CTC

Centro de Terapia Celular

Center for Cell-Based Therapy

CENTER FOR RESEARCH ON CELL-BASED THERAPY

Annual Report

Ribeirão Preto
University of São Paulo

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1. THE RESEARCH PROGRAM

The Research Project for the center is based on the broad concept of using cells for therapy, under different conditions and from several sources, including transfusion of blood components, hematopoietic stem cell transplantation from bone marrow, umbilical cord, and peripheral blood, for instance. The program considers also the actual or potential targets of the treatment, particularly individuals affected with neoplastic blood diseases.

> *The research project focuses on basic cellular mechanisms (cell differentiation, cell recognition, cell-to-cell interaction, cell mediators, inflammation, coagulation, and apoptosis) and processing (isolation, expansion, selection, purging) which are relevant for cell-based therapy and its relation with gene structure and protein expression, on four levels: a. Characteristics and manipulation of the cells used for therapy, b. Characteristics of the recipients, affected with neoplastic blood diseases, c. Relationship of the host with parasites transmitted by cell therapy, d. Transgenic animals as experimental models.*

Although the center focuses mainly on basic cellular mechanisms and processes that are relevant for cell-based therapy and its relation with gene and protein expression, we are progressively increasing the stress on clinical and applied research. Thus, mesenchymal stem cells are now starting to be tested for their possible therapeutic uses, and innovative clinical trials with hematopoietic stem cell transplantation are underway or starting, for autoimmune diseases and diabetes mellitus. We also are actively looking for therapeutic targets on the basis of gene expression studies.

2. QUALITATIVE ANALYSIS OF THE CENTER'S ACHIEVEMENTS

[References in brackets throughout the text refer to numbers of publication list starting page 11]

2a. RESEARCH

Young Researcher Award for 2005. Two students of the Center were awarded prizes in the annual national contest promoted by the CNPq (National Council for Science and Technology), among 181 candidates: Rodrigo A Panepucci won one of the three prizes in the Graduate category, with the work that was part of his PhD thesis, and Fabio M Nascimento won one of the three prizes for undergraduates with a work on the distribution of the PRAME antigen in normal cells.

Panepucci RA – ***Molecular bases of biology of the stem-cells from the hematopoietic system***. Supervisor: MA Zago

Nascimento FP – Analysis of the PRAME antigen expression in normal lymphocytes. Supervisor: Eduardo M. Rego

Regarding the isolation and characterization of mesenchymal and hematopoietic stem cells, four papers have been published [1, 2, 4, 34] in 2005/2006. Of particular relevance is the paper by Panepucci et al. in which the expression of approximately 10.000 genes were compared by serial analysis of gene expression (SAGE) of magnetically sorted $CD34^+$ cells from bone marrow (BM) and umbilical cord blood (UCB) [1]. The overrepresentation of NF-kappa B pathway components and targets was found to be a major characteristic of UCB progenitors. Additionally, promoter analysis of 41 UCB overrepresented genes revealed a significantly higher number of NF-kappa B *cis*-regulatory elements than would be expected by chance alone. This is the first study to point out the role of NF-kappa B pathway on stem cells homeostasis, and this finding is sufficient to explain most of the differences in the clinical outcomes observed when patients receive either bone marrow or UCB stem cell grafts. A follow-up of this study will be Panepucci's post-doctoral project entitled "Role of the NF kappa B pathway on the *in vitro* differentiation of T lymphocytes from human $CD34^+$ hematopoietic stem cells". Along with this study, our group developed an interactive web-based tool to analyze SAGE results which has been called Gene Class [34]. Another relevant point investigated by us is the wide spectrum of tissues from which mesenchymal stem cells (MSC) can be obtained. In 2003 our group obtained MSC from the wall of the umbilical cord vein, and in the following year we showed that the gene expression profiles of the MSC from the umbilical vein and from the bone marrow were highly similar, although not exactly identical. We now demonstrated that the same cell can also be retrieved form the wall of an adult vein, and again the gene expression profile is very similar both to umbilical vein and bone marrow MSC [2].

The clinical trial evaluating the use of a transplant approach for patients with severe newly diagnosed type-I diabetes mellitus (DM) made a significant progress in recruiting patients. Thus far, 12 patients have been submitted to autologous hematopoietic stem cell transplantation, and 11 are no longer insulin dependent [49]. In addition, nine patients with refractory multiple sclerosis [27] were transplanted with autologous hematopoietic stem cells, with clinical improvement or no disease progression in five of them. The results obtained, although still require longer observation and an increase in the number of subjects, corroborate our hypothesis that cell therapy may be a useful therapeutic strategy in autoimmune disorders [18, 27, 49, 55, 56].

Our studies searching for new therapeutic targets in hematological malignancies, melanoma and other cancers resulted in 12 papers [3, 5, 8-12, 17, 19, 26, 36, 47] published in international journals. In the study by de Souza et al. [3] we compared soluble proteins from murine melanoma lines Tm1 and Tm5 with proteins from the

nontumoral cell melan-a using 2-DE of total cell protein extracts. Seventy-one of the 452 spots (average) were differentially accumulated, i.e., increased or decreased twofold in melanoma. SAGE showed that 17/34 (50%) of the differentially accumulated proteins presented similar differences at the mRNA level. Major reductions in protein were observed in tumor cells of proteins that degrade reactive oxygen species (ROS). Our results suggest that melanoma cells can favor survival pathways activated by ROS by inhibiting p53 pathways and activation of Ras and c-myc pathways [3].

As follow up of our previous study analyzing the PRAME antigen as a putative therapeutic target in chronic lymphocytic leukemia (CLL) and non Hodgkin lymphoma, we published in 2006 the analysis of protein expression and subcellular localization of PRAME in CLL and mantle cell lymphoma [5]. Approximately 90% of the analyzed patients, but none of the normal controls, presented more than 20% of PRAME+ lymphocytes. By immunofluorescence microscopy and by permeabilized flow cytometry we demonstrated that PRAME is a membrane antigen and a cytoplasmic protein aberrantly expressed in malignant lymphoproliferative disorders. We also have expanded the analysis of PRAME and the related cancer testis antigens in head and neck squamous cell carcinomas [8]. The interest in this protein increased when we demonstrated that PRAME is one of the most frequently expressed CT antigen in other cancers as well; for instance, CT antigens are expressed in 67% in squamous cell carcinomas of the head and neck, and PRAME was the second most frequently expressed antigen. We have also unpublished data showing a high prevalence of expression also in osteosarcomas. Innovative approaches to chemotherapy, attempts to improve bone marrow transplantation protocols or the dynamics of the cells after transplantation have also been the focus of our attention [9, 15, 16, 25]

In 2006 we have published three articles (references 7, 12, 20) regarding animal models of human disease. As mentioned before, we study the molecular basis of leukemogenesis using the acute promyelocytic leukemia (APL) as a model. These transgenic mice (TM) expressing PML/RARalpha under the control of human cathepsin G promotor develop a form of leukemia that mimics the hematological findings of human APL. Leukemia is diagnosed after a long latency (approximately 12 months) during which no hematological abnormality is detected in peripheral blood (pre-leukemic phase). We have characterized the expression of myeloid antigens by leukemic cells from hCG-PML/RARalpha TM [12]. Flow cytometry analysis of bone marrow and spleen from leukemic TM identified the asynchronous co-expression of CD34, CD117, and CD11b. This abnormal phenotype was rarely detected prior to the diagnosis of leukemia and was present at similar frequencies in hematologically normal TM and wild-type controls of different ages. Our results suggest that the leukemic

transformation occurs in a specific and rare subset of myeloid progenitors, which then rapidly proliferates leading to full blown leukemia.

To analyze whether the variable N-terminal domain (the so called X moiety) of the different hybrid oncoproteins associated with APL (PML/RARalpha, NPM/RARα and PLZF/RARalpha) could affect the activity of the fusion protein in vivo, we generated and characterized NPM/RARalpha transgenic mice (TM) [20]. We then compared these TM with the PML/RARalpha and PLZF/RARalpha TM generated previously by the Memorial Sloan Kettering Cancer Center of New York. In the three models the fusion gene is expressed under the control of a human cathepsin G (hCG) minigene. The three leukemias displayed distinct cytomorphological features. hCG-NPM/RARalpha leukemic cells resembled monoblasts. This phenotype contrasts with what was observed in the hCG-PML/RARalpha TM model in which the leukemic phase was characterized by the proliferation of promyelocytic blasts. Similarly, hCG-PLZF/RARalpha TM displayed a different phenotype where terminally differentiated myeloid cells predominated. Importantly, the NPM/RARα oncoprotein was found to localize in the nucleolus, unlike PML//RARalpha and PLZF/RARalpha, thus possibly interfering with the normal function of NPM. Similarly to what was observed in human APL patients, we found that NPM/RARalpha and PML/RARalpha, but not PLZF/RARalpha leukemia, was responsive to all-trans retinoic acid (ATRA) or As_2O_3 treatments. Taken together, our results underscore the critical relevance of the X moiety in dictating the biology of the disease and the activity of the APL fusion oncoprotein [20].

Another field of interest is the analysis of the relationship between aberrant protein synthesis and oncogenesis. More specifically, we have been studying whether impairment of ribosome biogenesis may affect normal and aberrant hematopoiesis. Previously, Ruggero et al had reported the generation of mutant mice in which the expression of the DKC-1 gene was defective (hypomorphic mutants). The DKC1 gene encodes a pseudouridine synthase that modifies ribosomal RNA (rRNA). DKC1 is mutated in people with X-linked dyskeratosis congenita (X-DC), a disease characterized by bone marrow failure, skin abnormalities, and increased susceptibility to cancer. DKC-1 mutant mice develop a disease that resembles human X-DC. We have collaborated in the generation and characterization of this model. We have used an unbiased proteomics strategy to analyze cells from these mutants [7]. We discovered a specific defect in IRES (internal ribosome entry site)-dependent translation in Dkc1(m) mice and in cells from X-DC patients. This defect results in impaired translation of messenger RNAs containing IRES elements, including those encoding the tumor suppressor p27(Kip1) and the antiapoptotic factors Bcl-xL and

XIAP (X-linked Inhibitor of Apoptosis Protein). Moreover, Dkc1(m) ribosomes were unable to direct translation from IRES elements present in viral messenger RNAs. These findings reveal a potential mechanism by which defective ribosome activity leads to disease and cancer [7].

2b INNOVATION

Recently the main activity in innovation was the setup of the Small Business Incubator (INBIOS – Incubadora de Biotecnologia em Saúde) in 2002. Thus far, two small businesses have graduated, and five additional businesses are housed. The initiative is part of the aim to setup a Technological Park in the campus of Ribeirão Preto, dedicated to R&D in biotechnology.

Other technological projects are in development including the production of recombinant proteins (coagulation factor VIII, viral proteins, growth factors), and equipments and software for non-invasive iron quantification and blood irradiation (see, for instance, publications 45 and 57, and the article by Goes *et al*. in press in ***Transfusion***).

2c DIFFUSION

Book on Stem Cells. Two investigators of the center published a book on the subject of stem cells, comprising the basic aspects of stem cells, the medical applications and a part on ethical and legal issues, distributed into 15 chapters and written by 27 collaborators:

> Zago MA & Covas DT – ***Células-tronco: a Nova Fronteira da Medicina***. [Stem-cells: the new frontiers of medicine] Editora Atheneu, Rio de Janeiro, 2006, 245 pages. ISBN 85-7379-809-2

Vitae. In 2005, the education program that started with the CEPID received a financial support of US$ 100.000 from the prestigious *Vitae Foundation* for the project "***Consolidation of the Museum and Laboratory for Science Teaching***" [Consolidação do MuLEC], after reviewing by expert external referees.

In 2006, the educational program has maintained the activities with the participation of teachers and students of public elementary and middle schools. The activities are held in two facilities: the House of Science (Casa das Ciências), and Museum and Laboratory for Science Teaching (MuLEC). Among the new educational activities that have been carried out we can mention:

a. **Science Exhibitions** – Every Thursday the MuLEC is open to public visitation. The general population and students groups are guided by graduated students through the exposition that includes topics related to cell biology, botanic, genomics, zoology and others. In 2006, the MuLEC received the visits of 68 basic and middle schools from 12 municipalities.

b. **Science on Tuesdays** – Since January of 2006, we setup a special program dedicated to talented young students of public schools. Small groups of students meet with senior investigators to discuss topics such as diabetes, stem cells, embryology, virus diseases, genetics, evolution and Mendel's Laws, botany, and other scientific topics. In the second semester of 2006, the Center made an agreement with the municipality of Luiz Antonio (60 km of Ribeirão Preto) to extend these activities to the town itself, involving more than 1200 students.

c. **Tutoring Young Scientists** is a program designed to enroll University graduated students in the orientation of small groups of students from the public schools. The aim is the development of scientific initiation of talented students, narrowing the distance between research and the middle school. Thus far, more than 250 students from public schools have been involved.

d. **Educational Publications** – in the period 2005-2006 the Center produced various kinds of printed materials destined to the public schools, including: 4 numbers of the Science Newsletter, now in its 15th edition [*Jornal das Ciências*], with a circulation of 4,000; and a series of brief publications called "*Folhetim*" that are intended to build up the memory of the projects developed in the House of Science. This material is available on line in the Center's Educational site.

e. In 2006, the Center offered an **online certified course** using the COL platform developed by the University of São Paulo. The course was called "*A aula: um exercício de investigação*" [Teaching class as a research exercise] and was opened for the participation of 20 teachers from public schools.

3. SCIENTIFIC CHALLENGES OR OBSTACLES

The most important scientific challenge, which has obvious practical consequences, is the translation of the basic bench research into applied technology and medical practice. We have approached this topic cautiously, but have steadily moved to increase the practical component of our research. This was probably one of the most clear positive effects of the CEPID project: it brought together researchers who used to collaborate but did not have a common target. Setting a common target coupled with long term financing has changed the profile of the research carried out by

these researchers. Not only they have jointly coauthored a significantly higher number of articles after the starting of the center, but also the contents of the output focus increasingly on the actual or potential application for “using cells or changing cells for treating diseases”.

4. DIFFICULTIES FOR THE PROJECT`S DEVELOPMENT

The acquisition of NOD/SCID mice is essential for the development of xenotransplant models of human cancer and for the development of an *in vivo* model for the analysis of mesenchymal stem cell differentiation. Unfortunately, the process of importation was too morose, taking over 9 months for the animals to arrive. Actually, all the transnational transfer of biological material (to and from Brazil) is encumbered with difficulties sometimes unsurpassable. More than one we lost precious material retained in the Brazilian customs or violated and rendered useless.

5 . OBJECTIVES FOR THE NEXT YEAR

Concerning the isolation and characterization of stem cells, we will: a) improve the selection of hematopoietic stem cells (for instance, by using the CD133 antigen for isolation) and characterization of gene expression; b) expand the comparison of mesenchymal stem cells with pericytes isolated by antibodies, then comparing the cells on the basis of gene expression; c) carry out the proteomic analysis of mesenchymal and hematopoetic stem cells derived from different sources; d) develop an animal model which will would allow the study of mesenchymal stem cell differentiation *in vivo*; e) the effects of different stimuli (TNF-alpha, CD40L, IL18, LPS, and PGE2 or combinations) on the differentiation of mesenchymal stem cells on the biological properties and profile of protein and post-translational modification of proteins will be evaluated; f) the role of microRNAs (miR) on stem cell fate will be evaluated; we have started the characterization of miRr223 expression at different stages of differentiation and intend to explore the mechanisms controlling its expression. Following our demonstration that mesenchymal stem cells with similar gene expression profiles can be isolated form bone marrow, umbilical cord vein and adult saphena vein, we are evaluating the characteristics of MSC obtained form a large spectrum of tissues, and comparing the cells with pericytes and fibroblasts, since these cells share several biological properties with MSC.

Aiming at the use of mesenchymal stem cells as immuno-modulatory cells for treating and preventing immune disorders, such as graft-versus-host and autoimmune diseases, we will analyze the effect of mesenchymal cells on normal purified T-

lymphocytes, by evaluating the modifications of the gene expression profiles induced by *in vitro* co-culture of the two cells, followed by separation and gene expression analysis. As reported on page 4, the differences of the NF kappa B pathway activation observed when comparing bone marrow and umbilical cord $CD34^+$ led us to explore the effects of this pathway upon the early stages of human T lymphocytes differentiation.

The clinical trial evaluating the use of a transplant approach for treatment of patients with severe newly diagnosed type-I diabetes mellitus will be expanded. The treatment protocol for refractory multiple sclerosis has been modified in order to reduce toxicity and we will increase the accrual of patients in this study.

We plan to use the animal models of acute promyelocytic leukemia to develop new therapeutic strategies. We are currently analyzing the effect of alpha-tocopherol a derivative of vitamin E with pro-apoptotic activity. In addition, we will use these models to study the retinoic acid syndrome, a potentially fatal complication of APL treatment.

Regarding the search for new therapeutic targets, we will analyze the cytotoxicity induced by the PRAME antibody in order to determine if it may be useful in non-Hodgkin's lymphoma or chronic lymphocytic leukemia treatment. The analysis of the gene expression of chronic lymphocytic leukemia by SAGE is now complete, and we are reviewing the findings in search of the targets for the disease diagnosis or treatment. Experiments are being conducted to explore the finding of a higher expression of TGF-beta pathway in mantle cell lymphomas [10]; for this end, we are testing the effects of the inhibition of this pathway on the functional properties of cultured lymphoma cells.

ATTACHMENTS

6.1 PUBLICATIONS OF THE CENTER'S INVESTIGATORS

1. Panepucci RA, Calado RT, Rocha V, Proto-Siqueira R, Silva Jr WA, Zago MA. Higher Expression of Transcription Targets and Components of the NF-*kappa*B Pathway is a Distinctive Features of Umbilical Cord Blood CD34+ Precursors. **Stem Cells** 2006 Sep 14; [Epub ahead of print]

2. Covas DT, Piccinato CE, Orellana MD, Siufi JL, Silva JR WA, Proto-Siqueira R, Rizzatti EG, Neder L, Silva AR, Rocha V, Zago MA. Mesenchymal stem cells can be obtained from the human saphena vein. **Experimental Cell Research**, v. 309, n. 2, p. 340-344, 2005.

3. de Souza GA, Godoy LM, Teixeira VR, Otake AH, Sabino A, Rosa JC, Dinarte AR, Pinheiro DG, Silva WA Jr, Eberlin MN, Chammas R, Greene LJ. Proteomic and SAGE profiling of murine melanoma progression indicates the reduction of proteins responsible for ROS degradation. **Proteomics**, 2006, 6(5):1460-70.

4. Pereira SR, Faça VM, Gomes GG, Chammas R, Fontes AM, Covas DT, Greene LJ. Changes in the proteomic profile during differentiation and maturation of human monocyte-derived dendritic cells stimulated with granulocyte macrophage colony stimulating factor/interleukin-4 lipopolysaccharide. **Proteomics**, v. 5, p. 1186-1198, 2005.

5. Proto-Siqueira R, Figueiredo-Pontes LL, Panepucci RA, Garcia AB, Rizzatti EG, Nascimento FM, Ishikawa HC, Larson RE, Falcao RP, Simpson AJ, Gout I, Filonenko V, Rego EM, Zago MA. PRAME is a membrane and cytoplasmic protein aberrantly expressed in chronic lymphocytic leukemia and mantle cell lymphoma. **Leukemia Research,** 2006, 30(11):1333-9.

6. Yao YG, Ogasawara Y, Kajigaya S, Molldrem JJ, Falcao RP, Pintao MC, McCoy Jr JP, Rizzatti EG, Young NS. Mitochondrial DNA sequence variation in single cells from leukemia patients. **Blood**, 2006 Aug 31; [Epub ahead of print]

7. Toon A, Peng G, Bradenburg Y, Zollo O, Xu W, Rego EM, Ruggero D. Impaired control of IRES-mediated translation in X-linked dyskeratosis congenita. **Science**, v. 312, n. 5775, p. 902-906, 2006

8. Figueiredo DL, Mamede RC, Proto-Siqueira R, Neder L, Silva WA Jr, Zago MA. Expression of cancer testis antigens in head and neck squamous cell carcinomas. **Head and Neck** 28:614-619, 2006.

9. Fontes AM, Davis BM, Encell LP, Lingas K, Covas DT, Zago MA, Loeb LA, Pegg AE, Gerson SL. Differential competitive resistance to methylating versus chloroethylating agents among five O6-alkylguanine DNA alkyltransferases in human hematopoietic cells. **Molecular Cancer Thererapeutic*s*** 5:121-8, 2006

10. Rizzatti EG, Falcao RP, Panepucci RA, Proto-Siqueira R, Anselmo-Lima WT, Okamoto OK, Zago MA. Gene expression profiling of mantle cell lymphoma cells reveal aberrant expression of genes from the PI3K-AKT, WNT and TgF beta signaling pathways. **British Journal of Hematology,** v. 130, p. 516-526, 2005.

11. Lima RSA, Baruffi MR, Lima ASG, Oliveira FM, Pontes LLF, Tone LG, Rogatto SR, Falcao RP, Chauffaille MLLF, Rego EM. The co-expression of PML/RARalfa and

AML1/ETO fusion genes is associated with ATRA resistance. **British Journal of Haematology**, v. 128, p. 407-409, 2005.

12. Matsushita H, Scaglioni PP, Bhaumik M, Rego EM, Cai LF, Majid SM, Miyachi H, Kakizuka A, Miller WH Jr, Pandolfi PP. In vivo analysis of the role of aberrant histone deacetylase recruitment and RAR alpha blockade in the pathogenesis of acute promyelocytic leukemia. **Journal of Experimental Medicine,** 2006, 17;203(4):821-8.

13. Matos DM, Rizzatti EG, Fernandes M, Buccheri V, Falcao RP. Gamma/delta and alfa/beta T-cell acute lymphoblastic leukemia: comparison of the clinical and immunophenotypic features. **Haematologica**, v. 90, p. 264-266, 2005

14. Kashima S, Alcantara LC, Takayanagui OM, Cunha MA, Castro BG, Pombo-de-Oliveira MS, Zago MA, Covas DT. Distribution of human T cell lymphotropic virus type 1 (HTLV-1) subtypes in Brazil: genetic characterization of LTR and tax region. **AIDS Research and Human Retroviruses** 22:953-9, 2006.

15. Pieroni F, Oliveira FM, Panepucci RA, Voltarelli JC, Simoes BP, Falcao RP. Development of donor cell derived acute myeloid leukemia after stem cell transplantation for chronic myeloid leukemia. **Bone Marrow Transplantation,** 2006, 37(8):801-2.

16. Baldissera RC, Nucci M, Vigorito AC, Maiolino A, Simoes BP, Lorand-Metze I, Aranha FJ, Miranda EC, Pagnano KB, Ruiz MA, Moraes AA, De Souza CA. Frontline therapy with early intensification and autologous stem cell transplantation versus conentional chemotherapy in unselected high-risk, aggressive non-Hodgkin's lymphoma patients: a prospective randomized GEMOH report. **Acta Haemaologica**, 115(1-2), p. 15-21, 2006

17. dos Santos ML, Palanch CG, Salaorni S, Da Silva WA Jr, Nagai MA. Transcriptome characterization of human mammary cell lines expressing different levels of ERBB2 by serial analysis of gene expression. **International Journal of Oncology**, 2006, 28(6):1441-61.

18. Burt RK, Marmont A, Oyama Y, Slavin S, Arnold R, Hiepe F, Fassas A, Snowden J, Schuening F, Myint H, Patel DD, Collier D, Heslop H, Krance R, Statkute L, Verda L, Traynor A, Kozak T, Hintzen RQ, Rose JW, Voltarelli J, Loh Y, Territo M, Cohen BA, Craig RM, Varga J, Barr WG.. Randomized controlled trials of autologous stem cell transplantation for autoimmune diseases. **Arthritis & Rheumatism** 54: 3750-60, 2006.

19. Rodrigues-Lisoni FC, Mehemet DK, Peitl Jr P, John CD, Silva Jr WA, Tajara E, Buckingham JC, Solito E . *In vitro* and *in vivo* studies on CCR 10 regulation by annexin A1. **FEBS Letters**, v. 580, p. 1431-1438, 2006.

20. Rego EM, Ruggero D, Tribioli C, Cattoretti G, Kogan S, Redner RL, Pandolfi PP. Leukemia with distinct phenotypes in transgenic mice expressing PML/RAR alpha, PLZF/RAR alpha or NPM/RAR alpha. **Oncogene** 2006, 25(13):1974-9.

21. Souza-Costa DC, Sandrim VC, Lopes LF, Gerlach RF, Rego EM, Tanus-Santos JE. Anti-inflammatory effects of atorvastatin: Modulation by the T-786C polymorphism in the endothelial nitric oxide synthase gene. **Atherosclerosis** 2006, Aug 26; [Epub ahead of print]

22. Pereira TV, Salzano FM, Mostowska A, Trzeciak WH, Ruiz-Linhares A, Chies JA,

Saavedra C, Nagamachi C, Hurtado AM, Hill K, Castro-de-Guerra D, Silva Jr WA, Bortolini MC. Natural selection and molecular evolution in primate PAX9 gene, a major determinant of tooth development. **Proceedings of the National Academy of Sciences of USA**, v. 103, n. 15, p. 5676-5681, 2006.

23. Pereira AC, Lourenco DM, Maffei FH, Morelli VM, Rollo HA, Zago MA, Vannucchi H, Franco RF. A transcobalamin gene polymorphism and the risk of venous thrombosis. The BRATROS (Brazilian Thrombosis Study). **Thrombosis Research** 119:183-188, 2007.

24. Pieroni F, Lourenco DM, Morelli VM, Maffei FH, Zago MA, Franco RF. Cytokine gene variants and venous thrombotic risk in the BRATROS (BRAZILIAN THROMBOSIS STUDY). **Thrombosis Research** 2006 Nov 16; [Epub ahead of print]

25. Souza CA, Vigorito AC, Ruiz MA Nucci M, Dulley FL, Funcke V, Tabak D, Azevedo AM, Byington R, Macedo MC, Saboya R, Penteado Aranha FJ, Oliveira GB, Zulli R, Martins Miranda EC, Azevedo WM, Lodi FM, Voltarelli JC, Simoes BP, Colturato V, De Souza MP, Silla L, Bittencourt H, Piron-Ruiz L, Maiolino A, Gratwohl A, Pasquini R.Validation of the EBMT risk score in chronic myeloid leukemia in Brazil and allogeneic transplant outcome. **Haematologica** 90: 234-239, 2005

26. Bernardes ES, Silva NM, Ruas LP, Mineo JR, Loyola AM, Hsu DK, Liu FT, Chammas R, Roque-Barreira MC. *Toxoplasma gondii* infection reveals a novel regulatory role for galectin-3 in the interface of innate and adaptive immunity. **American Journal of Pathology,** 2006, 168(6):1910-20.

27. Burt RK, Cohen B, Rose J Rose J, Petersen F, Oyama Y, Stefoski D, Katsamakis G, Carrier E, Kozak T, Muraro PA, Martin R, Hintzen R, Slavin S, Karussis D, Haggiag S, Voltarelli JC, Ellison GW, Jovanovic B, Popat U, McGuirk J, Statkute L, Verda L, Haas J, Arnold R.Hematopoietic stem cell transplantation for multiple sclerosis. **Archives of Neurology,** 62: 860-864, 2005.

28. Marques VD, Barreira AA, Davis MB, Abou-Sleiman PM, Silva WA Jr, Zago MA, Sobreira C, Fazan V, Marques W Jr. Expanding the phenotypes of the Pro56Ser VAPB mutation: proximal SMA with dysautonomia. **Muscle Nerve** 34:731-9, 2006

29. Marrero AR, Silva Jr WA, Bravi CM, Hutz MH, Petzl-Erler ML, Ruiz-Linhares Adres,Salzano FM, Bortolini MC. The demographic and evolutionary trajectories of the Guarani and Kaingang natives of Brazil. **American Journal of Physical Anthropology**, 2006.

30. Silva WA, Bortolini MC, Schneider MP, Marrero A, Elion J, Krishnamoorthy R, Zago MA. MtDNA haplogroup analysis of black Brazilian and sub-Saharan populations: implications for the Atlantic slave trade. **Human Biology** 78:29-41, 2006.

31. Covas DT, Kashima S, Guerreiro JF, Santos SEB dos, Zago MA. Variation in the FC gamma R3B gene among distinct Brazilian populations. **Tissue Antigens**, v. 65, p. 178-182, 2005.

32. Estalote AC, Proto-Siqueira R, Silva-Jr WA, Zago MA, Palatnik M. The mutation G298A-->Ala100Thr on the coding sequence of the Duffy antigen/chemokine receptor gene in non-caucasian Brazilians. **Genetics and Molecular Research**, v. 4, p. 166-173, 2005.

33. Silva Jr WA, Marrero AR, Leite FPN, Carvalho BA, Peres LM, Kommers TC, Cruz

IM, Salzano FM, Ruiz-Linhares A, Bortolini MC. Heterogeneity of the genome ancestry of individuals classified as white in the state of Rio Grande do Sul, Brazil. **American Journal of Human Biolog***y*, v. 17, n. 1, p. 1-17, 2005.

34. Pereira GS, Brandao RM, Giuliatti S, Zago MA, Silva WA Jr. Gene Class expression: analysis tool of Gene Ontology terms with gene expression data. **Genetics and Molecular Research** 5:108-14, 2006

35. Nakahata AM, Bueno NR, Rocha HA, Franco CR, Chammas R, Nakaie CR, Jasiulionis MG, Nader HB, Santana LA, Sampaio MU, Oliva ML. Structural and inhibitory properties of a plant proteinase inhibitor containing the RGD motif. **International J Biol Macromol**. 2006 May 26; [Epub ahead of print]

36. Oba-Shinjo SM, Correa M, Ricca TI, Molognoni F, Pinhal MA, Neves IA, Marie SK, Sampaio LO, Nader HB, Chammas R, Jasiulionis MG. Melanocyte transformation associated with substrate adhesion impediment. **Neoplasia**, 2006, 8(3):231-41.

37. Cabral H, Leopoldino AM, Tajara EH, Greene LJ, Faca VM, Mateus RP, Ceron CR, de Souza Judice WA, Julianod L, Bonilla-Rodriguez GO. Preliminary functional characterization, cloning and primary sequence of Fastuosain, a cysteine peptidase isolated from fruits of *Bromelia fastuosa*. **Protein and Peptide Letters** 2006, 13(1):83-9.

38. de Oliveira AH, Ruiz JC, Cruz AK, Greene LJ, Rosa JC, Ward RJ. Expression in E. coli and purification of the nucleoside diphosphate kinase b from *Leishmania major*. **Protein Expression Purification,** 2006, 49(2):244-50.

39. Oliveira AHC, Ruiz JC, Cruz AK, Greene LJ, Rosa JC. and Ward, R.J. Expression in E.coli and purification of the nucleoside diphosphate kinase b from *Leishmania* major. **Protein Expression and Purification** 49: 244-250, 2006.

40. Ruller R, Rosa JC, Faca VM, Greene LJ, Ward RJ. Efficient constitutive expression of *Bacillus subtilis* xylanase A in *Escherichia coli* DH5alpha under the control of the *Bacillus BsXA* promoter. **Biotechnology and Applied Biochemistry** 2006, 43(Pt 1):9-15.

41. Laure HJ, Faca VM, Izumi C, Padovan JC, Greene LJ. Low molecular weight squash trypsin inhibitors from *Sechium edule* seeds. **Phytochemistry** 2006, 67(4):362-70.

42. Penteado FCL, Medeiros L, Orellana MD, Palma P, Fontes AM, Takayanagui OM, Covas DT. Clonagem e expressão da glicoproteína transmembrana do retrovírus HTLV-1 em células de mamíferos. **Revista da Sociedade Brasileira de Medicina Tropical**, v. 39, n. 2, p. 169-173, 2006.

43. Santana FA, Nunes FM, Vieira CU, Machado MA, Kerr WE, Silva WA Jr, Bonetti AM. Differentially displayed expressed sequence tags in *Melipona scutellaris* (*Hymenoptera, Apidae, Meliponini*) development. **An Acad Bras Cienc**. 2006, 78(1):69-75.

44. Almeida LM, Silva IT, Silva Jr WA, Riggs PK, Carareto CM, Amaral EJ . The contribution of transposable elements to *Bos taurus* gene structure. **Gene**, 2006.

45. Carneiro AA, Fernandes JP, Araujo DB, Elias JJr, Martinelli AL, Covas DT, Zago MA, Angulo IL, Baffa O. Liver iron concentration evaluated by two magnetic methods: Magnetic resonance imaging and magnetic susceptometry. **Magnetic**

Resonance in Medicine v. 54, p. 122-128, 2005.

46. de Souza DA, Greene LJ. Intestinal permeability and systemic infections in critically ill patients: Effect of glutamine. **Critical Care Medicine**, v. 33, n. 5, p. 1125-1135, 2005.

47. Matos DM, Rizzatti EG, Garcia AB, Gallo DA, Falcao RP. Adhesion molecule profiles of B-cell non-Hodgkin's lymphomas in the leukemic phase. **Brazilian Journal Medical Biological Research,** 2006, 39(10):1349-55.

48. Wunsch-Filho V, Eluf-Neto J, Lotufo PA, Silva WA Jr, Zago MA. Epidemiological studies in the information and genomics era: experience of the Clinical Genome of Cancer Project in Sao Paulo, Brazil. **Brazilian Journal of Medical and Biological Research** 39:545-53, 2006.

49. Couri CE, Foss MC, Voltarelli JC. Secondary prevention of type 1 diabetes mellitus: stopping immune destruction and promoting beta-cell regeneration. **Brazilian Journal Medical Biological Research,** 2006, 39(10):1271-80.

50. Santana BA, Pintao MC, Abreu e Lima RS, Scheucher PS, Santos GA, Garcia AB, Falcao RP, Rego EM. Asynchronous expression of myeloid antigens in leukemic cells in a PML/RARalpha transgenic mouse model. **Brazilian Journal Medical Biological Research,** 2006, 39(5):615-20.

51. Fontes AM, Orellana MD, Palma PVB, Covas DT. Maturation of dendritic cells following exposure to different maturational stimuli. **Revista Brasileira de Hematologia e Hemoterapia**, v. 28, p. 89-96, 2006.

52. Hamerschlak N, Maluf E, Pasquini R, Eluf-Neto, Cavalcanti AB, Okano IR, Falcao RP, Pita MT, Loggetto SR. Incidence of aplastic anemia and agranulocytosis in Latin America: the LATIN study. **São Paulo Medical Journal**, São Paulo, v. 123, p. 101-104, 2005.

53. Falcão RP . Proliferação monoclonal B $CD5^+$ subclínica. **Revista Brasileira de Hematologia e Hemoterapia**, Brasil, v. 27, p. 267-271, 2005

54. Valente VB, Covas DT, Passos ADC. Marcadores sorológicos das hepatites B e C em doadores de sangue do Hemocentro de Ribeirão Preto. **Revista da Sociedade Brasileira de Medicina Tropical**, v. 38, n. 6, p. 488-492,2005.

55. Voltarelli JC, Stracieri AB, Oliveira MCB et al. Transplante de células tronco hematopoéticas em doenças reumáticas. Parte 1: Experiência internacional. **Revista Brasileira Reumatologia,** 45: 229-241, 2005.

56. Voltarelli JC, Stracieri ABPL, Oliveira MCB et al. Transplante de células tronco hematopoéticas em doenças reumáticas. Parte 2: Experiência brasileira . **Revista Brasileira Reumatologia,** 45: 301-312, 2005.

57. Goes EG, Borges JC, Covas DT, Orellana MD, Palma PV, Morais FR, Pela CA. Quality control of blood irradiation: determination T cells radiosensitivity to cobalt-60 gamma rays. **Transfusion**, 46:34-40, 2006

58. Wunsch Filho V ; Zago MA . Modern cancer epidemiological research: genetic polymorphisms and environment. **Revista de Saúde Pública,** v. 39, p. 490-497, 2005.

6.2 ARTICLES IN PRESS

Covas DT, Oliveira FS, Rodrigues ES, Abe-Sendes K, Silva WA Jr, Fontes AM. Knops blood group haplotypes among distinct Brazilian populations. **Transfusion**

Carrara RCV, Orellana MD, Fontes AM, Palma PVB, Kashima S, Mendes MR, Coutinho MA, Voltarelli JC, Covas DT. Mesenquimal stem cells from patients with chronic mieloid leukemia do not express Bcr-Abl and show absence of chimerism after allogeneic bone marrow transplant. **Brazilian Journal of Medical and Biological Research**

Goes E, Covas DT, Ottoboni MA, Palma P, Morais F, Pelá CA, Borges JC. Quality control of blood irradiation using a teletherapy unit: damage to stored red blood cells after cobalt-60 gamma irradiation. **Transfusion**

6.3 PATENTS

Chammas R, Melo FHM, Butera D, Silva AM. Molécula híbrida para diagnóstico e/ou prognóstico de doenças crônico-degenerativas, infecciosas e do desenvolvimento. 2005.

6.4 ACTIVITIES RELATED TO KNOWLEDGE AND SCIENCE DIFFUSION

Articles

Zago MA – Terapia com células-tronco pode causar câncer? ***Scientific American Brasil***, no. 51, agosto de 2006, p. 45.

Mello LE, Zago MA – Eleito precisa liberar verbas para ciência e tecnologia. Opinião, Folha Ciênica. ***Folha de São Paulo***, 25/10/2006.

Zago MA – The 6th Joint Meeting of the Brazilian School of Hematology and the European School of Hematology. ***European School of Hematology Newsletter***, May 2006.

Interviews, News, Public Comments

Em Folha Ciência – Célula adulta pode “virar” embrionária [Entrevista com MA Zago]. ***Folha de São Paulo***, 11/08/2006

Em Vida& – Mapeado gene do cordão umbilical [sobre trabalho de RA Panepucci do Centro de Terapia Celular]. ***Estado de São Paulo***, 14/02/2006, pag A13.

Em Folha Ciência Medicina – Célula-tronco detém diabetes em um teste [sobre trabalho de tratamento de diabete com transplante no Centro de Terapia Celular e entrevista com JC Voltarelli]. ***Folha de São Paulo***, 19/01/2006

Em Ciência – Célula-tronco lembra ipê roxo [entrevista de MA Zago sobre livro sobre Células-tronco: a Nova Fronteira da Medicina] ***A Cidade*** 24/09/2006 (Ribeirão Preto)

Polêmica – Entrevista sobre pesquisa, células tronco e Ordem do Mérito Científico. ***TV Cultura e TV Thathi***, Ribeirão Preto, 22 de dezembro de 2006.

Eles vão voltar a andar? Entrevista sobre as aplicações médicas das células-tronco para a revista Época na seção Saúde. ***Época*** 28/08/2006, pag 76-79.

Entrevista sobre ´celulas-tronco e seu potencial terapêutico na seção de Saúde do programa "Mais Você". ***Rede Globo*** (rede nacional), 3/11/2006.

Dúvida atroz – Entrevista de MA Zago a Carlos Fioravanti sobre uso terapêutico de células-tronco. Revista ***Pesquisa*** FAPESP, n. 124, junho de 2006

As tribos do mundo – Entrevista MA Zago a Carlos Fioravanti sobre a diversidade geética humana e raças, e sobre seu artigo publicado em Human Biology. Revista ***Pesquisa*** FAPESP, n. 123, maio de 2006.

Ataque duplo – Reportagem sobre a abordagem para tratamento de diabete melito desenolvido por JC Voltarelli no Centro de Terapia Celuar. Revista ***Pesquisa*** FAPESP, n. 120, fevereiro de 2006.

Covas DT. Lançamento do livro "Células-Tronco. A nova fronteira da medicina". ***Rádio CBN Brasil***, 28 jun. 2006.

Covas DT. Importância da doação de sangue. ***Portal USP-SP***, 07 jul.2006.

Covas DT. A Qualidade do Ensino Básico no Brasil e em Batatais***. A Notícia, Batatai***s, v. 75, p. 3-3, 04 ago. 2006.

Covas DT. O Brasil Analfabeto. ***A Notícia, Batatais***, v. 77, p. 3-3, 11 ago.2006.

Covas DT. A Escola Pública e a Comunidade. ***A Notícia, Batatais***, v. 76,p. 3-3, 11 ago. 2006.

Covas DT. Projeto Educacional da Casa da Ciência. EPTV Comunidade, ***Rede Globo de Televisão***, 12 ago. 2006.

Covas DT. Casa da Ciência. ***A Notícia, Batatais***, v. 79, p. 3-3, 01 set. 2006.

Covas DT. Escolas em Tempo Integral. ***A Notícia, Batatais***, v. 80, p. 3-3, 09 set. 2006.

Covas DT. Avanço da Hemoterapia no Brasil e outros temas. ***Rádio CBN Brasil***, 13 outubro 2006.

6.5 PRINCIPAL RESEARCHERS AND GROUP LEADERS

Marco Antonio Zago
Professor of Clinical Medicine, Coordinator of the CTC Center. *Main research interests*: genome, gene expression, stem cell differentiation, gene abnormalities in neoplasias.

Roberto Passetto Falcão
Professor of Clinical Medicine. Deputy coordinator of the CTC Center. *Main research intierests*: flow cytometry, lymphoid cell differentiation, hematopoietic neoplasias

Dimas Tadeu Covas
Associate Professor of Medicine, Technology Transfer Coordinator. *Main research interests*: stem cell research, transfusion medicine, HIV, HTLV-II

Lewis Joel Greene
Professor of Biochemistry. *Main research interests*: protein chemistry, proteomics, dendritic cell differentiation.

Roger Chammas
Associate Professor of Medicine. *Main research interests*: oncology, cell biology, glycobiology.

Julio Cesar Voltarelli
Associate Professor of Medicine. *Main research interests*: applied human immunology, bone marrow transplantation.

Wilson Araujo Silva Jr
Assistant Professor of Genetics. *Main research interests*: genome, gene expression, population genetics, bioinformatics.

Eduardo Magalhães Rego
Associate Professor of Medicine. *Main research interests*: leukemia, leukemogenesis, animal model of human diseases.

Marisa Barbieri
Former High School Biology Teacher and Former Associated Professor of Biology. Coordinator of Education and Dissemination.

All researchers belong to the faculty of the Medical School of Ribeirão Preto, University of S. Paulo, except for R. Chammas, who is from the USP Medical School in S. Paulo, and M. Barbieri, who retired from the USP Faculty of Sciences in Ribeirão Preto.

International Collaboration

Many of the researchers of the center have scientific links with foreign researchers, forged outside the context of the CEPID. There are, however, two collaborations that are more constant and were established in the framework of the center. There are frequent exchages of visits and shared research activity:

Vanderson Rocha: Clinical coordinator of the EuroCord Project, Hôpital Saint-Louis, Paris
Pier Paolo Pandolfi: Professor of Genetics, Sloan-Kettering Cancer Institute, N. York
Davide Ruggero: Associate Professor Fox Chase Cancer Center, Philadelphia
Rodrigo Callado and **Neal S. Young:** Hematology Branch, National Heart Lung and Blood Institute, National Institutes of Health, Bethesda, USA

Principal Investigators (as recognized by FAPESP in the research grant document)

Dimas Tadeu Covas
Eduardo Magalhães Rego
Júlio César Voltarelli
Marco Antonio Zago
Lewis Joel Greene
Roberto Passetto Falcão
Roger Chammas

Center's Activities Coordinators

Name	Institution	Position/Responsibility
Marco Antonio Zago	FMRP USP	Coordinator of the Center of Cell Therapy
Roberto Passetto Falcão	FMRP USP	Deputy Coordinator
Dimas Tadeu Covas	FMRP USP	Coordinator of Technology Transfer
Marisa Ramos Barbieri	FUNDHERP	Coordinator of Education and Dissemination

Scientific Contributions to the Project Development

Marco Antonio Zago – FMRP USP
Subproject Coordinator:
- Functional genomics of B-cell malignancies: the gene expression profiles of chronic lymphocytic leukemias and mantle cell lymphomas
- The impact of gene polymorphisms on the response to treatment with cell therapy and on susceptibility to hematological diseases
- The functional genomics of cells used for cell therapy: the gene expression profiles of human mesenchymal stem cells obtained from different sites
- The functional genomics of cells used for cell therapy: the comparison of the gene expression profiles of human CD34+ cells obtained from bone marrow, umbilical cord and peripheral blood
- The early gene expression changes in the hematopoiesis: the erythroid and granulocytic-monocytic pathways

Dimas Tadeu Covas – FMRP USP
Subproject Coordinator:
- Generation, characterization and in vitro manipulations of mesenchymal stem cells aiming at their use for cell therapy
- The impact of gene polymorphisms on the response to HIV and HTLV infection.
- The functional genomics of cells used for cell therapy: the gene expression profiles of human mesenchymal stem cells obtained from different sites
- The functional genomics of cells used for cell therapy: the comparison of the gene expression profiles of human CD34+ cells obtained from bone marrow, the umbilical cord and peripheral blood
- Cloning and expression of recombinant human coagulation factor VIII in mammalian cells using retrovirus as a vector.
- Brazil Cord Blood Bank.
- Development of an animal model for the study of mesenchymal stem cell differentiation in vivo.
- Assessment and treatment of iron overload in β thalassemia homozygous patients.

Eduardo Magalhães Rego – FMRP USP

Subproject Coordinator:
- Animal model of dyskeratosis congenita
- Analysis of the molecular basis of leukemogenesis in the transgenic model of acute promyelocytic leukemia
- Analysis of leukemic cells adhesion and tethering upon histone deacetylases inhibitors and G-CSF treatment in acute promyelocytic leukemia
- Analysis of FLT-3 mutations in acute myelogenous leukemia by single strand polymorphism
- Analysis of the effect of vitamin E isomers in acute promyelocytic leukemia
- Study of the effect of histone deacetylase Inhibitors on gene transcription in acute promyelocytic leukemia cells.
- Analysis of PRAME antigen expression in normal lymphoid cells
- Study of the pathogenesis of disseminated intravascular coagulation in the transgenic model of acute promyelocytic leukemia.

Roberto Passetto Falcão – FMRP USP
Subproject Coordinator:
- The expression of adhesion molecules in the leukemic phase of non-Hodgkin's lymphomas
- Analysis of blasts adhesion and tethering upon histone decaetylase inhibitors and G-CSF treatment in acute promyelocytic leukemia
- Analysis of the expression of glucocorticoid receptors in non-Hodgkin's lymphomas
- Development of a method of cytotoxicity of leukemic cells based on the association of peroxidase with 3-indol-acetic acid

Júlio César Voltarelli – FMRP USP
Subproject Coordinator:
- Treatment of immunological diseases by high dose chemotherapy and autologous bone marrow transplantation.
- Treatment of severe type I diabetes mellitus by bone marrow transplantation
- Development of animal models for testing cell therapy for lung disorders.

Lewis Joel Greene – FMRP USP
Subproject Coordinator:
- Evaluation of gene expression during differentiation and maturation of cord blood CD34-derived dendritic cells using proteomic analysis.
- Proteome modification during the early stages of melanoma malignization.
- Proteomic analysis of human metastatic cells treated with antitumoral drugs.
- Proteomic and genomic analysis of target genes modulated by miRNA-155 in non Hodgkin lymphoma cells.
- Proteomic analysis of dendritic differentiation induced by different stimuli of CD34+ or monocytes
- Identification of ligants of galectin-3
- Proteomic analysis of osteogenic differentiation of mesenchimal stem cells Stro-1+
- Comparision of the proteomic profile of mesenchimal stem cells obtained from different sources
- Analysis of the post translational changes of proteins differentially expressed by Melan-A, Tm1 and Tm5 cell lines.

Roger Chammas – FM USP
Subproject Coordinator:
- The use of pulsed autologus dendritic cells for the treatment of melanoma
- Gene expression profile during melanoma progression
- Analysis of cell membrane molecules changes during melanoma progression
- Gangliosides in hematological malignancies and normal lymphoid cells

- Genes associated with melanoma progression and development of chemoresistance
- Analysis of cell membrane molecules changes during melanoma progression and development of chemoresistance
- Gangliosides and dendritic cell function
- Tumor cell interaction with microenvironmental cells

Senior Investigators

Marisa Ramos Barbieri - FUNDHERP
Coordinator of the Educational Project:
- The cells, the genome and you.

Aparecida Maria Fontes - FUNDHERP
Subproject Coordinator:
- Cancer vaccine for chronic myeloid leukemia.
- Cloning and expression of recombinant human coagulation factor VIII in mammalian cells
- Cloning and expression of recombinant human coagulation factor IX in mammalian cells
- Isolation and characterization of murine mesenchymal cells
- Gene modification of stem cells

Wilson Araújo da Silva Jr – FMRP USP
Subproject Coordinator:
- Initiative to validate of the human transciptome
- Bioinformatics high throughput approaches to analyzing gene expression of human tissues
- The comparison of gene expression in human neoplasias, with especial emphasis in interleukines, adhesion molecules and angiogenesis.
- Analysis of the sequences generated by the Human Genome of Cancer project.
- Clinical Genomics Project – Bioinformatics Laboratory
- Genome data mining.
- Gene expression of microRNAs in hematopoietic stem cells

Vanderson Rocha – EUROCORD/Paris, Hôpital S. Louis
Subproject Coordinator:
- Facilitating cord blood cells for engraftment: importance of specific lymphocyte subpopulations.
- Expansion of cord blood mononuclear cells in coculture with autologous human umbilical vein endothelial cells (HUVEC).
- The impact of gene polymorphisms on the response to treatment with cell therapy.
- The impact of gene polymorphisms on the susceptibility to hematological diseases

Belinda Pinto Simões – FMRP USP
Subproject Coordinator:
- Haploidentical bone marrow transplantation
- Strategies to reduce or avoid graft-versus-host disease
- Facilitating cord blood cells for engraftment: importance of specific lymphocyte subpopulations.
- The impact of gene polymorphisms on the susceptibility and evolution of GVHD

José César Rosa – FMRP USP
Subproject Coordinator:

- Proteome modification during the differentiation of dendritic cells from CD34+ cells of human umbilical cord, during the early stages of melanoma malignization, and of human metastatic cells treated with antitumoral drugs

Evamberto Garcia de Góes - FUNDHERP - FAPESP
Subproject Coordinator:
- Use of Telecobalt therapy for the prevention of graft versus host disease asociated with transfusion: dosimetry and quality control of irradiated blood
- Effects of diagnostic X-ray dose on peripheral blood mononuclear cells

Associate Investigators

Greice A Molfetta - FMRP/USP - FAPESP
Subproject
- Changes of gene expression in the early differentiation of CD34+ along the erythroid and the granulocytic-monocytic pathways

Rita de Cássia Viu Carrara - FUNDHERP - FAPESP
Subproject
- Identification of genes differentially expressed in CD34+ Bcr/Abl+ cells of patients with chronic myeloid leukemia

Clarice Izumi - FMRP/USP
Subproject
- Proteome modification during the differentiation of dendritic cells from CD34+ cells of human umbilical cord, during the early stages of melanoma malignization, and of human metastatic cells treated with antitumoral drugs

Paulo Peitl Junior - FUNDHERP - FAPESP
Subproject
- Changes of gene expression in human cells treated *in vitro* with antitumoral drugs

Simone Kashima Hadad - FUNDHERP
Subproject
- Genetic characterization of host factors and role of microRNA expression in HTLV-1 infection.

Post Doctoral Fellows

Name	Institution	Adviser
Paulo Peitl Jr *	FMRPUSP – FAPESP	Marco A. Zago
Rodrigo Proto-Siqueira *	FMRPUSP – FAPESP	Marco A. Zago
Rodrigo Alexandre Panepucci +	FMRPUSP – FAPESP	Marco A. Zago
Rita de Cássia Viu Carrara *	FMRPUSP – FAPESP	Dimas T. Covas
Idalete da Silva	FMRPUSP – FAPESP	Lewis J. Greene
Kelen Cristina M Farias +	FMRPUSP – FAPESP	Julio C. Voltarelli
Bárbara Amelia A Santana +	FMRPUSP – FAPESP	Eduardo M. Rego

* Finished during 2006
+ Started in December 2006

6.6 DOCTORAL AND MASTERS THESES COMPLETED IN 2005 AND 2006

Masters Theses

- Roberta Carreto. **Caracterização molecular de isolados de HIV-1 na região de Ribeirão Preto.** 2005. Faculdade de Ciências Farmacêuticas de Ribeirão Preto. Orientador: Prof. Dr. Dimas Tadeu Covas.

- Danielle Leão Cordeiro de Farias Souza. **Pesquisa de mutações nos exons 12 a 20 do gene FLT3 em pacientes com leucemia mielóide aguda.** 2005. Faculdade de Medicina de Ribeirão Preto. Orientador: Prof. Dr. Eduardo Magalhães Rego.

- Priscila Santos Scheucher. **Proliferação e morte celular programada na gênese da leucemia promielocítica aguda no modelo transgênico hCG-PML-RARalfa.** 2005. Faculdade de Medicina de Ribeirão Preto - USP, Fundação de Amparo à Pesquisa do Estado de São Paulo. Orientador: Prof. Dr. Eduardo Magalhães Rego.

- Fabíola Leslie A. C. Mestriner. **Caracterização de componente(s) sérico(s) envolvido(s) na ausência da migração de neutrófilos para o foco infeccioso na sepse.** Faculdade de Medicina de Ribeirão Preto-USP. 2006. Orientador: Prof.Dr. Lewis Joel Greene

- Alana Maria Cerqueira de Oliveira. **Isolamento de mitocôndrias de monócitos humanos para estudo de proteoma subcelular durante a diferenciação e maturação de células dendríticas.** 2006. Fundação de Amparo a Pesquisa do Estado de São Paulo. Orientador: Prof.Dr. Lewis Joel Greene.

- Maria Carolina Oliveira Rodrigues. **Transplante de células tronco hematopoéticas para doenças auto-imunes.** 2006. Faculdade de Medicina de Ribeirão Preto. Orientador: Prof. Dr. Julio Cesar Voltarelli.

- Daniel Mazza matos. **Expressão de moléculas de adesão na leucemia linfocítica crônica/linfoma linfocítico e em linfomas não-Hodgkin B em fase leucêmica.** 2005. Dissertação. Faculdade de Medicina de Ribeirão Preto da Universidade de São Paulo. Orientador: Prof. Dr. Roberto Passetto Falcao.

- Fabíola Singaretti de Oliveira. **Geração de Duas Populações Celulares Geneticamente Modificadas Super Expressando os genes BCR-ABL parcial e B7.1.** 2005. Faculdade de Medicina de Ribeirão Preto - USP, Fundação Hemocentro de Rib. Preto. Orientador: Profa. Dra. Aparecida Maria Fontes.

- Mara de Souza Junqueira. **Caracterização das vias de transformação maligna de uma nova linhagem estabelecida de melanoma murino.** 2006. Universidade de São Paulo. Orientador: Prof. Dr. Roger Chammas.

Doutorado

- Rodrigo Alexandre Panepucci. **Diferenças na expressão gênica de células CD34+ de medula óssea e de sangue de cordão umbilical.** 2006. Faculdade de Medicina de Ribeirão Preto da USP. Orientador: Prof. Dr. Marco Antonio Zago

- Virgínia Proença Picanço. **Clonagem e Expressão do Fator VIII Humano de Coagulação Humano.** 2006. Faculdade de Medicina de Ribeirão Preto Usp, Fundação de Amparo à Pesquisa do Estado de São Paulo. Orientador: Prof. Dr. Dimas Tadeu Covas.

- Barbara Amelia Aparecida Santana. **Determinacão do efeito dahaploinsuficiência do gene C/EBPalfa na gênese da leucemia promielocítica aguda do modelo transgênico hCG-PML-RARalfa.** 2006. Universidade de São Paulo, Fundação de Amparo à Pesquisa do Estado de São Paulo. Orientador: Prof. Dr. Eduardo Magalhães Rego.

- Kelen Cristina Malmegrim de Farias. **Reconstituição imunológica pós-transplante de células tronco hematopoéticas para diabete melito do tipo 1 e esclerose múltipla.** 2006. Faculdade de Medicina de Ribeirão Preto-USP, Fundação de Amparo à Pesquisa do Estado de São Paulo. Orientador: Prof. Dr. Julio Cesar Voltarelli.

- Luiz Paulo Cicogna Faggioni. **Fatores constitucionais e genéticos determinantes de microquimerismo pós-transfusional.** 2006. Faculdade de Medicina de Ribeirão Preto-USP. Orientador: Julio Cesar Voltarelli.

- Edgar Gil Rizzatti. **Análise do perfil de expressão gênica do linfoma de células do manto em fase leucêmica com microarrays de oligonucleotideos.** 2005. Faculdade de Medicina de Ribeirão Preto . Orientador: Prof. Dr. Roberto Passetto Falcao.

- Andréia Hanada Otake. **Papel de dissialogangliosídeos na proliferação e morte celular induzida de melanocitos e melanomas in vitro.** 2006. Universidade de São Paulo, Fundação de Amparo à Pesquisa do Estado de São Paulo. Orientador: Prof. Dr. Roger Chammas.

- Fabiana Henriques Machado de Melo. **Exploração funcional do processo de glicosilação aberrante em tumores: mecanismos envolvidos na atividade pró-migratória de galectina-3.** 2006. Universidade de São Paulo, Fundação de Amparo à Pesquisa do Estado de São Paulo. Orientador: Prof. Dr. Roger Chammas.

- A G Muras. **Avaliação da participação de prion celular em fenômenos associados a tumorigênese experimental.** 2005. Fundação Antônio Prudente. Co-Orientador: Prof. Dr. Roger Chammas.

6.7 GRADUATE STUDENTS (PhD AND MSc) ACTIVE

Name	Institution	Adviser
Evandra Strazza Rodrigues	FMRPUSP – FUNDHERP	Aparecida M Fontes
Elaine Cristina P. Vitorelli	FMRPUSP – FUNDHERP	Aparecida M Fontes
Rochele Azevedo	FMRPUSP	Dimas T Covas
Ana Cristina Silva Pinto	FMRPUSP	Dimas T Covas
Bruno Marcos Verbeno Azevedo	FMRPUSP	Dimas T Covas
Ana Valéria Gouveia Andrade	FMRPUSP	Dimas T Covas
Lucila Habib B de Oliveira	FMRPUSP	Dimas T Covas
Jorge Luis Curado Siufi	FMRPUSP	Dimas T Covas
Ana Paula C N Cunha Cozac	FMRPUSP	Dimas T Covas
Maria Fernanda Castro Amarante	FMRPUSP	Dimas T Covas
Flora Cristina Lobo Penteado	FCF/ARARAQUARA	Dimas T Covas
Rodrigo Haddad	FMRPUSP	Dimas T Covas
Antonio Roberto Lucena Araújo	FMRPUSP – FAPESP	Eduardo M Rego
Rafael H Jácomo	FMRPUSP – FAPESP	Eduardo M Rego
Luciana O. Oliveira	FMRPUSP	Eduardo M Rego

Mirela Tomazzini	FMRPUSP – FAPESP	Eduardo M Rego
Priscila Santos Scheucher	FMRPUSP – FAPESP	Eduardo M Rego
Maria Carolinia Tostes Pintão	FMRPUSP	Eduardo M Rego
Hamilton Luis G. Teixeira	FMRPUSP	Eduardo M Rego
Guilherme Augusto Silva Santos	FMRPUSP	Eduardo M Rego
Lorena Lobo e Figueiredo	FMRPUSP – FAPESP	Eduardo M Rego
Rodrigo Abreu e Lima	FMRPUSP – FAPESP	Eduardo M Rego
Vivian Toussef Khouri	FMRP - USP	Julio C Voltarelli
Alessandra de Paula Souza	FMRPUSP - FAPESP	Julio C Voltarelli
Marcia Pinho	FMRP - USP	Julio C Voltarelli
Danielle F Godoi	FMRP - USP	Julio C Voltarelli
Elisa Vendramini Nogueira	FMRP - USP	Julio C Voltarelli
Carolina Hassibe Thomé	CNPq	Lewis J Greene
Germano Aguiar Ferreira	FMRPUSP – FAPESP	Lewis J Greene
Glauce Gaspar Gomes	FMRPUSP – CAPES	Lewis J Greene
Ana Cristina D`Ávilla de Castro	UNIFESP – FAPESP	Lewis J Greene
Gisele Guiçardi Tomazella	UNIFESP – FAPESP	Lewis J Greene
Helen Cristina Miranda	FMRPUSP – FAPESP	Lewis J Greene
Nívea Maria Rocha Macedo	FMRPUSP – CAPES	LJ Greene/JC Rosa
Francisco Careta	FMRPUSP – FAPESP	Marco A Zago
Manuela Ramos Barbieri	FMRPUSP – FAPESP	Marco A Zago
Dalila Zanete	FMRPUSP – FAPESP	Marco A Zago
André Marinato	FMRPUSP	Roberto P Falcão
Daniel Mazza	FMRPUSP – FAPESP	Roberto P Falcão
Leandro Felipe Dalmazzo	FMRPUSP	Roberto P Falcão
Tharcisio Citrangulo Tortelli Jr	USP	Roger Chammas
Guilherme Francisco	Fund A Prudente - FAPESP	Roger Chammas
Fabio Luiz Navarro Marques	USP	Roger Chammas
Patrícia Leusa Nunes da Costa	Fund A Prudente - FAPESP	Roger Chammas
Luciana Nogueira Sousa Andrade	USP – FAPESP	Roger Chammas
Verônica Rodrigues Teixeira	USP – FAPESP	Roger Chammas

Masters and Doctoral Theses and Post-Doctoral Projects in Development

Mestrado

- Francisco Caretta. **Vias gênicas nas neoplasias linfóides**. Faculdade de Medicina de Ribeirão Preto. Orientador: Prof. Dr. Marco Antonio Zago

- Manuela Ramos Barbieri. **Padrão de expressão celular da proteína S100 calcium binding protein A7 (psoriasin).** Faculdade de Medicina de Ribeirão Preto. Orientador: Prof. Dr. Marco Antonio Zago

- Rochele Azevedo. **Fatores prognósticos envolvidos na patogênese da infecção pelo HTLV-1.** Início: 2005. Faculdade de Medicina de Ribeirão Preto Usp. Orientador: Prof. Dr. Dimas Tadeu Covas.

- Karen de Lima Prata. **Análise das Características Biológicas das Células Tronco Mesenquimais de Pacientes submetidos a altas doses de Rádio e/ou Quimioterapia.** Início: 2004. Faculdade de Medicina de Ribeirão Preto Usp. Orientador: Prof. Dr. Dimas Tadeu Covas.

- Ana Cristina Silva Pinto. **Efeito do Tratamento com Hidroxiuréia sobre as Células Hematopoéticas da Medula Óssea de Pacientes com Anemia Falciforme.** Início: 2004. Faculdade de Medicina de Ribeirão Preto USP. Orientador: Prof. Dr. Dimas Tadeu Covas.

- Bruno Marcos Verbeno Azevedo. **Avaliação do Potencial Vasculogênico de Células Progenitoras Endoteliais**. Início: 2006. Faculdade de Medicina de Ribeirão Preto Usp. Orientador: Prof. Dr. Dimas Tadeu Covas.

- Ana Valéria Gouveia Andrade. **Análise da Expressão do SDF-1 e do CXCR4 em células progenitoras mesenquimais fetais e avaliação do efeito das 3 isoformas do TGFBeta na expressão destes genes.** Início: 2005. Faculdade de Medicina de Ribeirão Preto USP. Orientador: Prof. Dr. Dimas Tadeu Covas.

- Lucila Habib B. Oliveira. **Análise de Expressão Gênica das Células AC 133+ Isoladas a partir do Sangue de Cordão Umbilical.** Início: 2006. Faculdade de Medicina de Ribeirão Preto USP. Orientador: Prof. Dr. Dimas Tadeu Covas.

- Antonio Roberto Lucena de Araújo. **Expressão das isoformas do gene p73: TAp73 e deltaNp73 em leucemia mielóide aguda.** Início: 2004. Faculdade de Medicina de Ribeirão Preto - USP. Orientador: Prof. Dr. Eduardo Magalhães Rego
- Carolina Hassibe Thomé. **Identificação e caracterização de modificações pós-traducionais em algumas proteínas diferencialmente expressas durante a maturação das células dendríticas humanas.** Início: 2005. Orientador: Prof. Dr. Lewis Joel Greene

- Germano Aguiar Ferreira. **Caracterização das modificações pós-traducionais em células dendríticas humanas.** Início: 2006. Orientador: Prof. Dr. Lewis Joel Greene

- Vivian Youssef Khouri. **Prevenção da mucosite pós-transplante de medula óssea alogênico com aplicação local de laser.** Início: 2004. Faculdade de Medicina de Ribeirão Preto-USP. Orientador: Prof. Dr. Julio César Voltarelli

- Elaine Cristina Pereira Vitorelli. **Isolamento e Caracterização de Células-Tronco Mesenquimais da Medula Óssea e do Tecido Mesotelial de Camundongos NODSCID.** Início: 2004. Faculdade de Medicina de Ribeirão Preto, Fundação Hemocentro de Rib. Preto. Orientador: Profa. Dra. Aparecida Maria Fontes

- Evandra Strazza Rodrigues. **Clonagem e Expressão do Fator VIII Recombinante em Células de Mamíferos.** Início: 2004. Faculdade de Medicina de Ribeirão Preto, Fundação Hemocentro de Rib. Preto. Orientador: Profa. Dra. Aparecida Maria Fontes

- Tharcisio Citrangulo Tortelli Jr. **Proibitina e seu papel na quimiorresistência de melanomas humanos.** Início: 2006. Universidade de São Paulo. Orientador: Roger Chammas

- Guilherme Francisco. **Polimorfismos em genes de reparo e susceptibilidade ao desenvolvimento de melanoma cutâneo.** Início: 2005. Fundação Antônio Prudente, Fundação de Amparo à Pesquisa do Estado de São Paulo. Orientador: Roger Chammas

Doutorado

- Dalila Zanete. **Influência da metilação e da acetilação na expressão gênica de células progenitoras hematopoéticas.** Faculdade de Medicina de Ribeirão Preto**.** Orientador: Prof. Dr. Marco Antonio Zago

- Jorge Luiz Curado Siufi. **Avaliação do potencial terapêutico das células tronco mesenquimais no tratamento da GVHD experimental.** Início: 2005. Faculdade de Medicina de Ribeirão Preto Usp. Orientador: Prof. Dr. Dimas Tadeu Covas.

- Ana Paula Costa Nunes da Cunha Cozac. **Estudo do potencial antigênico relativo dos antígenos de grupos sangüíneos menores em pacientes em esquema de transfusão da região de Ribeirão Preto.** Início: 2005. Faculdade de Medicina de Ribeirão Preto USP. Orientador: Prof. Dr. Dimas Tadeu Covas.

- Maria Fernanda Castro Amarante. **Isolamento, caracterização, clonagem e expressão dos genes de fatores de crescimento celular a partir de um banco de cDNA de fígado fetal.** Início: 2005. Faculdade de Medicina de Ribeirão Preto Usp. Orientador: Prof. Dr. Dimas Tadeu Covas.

- Flora C Lobo Penteado. **Homing e Diferenciação das Células Progenitoras Mesenquimais Humanas em Resposta ao Dano Hepático Reversível Induzido em Camundongo NOD-SCID.** Início: 2004. Faculdade de Ciências Farmacêuticas de Araraquara. Orientador: Prof. Dr. Dimas Tadeu Covas.

- Rodrigo Haddad. **Silenciamento da expressão de genes estruturais do HTLV-1 utilizando a técnica de RNA de interferência.** Início: 2006. Faculdade de Medicina de Ribeirão Preto USP. Orientador: Prof. Dr. Dimas Tadeu Covas.

- Rafael H Jacomo. **Estudo do papel da anexina II na ativação da coagulação na leucemia promielocítica aguda.** Início: 2006. Faculdade de Medicina de Ribeirão Preto - USP. Orientador: Prof. Dr. Eduardo Magalhães Rego

- Luciana C Oliveira Oliveira. **Estudo do papel das células progenitoras do endotélia na gênese e progressão do mieloma múltiplo.** Início: 2006. Faculdade de Medicina de Ribeirão Preto - USP. Orientador: Prof. Dr. Eduardo Magalhães Rego

- Mirela de Barros Tamarozzi. **Análise da fisiopatologia da lesão pulmonar aguda relacionada a transfusão (TRALI) em um modelo murino.** Início: 2006. Faculdade de Medicina de Ribeirão Preto - USP, Fundação de Amparo à Pesquisa do Estado de São Paulo. Orientador: Prof. Dr. Eduardo Magalhães Rego

- Priscila Santos Scheucher. **Estudo do efeito da própolis e do seu derivativo CAPE na leucemia mielóide aguda.** Início: 2005. Faculdade de Medicina de Ribeirão Preto - USP. Orientador: Prof. Dr. Eduardo Magalhães Rego

- Maria Carolina Tostes Pintão. **Análise da ativação da cascata de coagulação no modelo transgênico hCG-PML/RARalfa.** Início: 2005. Faculdade de Medicina de Ribeirão Preto - USP. Orientador: Prof. Dr. Eduardo Magalhães Rego

- Hamilton Luiz Gimenes Teixeira. **Análise da influência do C/EBPalfa na expressão do microRNA223 em células da leucemia promielocítica aguda.** Início: 2005. Faculdade de Medicina de Ribeirão Preto - USP, Conselho Nacional

de Desenvolvimento Científico e Tecnológico. Orientador: Prof. Dr. Eduardo Magalhães Rego

- Guilherme Augusto Silva dos Santos. **Estudo da atividade antileucêmica da rapamicina no modelo de xenotransplante de leucemia mielóide aguda.** Início: 2004. Faculdade de Medicina de Ribeirão Preto - USP. Orientador: Prof. Dr. Eduardo Magalhães Rego

- Lorena Lobo Figueiredo. **Análise da interferência do TGFbeta na leucemia promielocítica aguda induzida pelo gene de fusão PML-RARalfa.** Início: 2003. Faculdade de Medicina de Ribeirão Preto da Universidade de São Paulo, Fundação de Amparo à Pesquisa do Estado de São Paulo. Orientador: Prof. Dr. Eduardo Magalhães Rego

- Rodrigo S Abreu e Lima. **Estudo do efeito da alfa tocoferol no modelo transgênico de leucemia promielocítica aguda.** Início: 2003. Faculdade de Medicina de Ribeirão Preto da Universidade de São Paulo, Fundação de Amparo à Pesquisa do Estado de São Paulo. Orientador: Prof. Dr. Eduardo Magalhães Rego

- Glauce Gaspar Gomes. **Análise proteômica do processo de diferenciação de células progenitoras mesenquimais isoladas da medula óssea humana.** Início: 2005. Faculdade de Medicina de Ribeirão Preto-USP. Orientador: Prof. Dr. Lewis Joel Greene

- Ana Cristina D`Ávila de Castro. Análise funcional e perfil proteômico. **Efeito de diferentes estímulos sobre a diferenciação das células dendríticas plasmacitóides a partir de células CD34+ de sangue de cordão umbilical humano.** Início: 2005. Universidade Federal de São Paulo, Escola Paulista de Medicina. Orientador: Prof. Dr. Lewis Joel Greene

- Gisele Guiçardi Tomazella. **Identificação dos ligantes de galectina-3 a partir de células dendríticas e seus monócitos presursores e neutrófilos humanos.** Início: 2005. Universidade Federal de São Paulo, Escola Paulista de Medicina. Orientador: Prof. Dr. Lewis Joel Greene

- Helen Cristina Miranda. **Comparação da expressão gênica de células tronco mesenquimais obtidas de veia de cordão umbilical e medula óssea.** Início: 2005. Faculdade de Medicina de Ribeirão Preto-USP. Orientador: Prof. Dr. Lewis Joel Greene

- Nívea Macedo Rocha Martins. **Estudos das modificações pós-tradução em proteínas diferencialmente expressas nas linhagens celulares melan-A, TM1 e TM5. Um modelo murino de progressão de melanoma.** Início: 2006. Faculdade de Medicina de Ribeirão Preto-USP. Orientador: Prof. Dr. Lewis Joel Greene

- Alessandra de Paula Souza. **Influência do transplante de medula óssea autólogo na expressão gênica diferencial no sangue periférico de pacientes com esclerose múltipla.** Início: 2006. Faculdade de Medicina de Ribeirão Preto-USP, Fundação de Amparo à Pesquisa do Estado de São Paulo. Orientador: Prof. Dr. Julio César Voltarelli.

- Maria Carolina Oliveira Rodrigues. **Transplante de células tronco mesenquimais no diabete melito do tipo 1- Estudo clínico e experimental.** Início: 2006. Faculdade de Medicina de Ribeirão Preto-USP. Orientador: Prof. Dr. Julio César Voltarelli.

- Márcia Pinho. **Associação entre doença periodontal e artrite reumatóide.** Início: 2005. Faculdade de Medicina de Ribeirão Preto-USP. Orientador: Prof. Dr. Julio César Voltarelli.

- Dannielle F. Godoi. **Modelo experimental de transplante de células tronco hematopoéticas em doença inflamatória intestinal.** Início: 2004. Faculdade de Medicina de Ribeirão Preto-USP. Orientador: Prof. Dr. Julio César Voltarelli.

- Elisa Vendramini Nogueira. **Transferência de atopia cutânea e pulmonar no transplante alogênico de medula óssea.** Início: 2004. Faculdade de Medicina de Ribeirão Preto-USP. Co-orientador: Orientador: Prof. Dr. Julio César Voltarelli.

- Fabio Luiz Navarro Marques. **Desenvolvimento de novos radiofármacos para imagem molecular de tumores.** Início: 2006. Universidade de São Paulo. Orientador: Prof. Dr. Roger Chammas

- Patrícia Luisa Nunes da Costa. **Fatores microambientais no desenvolvimento do melanoma: implicações terapêuticas.** Início: 2005. Fundação Antônio Prudente, Fundação de Amparo à Pesquisa do Estado de São Paulo. Orientador: Prof. Dr. Roger Chammas

- Luciana Nogueira de Sousa Andrade. **Galectina-3 e angiogênese.** Início: 2004. Universidade de São Paulo, Fundação de Amparo à Pesquisa do Estado de São Paulo. Orientador: Prof. Dr. Roger Chammas

- Veronica Rodrigues Teixeira. **Controle de Expressão de Galectina-3.** Início: 2003. Universidade de São Paulo, Fundação de Amparo à Pesquisa do Estado de São Paulo. Orientador: Prof. Dr. Roger Chammas

Pós-Doutorado

- Carbolante EM. **Clonagem e expressão de proteínas antigênicas do vírus linfotrópico de células T humanas em sistema procarioto.** Em andamento. 2004 Faculdade de Medicina de Ribeirão Preto Usp, Conselho Nacional de Desenvolvimento Científico e Tecnológico. Supervisor: Prof. Dr. Dimas Tadeu Covas.

- Kelen Cristina Malmegrim de Farias. **Características biológicas e genéticas de células tronco hematopoéticas e mesenquimais de pacientes submetidos a transplante autólogo de células tronco hematopoéticas para doenças auto-imunes.** Início: 2006. Faculdade de Medicina de Ribeirão Preto-USP, Fundação de Amparo à Pesquisa do Estado de São Paulo. Supervisor: Prof. Dr. Julio César Voltarelli

- Rodrigo Alexandre Panepucci. **Papel da via NF kappa B na diferenciação *in vitro* de células T a partir de células tronco hematopoéticas CD34^{+}.** Início: 2006. Faculdade de Medicina de Ribeirão Preto-USP, Fundação de Amparo à Pesquisa do Estado de São Paulo. Supervisor: Prof. Dr. Marco Antonio Zago

6.8 Graduate Students (PhD and MsC) concluded in 2006

Name	Institution	Adviser
Virginia Proença Picanço	FUNDHERP	Dimas Tadeu Covas
Barbara Amélia A. Santana	FMRPUSP-FAPESP	Eduardo M Rego
Fabiola Leslie A C Mestriner	FMRPUSP	Lewis J Greene
Alana Maria Cerqueira de Oliveira	FMRPUSP, CNPq	Lewis J Greene
Maria Carolina Oliveira Rodrigues	FMRPUSP	Julio C Voltarelli
Luiz Paulo Cicogna Faggioni	FMRPUSP	Julio C Voltarelli
Mara de Souza Junqueira	USP	Roger Chammas
Andreia Hanada Otake	USP - FAPESP	Roger Chammas
Fabiana Henrique M Melo	USP - FAPESP	Roger Chammas
Karen Lima Prata	FMRPUSP	Dimas Tadeu Covas

FUNDHERP	Fundação Hemocentro de Ribeirão Preto
FAPESP	Fundação de Amparo à Pesquisa do Estado de São Paulo
HCRPUSP	Hospital das Clínicas de Ribeirão Preto / Universidade de São Paulo
FMRPUSP	Faculdade de Medicina de Ribeirão Preto / Universidade de São Paulo
FMUSP	Faculdade de Medicina da Universidade de São Paulo (São Paulo)
CAPES	Coordenação de Aperfeiçoamento de Pessoal de Nível Superior.
CEPID	Centro de Pesquisa Inovação e Difusão.
CNPq	Conselho Nacional de Desenvolvimento Cientifico e Tecnológico.

6.9 COMUNICATIONS IN CONGRESSES AND MEETINGS

PEREIRA AS, ALCÂNTARA LCJ, FIGUEIROA F, NUNES CLX, RIOS DLS, KASHIMA SH, COVAS DT, CASTRO B G. Study on the genetic polymorphism of the HTLV-1 U3-LTR region isolated from asymptomatic and symptomatic (TSP/HAM) infected individuals from Salvador-Brazil. In: IX SIMPÓSIO INTERNACIONAL SOBRE HTLV NO BRASIL, 2006, Belo Horizonte. Revista da Sociedade Brasileira de Medicina Tropical. 2006. v. 39, p. 96-96.

PRADO JR BPA, PRATA KL, BARROS GM, SANTIS GC, PINTO AC, DAVILA RB, FERNANDES AT, FERREIRA SI, OTTOBONI MA, COVAS DT. Platelet Aphaeresis: Effect on Donors Collecting Single and Double Bag. In: 59TH AABB ANNUAL MEETING, 2006, Miami Beach. Transfusion. 2006. v. 46, p. 40A-41A.

YOSHIOKA FKN, KASHIMA S, TAKAYANAGUI OM, PALMA PVB, MORAIS FR, SILVA ARL, ORELLANA MD, GUERREIRO JF, COVAS DT. Immunophenotypic characterization of denditric cells from patients asymptomatic HTLV-1 carriers and patients diagnosed as HAM/TSP. In: IX SIMPÓSIO INTERNACIONAL SOBRE HTLV NO BRASIL, 2006, Belo Horizonte. Revista da Sociedade Brasileira de Medicina Tropical. 2006. v. 39, p. 57-57.

KASHIMA S, SILVA IT, TAKAYANAGUI OM, OLIVEIRA MS Pombo de, COVAS DT. Full-length genome of two of HTLV-1 brazilian isolates. In: IX SIMPÓSIO INTERNACIONAL SOBRE HTLV NO BRASIL, 2006, Belo Horizonte. Revista da Sociedade Brasileira de Medicina Tropical. 2006. v. 39, p. 75-75.

COVAS DT, PANEPUCCI RA, FONTES AM, ORELLANA M, PRATA KL, PÉREZ LC, ARAÚJO AG, NEDER L, SILVA JR WA, ZAGO MA. Close Functional Similarities Between Human Mesenchymal Stem Cells, Pericytes and Fibroblasts. In: 11TH ANNUAL CONGRESS OF THE EUROPEAN HEMATOLOGY ASSOCIATION, 2006, Amsterdam. Haematologica. 2006. v. 91, p. 320-320.

PRATA KL, PRADO JÚNIOR BPA, SANTIS GC de, FERNANDES ATS, ORELLANA MD, PALMA PVB, OLIVEIRA MCB de, MORAES DA de, COVAS DT, VOLTARELLI JC. Avaliação da mobilização, coleta e infusão de células-tronco hematopoéticas autólogas de portadores de doenças auto-imunes submetidos a transplante. In: X CONGRESSO DA SOCIEDADE

BRASILEIRA DE TRANSPLANTE DE MEDULA ÓSSEA, 2006, Curitiba. Revista Brasileira de Hematologia e Hemoterapia. 2006. v. 28, p. 21-21.

AZEVEDO R, KASHIMA S, CASTELLI EC, TAKAYANAGUI OM, ALCÂNTARA LCJ, GADELHA S, OLIVEIRA MS Pombo de, COVAS DT. Associação entre carga proviral e polimorfismos dos genes IL-6 e IL-10 na infecção pelo HTLV-1. In: IX SIMPÓSIO INTERNACIONAL SOBRE HTLV NO BRASIL, 2006, Belo Horizonte. Revista da Sociedade Brasileira de Medicina Tropical. 2006. v. 39, p. 96-96.

RODRIGUES ES, AZEVEDO R, CASTELLI EC, YOSHIOKA FKN, SILVA IT, TAKAYANAGUI O M, KASHIMA S, COVAS DT. Associação dos polimorfismos da região promotora do gene DC-SIGN em pacientes HTLV-1 assintomáticos e HAM-TSP. In: IX SIMPÓSIO INTERNACIONAL SOBRE HTLV NO BRASIL, 2006, Belo Horizonte. Revista da Sociedade Brasileira de Medicina Tropical. 2006. v. 39, p. 92-92.

THOMÉ CH, FAÇA VM, FERREIRA GA, CATALÁN AMC, IZUMI C, ROSA JC and GREENE LJ. Passive Elution of intact proteins from SDS-PAGE for the identification of post translational modifications. XXXV Reunião Anual da Sociedade Brasileira de Bioquímica e Biologia Molecular, realizada em Águas de Lindóia/SP, de 1 a 4 julho de 2.006 (W49).

OLIVEIRA AHC, VIEIRA PS, RUIZ JC, CRUZ AK, GREENE LJ, ROSA JC.AND WARD RJ. Prokaryotic expression and purification of Nucleoside Diphosphate Kinase b from Leishmania major. XXXV Reunião Anual da Sociedade Brasileira de Bioquímica e Biologia Molecular, realizada em Águas de Lindóia/SP, de 1 a 4 julho de 2.006 (G11).

OTAKE AH, GODOY LMF, DE SOUZA GA, SCHWARZ N, SIUFI JLC, SABINO AA, ROSA JC, COVAS DT, CHAMMAS R, GREENE LJ. Prohibitin analysis in response of cisplatin in human melanoma cell line. XXI Reunião Anual da Federação de Sociedades de Biologia Experimental, 23 a 26 de agosto de 2006, Águas de Lindóia/SP/ Brasil. Publicado nos Anais do Congresso, Vol. 1, pg. 136, 2006.

SPILLER F, MESTRINER FLAC, LAURE HJ, TAVARES-MURTA BM, ROSA JC, BASILE-FILHO A, FERREIRA SH, GREENE LJ, CUNHA FQ. Alpha-1-Acid glicoprotein from serum of septic patients inhibitsw neurotrophil migration. Apresentado como Poster no 38º Congresso Brasileiro de Farmacologia, realizado de 18 a 21 de outubro de 2006, em Ribeirão Preto/SP. Foi finalista na Edição de 2006 do Prêmio José Ribeiro do Valle.

PONTES LLF, PINTAO MCT, Oliveira L, Dalmazzo LFF, Jácomo RH, GARCIA AB, FALCAO R P, REGO EM. Differential expression of P-glycoprotein, but not of MRP, LRP and BCRP in leukemic stem cells as comparaded to more differentiated CD34+ AML blasts. In: Congress of the European Hematology Association, 2006, Amsterdam. Haematologica/The Hematology Journal, 2006. v. 91.

PONTES LLF, GARCIA AB, LIMA RSA, PROTO-SIQUEIRA R, ZAGO MA, Nagler A, FALCAO RP, REGO EM. Proliferation or apoptosis induced by halofuginone in acute promyelocytic leukemia cells depend on the intensity of TGFbeta inhibition. In: Congress of the European Hematology Association, 2006, Amsterdam. Haematologica /The Hematology Journal, 2006. v. 91. p. 487-488.

MATOS DM, RIZZATTI EG, GARCIA AB, GALLO DAP, FALCAO RP. Different profiles of adhension molecules in B-cell non-Hodgkin lymphoma are associated with peripheral blood invasion. In: Congress of the European Hematology Association, 2006, Amsterdam. Haematologica/The Hematology Journal, 2006. v. 91. p. 494-495.

FAVARIN MC, BARROS GMN, PALMA LC, MADEIRA MIA, VELANO CEE, Straccieri ABL, Pieroni F, FALCAO RP, SIMÕES BP, VOLTARELLI JC. . Transplante alogênico não-mieloablativo com altas doses de rituximab em pacientes com linfoma da zona do manto em recaída pós-transplante autólogo. In: X Congresso da Sociedade Brasileira de Transplante de Medula Óssea, 2006, Curitiba. Revista Brasileira de hematologia e Hemoterapia. rio de Janeiro v. 28. p. 59-59.

LIMA RSA, LIMA ASG, Scheucher OS, PANEPUCCI RA, PROTO-SIQUEIRA R, SANTOS GAS, Teixeira HLG, FALCAO RP, REGO EM. In vivo analysis of the anti-leukemic activity of alpha tocopherol in acute promyelocytic leukemia. In: ASH, 2006, Orlando. Blood, 2006. v. 108. p. 569a-569a.

PONTES LLF, PINTAO MC, Oliveira L, Dalmazzo LFF, Jácomo RH, GARCIA AB, FALCAO R P, REGO EM. Differential expression of P-glycoprotein, but not MRP, LRP and BCRP in leukemic stem cells compared to more differentiated CD34+CD38+ acute myeloid leukemia blasts. In: ASH, 2006, Orlando. Blood, 2006. v. 108. p. 669a-669a.

OLIVEIRA FM, SCRIDELI C, SIMÕES BP, REGO E, FALCAO RP, TONE LG. Caracterização de novas alterações cromossômicas em neoplasias hematológicas (leucemias e linfomas) com a utilização do cariótipo espectral (SKY). In: Congresso Brasileiro de Hematologia e Hemoterapia - HEMO 2006, 2006, Recife. Revista Brasileira de Hematologia e Hemoterapia. Rio de Janeiro, 2006. v. 28. p. 110-111.

ARAÚJO ARL, LIMA A, GARCIA AB, Araújo AG, PANEPUCCI RA, FALCAO RP, REGO EM. Correlação entre expressão do deltaNp73 e TAP73 com rearranjos gênicos específicos e susceptibilidade e apoptose na leucemia mielóide aguda. In: Congresso Brasileiro de Hematologia e Hemoterapia - HEMO 2006, 2006, Recife. Revista Brasileira de Hematologia e Hemoterapia. Rio de Janeiro 2006. v. 28. p. 113-113.

LIMA RSA, GARCIA AB, SCHEUCHER OS, FALCAO RP, REGO EM. In vivo analysis of the anti-leukemic activity of alpha-tocopherol in acute promyelocytic leukemia. In: Congresso Brasileiro de Hematologia e Hemoterapia - HEMO 2006, 2006, Recife. Revista Brasileira de Hematologia e Hemoterapia. Rio de Janeiro, 2006. v. 28. p. 118-118.

SANTOS GAS, SCHEUCHER OS, LIMA A, ARAÚJO ARL, GARCIA AB, FALCAO RP, REGO E. O efeito anti-proliferativo e pró-apoptótico da 10-oxa-octadecilfosfocolina na leucemia mielóide aguda e relacionado à ativação de JNK. In: Congresso Brasileiro de Hematologia e Hemoterapia - HEMO 2006, 2006, Recife. Revista Brasileira de Hematologia e Hemoterapia. Rio de Janeiro, 2006. v. 28. p. 125-125.

SCHEUCHER OS, SANTOS GAS, ARAÚJO ARL, LIMA A, GARCIA AB, FALCAO RP, REGO E. O éster fenitílico do ácido cafeico ativa JNK e induz apoptose em células de leucemia promielocítica aguda resistentes ao ácido retinóico todo trans. In: Congresso Brasileiro de Hematologia e Hemoterapia - HEMO 2006, 2006, Recife. Revista Brasileira de Hematologia e Hemoterapia. Rio de Janeiro, 2006. v. 28.

PONTES LLF, PINTAO MC, OLIVEIRA L, DALMAZZO LFF, JÁCOMO RH, GARCIA AB, FALCAO RP, REGO E. p-glycoprotein is preferentially expressed in leukemic stem cells compared to more differentiated CD34+CD38+ Acute Myeloid Leukemia Blasts. In: Congresso Brasileiro de Hematologia e Hemoterapia - HEMO 2006, 2006, Recife. Revista Brasileira de Hematologia e Hemoterapia. Rio de Janeiro, 2006. v. 28. p. 126-126.

MARINATO AF,GARCIA AB, REGO EM, FALCAO RP. Análise da expressão do receptor de glicocorticóide e da proteína PRAME em neoplasias de linfócitos NK e NK/T. In: Congresso Brasileiro de Hematologia e Hemoterapia - HEMO 2006, 2006, Recife. Revista Brasileira de Hematologia e Hemoterapia. Rio de, 2006. v. 28. p. 133-133.

DALMAZZO LFF, MADEIRA MIA, PALMA LC, VELANO CEE, FAVARIN MC, BRUNETTI IL, PONTES LLF, SAGGIORO F, FALCAO RP. Progressão para LNH difuso de grandes células B disseminado em paciente com macroglobulinemia de Waldestron e linfoma T cutâneo: relato de caso. In: Congresso Brasileiro de Hematologia e Hemoterapia - HEMO 2006, 2006, Recife. Revista Brasileira de Hematologia e Hemoterapia. Rio de, 2006. v. 28

CARETA F, PROTO-SIQUEIRA R, PANEPUCCI RA, RIZZATTI EG, ZANETTE D, ARAÚJO AG, SILVA JR WA, DIGHIERO G, FALCAO RP, ZAGO MA. A expressão do gene antiapoptótico Toso é relacionada com o aumento de de Bcl2 e com os marcadores de prgnósticos Zap70 e LPL em Leucemia Linfocítica Crônica. In: Congresso Brasileiro de

Hematologia e Hemoterapia - HEMO 2006, 2006, Recife. Revista Brasileira de Hematologia e Hemoterapia. Rio de Janeiro, 2006. v. 28. p. 184-184.

VERISSIMO O, KOLB H, GARCIA AB, SCAFFO MH, Palma LC, FALCAO RP, ISMAEL SJ, SIMÕES BP, MARCO N . Análise in vitro do efeito citotóxico de um novo anticorpo biespecífico Bi20 (CD20XCD3). In: Congresso Brasileiro de Hematologia e Hemoterapia - HEMO 2006, 2006, Recife. Revista Brasileira de Hematologia e Hemoterapia. Rio de Janeiro, 2006. v. 28. p. 184-184.

VELANO CEE, FAVARIN MC, MADEIRA MIA, Palma LC, PERINI G, BRUNETTA D, KRUZICH C, CARDOSO L, REGO EM, FALCAO RP. Leucemia Pró-Linfocitica B com infiltração do sistema nervoso central - relato de um caso. In: Congresso Brasileiro de Hematologia e Hemoterapia - HEMO 2006, 2006, Recife. Revista Brasileira de Hematologia e Hemoterapia. Rio de, 2006. v. 28. p. 190-190.

6.8 CONFERENCES, LECTURES, SYMPOSIA, ROUND-TABLES

Zago MA – Stem cells from bone marrow and from other tissues: are they alike? International Symposium on Biological Cardiac Repair: a Critical Apprisal. Instituto do Coração (InCor), São Paulo, 18/09/2006

Zago MA – Células-tronco: mitos e verdades. Plenary Session. X Congresso da Sociedade Brasileira de Transplante de Medula Óssea, Curitiba 17/08/2006

Zago MA – Gene expression of mesenchymal stem cells derived from different sources. Conference at the ESH-EBMT – Eurocord Euroconference on Stem Cell Research, Cascais, Portugal, 15-17 April 2006.

Zago MA – Expressão gênica em neoplasias linfóides. Conference. V Congresso de Oncologia de Botucatu, Faculdade de Medicina de Botucatu, 5/8/2006.

Zago MA – Expressão gênica de células-tronco adultas hematopoéticas, mesenquimais e correlatas. Simpósio “Células-tronco adultas e embrionárias: a pesquisa antes do tratamento”. Instituto de Biociências da USP, 9/7/2006.

Zago MA – Diversidade e propriedades das células-tronco da medula óssea. Simpósio Multidisciplinar sobre Células-Tronco, Universidade Federal de São Paulo, 10/11/2006.

Zago MA – Células-tronco e genética: desafios atuais na pesquisa qlínica. Round table. 4º. Forum dos Comitês de Ética em Pesquisa do Estado de S. Paulo, 29/05/2006

Covas DT - Seminário sobre o tema “Células-Tronco”, realizado na Faculdade de Medicina de Ribeirão Preto, em 11 de maio de 2006.

Covas DT - Palestra proferida durante o II Seminário sobre Rotas Tecnológicas da Biotecnologia: Oportunidades de Investimentos e Inovações, realizado em Ribeirão Preto de 01 a 02 de junho de 2006.

Covas DT - Palestra sobre o tema “Aplicações Práticas das Pesquisas com Células-Tronco”, durante a XV Jornada do Departamento de Medicina da Santa Casa de São Paulo “Avanços no Diagnóstico e Tratamento em Clínica Médica”, em São Paulo no dia 11 de agosto de 2006.

Covas DT - Conferência da Mesa Redonda Inovação e Tecnologia, sobre o tema “Em Busca do Desenvolvimento de Tecnologia Nacional para Produção de Concentrado de Fatores VIII e IX de Origem Recombinante”, durante o I Simpósio de Hemostasia e Trombose, em Uberaba, de 21 a 23 de agosto de 2006.

Covas DT - Conferência sobre o tema “Terapia Celular” durante a Jornada Brasileira de Hemoterapia, realizada em São Paulo no dia 14 de outubro de 2006.

Chammas R - Melanomas, no ciclo de conferências do COPEA-UFRJ, em 18 de maio de 2006.

Chammas R - The double face of cell death within tumor microenvironments, no "6th International Cell Death Symposium", em 5 de junho de 2006, em Angra dos Reis, Rio de Janeiro.

Chammas R - Polimorfismos de genes de reparo de DNA e risco de melanoma maligno, no "I Simpósio Internacional de Pesquisa em Câncer: integrando pesquisa básica, clínica e epidemiológica", em 1 de dezembro de 2006, em São Paulo.

Falcao RP - NK and T-Cell Lymphomas, I Tutorial de Neoplasias Malignas: Foco em Neoplasias Linfóides, Escola Brasileira de Hematologia, Angra dos Reis, 6 /5/ 2006.

Voltarelli JC - Brazilian experience with BEAM for hematopoietic stem cell transplantation for multiple sclerosis. MIST trial meeting, Salt Lake City, UT, USA, 2/April/2005.

Voltarelli JC - Hematopoetic stem cell transplantation for early onset diabetes mellitus. Diabetes Research Institute, University of Miami, FL, USA, 21/April/2006.

Voltarelli JC - Hematopoietic stem cell transplantation for diabetes mellitus, Genzyme meeting, San Francisco, CA, 8/June/2006.

Voltarelli JC - Hematopoetic stem cell transplantation for diabetes mellitus, University of Florida, Gainesville, USA, 6/June/2006.

Voltarelli JC - Stem cells for diabetes mellitus, V Meeting of the Italian-Brazilian Society of Hematology, Rome, Italy, 24/May/2006.

Voltarelli JC - Terapia celular para doenças auto-imunes, Congresso Brasileiro de Hematologia e Hemoterapia – HEMO 2006, Recife, 4/11/2006.

Voltarelli JC - Indicações de TMO nas doenças auto-imunes, Congresso Brasileiro de Hematologia e Hemoterapia – HEMO 2005, Rio de Janeiro, 9/11/2006.

Rego EM - Leucemia linfóide aguda do adulto: protocolos de tratamento quimioterápico, Congresso Brasileiro de Hematologia e Hemoterapia – HEMO 2006, Recife, 4/11/2006.

Rego EM - Leucemia mielóide aguda: patobiologia, Congresso Brasileiro de Hematologia e Hemoterapia – HEMO 2006, Recife, 4/11/2006.

Rego EM - Participação como ‘Tutor’ no I Tutorial de Neoplasias Malignas: Foco em Neoplasias Linfóides, Escola Brasileira de Hematologia, Angra dos Reis, 6 /5/ 2006.

Rego EM - Fisiopatologia da leucemia mielóide aguda – novos alvos moleculares, Congresso Brasileiro de Hematologia e Hemoterapia – HEMO 2005, Rio de Janeiro, 8/11/2005.

Rego EM - Introdução às doenças mieloproliferativas crônicas, Curso da Escola Brasileira de Hematologia – Doenças Mieloproliferativas Crônica, São Paulo, 29/04/2005.

THE ADVISORY COMMITTEE

We selected the following Advisory Committee:

- Bob Löwenberg, Professor of Hematology, Erasmus University Medical Center, Rotterdam, the Netherlands
- Graça Almeida-Porada, Department of Animal Biotechnology, University of Nevada, Reno, USA
- Manoel Barral Netto, Professor Titular da Universidade Federal da Bahia e do Instituto Oswaldo Cruz, Salvador (BA)
- Rafael Linden, Professor Titular do Instituto de Biofísica da Universidade Federal do Rio de Janeiro (RJ)

The four researchers, two foreigners and two Brazilians, cover most of the aspects included in the Center's research program, especially: stem cell isolation and culture, animal models to study stem cell properties, stem cell differentiation, immunology of diseases and of transplantation, the molecular basis of cancer, diagnostic and therapeutic approaches to hematological malignancies.

We organized two visits for the members of the committee:

1-2 December, 2006: Manoel Barral-Netto and Graca Almeida-Porada

20-21 March, 2007: Bob Löwenberg and Rafael Linden

The schedule of the first visit and the written report is appended (it is written in Portuguese because Prof. Graça, although working in the USA for 15 years is form Portuguese origin).

Additionally, we have asked the two Brazilian researchers (Prof. Linden and Prof. Barral) to evaluate and send written report about the research proposal and curriculum of candidates to post-doctoral fellowship candidates.

Our personal evaluation of the first committee visit (December 1 and 2):

Very productive. It was a good opportunity to expose ideas and practical proposals to experienced researchers who felt at easy to discuss and analyze in depth our activities. Prof. Graça works actively in subjects very similar to those in which we focus at the moment; she came to Ribeirão Preto one day earlier, so she spent one day visiting the laboratories and discussing on-going research with many of the senior investigators.

Their report is appended. However, there was one comment, supported by both visitors, which should be transmitted to FAPESP. When asked if they thought that the investment of FAPESP was worth in view of the center's output, they answered that

considering the characteristics of the CEPID project, it should be measured by international standards, by which 7 principal investigators would receive 1.7-3.5 million dollars annually (each senior investigator would receive grants in the order of 250-500 thousand dollars annually).

Schedule for the visit by the Advisory Committee to the Center for Cell Therapy

1 December, 2006

8:30 h – 10:15 h. Visit to the University Hospital: Laboratory of Hematology, Bone Marrow Transplantation Unit
10:30 h – 12:45 h. Visit to the Laboratories at the Hemocentro (Flow Cytometry, Molecular Biology and DNA Sequencing, Bioinformatics, Protein Chemistry Laboratory), INBIOS (small business incubator)

13:00 – 13:30 h. Lunch

13:45 – 14:15 h. Visit to the House of Science

14:30 h – 18:00 h. Seminar with all the Center's Members

Introduction		
15 min	MA Zago	A general view of the Center for Cell Therapy
15 min	DT Covas	The education and technology program
10 min	M Barbieri	A movie clip of the activites of the House of Science
A summary of the research activities		
20 min	EM Rego + B Santana	Acute myeloid leukemias
20 min	MA Zago + RA Panepucci	Hematopoietic stem cells
20 min	DT Covas + AM Fontes	Mesenchymal stem cells
20 min	JC Voltarelli + K Farias	Treatment of autoimmune diseases
10 min	IT Silva	The bioinformatics laboratory
20 min	LJ Greene + R Chammas	Proteomics, dendritic cells and melanomas
15 min	BP Simões	Clinical testing the immunomodulatory effect of MSC
General discussion		

2 December, 2006

8:30 h – 10:30 h. Meeting with research leaders.
10:30 h – 12:30 h. Meeting of the advisory committee. Writing of the report.

Acompanhamento do CTC

Data: 01 e 02 de dezembro de 2006.

Estrutura da avaliação:

- Visita às instalações;
- Apresentação das linhas de pesquisa (apresentação geral por um investigador sênior e apresentação de dados pelos pós-doutorandos);
- Sessão de discussão dos avaliadores e investigadores sênior.

Comentários:

1. O CTC continua altamente produtivo com publicações internacionais em revistas de elevada qualidade;
2. Uma análise das citações do grupo demonstra uma elevação recente no número anual de citações, coincidindo com o período de financiamento do CEPID;
3. A formação de pessoal é, claramente, um aspecto importante do grupo. Todas as apresentações dos estudantes foram feitas de forma clara e segura, evidenciando o seu envolvimento ativo nos projetos;
4. Observa-se uma positiva interação intra-CTC, no compartilhamento de competências;
5. Valorizamos ainda a utilização compartilhada de equipamentos e infraestrutura;
6. É de grande interesse, ainda, o esforço de um grupo altamente produtivo no ensino de ciências no nível médio. A visita à Casa da Ciência foi valorizada pelos consultores. Para além do benefício na educação dos jovens secundaristas e seus professores, registra-se o benefício desta experiência na formação dos pós-graduandos do CTC ao ilustrar que a solidariedade científica pode conviver bem com produção qualificada.
7. Os objetivos propostos pelo CTC estão sendo alcançados. O grupo mantém o foco, assim como exercita um processo de análise crítica para revisão continuada de objetivos que podem haver perdido importância (exemplo da revisão da ênfase nas células dendríticas);
8. A qualidade da ciência os objetivos dos estudos a executar, a compreensão das dificuldades e proposição de métodos alternativos para obter melhores resultados, põe este grupo a par de grupos internacionais a fazer o mesmo tipo de ciência
9. Outro aspecto positivo e o fato de haver um forte componente de medicina translacional que põe este grupo numa situação única para abordar problemas que vão desde a ciência básica a clinica
10. Pareceu-nos que o CTC apresenta um adequado desempenho em todas as suas atividades. A impressão obtida é que trabalhando isoladamente os grupos participantes do CTC não teriam a mesma produtividade.
11. O nível de financiamento do CTC é razoável, considerando a sua produtividade. Observa-se grande racionalidade e eficiência na utilização de recursos. O aporte adicional de recursos permitiria ao grupo o aumento da sua inserção internacional.

Ribeirão Preto, 02 de dezembro de 2006.

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