General Information

Name of Research Unit: (LA-LVT-4) Instituto de Tecnologia Química e Biológica - ITQB

Coordinator: Luis Paulo da Silva Nieto Marques Rebelo

Main Scientific Domain: Engenharia Química e Biotecnologia

Other Subdomains: n/a

Host Institutions

Leading Host Institution: Instituto de Tecnologia Química e Biológica

Other Institutions Involved: Fundação Calouste GulbenkianFaculdade de Ciências Médicas - Universidade Nova de LisboaInstituto de Biologia Experimental e TecnológicaInstituto Gulbenkian de CiênciaInstituto de Tecnologia Química e Biológica

Objectives & Achievements

Unit Description

Since January 1, 2011, the current LA-ITQB is a successor of a previous, smaller consortium, signed in 2001, between ITQB, IBET, and a few groups of IGC, which, in turn, constituted one of the first Laboratórios Associados in Portugal. In its present form, it is now a much wider partnership involving the Instituto de Tecnologia Química e Biológia (ITQB; www.itqb.unl.pt), the Instituto Gulbenkian de Ciência (IGC; www.igc.gulbenkian.pt), the Instituto de Biologia Experimental e Tecnológica (IBET; www.ibet.pt) and the Centro de Estudos de Doenças Crónicas (CEDOC-UNL; www.cedoc.org). Detailed descriptions of the four institutes, their organization and management, can be found in their respective websites. It is at present one of the broadest in scientific expertise, spanning from Chemistry to Medicine, i.e., from "the molecule to the clinical".
In particular, the aforementioned expansion of the LA-ITQB was the natural outcome of a new architecture of the thematic lines (see next section), which aimed at increasing the breadth of the science and technology made in Oeiras, fostering the interaction between the partners, and optimizing the available resources.
Since 2001 (the original foundation date of the LA), its institutions published circa 2,800 WoS articles, received 47,000 WoS citations, and were responsible during the last five years for 50% of the national publications (as leading institution) in Nature and Science, 50 % of the ERC's in Life Sciences awarded to Portugal as well as 50 % of the Howard Huges Medical Institute grants in the country. On average, they have attracted more than 3 Meuros per year through contracts with private companies, and contributed to launch 9 spinoff companies (last five years).
The institutes have established an efficient communication network, which allows sharing infrastructures, such as libraries, scientific and academic services, and administration support. The network fosters the participation of staff in the scientific life of each one of the four institutes.
The organization and management of the LA can be summarized as follows:
The General Council is constituted by the Rector of the Universidade Nova de Lisboa, the President of the Administration Board of Fundação Calouste Gulbenkian, and the President of IBET. It meets once a year and supervises and establishes general guidelines for the partnership. The functions of the General Council are usually delegated to the Direction.
The Direction is composed of the Directors of the four institutes and ensures management of the common activities of the LA. It plays a central role in the choice of new collaborators, in the development of the scientific goals, and in the financial decisions.
The Scientific Advisory Board (SAB) of the LA is composed of representatives from the SABs of the institutions. The SAB elaborates periodical assessments, namely those related to the annual report and plan, and the activities of the LA.
The LA uses the ITQB Administrative Services for the management of its financial and human resources.

General Objectives

The objectives of this LA, one of very wide scientific expertise, can be summarized in the goals of its research themes. Briefly:
Theme 1 - Synthesis, structure, and function of biologically important molecules.
Understanding the living world, and actions to control health/disease, requires a deep knowledge of the composition and structure of biomolecules, their function, and mechanisms for their formation, fate, role in the cell, the organism, and in the environment. Emerging between chemistry and biology, this endeavour has reached medicine, as prime partner of the drug design process. A rare combination of expertises sets the LA to pursue fundamental and industrially relevant targets.
Theme 2 - From genetics, cell and developmental biology to pathogenesis and novel therapies.
Pursue cutting-edge fundamental studies in genetics, genomics, cell and molecular biology, and developmental biology. Apply this knowledge to understand the molecular, cellular and physiological basis of disease and develop animal models of human disease. Develop tools for cell- and gene-based therapies, test them in preclinical studies on disease models, and develop the infrastructure and know-how to carry out clinical trials.
Theme 3 - Computational and theoretical biology: from biochemistry to medicine.
Theoretical and computational approaches are now key players in biology. The LA has a privileged position, since it hosts the largest concentration of computational and theoretical biology groups in Portugal, working alongside experimental researchers in problems ranging from molecules to systems, organisms, and populations.
Theme 4 - Host-microbe and host-cancer interactions.
Pathogens induce tissue and cell-specific responses in the host. Similarly, in cancer, the "host" undergoes changes in response to the tumour. Research will focus on the induction of host-specific responses, including cell:pathogen, cell:cell, cell:matrix and cell:molecules communications, cell invasion and migration, and the selection of metabolic traits that accompany and determine the response of the host. This may contribute to the discovery and design of novel, host- and disease-specific targeted therapies.
Theme 5 - Plant genomics and stress responses.
Research in plants in the post-genomic era requires an integrated approach to the organism, considering its individual parts and their relationships, as well as its insertion in the environment, with both the biotic community and the abiotic surroundings. A variety of expertises and technologies is thus crucial, requiring the complementary competences available within the LA.
Theme 6 - Evolution of ecosystems, biological risk, and food safety.
Research will focus on microbial communities in the environment and their evolution, specially on human-associated microbial communities. The evaluation of tools for managing human and animal health and disease, like new diagnostic tools, vaccines, antibiotics, anti-inflammatories, and bioactive compounds (including food additives), are solid areas within the LA, setting the ground for further research and education in epidemiology, and biological risk.

Main Achievements during the year of 2011

Statistical highlights:
425 WoS articles
More than 10,000 WoS citations
45 Highly Cited Papers (world top 1%)
Average of one PhD thesis awarded per week
More than 380 running financed projects
More than 3.5 Meuros income in I&D contracts with the private sector
More than 5 Meuros income from European Projects
Scientific highlights:

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Relatório Científico

- Entrada
- Ajuda
- Print

FCT Relatório Científico 2011 Print: 23-04-2012 12:11:12 [Instituto de Tecnologia Química e Biológica]
Group Description

Title of Research Group:	(RG-LVT-50004-4026) Morphological Patterns of Disease and Tumor Microenvironment
Principal Investigator:	Ana Maria Félix de Campos Pinto
Main Scientific Domain:	n/a
Group Host Institution:	n/a

Funding, source, dates

Funding, source, dates

"Role of Lactate Rich Microenvironment in Uterine Cervix Cancer Progression", FLAD - Refª 094/2011, FLAD, 6.000 , from April 2011.

Merck Sharp & Dohme, Limitada, 500,00 (fund received during 2011).

"Os transportadores de monocarboxilatos (MCTs) como possíveis alvos terapêuticos em leucemia mielóide aguda (LMA)", Terry Fox 2011, LPCC-Canada Embassy, 15.000 , from March 2011.

Objectives & Achievements

Objectives

The main aim of our group is to analyse morphological patterns of disease with particular reference to tumor microenvironment, using human cancers.

More specifically:

- To study the role of HPV in human carcinomas

- To identify biomarkers in ovarian cancer cells that can serve as indicators for sensitivity or resistance to vorinostat

- To identify Biological Predictors of Survival in Lymphoma and Mechanisms Underlying Follicular Lymphoma Transformation Into Diffuse Large B-cell Lymphoma

Main Achievements

The progresses registered in 2011 are the following:

- prognosis in vaginal carcinoma regarding the role of HPV in human carcinomas

- establisment of primary cell lines regarding the identification of biomarkers in ovarian cancer cells that can serve as indicators for sensitivity or resistance to vorinostat.

Group Productivity

Internationalization

Collaboration with Randy D. Gascoyne from the institute British Columbia Cancer Agency, Canada, in several projects in the context of the theme Translational Research in Lymphoma.

Collaboration with Bosh X from the institution in Spain Servei d Epidemiologia i Registre del Càncer do Institut Catalá Oncologic Spain within the project International Epidemologic Study of Worldwide Distribution of Type-specific HPV DNA in Cancers of the Vulva, Vagina, Anus and Head and Neck Cancers (HPV VVAPO) Study Group .

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FCT Relatório Científico 2011 Print: 23-04-2012 12:11:13 [Instituto de Tecnologia Química e Biológica]
Group Description

Title of Research Group:	(RG-LVT-50004-4027) Molecular Endocrinology
Principal Investigator:	Branca Maria Prudêncio Limón Cavaco
Main Scientific Domain:	n/a
Group Host Institution:	n/a

Funding, source, dates

Funding, source, dates

Identification of genes involved in familial thyroid cancer using the new Single Nucleotide Polymorphisms (SNP)-Arrays and Large Scale Resequencing technologies ,NRS/LPCC-Terry-Fox 2009/2011, Núcleo Regional do Sul da Liga Portuguesa Contra o Cancro-Terry-Fox 2009/2011, 15000 , from 01-04-2009 to Extended end date 31-03-2012.

Evaluation of CDKN3, ESRP1 and ESRP2 genes as potential new targets for the treatment of anaplastic thyroid carcinomas , Sociedade Portuguesa de Endocrinologia Diabetes e Metabolismo (S.P.E.D.M.), SPEDM Scholarship for Research projects - 2010, 7500 euros, from 01-04-2011 to 31-03-2013.

Identification of novel genes associated with sporadic medullary thyroid carcinoma using the microarray technology , Sociedade Portuguesa de Endocrinologia Diabetes e Metabolismo (S.P.E.D.M.)./ Genzyme em Patologia da Tiróide, Scholarship Prof. E. Limbert SPEDM/Genzyme 2009, 5000 euros, from 22-03-2010 to 21-03-2011.

Objectives & Achievements

Objectives

Objectives for 2011:

1. To identify genes predisposing to familial nonmedullary thyroid carcinoma (FNMTC)

Molecular genetics studies suggest that FNMTC is a disease with high genetic heterogeneity, and the underlying molecular basis, which has been defined for less than 1% of the families, is virtually unknown.

In this topic, we aimed to identify potential pathogenic mutations in FNMTC candidate genes, selected either because they were located in previously mapped susceptibility regions, or because they were involved in thyroid differentiation and function. The functional characterisation of putative mutations identified, and the demonstration of their oncogenic role, was also pursued. Furthermore, we also aimed to explore the use of the new technology of whole-exome sequencing to identify pathogenic mutations in FNMTC susceptibility genes.

2. To discover novel therapeutic targets for poorly differentiated (PDTC) and anaplastic thyroid carcinomas (ATC)

Poorly-differentiated (PDTC) and, principally, the anaplastic (undifferentiated) thyroid carcinomas (ATC), present a rapid onset, extensive invasion and distant metastases. In fact, ATC are among the most lethal human malignancies, with a median survival of 3-4 months.

In this topic, we aimed to study genes involved in PDTC and ATC most deregulated molecular pathways, identified by genome-wide gene expression profiling. We specifically aimed to characterize the role of genes encoding critical regulators of cell cycle, such as cyclin-dependent kinase inhibitors (CDKI).

3. To unveil genetic alterations underlying medullary thyroid carcinoma (MTC) tumourigenesis and progression, which may represent novel therapeutic targets for MTC

We have earlier reported a series of fifty-one sporadic medullary thyroid carcinomas (MTC) with 64.7% of RET mutation positive and 35.3% of RET mutation negative cases.

In this topic, we aimed to define the role of the proto-oncogenes H, N and K-RAS, PIK3CA, AKT1, AKT2 and AKT3, in the development of sporadic RET negative MTC.

4. To study the familial predisposition to parathyroid-related endocrine neoplasia diseases

Our group has set up a collaboration with several Portuguese Departments of Endocrinology for the collection and genetic diagnosis of multiple endocrine neoplasia type 1 (MEN1), and the hereditary hyperparathyroidism and jaw tumour (HPT-JT) syndromes.

In this topic, we aimed to characterise the clinical and genetic features of patients with MEN1 and HPT-JT, in order to improve our understanding of these disorders.

Main Achievements

Main Achievements in 2011:

1. Identification of genes predisposing to familial nonmedullary thyroid carcinoma (FNMTC)

a) We found evidence of association between variants of a transcription factor required for thyroid differentiation and function (FOXE1) and thyroid cancer risk, in sporadic and familial NMTC cases from the Portuguese population.

b) We analysed transcription factors that play an essential role in thyroid development and differentiation (FOXE1, NKX2.1, HHEX and PAX8). Two missense variants, identified in the FOXE1 and HHEX genes, segregated with thyroid cancer in two families with FNMTC. These variants were absent in Portuguese controls, and affected evolutionarily conserved amino acid residues, suggesting that they could represent pathogenic mutations. We prepared plasmid vectors with FOXE1 mutated and wild type cDNA, and started functional characterization of the FOXE1 mutation. Preliminary data suggested that the mutated gene increased thyroid cell migration. One Master Thesis in this topic was completed.

c) We initiated whole-exome sequencing analyses of genomic DNA from the probands of two representative FNMTC families, in order to identify potential pathogenic variants. DNA samples were sent to a company, which provides whole-exome sequencing analysis, using Agilent and Illumina technologies. Sequencing results were only available in February 2012.

2. Identification of novel therapeutic targets for poorly differentiated (PDTC) and anaplastic thyroid carcinomas (ATC)

a) As both PDTC and ATC expression profiles suggested a highly deregulated proliferation, we searched for mutations in genes that encode critical regulators of cell cycle: TP53 (p53), and CDKIs, such as CDKN2A (p14/p16), CDKN2B (p15) and CDKN1B (p27). We analysed 24 PDTC and 19 ATC. We found mutations in the TP53 (PDTC 27%; ATC 56%), CDKN2A (PDTC 8%; ATC 16%) and CDKN2B (PDTC 0%; ATC 7%) genes. This preliminary data suggested that CDKN2A, CDKN2B and TP53 are involved in the development of PDTC and ATC, and may represent therapeutic targets for these tumours.

b) For another CDKI, CDKN3 (KAP), over-expressed in the ATC samples, we found an increasing expression of CDKN3 full-length transcript from normal tissues to WDTC and to PDTC. ATC had the highest mRNA levels, but these were associated to expression of both functional full-length transcripts and aberrant splice variants (predicted to originate truncated proteins). Characterisation of CDKN3 protein expression in ATC is ongoing.

This Project received a Research Grant from Sociedade Portuguesa de Endocrinologia Diabetes e Metabolismo (SPEDM).

3. Identification of genetic alterations underlying medullary thyroid carcinoma (MTC) development

a) We investigated the involvement of RAS proto-oncogene in the development of sporadic RET negative MTC. This study showed that RAS mutations were present in 68.0% of the RET negative and in only 2.5% of the RET positive MTC (P

b) We also initiated the analysis of novel candidate genes (PIK3CA, AKT1, AKT2 and AKT3) in 8 MTC, that were RET and RAS negative, but did not find potential pathogenic mutations.

4. Study the familial predisposition to parathyroid-related endocrine neoplasia diseases

We identified the first large germline deletion of the HRPT2 gene, a finding that emphasized that quantitative PCR should be implemented in HRPT2 molecular analysis, improving genetic assessment and clinical management of patients with HPT-JT. The results of this work were published in the Endocrine Pathology (Endocr Pathol 22:44 52, 2011).

Group Productivity

Publications in peer review Journals

1. Cavaco, B.M., et al. Identification of De Novo Germline Mutations in the HRPT2 Gene in Two Apparently Sporadic Cases with Challenging Parathyroid Tumor Diagnoses. Endocrine Pathology 22, 44-52 (2011). http://dx.doi.org/10.1007/s12022-011-9151-1; ISI IF: 1.568. This article was selected by Faculty of 1000 Medicine.

2. Moura, M.M., Cavaco, B.M., Pinto, A.E. & Leite, V. High Prevalence of RAS Mutations in RET-Negative Sporadic Medullary Thyroid Carcinomas. Journal of Clinical Endocrinology & Metabolism 96, E863-E868 (2011). http://dx.doi.org/10.1210/jc.2010-1921; ISI IF: 6.495

Internationalization

Collaborations with Graham Williams (Molecular Endocrinology Laboratory, Hammersmith Campus, London, UK) in the context of the project Identification of genes involved in familial thyroid cancer using the new Single Nucleotide Polymorphisms (SNP)-Arrays and Large Scale Resequencing technologies .

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Group Description

Title of Research Group:	(RG-LVT-50004-4028) Membrane Traffic in Disease
Principal Investigator:	Duarte Custal Ferreira Barral
Main Scientific Domain:	n/a
Group Host Institution:	n/a

Funding, source, dates

Funding, source, dates

"Role of Arl13b in endocytic trafficking", Research Executive Agency / EU, PIRG05-GA-2009-247726, 100.000,00 , from 01-10-2009 to 31-09-2013.

Objectives & Achievements

Objectives

Our general goal is to define regulatory mechanisms of intracellular vesicular trafficking and their role in infection and human disease. For this, we study the function of small GTPases of the Rab and Arf families.

Members of the Arf family, when mutated, affect primary cilia and cause ciliopathies, such as Bardet-Biedl and Joubert syndromes. These are characterized by obesity, polydactyly, renal cysts, retinal degeneration and neurological defects. Primary cilia are mechanosensory organelles that detect and transmit chemical and mechanical signals from the extracellular environment to the cell s interior and are present in almost all cell types in mammals. In particular, we are interested in studying the role of Arl13b, a member of the Arl (Arf-like) subfamily of small GTPases that we found to be involved in endocytic recycling trafficking. The function of Arl13b is currently unknown. However, some reports suggest that Arl13b is involved in the assembly of cilia. Therefore, we aim to determine the role of Arl13b in ciliary cargo trafficking and also the mechanism by which Arl13b could regulate endocytic trafficking. For 2011 our specific aims were:

- To discover Arl13b effectors

- To determine the role of the interaction between Arl13b and the actin cytoskeleton

- To investigate if Arl13b is involved in ciliary trafficking

- To produce recombinant Arl13b for crystallization studies

Membrane trafficking has also been shown to play essential roles in microbial infection. These families of proteins are prominently involved in phagocytosis, which normally leads to the degradation of the infectious agents. Moreover, several microbes can manipulate these proteins in order to escape degradation and evade the immune system. Recently, macrophage apoptosis was described as a novel defense mechanism against tuberculosis. Interestingly, it was also observed that ongoing membrane repair abrogates damage to the macrophages and prevents release of intracellular mycobacteria by resealing large pores in cellular membranes. However, virulent Mycobacterium tuberculosis (Mtb) can subvert membrane repair,

constituting an immune-evasion strategy. Therefore, membrane repair could be the critical mechanism that results in impermeability of the apoptotic macrophage leading to containment of Mtb and its products within the phagosome. Therefore, we aim to characterize the mechanisms involved in plasma membrane repair and the identification of mycobacterial factors that interfere with this process.

Main Achievements

We started the search for Arl13b effectors by co-imunoprecipitation and discovered an interacting protein, namely inositol 3-phosphate synthase 1. We plan now to validate this interaction and determine if it is a bona fide effector.

We also found that Arl13b localizes to circular dorsal ruffles (CDRs), which are actin-based structures involved in the internalization of signaling receptors from the plasma membrane and the recycling of integrins that are essential for cell migration, and that Arl13b could regulate the formation of these CDRs.

Finally, we succeeded in producing and purifying recombinant Arl13b that will now be used for crystallization studies, in collaboration with the group of Dr. Margarida Archer from ITQB.

We also participated in the characterization of the role of another Arl protein, Arl8b, in lysosomal trafficking, antigen presentation and microbial killing (Garg S, et al. Immunity 35(2):182-193).

Finally, the group was awarded a prestigious Harvard Medical School-Portugal Program grant to develop the project on the pathogenesis of Mtb and the work started at the end of the year.

Group Productivity

Publications in peer review Journals

1- Casalou, C., et al. Cholesterol Regulates VEGFR-1 (FLT-1) Expression and Signaling in Acute Leukemia Cells. Molecular Cancer Research 9, 215-224 (2011). http://dx.doi.org/10.1158/1541-7786.mcr-10-0155; ISI IF: 4.373

Internationalization

Collaborations with Michael B. Brenner (Brigham and Women´s Hospital, Harvard Medical School - USA) and Tamara Caspary (Emory University USA) in the context of the project: Role of Arl13b in endocytic trafficking.

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Group Description

Title of Research Group:	(RG-LVT-50004-4029) Purines and Anti-HIV Drugs Pharmacology
Principal Investigator:	Maria Emília Carreira Saraiva Monteiro
Main Scientific Domain:	n/a
Group Host Institution:	n/a

Funding, source, dates

Funding, source, dates

FCT/MCTES, PTDC/SAU-ORG/111417/2009, 100.000,00 , 01-03-2011 to 28-02-2014.

FCT/MCTES, PTDC/SAU-TOX/111663/2009, 131.188,00 (total) 75.388,00 (CEDOC), 15-03-2011 to 14-03-2014.

FCT/MCTES, PTDC/SAU-TOX/112264/2009, 194.240,00 , 15-03-2011 to 14-03-2014.

FCT/MCTES, PTDC/QUI-QUI/113910/2009, 133.000,00 , 01-02-2011 to 31-01-2014 (participant).

Accções Integradas - E-109/10, CRUP, 2.000,00 , 01-01-2010 to 2012.

FCT/CEDOC (I&D/LAO), 29.884,74 , 2011.

"Master in Clinical Research NOVA/Northeasthern University". APIFARMA; Fundação Calouste Gulbenkian; FLAD, 98.000,00 , 2010 to 2012.

"Produção e Monitorização de Normas de Orientação Clínica". DGS- Direcção Geral de Saúde, 153/2010/SCA/DGS, 31.000,00 , 01-12-2010 to 2012.

FCT/MCTES, PTDC/SAU-ORG/11149/2009, 100.000,00 , 2011 to 2014.

Objectives & Achievements

Objectives

The group includes 3 subareas that established the following main objectives for 2011:

1. Carotid Body:

1.1. Initiate the 2 FCT/MCTES projects in the area

1.2. Install the model of hypertension in rats caused by chronic intermittent hypoxia

1.3. Publish the results in aged animals

1.4. Publish the results related to the role of ATP/adenosine in carotid body function depending on the intensity of hypoxia

1.5. Follow a cohort of obstructive sleep apnea patients in Hospital Pulido Valente to identify the profile of consumption of anti.hypertensive drugs.

2. PK/PD of antiretrovirals:

2.1. Start the 2 FCT/MCTES projects in the field and obtain the first results in vitro and in humans concerning the identification of reactive metabolites and protein adducts of abacavir and nevirapine

3. Clinical Pharmacology:

3.1. Ensure the 1st curricular year of the Master in Clinical Research and identify the research projects of the 20 physicians enrolled in the course.

3.2. Prepare, and submit to public discussion the 4 guidelines for rational prescription included in the project with the Direção Geral de Saúde

3.3. Participate in the application to the 7FP European project that will allow the conditions to establish a Portuguese Platform for Clinical research Infrastructures

Main Achievements

The main achievements of each of the subareas were:

4. Carotid Body:

4.1. A PhD thesis of Teresa Monteiro was successfully discussed

4.2. The 2 FCT/MCTES grants in the area started in March 2011 and the model of hypertension in rats caused by chronic intermittent hypoxia is ongoing. The BIC were successfully recruited

4.3. At the end of 2011 , 189 patients were included in the cohort of obstructive sleep apnea patients in Hospital Pulido Valente followed to identify the profile of consumption of anti.hypertensive drugs includes.

Publications:

Monteiro TC, Batuca JR, Obeso A, Gonzalez C, Monteiro EC. Carotid Body Function in Aged Rats: responses to Hypoxia Ischemia, Dopamine and Adenosine. Age, 33:337-50. (FI: 6.280)

Nunes AR, Sample V, Monteiro EC, Gauda EB and Zhang J. Bicarbonate-sensitive soluble and trasmembrane adenylylcyclases in peripheral and central CO2 chemoreceptors. (submetido)

Conde SV, Obeso A, Monteiro EC and Gonzalez C. Mechanisms of carotid body acclimatization to sustained hypoxia effects of chronic caffeine ingestion. (submetido)

Conde SV, Monteiro EC, Rigual R, Obeso A and Gonzalez C. Hypoxic intensity: a determinant for the contribution of ATP and adenosine to the genesis of carotid body chemosensory activity. J. Appl. Physiol. (in press) (FI: 4.235)

Conde SV, Nunes da Silva T, Gonzalez C, Carmo MM, Monteiro EC and Guarino MP. Chronic caffeine intake decreases circulating catecholamines and prevents diet-induced insulin resistance and hypertension in rats. Br J Nutr. 107:86-95. (FI:3.072)

Gonzalez-Martín MC, Vega-Agapito MV, Conde SV, Castañeda J, Bustamante R, Olea E, Perez-Vizcaino F, Gonzalez C and Obeso A. Carotid body function and ventilatory responses in intermittent hypoxia. Evidence for anomalous brainstem integration of arterial chemoreceptor inputJ Cell Physiol. 226, 1961-1969. Factor impacto: 3.986.

5. PK/PD of antiretrovirals:

The two grants (Hepatic toxicity in HIV-infected individuals exposed to nevirapine , Hepatic toxicity in HIV-infected individuals exposed to nevirapine started in 15-03-2011; Bioactivation routes of the anti - HIV drug Nevirapine: identification of reactive metabolites and mutagenic potential., Bioactivation routes of the anti - HIV drug Nevirapine: identification of reactive metabolites and mutagenic potential. and the recruitment of the BIC completed.

Publications:

Charneira C, Godinho AL, Oliveira MC, Pereira SA, Monteiro EC, Marques MM, Antunes AM. Reactive aldehyde metabolites from the anti-HIV drug abacavir: amino acid-adducts as possible factors in abacavir toxicity. Chem Res Toxicol. 24 (12): 2129-41. (FI: 4.148)

Antunes A.M, Charneira C, Pereira SA, Monteiro EC, Marques MM. Abacavir hypersensitivity: hemoglobin N-terminal valine adduct as a possible biomarker. Mutagenesis, 26, 699.

Marinho A, Godinho A, Faustino I, Antunes A, Pereira S. Biomonitorização do fármaco anti-HIV Nevirapina: abordagem metodológica. Saúde & Tecnologia 2011 (Suplemento).

Caixas U, Antunes AMM, Marinho A, Godinho A, Marques MM, Oliveira MC, Branco T, Monteiro EC, Pereira SA. Hemoglobin n-terminal valine adducts from nevirapine in HIV-infected patients as evidence for nevirapine haptenation ability upon bioactivation. (submitted).

6. Clinical Pharmacology:

6.1. The 1st curricular year of the Master in Clinical Research was accomplished successfully with only 1 drop out. The 2 edition was launched

6.2. The 4 guidelines for rational prescription were published by Direção Geral de Saúde :

6.2.1. Supressão Ácida: Utilização dos Inibidores da Bomba de Protões e das suas Alternativas Terapêuticas (nº 036/2011)

6.2.2. Antibioterapia na Pneumonia Adquirida na Comunidade em Adultos Imunocompetentes (nº45/2011)

6.2.3. Anti-inflamatórios não esteróides sistémicos em adultos: orientações para a utilização de inibidores da COX-2 (nº 13/2011)

6.2.4. Utilização e seleção de anti-agregantes plaquetários (nº 014/2011)

6.3. The grant European Clinical Research Infrastructures Network Integrating activity (ECRIN - IA) - Facilities and resources for multinational clinical trials 7FP-CP-CSA-Infra Integrating Activities / e-Infrastructures nº 284395 was approved funded and initiates in January 2012

Group Productivity

Publications in peer review Journals

1 - Antunes, A., Charneira, C., Pereira, S., Monteiro, E. & Marques, M. Abacavir hypersensitivity: hemoglobin N-terminal valine adduct as a possible biomarker. Mutagenesis 26, 699. http://dx.doi.org/10.1093/mutage/ger026; IF: 3.983

2 - Charneira, C., et al. Reactive Aldehyde Metabolites from the Anti-HIV Drug Abacavir: Amino Acid Adducts as Possible Factors in Abacavir Toxicity. Chemical Research in Toxicology 24, 2129-2141 (2011). http://dx.doi.org/10.1021/tx200337b; ISI IF: 4.140

3 - Gonzalez-Martin, M.C., et al. Carotid Body Function and Ventilatory Responses in Intermittent Hypoxia. Evidence for Anomalous Brainstem Integration of Arterial Chemoreceptor Input. Journal of Cellular Physiology 226, 1961-1969 (2011). http://dx.doi.org/10.1002/jcp.22528; ISI IF:3.986

4 - Monteiro, T.C., Batuca, J.R., Obeso, A., Gonzalez, C. & Monteiro, E.C. Carotid body function in aged rats: responses to hypoxia, ischemia, dopamine, and adenosine. Age 33, 337-350 (2011). http://dx.doi.org/10.1007/s11357-010-9187-z; ISI IF:6.280

Other international publications

Conference Papers:

1 - Conde, S., Antunes, D., Ribeiro, M., Gonzalez, C. & Guarino, M. Effect of chronic caffeine administration on Glut4 expression and plasma catecholamines in high sucrose diet rats. Diabetologia 54, S227 (2011). 47th Annual Meeting, European Association for the study of diabetes. ISI IF: 6.973

2 - Guarino, M., Gonzalez, C., Monteiro, E., Carmo, M. & Conde, S. Carvedilol restores insulin sensitivity in high sucrose and high fat diets rats through blockade of the sympathetic nervous system. Diabetologia 54, S243 (2011). Conference paper. ISI IF: 6.973

Other national publications

1 - Marinho, A., Godinho, A., Faustino, I., Antunes, A. & Pereira, S. Biomonitorização do fármaco anti-HIV Nevirapina: abordagem metodológica. Saúde & Tecnologia (2011).

2 - Monteiro, E. Avaliação de tecnologias em saúde no contexto do sistema de saúde. Cadernos Saúde e Sociedade, Avaliação de Tecnologias em Saúde, 21-29 (2011).

3 - Monteiro, E. Em direção ao NOVO Currículo da FCM-UNL. Frontal 38, 17-18 (2011).

4 - Monteiro, E., Santos, I., Caetano, P., Pinto, D. & Heleno, B. Normas da Direção Geral de Saúde: Supressão Ácida: Utilização dos Inibidores da Bomba de Protões e das suas Alternativas Terapêuticas (nº 036/2011); Antibioterapia na Pneumonia Adquirida na Comunidade em Adultos Imunocompetentes (nº45/2011); Anti-inflamatórios não esteróides sistémicos em adultos: orientações para a utilização de inibidores da COX-2 (nº 13/2011); Utilização e seleção de anti-agregantes plaquetários (nº 014/2011). (Direção Geral de Saúde, 2011).

Ph.D. thesis completed

PhD thesis entitled "O corpo carotídeo na terapêutica da doença de Parkinson: estudo funcional em função da idade" from Teresa Maria de Castro Alves Monteiro. Faculdade de Ciências Médicas, October 2011.

Internationalization

Collaborations with Ana Obeso, Constancio Gonzalez and Elena Olea from Faculdade de Medicina/Universidade Valladolid Spain in the context of the project: Relative contribution of ATP and adenosine to carotid body chemotransduction in acute and chronic hypoxia.

Collaborations with Paul Kemp and Daniela Riccardi (Cardiff University, UK) in the context of the project Genomics and Biotechnology Applied to Therapeutic Innovation.

Collaborations with Eric Kupferberg (Vice-Dean coordinator) ; Sharon E. Smith; Jean M. Morrone (presencial 1st Module); NEU e-learning faculty from Northeastern University (NEU) (Boston/USA) in the context of the Masters programme Mestrado de Investigação clínica NOVA/Northeasthern University .

Collaborations with Ana Obeso and Constancio Gonzalez (Faculdade de Medicina/Universidade Valladolid - Spain) and with Paul Kemp and Daniela Riccardi (Cardiff University - UK) in the context of the project O papel do corpo carotídeo na genese da resistência à insulina e hipertensão .

Collaborations with John Seman and Jerry Avorn (Alosa Foundation; Harvard Medical School Boston, USA) in the context of the project Adaptation of Alosa Foundation prescription guidelines to Portugal .

Establishment of collaborations during 2011 with Jacques Demotes, INSERM (project Coordinator) + 32 partners from Europe (INSERM - France) in the context of the network project European Clinical Research Infrastructures Network Integrating activity (ECRIN - IA) to start in 2012.

Collaborations with Jan Hedner (University of Gothenburg - Sweden) and international collaborations with in the context of the project Chronic Intermitent Eucapnic Hypoxia: systemic effects and evaluation of anti-hypertensive drugs efficacy .

Collaborations with Frederick Beland and Igor Pogribny (Division of Biochemical Toxicology. National Center for Toxicology Research. Food and Drug Administration (NCTR, FDA) - USA) in the context of the project Bioactivation routes of the anti - HIV drug Nevirapine: identification of reactive metabolites and mutagenic potential .

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FCT Relatório Científico 2011 Print: 23-04-2012 12:11:14 [Instituto de Tecnologia Química e Biológica]
Group Description

Title of Research Group:	(RG-LVT-50004-4030) Metabolic Disorders Research
Principal Investigator:	Maria Paula Borges de Lemos Macedo
Main Scientific Domain:	n/a
Group Host Institution:	n/a

Funding, source, dates

Funding, source, dates

"Meal-induced insulin sensitization (MIS) - from basics to clinical studies"; FCT/MCTES; PIC/IC/82956/2007; 140.000,00 ; from 01-03-2009 to 29-02-2013.

"Condição do Sistema Nervoso Parassimpático e Intolerância à Glucose" ; SPD/Bayer; 5.000,00 ; from 01-04-2010 to 30-04-2012.

Awards:

"Hepatic Insulin Sensitizing Substance (HISS) - Target organs". Ernesto Roma Award, Portuguese Diabetes Association (APDP)/Merck Sharp & Dohme (award to Ana Fernandes, M. Paula Macedo); 10.000,00 .

The relevance of the glucagon pathway on HISS-dependent insulin sensitivity . Hargreaves Award SPD/JABA 2011 for Diabetes research, by Sociedade Portuguesa de Diabetologia (SPD) (award to Rita S. Patarrão, M. Paula Macedo); 7.500,00 .

Objectives & Achievements

Objectives

MEDIR: Metabolic DIsorders Research

The MEDIR group is committed simultaneously in establishing an integrated picture of the etiological processes that determine the development of prediabetes, diabetes and associated pathologies and to broaden the knowledge concerning specific molecular mechanisms that may contribute to these processes. Additionally, this basic research is readily translated into human studies. The main goal is thus to highlight clinically-relevant, early detecting, biomarkers and design new therapeutical approaches.

Main Achievements

In the context of the project Meal-induced insulin sensitization (MIS) - from basics to clinical studies , our objectives were: 1) to determine the site responsible for initiation of the MIS process; 2) to characterize the feeding signal; 3) to characterize the MIS in healthy human subjects; 4) to characterize the MIS effect in healthy, in 5) obese and in 6) type 2 diabetic human subjects. The main achievements were that a meal composed either by glucose + aminoacids, or by glucose + aminoacids + lipids (complete mixed meal) is capable of full meal-induced insulin sensitization (MIS) activation, whereas removal of glucose and/or aminoacids from the meal significantly impairs this capacity.

In the context of the project Condição do Sistema Nervoso Parassimpático e Intolerância à Glucose , our hypothesis is that both insulin secretion and action are acutely modulated by signals related to feeding; that after being integrated in central nervous system modify insulin secretion and action through the parasympathetic nervous system (PNS). Our work in 2011, led us to the conclusion that diurnal dysglycaemia is a reflex of autonomic dysfunction.

In the context of the project Estudo da Prevalência da Diabetes em Portugal; follow-up , the aims of the study were to determine the prevalence of diagnosed and undiagnosed Type 2 diabetes, impaired fasting glycaemia (IFG) and impaired glucose tolerance (IGT) in the Portuguese population aged between 20 and 79 years old. 5% of the portuguese are either diabetic or pre-diabetic. A follow up study was started in 2011 to reassess the pre-diabetic population.

The project Sweet will enhance health and quality of life of children and young people affected by type 1 and type 2 diabetes in Europe by improving secondary prevention; early dianosis and control; and effective management. SWEET will address this, e.g. by stimulating the exchange of information and good practice, developing recommendations for standards of care and education. In 2011, we audit 13 Health Care Centres in order to find their specific requirements for Health Care Professionals training and centre differences.

One of the aims of the MGSD is trying to meet the needs of information and training in diabetes on both sides of the Mediterranean, namely to health care professionals in charge of diabetic patients. In 2011, the progresses were: 2-yearly conference and post-graduate courses in French and English organized every year; Development of a website to improve the distribution of information and educational materials to Group members.

Group Productivity

Publications in peer review Journals

30. Fernandes, A.B., Patarrao, R.S., Videira, P.A. & Macedo, M.P. Understanding Postprandial Glucose Clearance by Peripheral Organs: The Role of the Hepatic Parasympathetic System. Journal of Neuroendocrinology 23, 1288-1295 (2011). http://dx.doi.org/10.1111/j.1365-2826.2011.02226.x; ISI IF: 4.650

43. Lautt, W.W., Schafer, J., Macedo, M.P. & Legare, D.J. Bethanechol and N-acetylcysteine mimic feeding signals and reverse insulin resistance in fasted and sucrose-induced diabetic rats. Canadian Journal of Physiology and Pharmacology 89, 135-142 (2011). http://dx.doi.org/10.1139/Y11-001; ISI IF:1.849

Other national publications

1 - Afonso, R. Insulin action in peripheral glucose uptake - the molecular perspective (Review). Rev. Port. Endocrinol. Diab. & Metab. 11, 87-95 (2011).

Internationalization

Collaborations with Wayne Lautt (Faculty of Medicine, University of Manitoba - Canada) in the context of the project Meal-induced insulin sensitization .

Collaborations with Andrea Mari (Institute of Biomedical Engineering, University of Padua - Italy) in the context of the project Insulin clearance modeling .

Collaborations with Robert O'Doherty (University of Pittsburgh - USA) in the context of the project Kupper cells and Diabetes .

Collaborations with Young-Bum Kim (BIDMC Endocrinology, Harvard University - USA) in the context of the project Postprandial insulin signalling .

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Group Description

Title of Research Group:	(RG-LVT-50004-4031) Molecular Mechanisms of Disease
Principal Investigator:	Miguel Seabra
Main Scientific Domain:	n/a
Group Host Institution:	n/a

Funding, source, dates

Funding, source, dates

"Functional genomis studies of phagocytosis in retinal pigment epithelium"; FCT-MCTES; PTDC/SAU-GMG/105175/2008; 199.920,00 ; from 1-04-2010 to 31-03-2013.

"Regulation of retinal growth factors GTPases"; FCT-MCTES; PTDC/SAU-OSM/104668/2008; 158.952,00 ; from 01-12-2010 to 31-12-2012.

"Rab GTPases expression in Breast Cancer"; LPCC- Terry Fox; 15.000,00 ; from 01-03-2010 to 28-02-2012.

"Molecular Mechanisms of melanosome transfer and processing by keratinocytes"; FCT-MCTES; PTDC/BIA-BCM/111735/2009; 193.060,00 ; from 01-01-2011 to 31-12-2013.

Objectives & Achievements

Objectives

The main aim of our group is to study the role of Rab GTPases and their interacting partners in the control of vesicle trafficking and organelle motility.

In 2011, we had several projects which have the following goals:

1) Molecular Dissection of the Intracellular Route of Plasmodium in Macrophages and Dendritic Cells . The aim of this project is to study membrane trafficking pathways relevant to dendritic cell and macrophage function, using malaria infection as a model system.

2) Subversion of the host endocytic pathway by Plasmodium sporozoites . We propose to study the role of the host hepatocyte endocytic and autophagic pathways during the course of malaria liver infection.

3) Functional genomis studies of phagocytosis in retinal pigment epithelium . The aim of this project is to study the function of conserved RabGTPases and of selected Rab effectors in the phagosome pathways of RPE.

4) Regulation of retinal growth factors GTPases . We propose to study the role of Rab proteins in Ca2+ signalling and release of VEGF following TGF-beta exposure.

5) Rab GTPases expression in Breast Cancer . The aim of this project is to study the expression of Rab27a and Rab27b on a series of 100 breast cancers and correlate the GTPase expression with the histologic type and grade, dimension, ER, PGR and HER2, lymph node and distant metastasis, in order to use these small GTPases as molecular markers of breast cancer prognosis and response to treatment.

6) Molecular Mechanisms of melanosome transfer and processing by keratinocytes . The aim of this project is to dissect the mechanism of melanosome transfer from melanocytes to keratinocytes and identify the RabGTPases involved in the pathway.

Main Achievements

The main achievements were the following regarding the indicated projects:

1) The malaria parasite is able to change the expression level of certain Rabs, such as Rab14, Rab27a, Rab32, on macrophages. From these Rabs, Rab14 showed to be involved in the phagocytosis process of the malaria parasite. On contrary, bacteria such as E. coli and Salmonella induce the increase in the expression level of Rab8 and Rab9a. From these Rabs, Rab9a showed to be involved in the phagocytosis process of the bacteria.

2) The association of the host autophagic pathway with Plasmodium parasites was evaluated: Parasites interact with mature vesicles - amphisomes- derived both from the autophagic and endocytic pathway. Depletion or progression deficiency of host autophagy renders parasite growth arrest. In vitro data is currently being confirmed in vivo system.

3) We observed an involvement of some RabGTPases in the phagosome pathway of RPE.

4) We have observed a relationship between some of RabGTPases and VEGF secretion pathways.

5) We observed by immunohistochemistry and by western-blot that increasing Rab27a expression correlates with higher grades of breast tumors, being the higher expression observed in Grade III tumors as compared with Grade II and Grade I tumors and with non-tumoral tissue.

6) We have optimised in vitro melanin exocytosis and melanin transfer assays. Using these assays we have confirmed our hypothesis that melanin transfer occurs predominantly by a coupled melanin exocytosis/phagocytosis mechanism. We find that melanin exocytosis from melanocytes is induced by keratinocytes. A siRNA screen of RabGTPases revealed that Rab11b is important for keratinocyte-induced melanin exocytosis from melanocytes. Furthermore depletion of Rab11b, which decreases melanin exocytosis, also decreases melanin transfer to keratinocytes.

Group Productivity

Publications in peer review Journals

1 - Bolasco, G., et al. Loss of Rab27 function results in abnormal lung epithelium structure in mice. American Journal of Physiology-Cell Physiology 300, C466-C476 (2011). http://dx.doi.org/10.1152/ajpcell.00446.2010

2 - Chiang, L., et al. Rab27b regulates exocytosis of secretory vesicles in acinar epithelial cells from the lacrimal gland. American Journal of Physiology-Cell Physiology 301, C507-C521 (2011). http://dx.doi.org/10.1152/ajpcell.00355.2010; ISI IF: 3.817

3 - Diekmann, Y., Seixas, E., Grouw, M., Tavares-Cadete, F., Seabra, M.C., Pereira-Leal, J.B. Thousands of Rab GTPases for the Cell Biologist. Plos Computational Biology 7(2011). http://dx.doi.org/10.1371/journal.pcbi.1002217; ISI IF: 5.515

4 - Hume, A.N. & Seabra, M.C. Melanosomes on the move: a model to understand organelle dynamics. Biochemical Society Transactions 39, 1191-1196 (2011). http://dx.doi.org/10.1042/bst0391191; ISI IF:3.989

5 - Mizuno, K., Ramalho, J.S. & Izumi, T. Exophilin8 transiently clusters insulin granules at the actin-rich cell cortex prior to exocytosis. Molecular Biology of the Cell 22, 1716-1726 (2011). http://dx.doi.org/10.1091/mbc.E10-05-0404; ISI IF:5.861

6 - Tarafder, A.K., et al. Rab27a Targeting to Melanosomes Requires Nucleotide Exchange but Not Effector Binding. Traffic 12, 1056-1066 (2011). http://dx.doi.org/10.1111/j.1600-0854.2011.01216.x; ISI IF:5.278
CEDOC

7 - Taylor, A., et al. Impaired prenylation of Rab GTPases in the gunmetal mouse causes defects in bone cell function. Small Gtpases 2, 131-142 (2011). http://dx.doi.org/10.4161/sgtp.2.3.16488

Ph.D. thesis completed

"Dissecting the molecular interaction between hepatocytes and Plasmodium liver parasites", Mafalda Pinto Baptista Lopes da Silva; Universidade Nova de Lisboa; May 27, 2011.

Internationalization

Collaborations with Sebastien Amigorena and Graça Raposo (Institut Curie, Paris - France) and Tanya Tolmachova, Robert Sinden (Imperial College London - UK) in the context of the project "Molecular mechanisms of parasitophorus vacule formation in Malaria infection .

Collaborations with Sebastien Amigorena (Institut Curie, Paris - France) in the context of the project "Molecular Dissection of the Intracellular Route of Plasmodium in Macrophages and Dendritic Cells".

Collaborations with Olaf Strauss (Bereich Experimentalle Ophthalmologie, Universitaetsklinikum Hamburg-Eppendorf - Germany), Clare Futter (Institute of Ophtalmology - UK) in the context of the project "Regulation of retinal growth factors GTPases".

Collaborations with Alistair Hume (University of Nottingham - UK), Clare Futter (Institute of Ophtalmology - UK) in the context of the project "Molecular mechanisms of melanosome transfer and processing by keratinocytes".

Collaborations with Graça Raposo (Institut Curie, Paris - France) and Clare Futter (Institute of Ophtalmology - UK) in the context of the project "Functional genomics studies of phagocytosis in retinal pigment epithelium .

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Group Description

Title of Research Group:	(RG-LVT-50004-4032) Glycoimmunology
Principal Investigator:	Paula Alexandra Quintela Videira
Main Scientific Domain:	n/a
Group Host Institution:	n/a

Funding, source, dates

Funding, source, dates

"The role of sialofucosylated antigens in the binding of Human Monocyte-derived Dendritic Cells to Selectins"; FCT/MCTES; PTDC/SAU-MII/67561/2006; 145.303,00 ; from 01-09-2007 to 28-02-2011.

"Non-small cell lung cancer: what can we learn from the crosstalk between immune cells and sialyl Lewis X?"; CEDOC donnation for clinical studies; 6.000,00

Award:

Paula Videira Invited Researcher at the Dermatology Department, Brigham and Women's Hospital - Harvard Institutes of Medicine, Boston USA. J EMBO- European Molecular Biology Organization Short Term Fellowship - 6.000,00 ; from 1 July 2011 to 30 September 2011.

Objectives & Achievements

Objectives

Our main interest is to understand how the immune cell responses and cancer biology can be modulated by their glycan phenotype. We anticipate that this understanding will permit the design of novel therapeutic strategies against cancer or infection. Specifically:

1) We aim to understand how the immune responses mediated by the dendritic cell (DC) are modulated by glycan structures. DCs are one of the most important leukocytes linking innate and adaptive immune responses and have been used in cellular therapies, therefore our results are expected to be relevant to fine tune the applicability of DC-based vaccines.

2) We aim to identify novel glycan-based biomarkers of cancer. A hallmark of malignancy is the deranged expression of glycans at tumour cell surface. By understanding the pathophysiological role of the tumour glycans we will be able to develop innovative therapeutic strategies to fight cancer progression.

Main Achievements

Regarding the 1st aim:

We identified the importance of sialyl Lewis X in the binding of human dendritic cells to E-, P- and L-selectins, in static and simulated physiological flow conditions. 2) We found that IFN-gamma is able to increase the expression of sialyl Lewis X by dendritic cells and probably its expression is modulated by

cytokine and other stimulus. 3) We published two papers regarding this subject (one was an invitation for a special issue), We found novel glycoprotein that act as selectin ligands under flow conditions.

Regarding the 2nd aim:

1) we have elucidated several aspects of the phagocytosis mechanism in human and mouse dendritic cells defficient for specific sialic acids; 2) we identified dendritic cell s receptor candidates); 4) we found that some of the opportunistic bacteria from the Burkholderia cepacia complex are also recognized by sialic acid recognizing receptors expressed by dendritic cells; 5) We submitted a manuscript to INFECTION AND IMMUNITY.

2) Regarding lung cancer:1) We have successfully analyzed lymph node aspirates from 58 patients, through different techniques (flow cytometry, histochemistry and Real time PCR) and studyed its efficacy in the screening patient's outcome. 2) We created a biobank consisting of tussue, serum and pleural effusions from patients. 3) We have established key collaborations to initiate the overall glycomics of lung cancer cells including those from lymph node metastasis Kelly Moremen (Georgia University, USA) and Pauline Rudd (NIBRT, Ireland) to study the overall glycosyltransferase transcripts and glycan structures in lung cells. 4) We are now preparing a manuscript comparing the relevance of the different techniques in identifying lung cancer cells in aspirates and cell lines.

3) Regarding bladder cancer: 1) We have analysed BCG on a glycan array and proved this microrganism binds glycans only expressed in cancer cells . 2) We have also found that sialyl-Tn influence the internalization of BCG into bladder cancer cells and its mechanism of action and we then hypothesised that bladder cell sialylation, in general, affects the efficacy of Bacilus Calmette-Guerin (BCG) treatment. 3) We have found that sialyl-Tn is able to hinder dendritic cells maturation, cytokine production and capacity for T cell priming. 4) We have also established important collaborations (Carlos Novo from IHMT and Michael Bachmann in Dresden University, Germany) in order to initiate the construction of cytotoxic antibodies specific for sialyl-Tn, an antigen that is also highly expressed in breast and gastric cancer.

4) Regarding pancreatic cancer: We established important collaborations with Hospitals to obtain patient samples . We analysed pancreatic cancer cell lines for the expression of selectin ligands.

Group Productivity

Publications in peer review Journals

1 - Lepper, P.M., et al. Superior Vena Cava Syndrome in Thoracic Malignancies. Respiratory Care 56, 653-666 (2011). http://dx.doi.org/10.4187/respcare.00947; ISI IF:1.534

2 - Lima, L., et al. IL-4 and TNF-alpha Polymorphisms Are Associated with Risk of Multiple Superficial Tumors or Carcinoma in situ Development. Urologia Internationalis 87, 457-463 (2011). http://dx.doi.org/10.1159/000331882; ISI IF:0.924

3 - Paixão, P., Almeida, S., Videira, P., Ligeiro, D. & Marques, T. Screening of congenital cytomegalovirus infection by real-time PCR in urine pools. European journal of pediatrics (2011). http://dx.doi.org/10.1007/s00431-011-1496-4; ISI IF: 1.644

4 - Silva, Z., et al. Sialyl Lewis(x)-dependent binding of human monocyte-derived dendritic cells to selectins. Biochemical and Biophysical Research Communications 409, 459-464 (2011). http://dx.doi.org/10.1016/j.bbrc.2011.05.026; ISI IF:20595

5 - Videira, P.A., et al. Effects of Bevacizumab on Autocrine VEGF Stimulation in Bladder Cancer Cell Lines. Urologia Internationalis 86, 95-101 (2011). http://dx.doi.org/10.1159/000321905; ISI IF:0.924

Other international publications

1 - Silva, Z., Konstantopoulos, K. & Videira, P. Sugars to move dendritic cells! Annals of Biomedical Engineering (Special Issue). (2011). ISI IF: 2.376

Organization of conferences

- International Workshop: "Glycosciences in The International Year of Chemistry- Applications to Human Health and Disease", European Science Foundation. Paula Videira made part of the ORGANIZING COMMITTEE. This event marked the International Year of Chemistry in Glycosciences and was a Forum of discussion and expertise in the field. This workshop aimed to foster collaboration between disciplines and generations, bringing together experts in Glycosciences, invited from across Europe. 8-10 September 2011.

- Seminar: The CDG Syndrome networking - CDG: Congenital diseases of Glycosylation ; organizer and speaker: Paula Videira; 2 June 2011.

- XV Pós-Graduation Course from Escola de Pneumologia: Pneumologia de Intervenção , organizer and speaker: Antonio Bugalho from the Sociedade Portuguesa de Pneumologia; Monte Real, Portugal; 14 - 15 May 2011.

Internationalization

Collaborations from Consortium for Functional Glycomics- National Institute of General Medical Sciences, USA; with Fabio Dall'Olio (Department of Experimental Pathology, University of Bologna, Bologna, Italy); Kelley Moremen (Complex Carbohydrate Research Center, University of Georgia, USA) and Pauline Rudd (Dublin Oxford Glycobiology Laboratory, University College of Dublin, Ireland) in the context of the project "Thomsen-Friedenreich glycosidic antigens in bladder cancer .

Collaborations from Consortium for Functional Glycomics- National Institute of General Medical Sciences, USA and with Joseph Lau (Department of Molecular & Cellular Biology, Roswell Park Cancer Institute, Buffalo, New York, U.S.A.); with Konstantino Konstantopoulos (Department of Chemical & Biomolecular Engineering; Johns Hopkins Engineering in Oncology Center; The Johns Hopkins University (Baltimore, MD/USA)), with Paul Wallace (Image and flow Cytometry Departmetn, Roswell Park Cancer Institute (Buffalo, NY/USA)), with Paul Crocker (College of Life Sciences, University of Dundee, Dundee - UK) in the context of the project "The role of sialic acid in the immunobiology of dendritic cells .

Collaborations with Kelley Moremen (Complex Carbohydrate Research Center, University of Georgia, USA) and Pauline Rudd (Dublin Oxford Glycobiology Laboratory, University College of Dublin, Ireland) in the context of the project "Glycan based biomarkers .

Collaborations with Paul Crocker (College of Life Sciences, University of Dundee, Dundee - UK) in the context of the project "The role of Siglec receptors in dendritic cell phagocytosis .

Collaborations with Robert Sackstein (Harvard Medical School - USA) in the context of the project "Development of dendritic cell-based vaccines with osteotropism for treatment of bone metastasis (proposal submitted to HMS Portugal Program) .

Collaborations with Yi Luo (Department of Urology, University of Iowa, USA) in the context of the project "(Sia)Signature And Enhancement Of Intravesical Bladder Cancer Therapy (collaborator in grant submitted to FCT) .

Collaborations with Michael Bachman (Dresden University - Germany) in the context of the project " Generation of Bispecific Antibodies for the Treatment of Breast cancer (collaborator in grant submitted to FCT) .

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Group Description

Title of Research Group:	(RG-LVT-50004-4033) Angiogenesis Laboratory
Principal Investigator:	Sérgio Jerónimo Rodrigues Dias
Main Scientific Domain:	n/a
Group Host Institution:	n/a

Funding, source, dates

Funding, source, dates

"Cholesterol promotes angiogenesis and metastasis formation?"; FCT; PTDC/SAU-ONC/114080/2009; 166.720,00 (total), 118.720,00 (CEDOC); from 01-03-2011 to 28-02-2014.

"Exploiting the molecular basis underlying an aberrant bone marrow vascular niche in malignant myeloma"; FCT; PTDC/SAU-ORG/113617/2009; 160.000,00 (total), 114.008,00 (CEDOC); from 01-03-2011 to 28-02-2014.

Objectives & Achievements

Objectives

The main objectives of the Angiogenesis group are: 1. To link endothelial function in solid tumors and in hematological malignancies with tumor progression; 2. To identify metabolic shifts and other systemic signals that trigger tumor progression or the onset of metastases.

Main Achievements

We identified the notch signaling pathway, via Dll4 expression and function, as a key component of the endothelial cells of multiple myeloma bone marrow microenvironment. In vivo and in vitro assays indicated that this signaling pathway conditions the bone marrow into a more lymphoid state, thereby supporting the expansion of the malignant multiple myeloma clones. Second, we identified LDL cholesterol as a key systemic factor in inducing tumor (breast and leukemia) expansion and invasion. Other systemic signals supporting tumor invasion include the LDL-induced chemokine fractalkine (in the case of leukemia) and angiopoietin-like factor 4 in the case of breast cancer.

Group Productivity

Publications in peer review Journals

1 - Caiado, F., et al. The role of fibrin E on the modulation of endothelial progenitors adhesion, differentiation and angiogenic growth factor production and the promotion of wound healing. Biomaterials 32, 7096-7105 (2011). http://dx.doi.org/10.1016/j.biomaterials.2011.06.022; ISI IF: 7.883

2 - Casalou, C., et al. Cholesterol Regulates VEGFR-1 (FLT-1) Expression and Signaling in Acute Leukemia Cells. Molecular Cancer Research 9, 215-224 (2011). http://dx.doi.org/10.1158/1541-7786.mcr-10-0155; ISI IF: 4.373

3 - Real, C., et al. Bone Marrow-Derived Endothelial Progenitors Expressing Delta-Like 4 (Dll4) Regulate Tumor Angiogenesis. Plos One 6(2011). http://dx.doi.org/10.1371/journal.pone.0018323; ISI IF:4.411

Ph.D. thesis completed

Francisco Caiado: "Role of the Notch-Delta signaling pathway on Bone Marrow derived cells function during wound healing and tumor progression" FCUL (Lisbon University); July 2011.

Internationalization

Collaborations with Julian Dye (UK) in the context of the project "The use of synthetic materials in wound healing .

Collaborations with Peter Carmeliet (Belgium) in the context of the project "PLGF neutralizing Antibodies .

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Group Description

Title of Research Group:	(RG-LVT-50004-4034) Biology of Cytoprotection
Principal Investigator:	Helena Luisa de Araujo Vieira
Main Scientific Domain:	n/a
Group Host Institution:	n/a

Funding, source, dates

Funding, source, dates

"Integrated strategies for expansion, neuronal differentiation and cryopreservation of human embryonic stem cells"; FCT/MCTES; PTDC/BIO/72755/2006; 123.000,00 (this project is at IBET)

"Preconditioning triggered by Carbon monoxide: new strategies to prevent brain damage due to hypoxia-ischemia and reperfusion"; FCT/MCTES; PTDC/SAU-NEU/089747/2008; 100.000,00 (this project is at IBET)

Objectives & Achievements

Objectives

The main project is PTDC/SAU-NEU/098747/2008 entitled Preconditioning triggered by Carbon monoxide: new strategies to prevent brain damage due to hypoxia-ischemia and reperfusion . The objective during 2011 was studying CO-induced preconditioning in several aspects: (i) modulation of astrocytic metabolism by carbon monoxide; (ii) influence of CO in astrocyte-neuron communication leading to neuronal cell death prevention;(iii) in vivo model of perinatal cerebral ischemia and reperfusion and reconditioning induction by changing gene expression, in particular anti-apoptotic and anti-oxidant genes. The lab is also involved in the project PTDC/SAU-TOX/112264/2009 entitled Chronic intermittent eucapnic hypoxia: systemic effects and evaluation of anti-hypertensive drugs efficacy , whose PI is Prof. Emília Monteiro. The general objective of this project is to contribute to identify more effective anti-hypertensive drugs for the treatment of hypertension (HT) in patients with sleep apnea/hypopnea (SAH) and investigate underlying mechanisms of systemic effects associated with SAH. In our lab, the rat experimental model of chronic intermittent eucapnic hypoxia (CIEH) will be used for searching cell death and preconditioning markers in CNS.

Main Achievements

PTDC/SAU-NEU/098747/2008 - Preconditioning triggered by Carbon monoxide: new strategies to prevent brain damage due to hypoxia-ischemia and reperfusion .

The main achievements concerning CO-induced cerebral preconditioning are: (i) The communication between neurons and astrocytes, in particular the role of P1 and P2 neuronal receptors during adenosine and ATP released from astrocytes, which is promoted by CO, and prevents neuronal cell death were studied during 2011. (ii) Neuroprotective role of CO in an animal model of perinatal cerebral ischemia was shown and these data are submitted for publication; (iii) Carbon monoxide modulates apoptosis by reinforcing oxidative metabolism in astrocytes: role of Bcl-2, these data were submitted and are in final review.

Indirectly related to this project, the lab has developed a scientific collaboration with Dr Claudia Santos from ITQB/IBET, which has generated one published article in 2011, and it is about the neuroprotective effect blackberry (Rubus fruticosus) polyphenols.

PTDC/SAU-TOX/112264/2009 - Chronic intermittent eucapnic hypoxia: systemic effects and evaluation of anti-hypertensive drugs efficacy . The results and progress are (i) The

experimental model has been under optimization and (ii) the sampling from CNS have been also optimized, in particular brain preparation for immunohistochemistry and cerebral spinal fluid (CSF) isolation.

Group Productivity

Internationalization

Collaborations with Alessandro Vercelli (Universidà degli studi di Torino - Italy), Catherine Brenner-Jan (Faculté de Pharmacie, Université de Paris-Sud - France) and Patricia Boya (Centro de Investigaciones Biológicas, CIB-CSIC - Spain) in the context of the project "Preconditioning triggered by Carbon monoxide: new strategies to prevent brain damage due to hypoxia-ischemia and reperfusion .

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FCT Relatório Científico 2011 Print: 23-04-2012 12:11:15 [Instituto de Tecnologia Química e Biológica]
Group Description

Title of Research Group:	(RG-LVT-50004-4035) Cilia Regulation and Disease
Principal Investigator:	Susana Santos Lopes
Main Scientific Domain:	n/a
Group Host Institution:	n/a
Funding, source, dates	
Funding, source, dates	

N/A

Objectives & Achievements

Objectives

The main objectives or the Cilia Regulation and Disease Laboratory for the year 2011 were to initiate the lab activity aiming at understanding ciliary length regulation in the context of ciliopathies. For this purpose we use zebrafish embryos as our main model organism.

As a new Lab the group leader needed to purchase equipment and consumables, start new fish lines in the fish facility, acquire a new aquarium system that allowed to control the fish light-cycle and recruit three lab members ideally including one Post-Doc.

During this first year it was crucial to train the new lab members in all the major techniques in a Developmental Biology lab. These techniques include live imaging of zebrafish embryos, in situ hybridization, RNA extraction, making RNA constructs for injection into zebrafish embryos and anti-sense oligonucleotide injections. The Master students to recruit were expected to finish their Master Thesis in one year.

In the first year of activities we aimed to complete a microarray experiment from an ongoing project that involved comparing a mutant embryos for the DeltaD gene and wild-type zebrafish embryos. This screen was tissue specific and aimed at isolating the cells from the Kupffer s vesicle by Fluorescent Activated Cell Sorting. These cells were then used to extract their RNA and to do a transcriptome comparative analysis. From the list of genes most significantly up-regulated or down-regulated we wanted to start the validation process of a sub-list of genes and to initiate a functional study on some of the most interesting genes.

Our objectives were to present our new work at National and International meetings and to have preliminary data to write new grant applications in the end of the first year. We also aimed at drafting our first lab publication by the end of the first year. One important goal was to establish collaborations with clinical groups within or outside CEDOC in the field of ciliopathies.

Main Achievements

In this first year of the Cilia Regulation and Disease Laboratory we have successfully initiated the lab activity. We have recruited a Post-Doc that applied for a FCT fellowship with success. We have employed two Master students that started their final projects in the lab. One of these students has completed her Thesis and is now on a shared PhD programme from the University of Minho, Coimbra and Nova de Lisboa. The other Master student started later and she is now doing experimental work that may lead to the development of a new technique useful for diagnosing humans ciliopathies. These experiments allowed us to develop a new ways of identifying cilia beat patterns.

The three lab members are fully trained in Developmental biology techniques including live imaging with confocal fluorescent microscopy and visualization of ciliary beating with very fast acquisition cameras.

In a screen by microarrays we have found 574 genes (p

One student has completed her Masters and we are preparing her results for publication. This study focused on characterizing the role of Arl13b, a ciliary membrane protein, in the zebrafish embryonic development. We have found that the overexpression of this protein results in the over-growth of cilia. This work is ongoing and we are now looking for arl13b effectors in collaboration with the lab of Dr. Barral from CEDOC.

In summary, we have started the lab activity and in one year we have formed one Master Student with promising results. We are all participating in an International Cilia meeting in London next May and were invited to present an oral presentation in a National meeting (SINAL 2012). In addition, we have preliminary results that we are using to write new grant applications to continue exploring the ciliary length regulation and motility.

In the context of translational research, one of the CEDOC main goals, we have established collaboration and applied for collaborative grants on the role of cilia in the nasal polyposis. We have teamed up with an Otorhinolaryngology team from the Hospital de São José and the Faculty of Medical Sciences/CEDOC.

Group
Productivity

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Group Description

Title of Research Group:	(RG-LVT-50004-4036) Nutraceuticals and Chronic Inflammation
Principal Investigator:	António José Murinello de Sousa Guerreiro
Main Scientific Domain:	n/a
Group Host Institution:	n/a

Funding, source, dates

Funding, source, dates

"Nutraceuticals: a shield against chronic disease? Contribution for the rationale of a new therapeutic option"; FCT; PTDC/SAU-OSM/66323/2006; 170.000,00 Euros (total), 50.651,00 (CEDOC); from 16-06-2008 to 14-02-2012.

Objectives & Achievements

Objectives

Our group is committed in the study of Nutraceuticals.

As a major objective for 2011 we want to test the efficacy of two nutraceuticals (Curcumin and Synbiotic 2000) in the development of chronic disease in three experimental models: gastric carcinoma; non-alcoholic steatohepatitis; chronic B viral hepatitis. The study of these nutraceuticals will be at a morphological, microbiological and molecular level.

Main Achievements

The main achievements for 2011 were:

the implementation of the three experimental models.

The development of the studies concerning: genetic expression profile; gut microbiota composition; histological and immunochemistry analysis. The data were partially presented and published.

Our findings in the context of infection by Helicobacter pylori allow the presentation of a future application in 2012 with the purpose of enhancing the work in the current project.

Group Productivity

Publications in peer review Journals

1 - Machado, J., et al. Helicobacter pylori infection: the role of intestinal microbiota modulation. Helicobacter 16, 140-140 (2011). Conference paper. http://dx.doi.org/10.1111/j.1523-5378.2011.00886.x; ISI IF:3.109

2 - Santos, A.M., et al. Role of (13)C-Urea Breath Test in Experimental Model of Helicobacter pylori Infection in Mice. Helicobacter 16, 320-326 (2011). http://dx.doi.org/10.1111/j.1523-5378.2011.00847.x; ISI IF:3.109

3 - Santos, A.M., et al. Nutraceuticals: a new therapeutic approach against Helicobacter pylori infection? Helicobacter 16, 140-140 (2011). http://dx.doi.org/10.1111/j.1523-5378.2011.00886.x; ISI IF:3.109

Other international publications

1 - Vale do Gato, I., Machado, J., Chaves, P., Cortez-Pinto, H. & Guerreiro, A.S. Comparison of mice gut microbiota composition between two diet models of non alcoholic steatohepatitis. [abstract] Journal of Hepatology 54, S504-S505 (2011). ISI IF:9.334

Other national publications

1 - Vale do Gato, I., et al. Comparação da composição da microbiota entre dois modelos de dieta de esteatohepatite não alcoólica no ratinho. GE-Jornal Português de Gastrenterologia 18(2011).

Internationalization

Collaborations with Mark Feitelson (Thomas Jefferson University, Philadelphia in USA) and Stig Bengmark (University College London in UK) in the context of the Project Nutraceuticals: a shield against chronic disease? Contribution for the rationale of a new therapeutic option .

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Group Description

Title of Research Group:	(RG-LVT-50004-4037) Immune Reconstitution
Principal Investigator:	Cristina Maria Godinho Pires João, M.D.
Main Scientific Domain:	n/a
Group Host Institution:	n/a

Funding, source, dates

Funding, source, dates

"B cell modulation of T cells function and repertoire - immune characterization of lymphoma patients receiving chemotherapy with or without a B cell depleting agent, Rituximab"; Associação Portuguesa Contra Leucemia 2007; 40.000,00 ; from 01-07-2008 to 31-03-2012.

"Examine the role of VEGF isotypes and TGFb on various aspects of dendritic and T cell function in healthy volunteers and cancer patients". FLAD; 12.000 ; from 01-10-2011.

Objectives & Achievements

Objectives

In 2011, the main objective of the group were: 1. to conclude the studies of TCR diversity with our collaborators in france, what occured. The manuscript will be prepared and submitted in 2012; 2. To conclude the studies of the human project on NHL patients treated or not with depletion of B cells. This procet correspond to the Master project of Dr. Ana Afonso. This master will be defended in 2012; 3. To write the PhD project of Dr. Ana Queiros. Dr. Queiros is developing her studied in Barcelona since 2011.

Main Achievements

1. Preparation of a manuscript to be published in 2011;

2. One lab. Prize;

3. One collaborator workinh at the Mayo Clinic;

4. Develop new collaborations - with Prof. Elias Campo and Prof Inaki Subero at Barcelona (Ana Queiros PhD project).

Group Productivity

Internationalization

Collaborations with Luis Porrata and Svetomir Markovic (Mayo Clinic USA); Adrien Six (Hôpital Pitié Salpétrière-UPMC and Centre de Recherche des Cordeliers France) and Anton W. Langerak (Erasmus Medical Center Netherlands) in the context of the project: "Immune recovery after Autologous Stem Cell Transplantation - modulation by Ig and potential clinical application".

Collaborations with Elias Campo and Inaki Subero (Clinic Hospital, Universidade de Barcelona - Spain) in the context of the project: "Unraveling the epigenome and microenvironment interactions of B-Cell Chronic

Lymphocytic Leukemia".

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Group Description

Title of Research Group:	(RG-LVT-50004-4038) Heart Failure, Atrial Fibrillation & Thromboembolism
Principal Investigator:	Maria de Fatima Matias de Ceia Gomes
Main Scientific Domain:	n/a
Group Host Institution:	n/a
Funding, source, dates	
Funding, source, dates	

N/A

Objectives & Achievements

Objectives

The main objectives of this group are to contribute to the knowledge in the following areas:

1. Heart failure

1.1. Chronic heart failure (CHF)

CHF patients in the community, followed up at Hospital consultation and at Day-Hospital: epidemiology, survival, quality of life, drug therapy compliance, and education of the patients, and families.

International multicentric studies on drug therapy

National multicentric study on drug therapy and resynchronization therapy

1.2. Acute heart failure (AHF)

Patients hospitalized at a Heart Failure Unit: cost-effectiveness of the management at this structure, diagnostic and prognostic role of biomarkers, drug therapy, other therapeutic interventions.

2. Oral Anticoagulation

Development of programs of decentralization of warfarin therapy programs for ambulatory patients involving community Health Centers, namely family practitioners and nurses.

Studies of oral inhibitors of coagulation factors (acute venous thrombosis, pulmonary thromboembolism)

3. CV risk factors

Participation in multidisciplinary teams for the management of obesity (bariatric team approach, Centro Hospitalar de Lisboa Ocidental, Lisbon).

Studies on new drugs and formulations for diabetes mellitus therapy.

Main Achievements

1. Organization of the Acute Heart Failure Unit at the 3rd Medicine Ward, Hospital de S. Francisco Xavier (HSFX), Lisbon (equipments, protocols, training of health workers), that opens Feb 2012.

2. Studies and surveys, 2011:

The effect of Eplerenone versus placebo on cardiovascular mortality and heart faillure hospitalization with NYHA class II chronic systolic heart failure (EMPHASIS) Prof C. Fonseca MD PhD, Main investigator, HSFX.

Evaluation of feasibility, quality and cost-effectiveness of a decentralized oral anticoagulation program, Prof. C. Fonseca MD PhD, Dr. Ana Leitão MD. Main investigators, HSFX.

Aliskiren Trial to Minimize OutcomeS in Patients with HEart failure (ATMOSPHERE) Prof. C. Fonseca MD PhD, Member of the Steering Committee, HSFX main investigator

Design of the Reduction of Events with Darbepoetin alfa in Heart Failure (RED-HF): a Phase III, anaemia correction, morbidity-mortality trial, Dr. Pedro Sarmento MD, main investigator, HSFX.

CL2- 44121 004 Betablockers in Heart Failure: a new molecule. A phase III study Profª C. Fonseca MD PhD, HSFX main investigator

C-SCADE 6 (BI 1245.33) 2010-2012 Drª Ana Leitão MD, HSFX main investigator

C-SCADE 8 (BI 1245.25) 2011-2012 Drª Ana Leitão MD, HSFX main investigator

C-SCADE 7 (BI 1245.28) 2011-2012 Drª Ana Leitão MD HSFX main investigator

SINCRONE Observational study for the characterization of heart failure patients with asynchrony, before and after resynchronization in Portugal, Profª C. Fonseca MD PhD, member of the Steering Committee, HSX main investigator, Prof Fátima Ceia MD PhD, member of the Steering Committee

3. Activities related to the design, coordination and implementation of European studies and surveys:

HF Long-term Registry. EURObservacional Research Programme - Profª C. Fonseca MD PhD, Member of the European Board and National Coordinator

Member of the Task Force for the Revision of Acute and Chronic Heart Failure Management European Guidelines - Profª C. Fonseca MD PhD.

4. PhD students: three. Subjects: Patients Rights and Duties, Oral Hypocoagulation, and Organization, management and performance evaluation of Emergency Departments in urban Central Hospitals.

5. Publications

Dores H, Cardiga R, Ricardo F, Araujo I, Gândara F, Abreu A, Marques F, Leitão A, Fonseca C, Ceia C. Atrial fibrillation and thromboembolic risk: what is the extent of adherence to guidelines in clinical practice? Rev Port Cardiol 2011; 30: 171-180.

6. Participation as lecturers or in workshops in National and International Congresses.

Group Productivity

Other national publications

Dores H, Cardiga R, Ricardo F, Araujo I, Gândara F, Abreu A, Marques F, Leitão A, Fonseca C, Ceia C. Atrial fibrillation and thromboembolic risk: what is the extent of adherence to guidelines in clinical practice? Rev Port Cardiol 2011; 30: 171-180.

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Group Description

Title of Research Group:	(RG-LVT-50004-4039) Immune Response and Vascular Disease
Principal Investigator:	Jose Antonio Pereira Delgado Alves
Main Scientific Domain:	n/a
Group Host Institution:	n/a

Funding, source, dates

Funding, source, dates

"Effect of Probiotics in intestinal permeability mediated by zonulin in Crohn's Disease"; Merck Serono SA /BMS; 30.000,00 ; from 01-10-2010 to 31-12-2012.

"Neutralizing antibodies in anti-TNF therapy"; Merck Sharp & Dohme; 45.000,00 ; from 01-10-2010 to 31-12-2012.

"HDL in regulation of T cell activation"; Fundação Amadeu Cardoso; 20.000,00 ; from 01-09-2010 to 30-09-2012.

"Capillaroscopy in diabetic retinopathy: evaluation of the micro-vasculature as a factor in evaluating inflammation"; Actelion International; 15.000,00 ; from 01-10-2010 to 31-12-2012.

"Angiogenesis and clinical remission in juvenile idiopathic arthritis"; Prémio de Investigação da Sociedade Portuguesa de Pediatria; 15.000,00 ; from 01-01-2011 to 31-12-2012.

Clinical trial EXPLORE: Exploratory, double blind placebo controlled, randomized, single cross-over study to evaluate the potential anti-oxidant action of Niaspan ; Merck Serono S.A.; 47.190,00 ; from 01-01-2008 to 30-06-2011.

Humoral response towards HDL evaluation of their impact on the HDL anti-atherogenic functions ; Prémio NEDAI da SPMI/ Several private sponsorships; 18.500,00 ; from 01-01-2007 to 31-12-2012.

"Humoral response in atherogenesis"; Merck, SA, Prémio de Investigação em Autoimunidade NEDAI/SPMI, 2010; 24.000,00 , from Jan-08 to Jun-11.

Objectives & Achievements

Objectives

Our group has been studying the importance of HDL in atherogenesis for the last few years and has proposed that humoral response towards the HDL complex through antibody production against different antigens within HDL could account for this quantitative and/or qualitative fault.

We show the presence of anti-HDL antibodies and more particularly anti-Apo A-I antibodies (the main apolipoprotein contained in HDL) and anti-paraoxonase 1 (the main antioxidant enzyme in HDL) in patients

with autoimmune diseases but also in patients with atherosclerosis-associated clinical events outside the context of autoimmune diseases. Furthermore we established an association between the titres of these antibodies and some markers of endothelial dysfunction.

Despite these reports, the interaction of the immune system and HDL has never been thoroughly addressed nor has the pathogenicity of these antibodies been determined.

Our current aims are:

a) Identify which CD8+ T a cell are responsive to HDL stimuli, by which mechanism and in what way does HDL blocking by anti-HDL antibodies affects T cell interactions, regulation and cell signalling.

b)Establish whether anti-HDL antibodies are biologically active and therefore their presence is associated with blocking of some of the most relevant anti-atherogenic properties of HDL

Main Achievements

In the context of the project Humoral response towards HDL evaluation of their impact on the HDL anti-atherogenic functions , we identified IgG aHDL, aApo A-I and aPON1 antibodies in autoimmune patients and in patients with ischemic stroke or coronary heart disease, with no clinical features of autoimmune disease. These results suggest that aHDL antibodies might be a family of auto-antibodies of which Apo A-I and PON1 seem to be the main targets. We also show that these antibodies are biologically active and consequently pathogenic by blocking HDL anti-oxidant and anti-inflammatory properties. Published papers in top scientific journals and presented at several prestigious international meetings.

At a general level ours studies will provide evidence of the main targets as well as the mechanisms by which the antibodies disrupt the normal HDL function, leading to atheroma development and clinical manifestations and may also provide background information for potential new drugs and/or vaccines for primary or secondary prevention of this disease.

Group Productivity

Publications in peer review Journals

1 - Alves, J.D., Marinho, A. & Serra, M.J. Tocilizumab: is there life beyond anti-TNF blockade? International Journal of Clinical Practice 65, 508-513 (2011). http://dx.doi.org/10.1111/j.1742-1241.2010.02612.x; ISI IF: 2.309.

2 - Ferreira, I., Neves, M. & Delgado Alves, J. Atherosclerosis risk in antiphospholipid syndrome. International Journal of Clinical Rheumatology 6, 583-593 (2011).

3 - Neves, M. & Alves, J.D. Factors implicated in the generation and persistence of long-lived plasma cell-mediated autoimmunity. Autoimmunity Reviews 10, 375-382 (2011). http://dx.doi.org/10.1016/j.autrev.2010.12.007; ISI IF:6.556

Other international publications

Chapter in book:

1 - Ferreira, I. & Delgado Alves, J. Chapter "Atherogenesis and vascular disease in SLE", Book "Systemic Lupus Erythematosus", (InTech, in print, 2011).

Internationalization

Collaboration with Paul Ames (Rheumatology and Haematology Airedale District General Hospital - United Kingdom) in the context of the project "Thrombotic primary antiphospholipid syndrome: oxidative and nitrative stress".

Collaboration with Luis Lopez (Corgenix Inc, Colorado - USA) in the context of the project "Rosuvastatin promotes antioxidant effect through nitric oxide pathway and reduces serum levels of oxidized-LDL/ B2GPI complexes in patients with diabetes mellitus".

Collaboration with Elizabeht C. Jury (Centre for Rheumatology Research, University College London - United Kingdom) in the context of the project "HDL in regulation of T cell activation"

Collaboration with Marietta Charakida (Department of Vascular Physiology, The Institute of Child Health, University College London - United Kingdom) in the context of the project "Vascular dysfunction in primary antiphospholipid syndrome; role of dysfunctional high density lipoprotein"

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Group Description

Title of Research Group:	(RG-LVT-50004-4040) Stroke and Dementia
Principal Investigator:	Miguel José de Carvalho Viana Baptista
Main Scientific Domain:	n/a
Group Host Institution:	n/a

Funding, source, dates

Funding, source, dates

PORTYSTROKE Screening genetic conditions in Young Stroke patients; Genzyme, Portugal; 38.816,00 ; from 01-10-2006 to 31-12-2012.

Objectives & Achievements

Objectives

Our lab main scientific interests are related to cerebrovascular disease, dementia, vascular dementia and age related white matter changes and uncommon causes of stroke.

Regarding our main research project, PORTYSTROKE the main objective is to screen genetic conditions in Young Stroke patients.

Main Achievements

Our main achievements regarding PORTYSTROKE was the launch of the 5 year follow-up of patients, with the Publication of a letter.

Group Productivity

Publications in peer review Journals

1 - Barahona-Correa, B., Bugalho, P., Guimaraes, J. & Xavier, M. Obsessive-Compulsive Symptoms in Primary Focal Dystonia: A Controlled Study. Movement Disorders 26, 2274-2278 (2011). http://dx.doi.org/10.1002/mds.23906; ISI IF: 4.480

2 - Bugalho, P. & Vale, J. Brief Cognitive Assessment in the Early Stages of Parkinson Disease. Cognitive and Behavioral Neurology 24, 169-173 (2011). http://dx.doi.org/10.1097/WNN.0b013e3182350a1f; ISI IF:1.247

3 - Viana-Baptista, M. Stroke and Fabry Disease (Review). Journal of Neurology (2011). http://dx.doi.org/10.1007/s00415-011-6278-4; ISI IF: 3.853

4 - Viana-Baptista, M., et al. Motor dysfunction correlates with frontal white matter ischemic changes in patients with leukoaraiosis. Journal of aging research 2011, 950341 (2011). http://dx.doi.org/10.4061/2011/950341

5 - Viana-Baptista, M. & for the PORTYSTROKE investigators. Response to Letter Regarding Article, Mutations of the GLA Gene in Young Patients With Stroke: The PORTYSTROKE Study Screening

Genetic Conditions in Portuguese Young STROKE Patients . Stroke 42(2011). http://dx.doi.org/10.1161/STROKEAHA.110.601963; ISI IF: 5.756

Other international publications

Conference papers

1 - Calado, S., Matias, G., Ferreira, S., Oliveira, J. & Viana Baptista, M. CADASIL-like Phenotypes and NOTCH3 gene alterations: Missense sequence variants or cysteine-sparing mutations? in XX European Stroke Conference. May 2011, Vol. 31 1-322 (Cerebrovascular Diseases, Hamburg, Germany., 2011).

2 - Correia, A.S.A., et al. Bilateral anterior cerebral artery territory infarction: a diagnostic dilemma. European Journal of Neurology 18, 387-387 (2011). 15th Congress of the European Federation of Neurological Societies. ISI IF:3.765

Other national publications

Conference papers

1 - Grunho, M. & Viana-Baptista, M. Dilatação extrema de espaços peri-vasculares de Virchow-Robin: The Swiss Cheese Brain . in Congresso de Neurologia 2011., Vol. 11 (Sinapse, Lisboa, Portugal, 2011).

Organization of conferences

Two-day seminar on eurological problems of pregnancy: "Advanced course on internal medicine in Pregnancy"; Maternidade Alfredo da Costa (MAC) / FCM.

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Group Description

Title of Research Group:	(RG-LVT-50004-4041) Rheumatological Diseases
Principal Investigator:	Jaime da Cunha Branco
Main Scientific Domain:	n/a
Group Host Institution:	n/a

Funding, source, dates

Funding, source, dates

"EpiReumaPt"; DGS, Pharmaceutical companies; 1,6M (total) from Sep 2011 to 2015.

"Ankylosing Spondylitis: genomic and functional characterization of candidate genes and its repercussion in clinical practice"; Pharmaceutical companies and CEDOC; from 01-01-2008.

Objectives & Achievements

Objectives

A. Ankylosing Spondylitis: genomic and functional characterization of candidate genes and its repercussion in clinical practice.

The objectives of the present study were:

1. To collect a representative sample of AS Portuguese patients to characterize the disease both epidemiologically and clinically in Portugal;

2. To validate the instruments used currently in clinical practice - the Bath AS indices - to Portuguese language;

3. To create new tools to monitor AS;

4. To evaluate the socio economic burden of AS;

5. To contribute to the identification of biomarkers with potential interest for diagnosis, clinical response to therapy, and prognosis in AS patients.

B. We aim to performed a prospective clinical, laboratorial and radiological evaluation of a cohort of Portuguese patients with JIA (n= 300)

C. The main objective of the study is to understand the entheseal structural damage in spondyloarthritis (SpA) evaluated by Doppler ultrasound.

Our specific objectives are:

1. To assess the prevalence and the relevance of the bursa-synovial lesion in SpA; and to evaluate the persistence, increase or resolution of entheseal erosion in SpA using the Achilles enthesis as a model.

2. To determine the predictive value of entheseal damage in SpA; and its relationship with other well-established SpA outcome measures.

Main Achievements

A. 1. AS Portuguese characterization performe; results submited as a paper;

2. BASDAI, BASFI, BASMI and BASG validate into Portuguese, widespread and an ongoing use by Portuguese rheumatologists; published as paper;

3. BASDAI, BASFI, BASFI and mSASSS charts performed for both genders in Portuguese population;; published as a paper; ongoing validation;

4. Socio economic burdem of AS in Portugal; Ongoing;

5. New locus -SPA2 identification and establishement of association between the gene TNFSF8 and susceptibility to spondyloarthritis; ANKH variants not associated with susceptibility or severety of AS; ERAP1 and IL23R variants associated with AS in Portuguese population; A gene signature establish the difference between AS patients and healthy controls; all results published as papers.

B. We ve started to analyse the data to correlate the association between susceptibility, prognosis and response to treatment of JIA patients and TNF -308G/A, PTPN22 1858C/T, MIF -173G/C, IL-1A -889C/T, IL2RA/CD25 rs2104286 (A/G), IL-6 -174G/C and IL-17 polymorphisms.

C. A prospective study of 68 SpA patients have been developed in cooperation with La Paz Hospital (Madrid). The first data about progression of erosions in Achilles enthesis have been published.

Group Productivity

Publications in peer review Journals

1 - Baptista, F., Fragoso, I., Branco, J., de Matos, A.A. & Sardinha, L.B. Reference Data for Bone Speed of Sound in Portuguese Girls and Boys Aged 9-13 Years. Journal of Clinical Densitometry 14, 484-491 (2011). http://dx.doi.org/10.1016/j.jocd.2011.05.019; ISI IF: 2.0321

2 - Branco, J.C., Cherin, P., Montagne, A., Bouroubi, A. & Multinatl Coordinator Study, G. Longterm Therapeutic Response to Milnacipran Treatment for Fibromyalgia. A European 1-Year Extension Study Following a 3-Month Study. Journal of Rheumatology 38, 1403-1412 (2011). http://dx.doi.org/10.3899/jrheum.101025; ISI IF: 3.551

3 - Branco, J.C., Tome, A.M., Cruz, M.R. & Filipe, A. Pirlindole in the Treatment of Depression and Fibromyalgia Syndrome. Clinical Drug Investigation 31, 675-689 (2011). http://dx.doi.org/10.2165/11595410-000000000-00000; ISI IF: 1.622

4 - de Miguel, E., et al. Enthesis erosion in spondyloarthritis is not a persistent structural lesion. Annals of the Rheumatic Diseases 70, 2008-2010 (2011). http://dx.doi.org/10.1136/annrheumdis-2011-200352; ISI IF: 9.082

5 - Pereira, D., et al. The effect of osteoarthritis definition on prevalence and incidence estimates: a systematic review. Osteoarthritis and Cartilage 19, 1270-1285 (2011). http://dx.doi.org/10.1016/j.joca.2011.08.009; ISI IF: 3.953

6 - Perez Alamino, R., et al. Differential features between primary ankylosing spondylitis and spondylitis associated with psoriasis and inflammatory bowel disease. The Journal of rheumatology 38, 1656-1660 (2011). http://dx.doi.org/10.3899/jrheum.101049; ISI IF: 3.551

7 - Pimentel-Santos, F.M., et al. Whole blood transcriptional profiling in ankylosing spondylitis identifies novel candidate genes that might contribute to the inflammatory and tissue-destructive disease aspects. Arthritis Research & Therapy 13(2), R57 (2011). http://dx.doi.org/10.1186/ar3309; ISI IF: 4.357

Other international publications

1 - Alamino, R.P., Maldonado Cocco, J., Citera, G., Arturi, P., Vazquez-Mellado, J., Sampaio Barros, P., Flores, D., Burgos-Vargas, R., Santos, H., Chavez Corrales, J., Palleiro, D., Gutierrez, M., Sousa, E., Pimentel-Santos, F.M., Paira, S., Berman, A., Moreno, M., Collantez-Estevez, E., on behalf of RESPONDIA GROUP. Differential features between pure AS and Spondylitis associated with Psoriasis and Inflammatory Bowel Disease. J Rheumatol 38(8): 1656-60 (2011).

2 - Silva, I., Mateus, M. & Branco, J. Characterization and Assessment of Infections in Patients Undergoing Biologic Therapies. Ann Rheum Dis 70 (Suppl 3), 568 (2011).

3 - Silva, I., Mateus, M. & Branco, J. Maladie de Poncet: un cas de Polyarthrite Symétrique Séronégative avec Enthésiopathie Réfractaire à la Thérapeutique. [abstract] Revue Rheumatism 78 (Suppl 5), A165-A166 (2011).

Other national publications

1 - Branco, J.C. Avaliação Diagnóstica em Reumatologia., (Lidel Lda, Lisboa, 2011). ISI IF: 0.451 - BOOK

2 - Branco, J.C. & Canhao, H. Epidemiological Study of Rheumatic Diseases in Portugal - EpiReumaPt. Acta Reumatologica Portuguesa 36, 203-204 (2011). IF: 0.73

3 - Canhao, H., Faustino, A., Martins, F., Fonseca, J.E. & Rheumatic Dis Portuguese, R. Reuma.PT - The Rheumatic Diseases Portuguese Register. Acta Reumatologica Portuguesa 36, 45-56 (2011). ISI IF: 0.451

4 - Carvalho, J.F., Barros, S.M., Branco, J.C. & Fonseca, J.E. Asia or Shoenfeld's Syndrome: highlighting different perspectives for diffuse chronic pain. Acta Reumatologica Portuguesa 36, 10-12 (2011).

5 - Cruz, M. & Branco, J. Porque Cai o Mundo? A Problemática das Quedas e o Impacto Sócio-Económico das Fracturas Osteoporóticas. Cadernos Ortopedia 7, 8-11 (2011).

6 - Diamantopoulos, et al. Cost-effectiveness of Tocilizumab Compared to Standard Therapeutic Sequences for the Treatment of Moderate/Severe Rheumatoid Arthritis (RA). Patients in Portugal. Value in Health 14, A307 (2011).

7 - Fonseca, J., et al. Portuguese Guidelines for the use of Biological Agents in Rheumatoid Arthritis October 2011 Update. Acta Reumatol Port 36, 385-388 (2011).

8 - Fonseca, J. & Branco, J. Uma Visão para a Reumatologia: B.I. da SPR. Sociedade Portuguesa de Reumatologia III série, 10-12 (2011).

9 - Mourao, A.F., et al. Markers of progression to rheumatoid arthritis: discriminative value of the new ACR/EULAR rheumatoid arthritis criteria in a Portuguese population with early polyarthritis. Acta Reumatologica Portuguesa 36, 370-376 (2011). ISI IF:0.451

10 - Mourao, A.F., et al. Practical guide to the use of biotherapeutic technologies in rheumatoid arthritis - update on December 2011. Acta Reumatologica Portuguesa 36, 389-395 (2011). ISI IF:0.451

11 - Pimentel-Santos, F., et al. SPOCK2 e EP300: Dois Novos Genes Envolvidos na Neo-formação Óssea da Espondilite Anquilosante? Acta Reumatol Port 36, 35 (2011).

12 - Pimentel-Santos, F., et al. Manifestações Clínicas e Radiológicas da Espondilite Anquilosante numa População Portuguesa: A Influência do Sexo. Acta Reumatol Port 36, 86 (2011).

13 - Silva, I. & Branco, J.C. RANK/RANKL/OPG: Literature review. Acta Reumatologica Portuguesa 36, 209-218 (2011).

14 - Silva, I., Mateus, M. & Branco, J. Caracterización y Evaluación de Infecciones en Patientes Bajo Terapéutica Biológica. Reumatologia Clínica 7, 94 (2011).

15 - Silva, I., Ribeiro, C., Araújo, F., Nero, P. & Branco, J. Vasculite Reumatóide: um Caso de Incumprimento Terapêutico. Acta Reumatol Port 36 (Supl 1), 65 (2011).

Internationalization

Collaborations with Pedro Machado and Inês Silva (Maastrich University - Netherlands), and Leiden University) in the context of the project " EpiRheumaPt - Epidemiology Rheumatic Diseases in Portugal ".

Collaborations with Maxime Breban (INSERM, Hôpital Cochin, Paris - France) in the context of the project "Systematic candidate-gene investigations in the SPA2 locus (9q32) show an association between the gene TNFSF8 and susceptibility to spondyloarthritis".

Collaborations with Carlos Lopez Larrea (Universidade Complutense de Madrid e Hospital Central de Astúrias, Unidad de Histocompatibilidad, Oviedo - Spain) in the context of the project "cnot3 polymorphism and ankylosing spondylitis".

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FCT Relatório Científico 2011 Print: 23-04-2012 12:11:19 [Instituto de Tecnologia Química e Biológica]
Group Description

Title of Research Group:	(RG-LVT-50004-4042) Psychiatric Epidemiology
Principal Investigator:	José Miguel Barros Caldas de Almeida
Main Scientific Domain:	n/a
Group Host Institution:	n/a

Funding, source, dates

Funding, source, dates

"National psychiatric survey: Study of prevalences of mental disorders, risk factors, social and economic burden, and utilization of services"; FCT; PTDC/SAU-ESA/64632/2006 TOTAL: 170. 000,00 (FCT) + 300.000,00 (F. Champalimaud) + 200.000,00 (F. Gulbenkian) +320.000,00 (Min. Saúde) FOR CEDOC: 170.000,00 ; from 21-05-2008 to 20-05-2011.

"The EU Contribution to the World Mental Health (WMH) Surveys Initiative"; EU; 2008308-DG SANCO 37.500,00 ; from 01-03-2009 to 31-07-2011.

"Factors associated to depression, anxiety and quality of life in the course of chemotherapy"; Liga Portuguesa Contra o Cancro Terry Fox (2011-2013); 15.000,00 ; from 01-03-2011 to 01-03-2013.

Objectives & Achievements

Objectives

To start data analysis, present the first results of the study Development of a European Measure of Best Practice for People with Long Term Mental Illness in Institutional Care (DEMoB.inc) and disseminate the toolkit Quirck developed by this study;

To start data analysis and present the first results of the National Psychiatric Survey , and collaborate in the preparation of papers based on the international results;

To complete the tasks included in the Work Package 2 (Dissemination of the results) of the study The EU Contribution to the World Mental Health (WMH) Surveys Initiative ;

Main Achievements

Analysis of the data from the study Development of a European Measure of Best Practice for People with Long Term Mental Illness in Institutional Care (DEMoB.inc) was started. Results from the national study were presented in two international meetings and the results from the European data were presented with our collaboration in two international conferences. Preparation of 2 papers was initiated in collaboration with our partners. One paper was published in BMC Psychiatry and another was submitted to publication.

Analysis of the data from the Psychiatric Survey was started at 3 levels: national, European and world level. Preparation of 9 papers was intiated in collaboration with our partners of the European group and the

World Consortium. One of the papers was published as a chapter of a book of Oxford University Press; three others were submitted to publication.

The project The EU Contribution to the World Mental Health (WMH) Surveys Initiative was concluded. Reports on burden of mental disorders, gender and mental health and inequalities and mental health were presented to the European Commission. Fact sheets with the main results of the project were published and disseminated. Contacts to publish the three reports were initiated with the Journal "Social Psychiatry and Psychiatric Epidemiology".

Intiated the study Factors associated to depression, anxiety and quality of life in the course of chemotherapy .

Group Productivity

Publications in peer review Journals

1 - Cardoso, G., et al. Frequent users of an acute psychiatric inpatient unit: a 5-year retrospective study. Eur Psychiatry 26, 518 (2011). Abstracts of the 19th European Congress of Psychiatry. http://dx.doi.org/10.1016/S0924-9338(11)72225-8; ISI IF:3.365 fcm

2 - Cardoso, G., Pacheco, C. & Caldas-de-Almeida, J. Quality of care in longer term mental health institutions in Portugal. Eur Psychiatry 26, S1, 2148, XX (2011). http://dx.doi.org/10.1016/S0924-9338(11)73851-2; ISI IF:3.365 ORAL COMMUNICATIONS

3 - Killaspy, H., et al. The development of the Quality Indicator for Rehabilitative Care (QuIRC): a measure of best practice for facilities for people with longer term mental health problems. BMC Psychiatry 11(2011). http://dx.doi.org/10.1186/1471-244X-11-35; ISI IF:2.891

4 - Martins, M., et al. A case of chronic mania in a patient with a double diagnosis of Bipolar I and Delusional Disorders. Internat Clin Psychopharmacol 26, 31 (2011). http://dx.doi.org/10.1097/01.yic.0000405678.41567.4e; ISI IF: 2.762

5 - Wright, C. & Cardoso, G. Quality of care and its determinants in rehabilitative mental health care across Europe. Psychiatrische Praxis 37(2011). http://dx.doi.org/10.1016/S0924-9338(11)73848-2. Deve ter FCM

6 - Xavier, S., et al. Somatoparaphrenia in a patient with schizophrenia. Eur Psychiatry 26, 1216 (2011). http://dx.doi.org/10.1016/S0924-9338(11)72921-2

Other international publications

1 - Cardoso, G., Pacheco, C. & Caldas-de-Almeida, J. Quality of care in longer term mental health institutions in Portugal. Psychiatrische Praxis 38 (2011).

Book:

1 - Wang, P., et al. Treated and untreated prevalence of mental disorders: Results from the World Health Organization World Mental Health (WMH) Surveys., (Oxford Textbook of Community Psychiatry. Oxford Univ. Press.).

Conference paper:

1 - Cardoso, G., et al. Psychological distress and gender in patients undergoing chemotherapy. J Psychosom Res 70, 580 (2011). [Meeting Abstract] ISI IF: 2.842

Other national publications

Books:

1 - Caldas de Almeida, J. Melhoria dos cuidados de saúde mental em Portugal: O que falta fazer?, (In: Mind Faces, as diferentes faces da Saúde Mental. Fundação Calouste Gulbenkian, Lisboa, 2011).

2 - Cardoso, G. Perturbações psicológicas na doença física: implicações para o tratamento e organização de serviços., (In: Mind Faces, as diferentes faces da Saúde Mental. Fundação Calouste Gulbenkian, Lisboa, 2011).

Internationalization

Collaborations with Jordi Alonso (IMIM - Spain) in the context of the project: The EU Contribution to the World Mental Health (WMH) Surveys Initiative.

Collaborations with Ron Kessler (Harvard University - USA) in the context of the project: National psychiatric survey: Study of prevalences of mental disorders, risk factors, social and economic burden, and utilization of services .

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Group Description

Title of Research Group:	(RG-LVT-50004-4043) Mental Health Needs and Interventions
Principal Investigator:	Fernando Miguel Teixeira Xavier
Main Scientific Domain:	n/a
Group Host Institution:	n/a

Funding, source, dates

Funding, source, dates

"Needs For Care Assessment in Mentally Disorderd Inmates"; FCT; PIC/IC/83257/2007; 22.000 ; from 1-12-2008 to 31-03-2011.

"Prevalence of old age neuropsychiatric disorders: contribution to mental health policy in Portugal"; FCT; PTDC/SAU-EPI/113652/2009; 124.274,00 ; from 1-4-2011 to 31-03-2014.

Objectives & Achievements

Objectives

1. To develop research in old age psychiatry and related epidemiology in Portuguese settings.

2. To perform needs assessment studies in several clinical contexts, namely the severe mentally ill, forensic populations and the frail elderly.

3. To explore the circular pathways underlying family dynamics, mental health and mental illness (as well as the impact of psychopathology on relatives, and ways to ease their burden of care).

4. To conduct research in neuropsychiatric disorders related to neurological conditions.

5. To start a collaboration with basic research in the field of neurosciences.

6. To strengthen the collaboration with excellent international groups

7. To improve the number of PhD dissertations in the group members

Main Achievements

1. A FCT-granted project has started, focused on the epidemiology of dementia and depression in the elderly.

2. A member of the team started a new collaborative work with the Neuroscience team from the Champalimaud Foundation.

3. A PhD thesis in neuropsychiatry has been finished, and directed for public discussion. Another PhD dissertation about Needs Assessment in forensic settings is being finished.

4. The team reinforced its collaboration with the Institute of Psychiatry (UK), integrating the 10/66 Dementia Research Study.

5. The team has given several talks in some of the most relevant congresses of psychiatry (EPA, WPA).

6. From 2010, the team increased the number of peer-reviewed publications

7. Two members of the team have participated as module-coordinators in the MSc and PhD programs of the FCM-UNL.

Group Productivity

Publications in peer review Journals

1 - Alves da Silva, J. Are affective disorders risk factors for dementia? A systematic review. in 7th EAGP/APG Congress, Vol. 15, 20 (Aging & Mental Health, Portugal, Oporto, 2011). http://dx.doi.org/10.1080/13607863.2011.646469

2 - Barahona-Correa, B., Bugalho, P., Guimaraes, J. & Xavier, M. Obsessive-Compulsive Symptoms in Primary Focal Dystonia: A Controlled Study. Movement Disorders 26, 2274-2278 (2011). http://dx.doi.org/10.1002/mds.23906; ISI IF: 4.480

3 - Bellon, J.A., et al. Predicting the onset of major depression in primary care: international validation of a risk prediction algorithm from Spain. Psychological Medicine 41, 2075-2088 (2011). http://dx.doi.org/10.1017/s0033291711000468; ISI IF: 5.200

4 - Gonçalves Pereira, M. The art and science of assessing the family in psychogeriatrics. Aging & Mental Health 15, 14. http://dx.doi.org/10.1080/13607863.2011.646469

5 - Jefferis, B.J., et al. Associations between unemployment and major depressive disorder: Evidence from an international, prospective study (the predict cohort). Social Science & Medicine 73, 1627-1634 (2011). http://dx.doi.org/10.1016/j.socscimed.2011.09.029; ISI IF:2.742

6 - King, M., et al. An international risk prediction algorithm for the onset of generalized anxiety and panic syndromes in general practice attendees: predictA. Psychological Medicine 41, 1625-1639 (2011). http://dx.doi.org/10.1017/S0033291710002400; ISI IF:5.200

7 - King, M., et al. Development and Validation of a Risk Model for Prediction of Hazardous Alcohol Consumption in General Practice Attendees: The PredictAL Study. Plos One 6(2011). http://dx.doi.org/10.1371/journal.pone.0022175; ISI IF:4.411

8 - Nazareth, I., et al. Heavy Episodic Drinking in Europe: A Cross Section Study in Primary Care in Six European Countries. Alcohol and Alcoholism 46, 600-606 (2011). http://dx.doi.org/10.1093/alcalc/agr078; ISI IF:2.599

9 - Stegenga, B., et al. Depression, anxiety and physical function: exploring the strength of causality. J Epidemiol Community Health (2011). http://dx.doi.org/10.1136/jech.2010.128371; ISI IF:20983

Other international publications

1 - Gonçalves Pereira, M., Martín-Carrasco, M. & Sampaio, S. Aspectos práticos da intervenção familiar na clínica psicogeriátrica. Mosaico (Revista de la Federación Española de Asociaciones de Terapia Familiar com a colaboração da SPTF) 47, 14-22 (2011).

Other national publications

1 - Gonçalves-Pereira, M. & Sampaio, D. Psicoeducação familiar na demência. Da clínica à saúde pública. Revista Portuguesa de Saúde Pública 29, 3-10 (2011).

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Group Description

Title of Research Group:	(RG-LVT-50004-4044) Respiratory Diseases
Principal Investigator:	Nuno Manuel Barreiros Neuparth
Main Scientific Domain:	n/a
Group Host Institution:	n/a

Funding, source, dates

Funding, source, dates

"ENVIRH - Environment and Health in children day care centres"; FCT; PTDC/SAU-ESA/100275/2008; 180.000,00 (total) 63.603,60 (CEDOC); from 01-02-2010 to 31-01-2013.

"INSPIRAR - Air Quality Exposure and Human Health in Industrialized Urban Areas"; FCT; PTDC/AAC-AMB/103895/2008; 180.000,00 (total) 61.415,00 (FCM) ; from 01-04-2010 to 31-03-2013.

Prémio SPAIC/Bial-Aristegui 2011; SPAIC; 3.500,00 .

Objectives & Achievements

Objectives

Our main objective is the environmental impact on respiration and its mechanisms of disease.

More specifically, with the ENVIRH - Environment and Health in children day care centres project we want to study the impact of indoor air quality in the health of chidren attending day care centers . As what refers to the INSPIRAR - Air Quality Exposure and Human Health in Industrialized Urban Areas project we aim at developing a multidisciplinary methodology for air quality, exposure and population health impacts assessment, from the emission of industrial pollutants in an industrialized urban area.

Main Achievements

In 2011 the main achievements were:

For the ENVIRH project, we received 3185 questionnaires from 46 day care centers (success rate - 61,7%). At this phase, we found an association between CO2 and wheezing through multivariate analysis. At phase 2, 20 day care centers were selected through cluster analysis (11 in Lisbon, 9 in Oporto). Molecular biology techniques to viruses were installed. Secretions were collected to 34 children with symptoms of respiratory infection, signaled by their tutors through a special free phone number. During phase 2 (spring/summer period), indoor air quality and thermal comfort were measured in 19 day care centers (one dropout). Essays related with permeability of buildings to outdoor air and with room ventilation were performed by engineers.

For the INSPIRAR project, the main achievements were: human health characterization (population health indicators, prospective study); case-study characterization: Estarreja (geographical data, population and socio-economical data, industrial source activity data, emission inventory/estimulations); air quality and exposure assessment (air quality and population exposure under accidental releases, individual exposure -

prospective study).

Group Productivity

Publications in peer review Journals

1 - Martins, P., et al. Airways changes related to air pollution exposure in wheezing children. Eur Respir J 39, 246-253 (2011). http://dx.doi.org/10.1183/09031936.00025111; ISI IF:5.922

Other national publications

1 - Gaspar Marques, J. Factores de risco para doença respiratória crónica: resultados preliminares da fase 1 do projecto "Qualidade do ar, exposição e saúde humana em zonas urbanas industrializadas (INSPIRAR). (Rev Port de Pneumol 2011 (Especial Congresso 3, 2011).

2 - Leiria-Pinto, P. Grau de concordância da obstrução brônquica com o resultado da prova de broncodilatação e com o aumento do volume residual. Vol. 19 (Rev Port Imunoalergol, 2011).

3 - Martins, P. Factores de risco para sibilância: resultados da Fase 1 do Projecto Ambiente e Saúde em creches e infantários (ENVIRH). Rev Port Imunoalergol 19, S1 (2011).

4 - Martins, P., et al. Efeito conjunto da exposição à poluição do ar e aos ácaros do pó, sobre as vias aéreas. Rev Port Imunoalergologia (aceite para publicação no âmbito do 1º classificado do Prémio SPAIC Bial Aristegui 2011) (2011).

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Group Description

Title of Research Group:	(RG-LVT-50004-4045) Affective Disorders and Suicide Prevention
Principal Investigator:	Ricardo Duarte Miranda de Gusmão
Main Scientific Domain:	n/a
Group Host Institution:	n/a

Funding, source, dates

Funding, source, dates

"OSPI-Europe - Optimizing Suicide Prevention Programs and their Implementation in Europe". EC/FP7 OSPI/EC/FP7/223138; 299.656,01 ; from 01-10-2008 to 30-09-2012.

"WHY - Why Youth Mental Health? Young people school-based suicide prevention". Municipalities Cascais, Oeira. Informal support with no reference number. 16.363,70 ; from 01-01-2009 to 31-12-2011.

"PSITRAIN - Suicide prevention and improved management of common mental health disorders". FCT; PIC/IC/82737/2007; 82.120,00 ; from 01-07-2010 to 30-06-2013

"PREDI-NU - Preventing Depression and Improving Awareness through Networking in the European Union". EAHC; PREDI-NU/EC/EAHC/20101214; 114.777,00 ; from 01-09-2011 to 31-08-2014.

Objectives & Achievements

Objectives

General and specific objectives of group Affective Disorders and Suicide Prevention for 2011

1. Keep the daily workflow consistently ongoing

1.1. to maintain the ability to advance new ideas and look for new opportunities, invest in new studies design and preparation, and search for partnership and feasibility;

1.2. to maintain capacity for regular submission of proposals;

1.3. to maintain the capacity for fieldwork implementation;

1.4. to maintain the capacity to collect and analyse data;

1.5. to maintain the capacity to present and disseminate outcomes;

1.6. to continue to improve the capacity to comment, collaborate and write up papers;

1.7. to maintain the capacity of networking;

1.8. to maintain the capacity of innovating and pursuing interdisciplinary work;

1.9. to maintain the capacity of multiple studies coordination and regular reporting of ongoing outcomes.

2. Group definition & development

2.1. to define our research and action aims in the short-medium (3 years) and long run periods (10 years), producing an internal strategic and policy statement document;

2.2. to create a clinical unit for health care and clinical research Clínica de Suicidologia based in the Psychiatry Department, Centro Hospitalar de Lisboa-Ocidental, through a specific protocol;

2.3. to preview and strengthen collaboration and synergies with different teams within CEDOC, through brain storming, aiming new ideas for research and deliver collaboration study proposals into the pipeline;

2.4. to strengthen collaboration between the different teams of the Epidemiology Group;

2.5. to create synergies between research activities of our group and the development of PhD Programs and the international masters in mental health policy and services;

2.6. to maintain and foster the participation of the group in international networks.

3. Sustainability & strategic challenges towards excellence

3.1. to improve general performance;

3.2. to increase the capacity to mobilize financial and human resources for the sustainability of the group and our future projects;

3.3. to create conditions to increase the number of papers published by our group;

3.4. to manage accessibility to national and local data on affective disorders and suicidality;

3.5. to influence suicide prevention policy delineation at local, national and European level.

Main Achievements

The main achievement in 2011 was the ability to succeed simultaneously in all specific objectives pertaining to point 1. Keep the daily workflow consistently ongoing.

Thus, we have finished implementation, data analysis, issued a report, and prepared a paper on the pilot project Why Youth Mental Health? Young people school-based suicide prevention (WHY) that ended the 31st December.

We continued to implement and field working until 31st September (involving a huge number of different actions) the multicentre European research study Optimizing Suicide Prevention Programs and their Implementation in Europe (OSPI-Europe), and data collection and analysis, presentation in international and national expert meetings, and collaboration in the preparation of papers based on international results, were all ongoing through 2011; an interim report was submitted to the EC officials; the project will continue until October 2012.

We finished the longer than expected preparation and initiate the implementation of the RCT study Suicide prevention and improved management of common mental health disorders. Combined intervention of psychoeducation for patients and training for primary care practitioners (PSITRAIN), with all randomized cases and controls recruited and almost all baseline assessment finished the 31st December; an interim report was submitted.

We collaborated in the preparation and negotiation of the proposal for the action-research project Preventing Depression and Improving Awareness through Networking in the European Union that was previously submitted and funded, and initiated preparation and task completion the 1st September 2011, and we finished the year ahead of deliverables previewed.

We started to negotiate and elaborate a protocol for a new international multicentre RCT study, Methylphenidate in Mania Project (MEMAP) that will start in 2012, though it had no funding the 31st December.

We have submitted other proposals on bipolar disorders and functioning (FUNIBODI project) that were not awarded but we are improving them.

We continued to collect data and build national databases for self-aggressive behaviour, suicide and violent deaths, psychotropics utilization and prescription, depression risk factors, diagnosis, treatment and attitudes and knowledge on depression and suicidality, within the global research line Affective Disorders and Suicide Prevention.

We continued our long run work of public relations, networking at national and international level.

Another important achievement relates with objective 2. Group definition & development

The group has been working in Neuropsychiatry and Mental Health, with core competencies in epidemiology and services research but is evolving in new directions, such as E-health (PREDI-NU) and clinical research (MEMAP and FUNIBODI) and plans to go into genetics of depression and suicide.

We are maintaining fruitful international cooperation.

A program and protocol to develop a specialised health care unit in suicidology were delivered to the Head of FCM-UNL and we are waiting a protocol signature with CHLO general hospital.

Nevertheless, points 2.3, 2.4, 2.5 didn t advance as desired. These depend specifically on the policy and facilitation by CEDOC coordination, epidemiology group coordination, and PhD and MSc programmes. We should be able to manage collaboration internally. PhD and MSc students available to work on our research lines are needed and haven t been available at a desired pace. Also, staff members of the group, partners, fellows and scholarships, don t have access to the graduation programmes, and we do not have a specific financing system to make them accessible. Graduation might be a powerful quality selection and motivator tool that we don t have access to. We would like to be heard on our needs and suggestions to make these resources synergic and effective.

Finally, our major achievement regarding item 3. Sustainability & strategic challenges towards excellence, was the nomination to write the National Strategy for Suicide Prevention.

Group Productivity

Publications in peer review Journals

1 - Vaernik, A., et al. Drug suicide: a sex-equal cause of death in 16 European countries. BMC Public Health 11(2011). http://dx.doi.org/10.1186/1471-2458-11-61; ISI IF:2.364

2 - van der Feltz-Cornelis, C.M., et al. Best Practice Elements of Multilevel Suicide Prevention Strategies A Review of Systematic Reviews. Crisis-the Journal of Crisis Intervention and Suicide Prevention 32, 319-333 (2011). http://dx.doi.org/10.1027/0227-5910/a000109; ISI IF: 1.383

Internationalization

Collaborations with Stanley Kutcher (University of Dalhousie - Canada) in the context of the projects: Why; PsiTrain; PREDI-NU.

Collaborations with Ulrich Hegerl (University of Leipzig - Germany) in the context of the projects: OSPI; PREDI-NU; MEMAP.

Collaborations with Ella Arensman (National Suicide Research Foundation - Ireland) in the context of the projects: OSPI; PREDI-NU.

Collaborations with James Coyne (University of Pennsylvania - USA) in the context of the project OSPI.

Collaborations with Airi Varnik (Estonian-Swedish Mental Health and Suicidology Institute - Estonia) in the context of the projects: OSPI; PREDI-NU.

Collaborations with José-Luis Ayuso (Universidad Autonoma de Madrid - Spain) in the context of the project MEMAP.