervisor: Rui Reis

Institution: School of Health Sciences, University of Minho

9.

Student: Susana Roque

Title: Infection and mood disorders: A bidirectional interaction?

Supervisor: Margarida Correia Neves

Co-supervisor: Joana Palha

Institution: School of Health Sciences, University of Minho

10.

Student: Tatiana Resende

Title: Temporal control of vertebrate embryo development: the role of Sonic Hedgehog in somite segmentation

Supervisor: Isabel Palmeirim

Co-supervisor: Raquel Andrade

Institution: School of Health Sciences, University of Minho

### **Patents/propotypes**

1. Luisa Pinto, António Pinheiro, João Bessa, Mónica Morais, Nuno Sousa. "Immuno-Golgi as a tool for analyzing neuronal 3D-dendritic structure in phenotypically characterized neurons", National patent nº105555, 2011.

### **Organization of conferences**

- Scientific Meetings/Committees:

1. Correia-Neves. "Thymus". Porto.

2. Pedrosa, Rodrigues, Ludovico, Sturme. "Microbiotec11". Braga.

3. Correia-Neves, Saraiva. "SPI International Immunology School". Tavira.

4. Ludovico. "8th International Meeting on Yeast Apoptosis (IMYA)". Kent, UK.

- ICVS Courses/Workshops:

1. Salgado, Pinto. Stem cells (...). Jan 31 - Feb 4.
2. Sousa, Cunha, Cotter. Arterial stiffness (...). Feb 16-17.
3. Salgado, Saraiva, Correia-Neves, Ludovico. (...) cell and tissue culture, flow cytometry and microscopy. Feb 21 - Mar 4.
4. Correia-Pinto, Henriques-Coelho. Fetal/neonatal endoscopic surgery. Mar 14-16.
5. Moreira-Pinto, Dias, Nogueira-Silva. Basic laparoscopy (...). Mar 25-26.
6. Lima, Autorino, Rassweiler, Correia-Pinto. Urological Laparoscopy (...). Apr 11-12.
7. Lima, Autorino, Rassweiler, Correia-Pinto. Urological LESS and NOTES (...). Apr 13-14.
8. Maciel, Rodrigues, Costa. DNA analysis (...). Apr 11-21.
9. Alves, Setúbal, Correia-Pinto. Gynecological laparoscopy. Apr 28-30.
10. Capela, Baltazar. (...) antibiotics. May 6-7.
11. Palha, Antunes, Pereira, Maciel. Obesity/metabolic syndrome (...). Jun 16-17.
12. Maciel, Barbosa. Mental retardation (...). Jul 4-8.
13. Sousa, Alegria. (...) sulci, gyri, ventricles and dissecting fibers. Aug 29 - Sep 2.
14. Costa. Feasible bologna for teachers (...). Sep 5-6.
15. Seivas, Oliveira, Leão. Microsurgical anastomosis. Sep 7-9.
16. Antunes, Correia-Pinto. Pediatric endoscopy. Sep 8.
17. Sousa, Cerqueira, Pêgo. Fundamentals in neuroscience. Sep 12-23.
18. Matos, Correia-Pinto. Digestive laparoscopy (...). Sep 26-29.
19. Ludovico, Castro. (...) immunology/infection. Sep 26 - Oct 7.

20. Duarte, Ferreira, Fidalgo, Vieira da Silva, Correia-Pinto. (...) arthroscopy. Oct 3-4.

21. Andrade. Bioinformatics (...). Oct 10-21.

22. Rolanda, Correia-Pinto. (...) endoscopy. Oct 13-14.

23. Vilaça, Leão, Correia-Pinto. Biliary laparoscopy. Oct 17-19.

24. Castelhana-Carlos, Correia-Neves. Laboratory animal science. Oct 24 - Nov 4.

25. Martins, Baltazar, Amorim, Macedo, Rodrigues. (...) rectal cancer. Nov 5.

26. Costa. Research methodologies. Dec 5-16.

### **Industry contract research**

In 2011, 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 neuropathic 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. Fundação Bial; the translation of neuro-glia interactions in complex cognitive functions. João Oliveira (coordinator).

6. Fundação Bial; the studies are designed to characterize how does cognitive enrichment impact on neuronal networks and behavioral performance. João Cerqueira (coordinator).

7. 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).

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



9. European Society of Clinical Microbiology and Infectious Diseases (ESCMID); the studies are designed to characterize the genetic variants of PTX3 and invasive aspergillosis: from risk assessment to mechanistic insights. Agostinho Carvalho (coordinator).

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

### **Internationalization**

- Reflecting the growing internationalization of ICVS, researchers from 15 foreign countries were part of the ICVS teams during 2011;

- Among the ICVS papers published in international peer-reviewed journals during 2011, 58 (78% of the overall production) resulted from partnerships involving research teams from institutions outside Portugal;

- In addition, the ICVS members were involved in 35 conferences and seminars in the context of international meetings outside Portugal during 2011;

- In 2011, the involvement of the ICVS in international networks with specific funding included:

5 European research projects (4 FP7 grants and 1 Marie Curie ITN);

2 Industry research contracts;

2 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 5 International awards, including the Jon J van Rood Award 2011, and the ISOBM 2011 Award;

- The Post-graduation program of ICVS/ECS promoted 26 international post-graduation courses that included the participation of 53 foreign students and 58 foreign Professors;

- Additionally, during 2011, researchers from the ICVS were:

ad-hoc reviewers in more than 50 peer-reviewed international journals;

evaluators of 8 international funding agencies;

members of 4 International Boards;

# Outreach Activities

## Activities

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.

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 in life and health sciences;
- health education and healthier lifestyles.
- advanced technologies in biomedicine.

The younger population is considered a crucial target, in the context of a network comprising over 80 schools, since first year to the pre-university stage.

In 2011, the activities were organized in 6 major events: the “Open Doors to high schools”, the “International Brain Awareness Week”, the “Science Outbreak Week”, the “Summer in the Campus”, the “ABCs of Surgery: present and future” and the “Science and Technology Week”. These initiatives included interactive talks in schools, experimental activities at the ICVS laboratories, exhibitions, guided tours to ICVS facilities and seminars. Overall, these activities counted with more than 3100 participants and their organization and implementation involved up to 57 ICVS researchers.

# Internal services and resources

## Other activities

At the ICVS facilities, all the scientific equipments from the installed technological platform are 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, these equipments are also available under request to the other research units of the University of Minho and to the Portuguese scientific community.

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 equipments, 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.

# 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 past recent years, the ICVS provided, 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 FOXP1 genes). Following the latest guidelines in the clinical and genetic diagnostics of development disorders, in the last year the SDM offers CGH 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. To the pharmaceutical industry, the ICVS has provided screening of drug effects for the behavioral rescue of neurological and psychiatric disorders. Furthermore, it has developed a protocol for the improvement of umbilical cord stem cells bio banking.

## Research Line Description

**Title of Research Line:** Microbiology and Infection

**Coordinator:** Gil Castro

22 Microbiology and Infection

24 Objectives & Achievements

General objectives

Main achievements

25 Research Line output

Ten selected publications in peer reviewed journals

Collaborative publications within the Associate Laboratory in peer reviewed journals

PHD thesis completed







# Objectives & Achievements

## 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.

## 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, in an increasing number, MDs. Research within the MIRD is supported by 7 projects funded by FCT, 2 FP7 grants and 2 contracts with industry.

During the year of 2011, researchers from MIRD published 18 papers in international peer-reviewed journals, including 8 in Q1, and with an average IF of 3.6, with 1 paper in a journal with an IF around 10, and submitted 19 abstracts to International Meetings.

Researches within the MIRD were granted with 1 International and 2 National awards (Prémio Pulido Valente Ciência 2010; Best Oral Presentation MICRO-BIOTEC’11).

The MIRD organized 5 scientific meetings and 5 post-graduation courses and workshops and graduated 2 PhD-students and 4 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.

## Ten selected publications in peer reviewed journals

1. Madureira P, Andrade EB, Gama B, Oliveira L, Moreira S, Ribeiro A, Correia-Neves M, Trieu-Cuot P, Vilanova M, Ferreira P. Inhibition of IL-10 Production by Maternal Antibodies against Group B Streptococcus GAPDH Confers Immunity to Offspring by Favoring Neutrophil Recruitment. *PLoS Pathog.* 2011 Nov;7(11):e1002363. (IF=9,079)
2. Cunha C, Giovannini G, Pierini A, Bell AS, Sorci G, Riuzzi F, Donato R, Rodrigues F, Velardi A, Aversa F, Romani L, Carvalho A. Genetically-Determined Hyperfunction of the S100B/RAGE Axis Is a Risk Factor for Aspergillosis in Stem Cell Transplant Recipients. *PLoS One.* 2011;6(11):e27962. (IF=4,411)
3. Agostinho Carvalho, Nuno S. Osório, Margarida Saraiva, Cristina Cunha, Agostinho J. Almeida, Maria Teixeira-Coelho, Paula Ludovico, Jorge Pedrosa, Lucia Pitzurra, Franco Aversa, Luigina Romani, António G. Castro, Fernando Rodrigues. The C Allele of rs5743836 Polymorphism in the Human TLR9 Promoter Links IL-6 and TLR9 Up-Regulation and Confers Increased B-Cell Proliferation. *PLoS One.* 2011;6(11):e28256. (IF=4,411)
4. Silva A, Almeida B, Sampaio-Marques B, Reis MI, Ohlmeier S, Rodrigues F, Vale AD, Ludovico P. Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) is a specific substrate of yeast metacaspase. *Biochim Biophys Acta.* 2011 Dec;1813(12):2044-9. (IF=4,374)
5. Fraga AG, Cruz A, Martins TG, Torrado E, Saraiva M, Pereira DR, Meyers WM, Portaels F, Silva MT, Castro AG, Pedrosa J. *Mycobacterium ulcerans* triggers T cell immunity followed by local and regional but not systemic immunosuppression. *Infect Immun.* 2011 Jan;79(1):421-30. (IF=4,205)
6. Rodrigues PN, Gomes SS, Neves JV, Gomes-Pereira S, Correia-Neves M, Nunes-Alves C, Stolte J, Sanchez M, Appelberg R, Muckenthaler MU, Gomes MS. *Mycobacteria*-induced anaemia revisited: A molecular approach reveals the involvement of NRAMP1 and lipocalin-2, but not of hepcidin. *Immunobiology.* 2011 Oct;216(10):1127-34. (IF=4,114)
7. Sampaio-Marques B, Felgueiras C, Silva A, Rodrigues F, Ludovico P. Yeast chronological lifespan and proteotoxic stress: is autophagy good or bad? *Biochem Soc Trans.* 2011 Oct 1;39(5):1466-70. (IF=3,989)

8. Teixeira-Coelho M, Cruz A, Carmona J, Sousa C, Ramos-Pereira D, Saraiva AL, Veldhoen M, Pedrosa J, Castro AG, Saraiva M. TLR2 deficiency by compromising p19 (IL-23) expression limits T helper 17 cell responses to Mycobacterium tuberculosis. *Int Immunol*. 2011 Feb;23(2):89-96. (IF=3,403)
9. Costa-Ramos C, do Vale A, Ludovico P, dos Santos NM, Silva MT. The bacterial exotoxin AIP56 induces fish macrophage and neutrophil apoptosis using mechanisms of the extrinsic and intrinsic pathways. *Fish Shellfish Immunol*. 2011 Jan;30(1):173-81. (IF=2,892)
10. Carvalho A, Cunha C, Romani L. Immunity and tolerance to infections in experimental hematopoietic transplantation. *Best Pract Res Clin Haematol*. 2011 Sep;24(3):435-42. (IF=2,178)

#### **Collaborative publications within the Associate Laboratory in peer reviewed journals**

1. Pereira VH, Salgado AJ, Oliveira JM, Cerqueira SR, Frias AM, Fraga JS, Roque S, Falcão AM, Marques FM, Neves NM, Mano JF, Reis RL, Sousa N. In Vivo Biodistribution of arboxymethylchitosan/ Poly(amidoamine) Dendrimer Nanoparticles Following Intravenous Injection in Rats. *J Bioact Comp Polym*, 26:619-627 (2011).
2. Marques F, Sousa JC, Coppola G, Gao F, Puga R, Brentani H, Geschwind DH, Sousa N, Correia-Neves M, Palha JA. Transcriptome signature of the adult mouse choroid plexus. *Fluids Barriers CNS*, 8(1):10 (2011)
3. Roque R, Oliveira TG, Nobrega C, Barreira-Silva P, Nunes-Alves C, Sousa N, Palha JA, Correia-Neves M. Interplay between depressive-like behavior and the immune system in an animal model of prenatal dexamethasone administration. *Front Behav Neurosci*, 5:4 (2011)
4. Rada T, Santos TC, Marques AP, Correló VM, Frias AM, Castro AG, Neves NM, Gomes ME, Reis RL. Osteogenic differentiation of two distinct subpopulations of human adipose-derived stem cells: an in vitro and in vivo study". *J Tissue Eng Regen Med*. In press.

#### **PhD thesis completed**

1.

Student: Ana Mesquita

Title: New insights into the effects of caloric restriction on *Saccharomyces cerevisiae* chronological lifespan

Supervisor: Paula Ludovico

Institution: School of Health Sciences, University of Minho

2.

Student: Susana Roque

Title: Infection and mood disorders: A bidirectional interaction?

Supervisor: Margarida Correia Neves

Co-supervisor: Joana Palha

Institution: School of Health Sciences, University of Minho

## Research Line Description

**Title of Research Line:** Neurosciences

**Coordinator:** Nuno Sousa

28    Neurosciences

30    Objectives & Achievements

General objectives

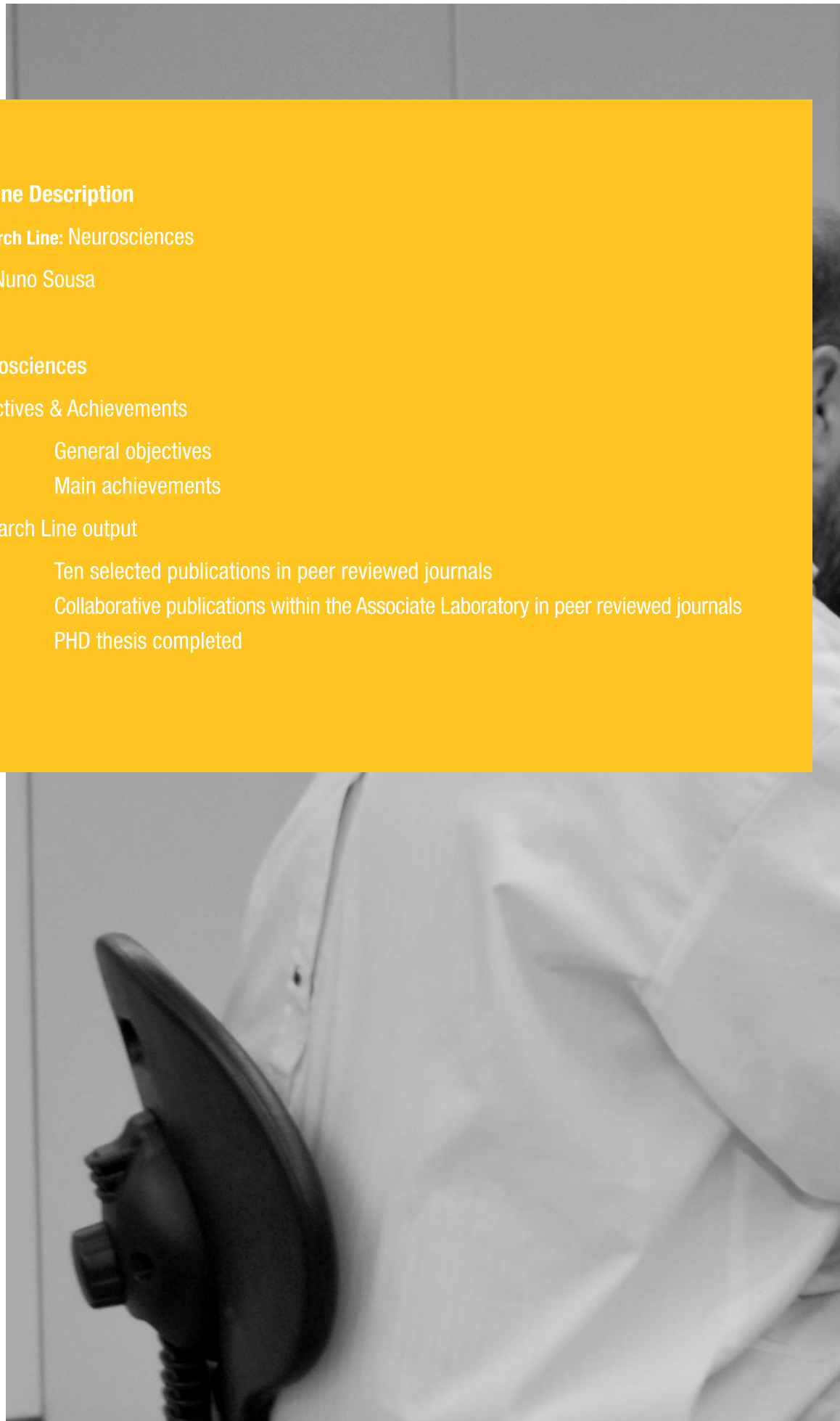
Main achievements

32    Research Line output

Ten selected publications in peer reviewed journals

Collaborative publications within the Associate Laboratory in peer reviewed journals

PHD thesis completed









# Objectives & Achievements

## 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.

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

## Main achievements

In 2011 the NERD published 31 papers in peer-reviewed journals.

In the last 5 years the NERD has published 129 papers in peer-reviewed journals. The mean impact factor is 4.8; of these, 3 have impact factor >25 and 8 >10. We have successfully finished 25 PhD and 24 Master theses. We have organized 13 international conferences/workshops.

Members of the NERD serve as members of Editorial Journals, and have reviewed for 33 journals. They have also integrated 6 review panels for international agencies and prizes.

Altogether, during this 5-year period, the NERD has been involved in 56 funded projects, of which we have led 95%. The source of funding is broad: 29% of projects are international and the remaining are supported by several national agencies (47% from FCT).

We have reinforced the translational/clinical focus of research; importantly, we successfully applied for a EU-FP7 Grant that involves preclinical and clinical studies, a multi-centered clinical consortium (HCP/QREN) and we initiated five clinical projects (in the scope of a recently created Clinical Academic Center).

The NERD has demonstrated an important capacity of continuity, renovation and expansion. Presently, the team is composed by 105 members, of which 35

hold a PhD (including members of the 3B's) and 70 are PhD and MSc students. 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). This increase in staff numbers has been planned according to the specific needs of the NERD available funding and development/implementation of new technical approaches.

# Research line output

## Ten selected publications in peer reviewed journals

1. Teixeira-Castro A, Ailion M, Jalles A, Brignull HR, Vilaça JL, Dias N, Rodrigues P, Oliveira JF, Neves-Carvalho A, Morimoto RI, Maciel P. Neuron-specific proteotoxicity of mutant ataxin-3 in *C. elegans*: rescue by the DAF-16 and HSF1 pathways. *Hum Mol Genet*, 20:2996-3009 (2011). (IF= 8,1)
2. Sotiropoulos I, Catania C, Pinto LG, Silva R, Pollerberg GE, Takashima A, Sousa N, Almeida O.F.X. Stress acts cumulatively to precipitate Alzheimer's disease-like TAU pathology and cognitive deficits. *J Neuroscience*, 31:7840-7847 (2011). (IF= 7.3)
3. Bettencourt C, Raposo M, Kazachkova N, Cymbron T, Santos C, Kay T, Vasconcelos J, Maciel P, Jardim L, Sequeiros J & Lima M. The  $\epsilon 2$  allele of APOE increases the risk of earlier age-at-onset in Machado-Joseph Disease (MJD/SCA3). *Arch Neurol*, 68:1580-1583 (2011). (IF= 7,1)
4. Butowski N, Chang S, Lamborn KR, Polley MY, Pieper R, Costa BM, Reis RM, Costello J, Vandenberg S, Parvataneni R, Nicole A, Kazmierski MH, Nicol S, Thornton DE, Prados MD. Phase II and Pharmacogenomics Study of Enzastaurin Plus Temozolomide During and Following Radiation Therapy in Patients With Newly Diagnosed Glioblastoma Multiforme and Gliosarcoma. *Neuro Oncology*, 12:1331-1338 (2011). (IF= 5,5)
5. Pereira DR, Silva-Correia J, Caridade SG, Oliveira JT, Sousa RA, Salgado AJ, Oliveira JM, Mano JF, Sousa N, Reis RL. Development of Gellan-Gum based Microparticles/Hydrogel Matrices for Application in the Intervertebral Disc Regeneration. *Tissue Eng Part C Methods*, 17:961-972 (2011). (IF= 4,6)
6. Paulo AC, Sampaio A, Santos NC, Costa PS, Cunha P, Zihl J, Cerqueira JJ, Palha JA, Sousa N. (2011). Patterns of Cognitive Performance in Healthy Ageing in Northern Portugal: A Cross-Sectional Analysis. *PLoS ONE*, 6(9):e24553. (IF= 4,4)
7. Yu S, Yang S, Holsboer F, Sousa N, Almeida OF. Glucocorticoid regulation of astrocytic fate and function. *PLoS One*, 6(7):e22419 (2011). (IF= 4,4)
8. Rodrigues AJ, Neves-Carvalho A, Teixeira-Castro A, Rokka A, Logarinho E, Maciel P. Absence of ataxin-3 leads to enhanced stress response in *C. elegans*. *PLoS One*, 6(4):e18512 (2011). (IF= 4,4)

9. Viana-Pereira M, Lee A, Popov S, Bax DA, Al-Sarraj S, Bridges L, Stávale JN, Hargrave D, Jones C, Reis RM. Microsatellite instability in paediatric high grade glioma is associated with genomic profile and differential target gene inactivation. *PlosOne*, 6(5): e20588 (2011). (IF= 4,4)

10. Costeira MJ, Oliveira P, Santos N, Ares S, Saenz-Rico B, Morreale de Escobar G, Palha JA. Psychomotor development of children from an iodine-deficient region. *J Pediatr*, 159:447-453 (2011). (IF=4,1)

#### **Collaborative publications within the Associate Laboratory in peer reviewed journals**

1. Carvalho MM, Teixeira FG, Sousa N, Salgado AJ. “Mesenchymal Stem Cells in the Umbilical Cord: Phenotypic Characterization, Secretome and Applications in Central Nervous System Regenerative Medicine”. *Current Stem Cell Research and Therapy*, 6(3): 221-228 (2011).

2. Cerqueira SR, Silva BL, Oliveira JM, Mano JF, Sousa N, Salgado AJ, Reis RL. Multifunctionalized CMChT/PAMAM dendrimer nanoparticles modulate the cellular uptake by astrocytes and oligodendrocytes in primary cultures of glial cells. *Macromolecular Bioscience*, 2011, in press.

3. Pereira DR, Silva-Correia J, Caridade SG, Oliveira JT, Sousa RA, Salgado AJ, Oliveira JM, Mano J, Sousa N, Reis RL. Development of Gellan-Gum based Microparticles/Hydrogel Matrices for Application in the Intervertebral Disc Regeneration. *Tissue Engineering – Part C*, 17(10): 961-972 (2011).

4. Pereira VH, Salgado AJ, Oliveira JM, Cerqueira SR, Frias AM, Fraga JS, Roque S, Falcão AM, Marques FM, Neves NM, Mano JF, Reis RL, Sousa N. In Vivo Biodistribution of Carboxymethylchitosan/Poly (amidoamine) Dendrimer Nanoparticles in Rats. *J Bioact Comp Polym*, 26:619-627 (2011)

5. Ribeiro CA, Salgado AJ, Fraga JS, Silva NA, Reis RI, Sousa N. The secretome of bone marrow Mesenchymal stem cells conditioned media varies with time and drives a distinct effect on mature neurons and glial cells (primary cultures). *J Tiss Engin Regen Med (TERM)*, 5:668-672 (2011).

6. Silva NA, Pires AO, Sousa RA, Sousa N, Salgado AJ, Reis RL. Interactions Between Schwann and Olfactory Ensheathing Cells with a Starch/Polycaprolactone Scaffold aimed at Spinal Cord Injury Repair. *Journal of Biomedical Materials Research – Part A*, 2011, in press.

## **PhD thesis completed**

1.

Student: Andreia Castro

Title: Identification of modulators of ataxin-3 proteotoxicity in animal models of Machado Joseph disease

Supervisor: Patrícia Maciel

Co-supervisor: Richard Morimoto

Institution: School of Health Sciences, University of Minho

2.

Student: Hugo Almeida

Title: Impact of chronic pain in emotional and cognitive behaviour in the rat: the effects of age and lateralization

Supervisor: Armando Almeida

Co-supervisor: Nuno Sousa

Institution: School of Health Sciences, University of Minho

3.

Student: Mário Oliveira

Title: The programming effects of antenatal exposure to corticosteroids in the brain

Supervisor: Nuno Sousa

Institution: School of Health Sciences, University of Minho

4.

Student: Marta Viana Pereira

Title: Molecular Genetics of Paediatric versus Adult Brain Tumours

Supervisor: Rui Manuel Vieira Reis

Institution: School of Health Sciences, University of Minho

5.

Student: Olga Martinho

Title: RTKs and MAPK pathway alterations in solid tumors: dissecting prognostic and therapeutic biomarkers

Supervisor: Rui Reis

Institution: School of Health Sciences, University of Minho

6.

Student: Susana Roque

Title: Infection and mood disorders: A bidirectional interaction?

Supervisor: Margarida Correia Neves

Co-supervisor: Joana Palha

Institution: School of Health Sciences, University of Minho

## Research Line Description

**Title of Research Line:** Surgical Sciences

**Coordinator:** Jorge Correia-Pinto

36 Surgical Sciences

38 Objectives & Achievements

General objectives

Main achievements

39 Research Line output

Ten selected publications in peer reviewed journals

Collaborative publications within the Associate Laboratory in peer reviewed journals

PHD thesis completed







# Objectives & Achievements

## 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.

## Main achievements

In 2011, the SSRD:

- i. Contributed for 31 papers published in peer-reviewed journals, which correspond to an accumulated IF of 123.3 (mean IF/paper of 4.2), from all publications we would like to emphasize one paper published in Nature;
- ii. Opened the “Endoscopic Research Lab” fully supported by KARL STORZ GmbH & Co. KG, which corresponded to an investment in equipment of over one Million of Euros;
- iii. Provided ten hand-on courses totally dedicated to surgeons from different specialties (ENT, Gastroenterology, General Surgery, Gynecology, Orthopedics, Pediatric Surgery, Urology) that were attended by over 100 MDs, most of them coming from abroad;
- iv. Got CE mark for personalized prosthesis and application devices to treat surgically Pectus Excavatum and other deformities of the thoracic cavity, through the iSurgical3D, Ltd (Spin-off from University of Minho emanated from our research activities).

# Research line output

## Ten selected publications in peer reviewed journals

1. Takeda Y, Costa S, Delamarre E, Roncal C, Leite De Oliveira R, Squadrito ML, Finisguerra V, Deschoemaeker S, Bruyère F, Wenes M, Hamm A, Sern-eels J, Magat J, Bhattacharyya T, Anisimov A, Jordan BF, Alitalo K, Maxwell P, Gallez B, Zhuang ZW, Saito Y, Simons M, De Palma M, Mazzone M. A switch in macrophage polarization induced by PHD2 haploinsufficiency prevents ischemic damage by inducing arteriogenesis. *Nature*. 479:122-26; 2011. (IF 36.104)
2. Olaru AV, Ghiaur G, Yamanaka S, Luvsanjav D, An F, Popescu I, Alexandrescu S, Allen S, Pawlik TM, Torbenson M, Georgiades C, Roberts LR, Gores GJ, Ferguson-Smith A, Almeida MI, Calin GA, Mezey E, Selaru FM. A microRNA downregulated in human cholangiocarcinoma controls cell cycle through multiple targets involved in the G1/S checkpoint. *Hepatology*. 54:2089-98; 2011. (IF 10.885)
3. Autorino R, Cadeddu JA, Desai MM, Gettman M, Gill IS, Kavoussi LR, Lima E, Montorsi F, Richstone L, Stolzenburg JU, Kaouk JH. Laparoendoscopic single-site and natural orifice transluminal endoscopic surgery in urology: a critical analysis of the literature. *Eur Urol*. 59:26-45; 2011. (IF 8.843)
4. Gettman MT, White WM, Aron M, Autorino R, Averch T, Box G, Cadeddu JA, Canes D, Cherullo E, Desai MM, Frank I, Gill IS, Gupta M, Haber GP, Humphreys MR, Irwin BH, Kaouk JH, Kavoussi LR, Landman J, Liatsikos EN, Lima E, Ponsky LE, Rane A, Ribal M, Rabenhalt R, Rao P, Richstone L, Sawyer MD, Sotelo R, Stolzenburg JU, Tracy CR, Stein RJ. Endourological Society NOTES and LESS Working Group; European Society of Urotechnology NOTES and LESS Working Group. Where Do We Really Stand With LESS and NOTES? *Eur Urol*. 59:231-4; 2011. (IF 8.843)
5. Teixeira-Castro A, Ailion M, Jalles A, Brignull HR, Vilaça JL, Dias N, Rodrigues P, Oliveira JF, Neves-Carvalho A, Morimoto RI, Maciel P. Neuron-specific proteotoxicity of mutant ataxin-3 in *C. elegans*: rescue by the DAF-16 and HSF1 pathways. *Hum Mol Genet*. 20:2996-3009; 2011. (IF 8.058)
6. Rolanda C, Silva D, Branco C, Moreira I, Macedo G, Correia-Pinto J. Peroral esophageal segmentectomy and anastomosis with single transthoracic trocar: a step forward in thoracic NOTES. *Endoscopy*. 43:14-20; 2011. (IF 6.096)

7. Soares JB, Gonçalves R, Rolanda C. Endoscopic resection of a large colonic lipoma by unroofing technique. *Endoscopy*. 43:E407; 2011. (IF 6.096)
8. Almeida MI, Reis RM, Calin GA. BRCA1, microRNAs and cancer predisposition: Challenging the dogma. *Cell Cycle*. 10:377; 2011. (IF 4.999)
9. Moura RS, Coutinho-Borges JP, Pacheco AP, daMota PO, Correia-Pinto J. 2011. FGF signaling pathway in the developing chick lung: expression and inhibition studies. *PLoS ONE*. 6:e17660; 2011. (IF 4.411)
10. Goers TA, Leão P, Cassera MA, Dunst CM, Swanström LL. Concomitant Endoscopic Radiofrequency Ablation and Laparoscopic Reflux Operative Results in More Effective and Efficient Treatment of Barrett Esophagus. *J Am Coll Surgeons*. 213: 486-92; 2011 (IF 4.241)

#### **Collaborative publications within the Associate Laboratory in peer reviewed journals**

1. Costa BM, Viana-Pereira M, Fernandes R, Costa S, Linhares P, Vaz R, Pinheiro C, Lima J, Soares P, Silva A, Pardal F, Amorim J, Nabiço R, Almeida R, Alegria C, Pires MM, Pinheiro C, Carvalho E, Oliveira P, Lopes JM, Reis RM. Impact of EGFR genetic variants on glioma risk and patient outcome. *Cancer Epidemiol Biomarkers Prev*, 20:2610-7 (2011).
2. de Mello RA, Ferreira M, Costa BM, Pires F, Neves I, Duarte N, Figueiredo F, Guimaraes J T, Hespanhol V, Reis RM. Association Between +61 A/G Polymorphism in the EGF Gene and Non-Small Cell Lung Cancer Risk in Male. *European Journal of Cancer*, 47 (1):635-635 (2011).
3. Vilaça N, Amorim R, Martinho O, Reis RM, Baltazar F, Fonseca AM, Neves IC. Encapsulation of a-cyano-4-hydroxycinnamic acid into a NaY zeolite, *J Mater Sci*. 46:7511-7516 (2011).

#### **PhD thesis completed**

1.

Student: Caroline Sheeba

Title: Molecular parallelism between vertebrate limb development and somitogenesis

Supervisor: Isabel Palmeirim

Co-supervisor: Jorge Correia-Pinto

Institution: School of Health Sciences, University of Minho

2.

Student: Marta Viana Pereira

Title: Molecular Genetics of Paediatric versus Adult Brain Tumours

Supervisor: Rui Manuel Vieira Reis

Institution: School of Health Sciences, University of Minho

3.

Student: Olga Martinho

Title: RTKs and MAPK pathway alterations in solid tumors: dissecting prognostic and therapeutic biomarkers

Supervisor: Rui Reis

Institution: School of Health Sciences, University of Minho

4.

Student: Tatiana Resende

Title: Temporal control of vertebrate embryo development: the role of Sonic Hedgehog in somite segmentation

Supervisor: Isabel Palmeirim

Co-supervisor: Raquel Andrade

Institution: School of Health Sciences, University of Minho







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