HUMAN GENOME RESEARCH CENTER (HGRC)

Departamento de Genética e Biologia Evolutiva
Instituto de Biociências
Universidade de São Paulo

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PART 1 - RESEARCH

GENOME RESEARCH

I- Neuromuscular and Neurodegenerative Disorders

a) Search of new genes: LGMD1G and SPOAN

We were able to refine the region for both genes and exclude more candidate genes, but the search for both LGMD1G and the SPOAN gene is still undergoing. The work with LGMD1G is being undertaken by Luciana Licinio as part of her MS thesis (supervision of MZ). The SPOAN gene is under the responsibility of the post-doctoral student Lucia Inês Macedo-Souza (supervised by Dr. Fernando Kok).

b) African Ancestry protects against dementia-related neuropathology

Previous studies in dementia epidemiology have reported higher Alzheimer's disease rates in subjects from African descent than Caucasians. We conducted a population-based study to determine whether genetically-determined African ancestry is associated with neuropathological changes commonly associated with dementia.

We studied 202 brains obtained in the brain bank of the Brazilian Aging Brain Study Group of the University of Sao Paulo between 2004 and 2008 for presence of amyloid plaques, neurofibrillary tangles, atherosclerosis, brain infarcts, and Lewy bodies. African ancestry was determined through the use of ancestry-informative markers. We also adjusted the results for multiple environmental risk factors (including socio-economic levels) and APOE genotype.

Subjects with African ancestry showed lower prevalence of amyloid plaques in the univariate analysis (OR 0.72, 95% CI 0.55-0.95, $p = 0.01$) and when adjusted for age, sex, APOE genotype, and environmental risk factors (OR 0.43, 95% CI 0.21-0.89, $p = 0.02$). Contrary to previous studies, our results show that African ancestry is highly protective of Alzheimer's disease neuropathology (amyloid plaques), with an adjusted odds ratio of 0.43. This suggests that unknown variants more frequent in the “African” genome reduce the accumulation of amyloid beta or increase its clearance, when compared to the “European” genome. This work was undertaken by David Schlesinger for his PhD thesis (supervision MZ) and the paper will be submitted for publication.

c) Insights from exceptional cases

Patients with atypical phenotypes may contribute to our comprehension on the mechanisms underlying phenotypic variability. A boy with a nonsense mutation in the dystrophin gene who is still asymptomatic at age 7 was reported (Dubowitz, 2006). We have observed a comparable situation in Ringo, a Golden Retriever muscular dystrophy dog, who is almost asymptomatic at age 7 years and 5 months. Among his offspring, one dog, Suflair, born in April 2004 is also almost asymptomatic. In order to try to identify potential “protective” genes a microarray study was performed (in collaboration with the group of Dr. Sergio Verjovski-Almeida from IQUSP) comparing these two dogs with severely affected and normal dogs related to Ringo. This work is being undertaken by Natassia Vieira as part of her PhD which will be continued as her post-doctoral research (MZ supervision). Four genes were found to be differentially expressed. Of these, one in

particular is now being tested in zebrafish (in a collaborative study with Lou Kunkel from Harvard, USA). More recently, we established a new collaboration with Dr. Diane Shelton, a researcher from University of California at San Diego. She identified asymptomatic Labrador dogs with the same characteristics as Ringo. They have no muscle dystrophin and no phenotype. Dr. Shelton sent us muscle samples from these dogs which will be compared with Ringo and Suflair. The identification of these dogs showed for the first time that skeletal muscle of large size may be functional even without dystrophin. The search for the underlying mechanism is of utmost importance in an attempt to find new pathways leading to the treatment of Duchenne muscular dystrophy.

d) Phenotypic variability

The possible modifier effect of the myostatin gene modulation in the hypermusculature phenotype of patients with congenital myotonia was evaluated and excluded (Muniz et al, 2010). Additionally, our group participated in complementary studies on the mdx mouse, which demonstrated alteration in the mitochondrial respiratory chain in the brain (Tulon et al, 2010). The analysis of proteins of the glycosilation pathway of a-DG was finalized (Poliana Martins, PhD thesis) and the pattern of expression of genes related to the degeneration and regeneration cascades were evaluated in the mouse models for muscular dystrophies (Paula Onofre, manuscript submitted).

II- Developmental Disorders: Craniofacial defects, autism, neurodevelopmental disorders, mental retardation associated or not with malformation, obesity and deafness

a) Identification of candidate genes for autism.

We have cloned a chromosome breakpoint from a patient with autism and identified a new locus for autism. We have established iPS cells from dental pulp stem cells of this patient and of a control. These cells were induced to neurons and functional analysis decreased Ca2+ influx in neuronal derived cells of the patient. We are finishing the characterization of a mouse knockout for this gene. This project is being developed by the PhD student Karina Oliveira in collaboration with Dr. Muotri, at University of California, USA (Griese-Oliveira et al, 2010. Conference: “The Emerging Neuroscience of Autism Spectrum Disorders”). Furthermore, we have demonstrated that collybistin and gephyrin are components of the eukaryotic translation initiation factor 3 complex. We have also demonstrated that due to their putatitve functional role in neuronal synapses, they became important functional candidates for autism (Sertie et al, 2010).

b) Identification of at-risk alleles and signaling pathways in non syndromic cleft lip and palate (NSCLP).

We have analyzed two SNPs at *IRF6,* a candidate locus for NSCL/P and 44 ancestrality markers in 600 patients and 250 controls. We confirmed association of this locus with the malformation, but interestingly the importance of the association depends on the ascertained population across the country (Brito et al, 2010. ASHG Annual Meeting). Besides, we have observed that heritability in NSCLP varies in different populations of the country, with the lowest values in patients ascertained in Maceio and the highest in patients ascertained in Barbalha, CE (Brito et al, 2010, submitted manuscript). Finally, we have shown that the transcriptome analysis of stem cells of NSCLP is significantly different

from controls, and a relevant pathway that involved modeling of extracellular matrix was identified (Bueno DF et al, 2010). These results have open a new perspective for the study of NSCLP as well as other complex disorders.

c) Possible new functions of *COL18A1*.

In collaboration with Dr. Esko, University of California at San Diego, we have shown that patients with Knobloch syndrome, a rare disease characterized by high myopia and occipital encephalocele, also present high levels of triglicerides. These results have open a new perspective for this molecule, as, unexpectedly, it also might play a role in lipid metabolism (Bishop et al, 2010).

d) Craniofacial syndromes.

We have collaborated in the molecular characterization of a new form of mandibulofacial syndrome (Zechi-Ceide et al, 2010). In addition, we have shown that craniosynostosis seems to be a common feature in pycnodysotosis, implying that cathepsin K has also an important role in suture homeostasis (Bertola et al, 2010). We have contributed for further characterization of the Saethre-Chotzen syndrome by describing a family with complex alterations of the ear (Lamônica et al, 2010).

e) Limb defects.

Three families with limb defects are under investigation with linkage studies and candidate gene analysis. In one of them, a collaborative study stablished with Dr. Stefan Mundlos, Institut für Medizinische Genetik Charité, Universitätsmedizin Berlin, Germany allowed to identify the causative mutation, a small genomic rearrangement. A collaborative publication is under preparation, which will indicate the novel gene. In the other two families, linkage analysis with SNP arrays did not allow identification of a candidate region and known candidate genes related to gene defects were excluded after sequencing.

f) **Deafness.**

Our work on the molecular diagnosis of deafness, related to mitochondrial mutations, resulted in one publication (Uehara et al, 2010). Besides, a report on association studies and mutation screening in patients with noise-induced hearing loss was published (Abreu-Silva et al, 2010).The development of a MLPA Kit to investigate copy number variation in those selected genes in a larger series of patients presenting with syndromic or non-syndromic deafness revealed an inherited genomic rearrangement leading to deafness in one pedigree, which allows to postulate a novel candidate gene for deafness, still under investigation (Daniela Uehara, MS dissertation, 2010).

g) **Genetic factors associated with hypertension and obesity in Afro-Brazilian partially isolated populations.**

A report including the results of our association studies regarding obesity-related phenotypes was accepted for publication (Angeli et al, *Obesity*, in press) and replication of our results in another population, in a collaborative study, was presented in another manuscript (Pereira et al, *Obesity*, in press). A large sample of African-Brazilians from the same populations was genotyped with a set of 48 autosomal population-specific alleles

and association studies of several genes with the phenotypes related to hypertension were performed (Lilian Kimura, PhD thesis, 2010 and manuscript in preparation).

h) Syndromic obesity.

In our search for the genetic causes of obesity, we screened for chromosome 1p36 deletion in a group of 154 hyperphagic and obese, PWS-negative patients, and our work reinforces the association between a submicroscopic 1p36 deletion of ~2 to 3 Mb in size and obesity and hyperphagia. Important nervous system and glucose or lipid metabolism genes are mapped to this region (D´Angelo et al, 2010a).

We describe novel CNVs of *de novo* occurrence found in patients with syndromic obesity that overlap with those of patients with developmental delay/mental retardation (DD/MR). Of these, five loci (2p25.3, 3p26.3, 6q16.3q21, 7q22.2, and 10p15.3) were recurrent among patients who also had obesity. In some instances, the CNVs overlapped genes already confirmed to be associated with BMI (*TMEM18*) or monogenic obesity (*SIM1),* and recently discovered genes mapped to rare recurrent CNV associated with severe early-onset obesity (*DIP2C)*. Most important, we found a single-gene deletion at 14q12 (*PRKD1*) and three independent CNVs at 11q22.3, 12q15q21.1, and 14q11.2 harboring genes in the same family as *RAB23*, which is associated with obesity in Carpenter syndrome (D´Angelo et al, 2010 ASHG Annual Meeting; Kohl, PhD Thesis).

i) Prader-Willi and Angelman syndromes.

In this ongoing project, the sample of PWS and AS patients was increased, and screening of *UBE3A* mutations in AS patients was finished. We also finished the screening of 70 patients with Angelman-like phenotypes for 22q13 deletions and five 22q chromosome alterations are currently under investigation.

j) Mental retardation.

SYNGAP1 (synaptic RAS-GTPase activating protein 1) is a component of the NMDAR (N-methyl-D-aspartate receptor) complex and blocks the insertion of AMPAR (a-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor) at the postsynaptic membrane by inhibiting the RAS-ERK pathway. Point mutations in the *SYNGAP1* gene have been described recently as a relatively frequent cause of mental retardation, present in about 3% of nonsyndromic individuals with mental retardation. These de novo mutations resulted in premature stop codons, and the produced proteins would lack important functional domains. We detected a carrier of a chromosomal deletion encompassing *SYNGAP1* among 300 patients with mental retardation studied by 1Mb array-comparative genomic hybridization (a-CGH). This finding confirms *SYNGAP1* haploinsuffiency as the cause of nonsyndromic mental retardation (Krepischi et al, 2010).

In 2006, we reported the first mutation in a ubiquitin-conjugating enzyme gene as the cause of a human disease: a mutation of *UBE2A,* causing a novel X-linked mental retardation (XLMR) syndrome (Nascimento et al. Am J Hum Genet 79:549, 2006). This finding prompted us and other groups to investigate *UBE2A* mutations in patients with XLMR mapped to intervals encompassing UBE2A. Although we did not detect mutations in 22 probands, others described point mutations, and the finding of deletions encompassing *UBE2A* in patients with clinical phenotypes similar to those of the first patients described by us confirms *UBE2A* haploinsufficiency as the cause of a specific mental retardation syndrome (de Leeuw et al, 2010). Interestingly, while microcephally was present in

patients carrying *UBE2A* deletions, carriers of missense or nonsense mutations showed macrocephaly.

We are conducting functional studies to understand the effect of the detected *UBE2A*:c.382C>T mutation on transcription and translation and to evaluate the ubiquitin conjugating activity of UBE2A isoforms *in vitro* e *in vivo*. Our *in vitro* analysis showed that only isoform 1 was able to ubiquitinate H2A histones. The mutated isoform was able to interact with ubiquitin, but failed to transfer it to histones. Functional complementation analysis of yeast ΔRAD6 mutation (conserved ortholog) by normal and mutated human isoforms showed that only the normal human transcript 1 restored the rad6-null yeast phenotypes, thus indicating that it differs functionally from the other two normal transcripts. The expression of the alternative isoforms 2 and 3 was partially toxic to this yeast strain, and toxicity increased under heat shock conditions. However, these two isoforms did not seem to be stable in yeast cells: as in human tissues, we failed to detect UBE2A isoforms 2 and 3 in yeast cells expressing the corresponding transcripts. We have confirmed, by proteasome inhibition assays, that the human isoform 2 is in fact not stable in yeast, and its degradation is proteasome-dependent. The mutant isoform was stable in yeast, but was unable to rescue the UV-sensitivity phenotype, its expression resulting in severe toxicity to the Δrad6 strain. (Part of the results in Nascimento RMP, PhD Thesis, 2010).

Nearly a third of obligate carriers of mutations causative of X-linked mental retardation (XLMR) have extreme X-inactivation skewing (≥ 90:10) in peripheral blood cells. We used the pattern of X-inactivation in 100 mothers of mentally retarded boys as a parameter to evaluate the frequency of XLMR among non-familial cases. Ten women (10%) had completely skewed X-inactivation (100:0), a frequency significantly higher (P = 0.0001) than that among adult women from the general population (~2%). Assuming that every mother with completely skewed X-inactivation is a carrier of an X-chromosome mutation that causes mental retardation in her son, the frequency of XLMR in our sample of 100 boys is 10% (95% CI = 0.0490 - 0.1762), the fragile X syndrome being excluded. Although these figures are quite in agreement with previous estimations of the frequency of XLMR among mentally retarded men, they might be an underestimation, since only about a third of obligate carriers of XLMR mutations have highly skewed X inactivation. (Vianna-Morgante et al, 2010. ASHG Annual Meeting).

III- <u>Chromosomal Studies</u>

a) Mechanisms originating chromosomal rearrangements.

A maternal inherited direct tandem duplication 20p11.2p13 associated with a contiguous 20p11.21proximal microdeletion, in a patient with clinical features of trisomy 20p, was also characterized with array technology and a more precise genotype-phenotype correlation was established in order to delineate the trisomy 20p syndrome (D´Angelo et al, 2010b)

To understand the mechanisms that predispose to chromosomal rearrangements, a rare case of trisomy 15pter-q21.2 due to a de novo marker chromosome presenting an interstitial deletion or a terminal deletion stabilized by a telomere capture mechanism was reported (Pacanaro et al, 2010).

b) Evolutionary studies.

To determine the relationship between mtDNA and chromosomal variation, analyses of chromosomal diversity in *A. guariba* were performed in individuals from the

state of São Paulo presenting a diploid number (2N) of 49 (♂♂) or 50 (♀♀) and *A. guariba* from the more southern states of Paraná and Santa Catarina. The differences and a north/south structuring of chromosomal variation may indicate that the two groups are reproductively isolated from each other and that the southern subspecies of *A. guariba* (*A. g. guariba*) in fact constitutes two different subspecies or potentially different species (Martins et al, 2010)

IV- Interfering in the Human Genome

In this part of the project, we have mainly analyzed DNA repair defects and cells' responses to DNA damaging agents. During this period we have identified two new mutations (base substitutions) in two siblings with defect in the XPG gene. Interestingly up to now, there are only four other mutations identified in xeroderma pigmentosum (XP) patients in this gene, and apparently in Brazil, other alleles exist. Functional analysis are being performed to confirm the pathological effects of these mutations (Soltys et al, in preparation). Meanwhile, we have discovered a community in an isolated area of Goiás (in the very heart of this large country) who suffer with XP. There are more than 20 patients diagnosed XP, although with very heterogeneous clinical phenotype, within a population of less than a 1,000 people. This high frequency of XP patients is unique in the world, and may be underestimated, as the allele may affect other close communities. We have initiated studies with cells from these patients in order to identify the mutation. Apparently the defect does involve DNA damage removal, but tolerance.

During this period we also have investigated the cells' responses and DNA repair of chemotherapeutic agents. Two articles were published which indicate the participation of nucleotide excision repair for the removal of lesions induced by doxorubicin. More recently, an effort has been made in order to investigate the repair of other agents, mainly chloroethylating agents (ACNU and BCNU). Moreover, we initiated two different strategies that may be useful for many of laboratories of the Human Genome Center, that is the use of nanoparticles containing chemotherapeutic agents and the use of lentivirus vectors expressing shRNA for silencing human genes.

STEM CELLS

V- Human stem cells

a) Craniofacial bone reconstruction

We have redefined some craniofacial animal models that better represent some craniofacial human defects, such as alveolar bone deficiency, which will allow us a evaluation of bone reconstruction with stem cells (Costa et al, 2010; Raposo-Amaral et al, 2010). Besides, we have invested in the screening of 10 biomaterials to evaluate the best ones for craniofacial bone reconstruction associated with stem cells. Up to now, two have shown promising results (Fanganiello et al, 2010). We are also establishing clones of dental pulp stem cell cultures in order to identify markers that allow to discriminate cells with better potential to bone differentiation. We have also characterized two stem cell populations derived from palatal muscle and neonatal dental tooth (Bueno DF, manuscript in preparation).

A clinical trial with enrichment of adipose mesenchymal cells to rehabilitate patients with microssomia and Parry-Romberg syndrome has also been initiated. Up to now, 8

patients have been submitted to this protocol. This project is being developed in collaboration with the group of Dr. Alonso, Dept. Plastic Surgery, University of São Paulo.

b) Bone regeneration

In 2009 we identified a new source of mesenchymal stem cells in the Fallopian tube (Jadezje et al, 2009b). Now we have analyzed the potential of these cells to regenerate bone in a rat model designed by Dr. Daniela Bueno (supervision MRPB). The results showed that the potential of these cells is comparable to those obtained from dental pulp to regenerate bone. This work undertaken by the pos-doc students Tatiana Jadezje (MZ) and Daniela Bueno (MRPB) won the prize SAÚDE DA MULHER- EDITORA ABRIL, in December of 2010 and a paper will be submitted to publication.

c) Muscle regeneration

We performed several in vivo experiments with human stem-cells injected in animal models: SJL mice and GRMD dogs. This work is being undertaken by the PhD students Natassia Vieira, Mariane Secco, Marcos Valadares and Carlos Bueno Jr. The results from these experiments showed that:

- Human adipose derived mesenchymal stem-cells (hAMSC) injected systemically in SJL mice and GRMD dogs are able to reach the muscle, engraft and express human muscle proteins without immunosupression
- hAMSC are better than umbilical cord mesenchymal stem-cells (MSCs) to differentiate in muscle cells after systemic delivery
- hAMSC injected systemically improved the phenotype in SJL mice and proved to be safe in GRMD dogs
- No human cells were found after local injections of MSCs in muscle of GRMD dogs
- No human cells were found after systemic injections of hASCS in normal mice suggesting that factors released by the dystrophic muscle direct homing
- Human muscle dystrophin was found in muscle of injected GRMD dogs up to 6 months after the last injection
- For therapeutic purposes, systemic delivery of stem-cells should be repeated at least every 6 months

d) Stem-cell bank from families with patients affected by genetic disorders

Up to now, the bank has collected 342 samples with the following distribution:

- **176** from patients affected by different genetic disorders, including craniofacial syndromes, Angelman syndrome, autism and neuromuscular disorders;
- **158** stem cell lines from normal volunteers or healthy relatives
- **8** iPS cell lines (autism, ALS, normal controls)

VI- <u>Animal Stem Cells</u>

a) Canine stem cells

We identified and characterized a new source of canine stem-cells from adipose tissue (Vieira et al, 2010).

b) Murine stem cells

The therapeutic potential of murine mesenchymal stem cells (MSC) from adipose tissue in the treatment of muscular dystrophy in the new double mutant mouse model for the genes Dystrophin and Large was tested (Martins et al, 2010. 8th ISSCR) and the therapeutic potential of murine mesenchymal stem cells (MSC) from different origins in the treatment of muscular dystrophy was compared (Onofre-Oliveira et al, 2010. ASHG Annual Meeting).

Murine embrionic stem cells were induced to originate muscle through different methdologies (Freitas Almeida, 2010. SIICUSP), and this also was done using mesenchymal stem cells from different animal models (Pessotti et al, 2009 – TCC).

Our experience in studies with animal models was reported in the Simposio "Animal models for neuromuscular diseases". XII International Congress on Neuromuscular Disease, Naple, Italy, and a new mouse model, double mutant for dystrophin and dysferlin was generated in our lab (Lanzoti et al, 2010. SIICUSP).

c) Murine and guinea pig ear progenitor cells

Culturing cells from organ of Corti is a starting point to the development of cell therapy for deafness. The aim of the study was to compare conditions and outcomes of otosphere suspension cultures from dissociated organ of Corti of either newborn mouse or guinea pig and to evaluate the guinea pig as a potential cochlea donor for preclinical cell therapy. Dissociated guinea pig cochlea produced otospheres *in vitro*, expressing stem cell markers, similarly to mouse otospheres. However, there was limited viability for these cells when compared to the mouse. The results were published in Oiticica et al (2010).

PROJECT 80 PLUS

In this project we plan to collect 1000 samples from healthy individuals older than 80 years old with the following objectives:

- To contribute to the understanding of genetic parameters responsible for healthy aging;
- To serve as a parameter to novel findings in the genome of younger people.

This is a collaborative project with Prof. Maria Lucia Lebrão - School of Public Health and Prof. Yeda A. de Oliveira Duarte - The School of Nursery, from USP.

Clinical data regarding cognitive and motor function as well as social-economic and habits/behavior aspects are being collected for further correlation studies with other genetic variables.

Until now, samples from 224 individuals older than 80 were collected. In addition, we have also planned a collaborative study with Institute Albert Einstein for functional MRI in this group.

This work is being undertaken by Michel Naslavsky (as part of his MS degree, supervision of MZ) and by Dr. David Schlesinger as a post-doc project (MZ)

INTERNATIONAL PUBLICATIONS

a) Articles

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accompanied by seizures, absent speech, urogenital, and skin anomalies in male patients. Am J Med Genet A. 152A**:** 3084-3090, 2010.

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b) Chapters in Books

1. Haddad, LA, Pena, SDJ. Biologia Molecular em Neuropediatria In: Fonseca LF, Pianetti G e Xavier CC. Compêndio de Neurologia Infantil, 2ª ed., Rio de Janeiro: Medbook, 2010, pp. 629-642 - ISBN-10: 978-85-99977-53-8

2. Koiffman CP, Diament A. Cromossomopatias In: Diament, A, Cypel, S e Reed, UC (eds.) – Neurologia Infantil. 5ª edição, São Paulo. Editora Atheneu, 2010. Vol. 1, p. 393-427.
3. Nascimento RMP e Vianna-Morgante AM. Síndrome do cromossomo X frágil: a importância do diagnóstico precoce na prevenção da deficiência mental. **In:** Kim CA, Albano LMJ e Bertola DR (Eds.) - Genética na Prática Pediátrica. 1ª. Edição, São Paulo. Editora Manole, 2010. Pp. 403-416.
4. Vainzof M, Bushby K. Muscular dystrophies presenting with proximal muscle weakness. In Karpati G, Hilton-Jones D, Griggs RC and Bushby. Disorders of Voluntary Muscle, 8th Edition, Cambridge University Press, Nicholas Dunton Senior Commissioning Editor, Medicine, 2010
5. Vianna-Morgante AM. A Transmissão das Doenças Genéticas: Padrões Mendelianos e Complexos. In: Diament, A, Cypel, S e Reed, UC (eds.) – Neurologia Infantil. 5ª edição, São Paulo. Editora Atheneu, 2010. Vol. 1, pp. 721-729.
6. Zatz M, Vainzof M. Distrofias Musculares Progressivas. In: Beçak W. Genetica Medica. Ed. Manole, 2010, (in press)

c) Abstracts

c.1) International Meetings

International Meetings/Conferences attended: 17
Abstracts presented: 44

1. Brito LA, Silva CBF, Rocha KM, Cruz LA, Meyer D, Schlesinger D, Kobayashi LB, Aguena M, Bertola D, Bueno DF, Alonso N, Passos-Bueno MRS. IRF6 and 8q24 SNPs contribution to nonsyndromic cleft lip with or without cleft palate predisposition varies according to the geographic region in Brazil. 2010. 60th Annual meeting of the American Society for Human Genetics. Washington, USA.
2. Bueno DF, Almada BV, Kobayashi GS, Amaral CER, Aguena M, Jazedje T, Passos-Bueno MRita. Stem cells from dental pulp of neonatal tooth: characterization and expression of neural crest markers. 2010. III International Symposium of Stem Cells. Gramado, RS.
3. Cruvinel EM, Secco M, Almeida CNA, Zatz M, Koiffmann CP. Neuronal differentiation of human mesenchymal stem cells from exfoliated deciduous teeth obtained from Angelman syndrome patients. 2010. ISSCR 8th Annual Meeting, San Francisco, USA.
4. Cussiol JRR, Alegria TGP, Szweda LI, Netto LES. Ohr (Organic hydroperoxide resistance protein) possesses a previously undescribed activity: Lipoyl-dependent peroxidase. 2010. Society for Free Radical Biology and Medicine (SFRBM) 17th Annual Meeting. Orlando, USA.
5. D´Angelo CS, Kohl I, Koiffman CP. Identification of pathogenic copy number variants and of a novel single-gene deletion on syndromic obesity. 2010. 60th Annual meeting of the American Society for Human Genetics. Washington, USA.

6. Discola KF, Oliveira MA, Guimarães BG, Netto LES. Residue 23 of yeast classic dithiol glutaredoxins has a prominent influence on their oxido-reductase activities. 2010. Gordon Research Conferences: Diffraction Methods in Structural Biology. Lewiston, USA.

7. Fanganiello R, Kimonis V, Corte C, Nitrini R, Passos-Bueno MR. A Brazilian family with IBMPFD caused by p.R93C mutation in the VCP gene and literature review for genotype-phenotype correlations. 2010. 60th Annual meeting of the American Society for Human Genetics. Washington, USA.

8. Fanganiello RD, Ishy FAA, Ribeiro C, Bueno DF, Bressiani AHA, Passos-Bueno MR. Enhanced healing of rat calvarial critical size defects with beta-tricalcium phosphate (beta-TCP) discs associated with dental pulp and adipose-derived stem cells. 2010. The American Society of Bone and Mineral Research Meeting. Toronto, Canada.

9. Fontes L, Haddad LA, Borges Jr E, Iaconelli Jr A, Braga DPF, Vianna-Morgante AM. The *FMR1* Gene In The Ovary: Expression And Functional Insights. 2010. 26th Annual Meeting of the European Society of Human Reproduction and Embryology. Rome, Italy.

10. Freitas EL, Cheroki C, Krepischi AC, Otto PA, Rosenberg C. High-resolution 44K array and 1 Mb array detect similar rates of chromosomal imbalances in patients with müllerian defects (MD). 2010. European Society of Human Genetics. Gotemburg, Sweden.

11. Griesi-Oliveira K, Nicol X, Vadasz E, State MW, Passos-Bueno MR, Muotri AR. Implications of TRPC6 expression to the neuronal phenotype of an autistic patient: using human induced pluripotent cells to model autism spectrum disorders. 2010. Brain Research Meeting: The Emerging Neuroscience of Autism Spectrum Disorders: Etiologic Insights; Treatment Opportunities. San Diego, USA.

12. Gurgel-Giannetti J, Silva M, Meira Z, Ferreira RZ, Yamamoto LU, Vainzof M, Zatz M. The value of cardiovascular magnetic resonance in the follow-up of Duchenne/Becker muscular dystrophy. 2010. XII ICNMD. Napoli, Italy.

13. Gurgel-Giannetti J, Lara MT, Nahim MJS, Siqueira CM, Concentino ELC, Martins-Machado MCP, Yamamoto LU, Onofre-Oliveira P, Vainzof M. Mitochondrial Cardioencephalomyopathy: new SCO2 gene mutations in a Brazilian patient. 2010. XII ICNMD. Napoli, Italy.

14. Haddad LA, Correa JC, Fontes L, Azzi-Nogueira D, Vianna-Morgante AM. Developmentally regulated FMRP isoforms expressing *Fmr1* exon 12 in the brain. 2010. 2010 Monod Conferences, Mental Retardation: from genes to synapses, functions and dysfunctions. Roscoff, France.

15. Horta BB, Oliveira MA, Discola KF, Cussiol JRR, Netto LES. Peroxiredoxin Qß is a bacterial Cys-based peroxidase that presents unique structural redox rearrangements and is highly reactive towards hydrogen peroxide and peroxynitrite. 2010. Society for Free Radical Biology and Medicine (SFRBM) 17th Annual Meeting. Orlando, USA.

16. Jazedje T, Bueno DF, Czeresnia CE, Perin PM, Halpern S, Maluf M, Martins MT, Passos-Bueno MR, Zatz M. Human fallopian tube stem cells are able to produce bone in vivo. 2010. ISSCR 8th Annual Meeting, San Francisco, USA.

17. Krepischi AC, Knijnenburg J, Bertola DR, Kim CA, Kok F, Vianna-Morgante AM, Rosenberg C. 2q24.2 microdeletions encompassing SLC4A10 gene are associated with idiopathic epilepsy and mental impairment. 2009. 14th international workshop on Fragile X and X-linked mental retardation. Salvador, BA.

18. Martins-Machado P, Ayub-Guerrieri D, Onofre-Oliveira PCG, Monteiro G, Zilbersztajn-Gotlieb D, Netto LES, Vainzof M. Fukutin-related protein localizes on the endoplasmic reticulum and perinuclear region in muscle of dystrophic animal models2010. XII ICNMD. Napoli, Italy.

19. Martins-Machado PCM, Onofre-Oliveira PCG, Ayub-Guerrieri D, Gotlieb D, Fernandes A, Pessoti N, Vainzof M. Therapeutic potential of murine mesenchymal stem cells (MSC) from adipose tissue in the treatment of muscular dystrophy in the new double mutant mouse model for the genes Dystrophin and Large. 2010. ISSCR 8th Annual Meeting, San Francisco, USA.

20. Martins-Machado PCM, Onofre-Oliveira PCG, Ayub-Guerrieri D, Gotlieb D, Fernandes A, Pessoti N, Yamamoto LU, Vainzof M. Therapeutic potential of murine mesenchymal stem cells (MSC) from adipose tissue in the treatment of muscular dystrophy in the new double mutant mouse model for the genes Dystrophin and Large. 2010. 15th International Congress of the World Muscle Society. Kumamoto, Japan.

21. Martyn M, Leão EE, Krepischi AC, Rosenberg C, Kok F. Investigation of chromosomal rearrangements by comparative genomic hybridization on arrays (CGH) in patients with mental retardation and agenesis of the corpus callosum. 2010. XI International Child Neurology Congress. Cairo, Egypt.

22. Mazzeu JF, Zhang F, Carvalho CM, Krepischi AC, Yatsenko S, Pardono E, Otto PA, Rosenberg C, Lupski J, Vianna-Morgante AM. Homozygous duplication at 10p11.21 in a boy with clinical manifestations of Lin-Gettig syndrome. 2010. 60th Annual meeting of the American Society for Human Genetics. Washington, USA.

23. Munhoz-Costa I, Netto LES, Nascimento RM, Demasi M, Monteiro G. Characterization of YCL047C, a Putative Adenylyltransferase Involved in the Saccharomyces cerevisiae Oxidative Stress Response. 2010. Yeast Genetics and Molecular Biology Meeting. British Columbia, Canada.

24. Nakamatsu EH, Monteiro G, Discola KF, Murakami MT, Netto LES. Investigation on the molecular aspects of substrate specificity of mitochondrial Thioredoxin Reductase 2 from Saccharomyces cerevisiae. 2010. 3rd Latin American Protein Society Meeting. Salta, Argentina.

25. Netto LES, Cussiol JRR, Oliveira MA, Alegria TGP. Ohr ("Organic Hydroperoxide Resistance protein") is a novel thiol-dependent, Cys-based peroxidase that possesses unique structure and biochemical properties. 2010. Gordon Research Conferences: Thiol-Based Redox Regulation & Signaling. Il Ciocco, Italy.

26. Oiticica J, Barboza-Junior LC, Batissoco AC, Haddad LA, Mingroni-Netto RC, Bento RF. Comparable phenotypes for otospheres from guinea pig and mouse cochlea. 2010. III International Symposium of Stem Cells. Gramado, RS.

27. Onofre-Oliveira PCG, Ayub-Guerrieri D, Martins-Machado P, Pessoti N, Gotlieb D, Fernandes A, Vainzof M. Therapeutic potential of murine mesenchymal stem cells (MSC) from different origins in the treatment of muscular dystrophy. 2010. ISSCR 8th Annual Meeting, San Francisco, USA.

28. Onofre-Oliveira PCG, Martins-Machado P, Ayub-Guerrieri D, Gotlieb D, Fernandes A, Yamamoto LU, Vainzof M. Therapeutic potential of murine mesenchymal stem cells (MSC) from different origins in the treatment of muscular dystrophy. 2010. 15th International Congress of the World Muscle Society. Kumamoto, Japan.

29. Onofre-Oliveira PCG, Martins-Machado P, Ayub-Guerrieri D, Zilbersztajn-Gotlieb D, Santos AF, Vainzof M. Potential of murine bone-marrow mesenchymal stem cells (BM-MSC) in treatment of muscular dystrophy. 2010. 60th Annual meeting of the American Society for Human Genetics. Washington, USA.

30. Passos-Bueno MRS, Brito LA, Cruz LA, Aguena M, Kobayashi LB, Bueno DF, Franco D, Mendonça A, Alonso N, Bertola D, Otto PA. Variability in heritability estimates as a confounding effect for association studies in nonsyndromic cleft lip and palate in Brazilian populations. 2010. 60th Annual meeting of the American Society for Human Genetics. Washington, USA.

31. Pearson PL, Costa SS, Vianna-Morgante AM. Back to family values: Replacing population based association analysis for mapping menopause genes by a novel family approach. 2010. 60th Annual Meeting of The American Society of Human Genetics. Washington, USA.

32. Pereira MCL, Secco M, Janjoppi L, Oliveira CR, Suzuki DE, Gonçalves AS, Zatz M, Okamoto OK. Preclinical study of mesenchymal stem cell human umbilical cord transplantation in an experimental model of parkinson's disease. 2010. ISSCR 8th Annual Meeting, San Francisco, USA.

33. Rosenberg C, Pearson PL. Is the excess of male mental retardation caused by functional and structural peculiarities of the X Chromosome? 2009. 14th international workshop on Fragile X and X-linked mental retardation. Salvador, BA.

34. Secco M, Vieira NM, Jazedje T, Bueno Junior CR, Valadares M, Okamoto OK, Zatz M. Do factors released from dystrophic muscle enhance myogenic differentiation of mesenchymal stem cells from human umbilical cord tissue? 2010. ISSCR 8th Annual Meeting, San Francisco, USA.

35. Secco M, Vieira NM, Jazedje T, Bueno Junior CR, Valadares M, Okamoto OK, Zatz M. Do factors released from dystrophic muscle enhance myogenic differentiation of mesenchymal stem cells from human umbilical cord tissue? 2010. 15th International Congress of the World Muscle Society. Kumamoto, Japan.

36. Tairum-Jr CA, Horta BB, Oliveira MA, Netto LES. Investigating the Redox Structural Transitions of Saccharomyces cereviseae Tsa1p. 2010. Society for Free Radical Biology and Medicine (SFRBM) 17th Annual Meeting. Orlando, USA.

37. Twigg SRF, Babbs C, Goriely A, Brunner HG, Toriello HV, Mathijssen IMJ, Hoogeboom AJM, Pober BR, Passos-Bueno MR, Wall SA, AOM Wilkie. A paradoxical genotype-phenotype correlation for *EFNB1* mutations: worse outcome in mosaic than constitutionally-deficient males. 2010. 60th Annual meeting of the American Society for Human Genetics. Washington, USA.

38. Vainzof M, Martins-Machado PCM, Onofre-Oliveira PCG, Gotlieb D, Fernandes A, Lopes V, Yamamoto LU. Mice models deficient for two muscle proteins helping to understand protein complexes organization and function. 2010. XII ICNMD. Napoli, Italy.

39. Vianna-Morgante AM, Coqueti KN e Otto PA. The maternal pattern of X-cheomosome inactivation as a parameter for evaluating the contribution of X-

chromosome mutation to mental retardation in males. 2010. 60th Annual Meeting of The American Society of Human Genetics. Washington, USA.

40. Vieira N, Bueno CRJ, Brandalise V, Caetano HVA, Zucconi E, Secco M, Vainzof M, Zatz M. Systemic transplantation of human adipose-derived stem cells into the golden retriever dystrophic dog. 2010. XII ICNMD. Napoli, Italy.
41. Vieira N, Zucconi E, Bueno Junior C, Secco M, Brandalise V, Suzuki MF, Bartolini P, Vainzof M, Zatz M. Do mesenchymal stem-cells from different sources have the same potential to originate muscle cells when injected into the dystrophic sjl mice? 2010. ISSCR 8th Annual Meeting, San Francisco, USA.
42. Vieira NM, Bueno Junior CR, Brandalise V, Caetano HVA, Zucconi E, Secco M, Vainzof M, Zatz M. Local and systemic transplantation of human adipose-derived stem cells into the GRMD dog. 2010. 15th International Congress of the World Muscle Society. Kumamoto, Japan.
43. Yeh E, Fanganiello RD, Sunaga DY, Passos-Bueno MR. How different FGFs contribute to Apert Syndrome phenotype. 2010. 60th Annual meeting of the American Society for Human Genetics. Washington, USA.
44. Zilbersztajn-Gotlieb D, Ayub-Guerrieri D, Onofre-Oliveira CG, Martins-Machado P, Santos AF, Martins A, Vainzof M. Myostatin expression in different mice models for neuromuscular disorders. 2010. 60th Annual meeting of the American Society for Human Genetics. Washington, USA.

c.2) National Meetings

National Meetings/Conferences attended: 11
Abstracts presented: 35

1. Alcântara S, Ayub D, Martins P, Vainzof M. Comparação do potencial miogênico “in vitro” de células-tronco mesenquimais de tecido adiposo e medula óssea em modelos murinos para distrofias musculares. 2010. SIICUSP. São Paulo, SP.
2. Atique RFT, Yeh E, Fanganiello R, Passos-Bueno MR. Células tronco mesenquimais como modelo para screening de drogas para o tratamento da síndrome de Apert. 2010. 56º Congresso Brasileiro de Genetica. Guarujá, SP.
3. Batissoco AC, Barboza-Junior LC, Lezirovtz K, Haddad LA, Mingroni-Netto RC, Bento RF, Oiticica J. Postnatal mouse and mature guinea pig cochlea as potential source of Sox2 and nestin positive otospheres. 2010. 1st meeting on Stem Cell Research of the Instituto de Química: Perspectives of Stem Cells. São Paulo, SP.
4. Bonaldi A, Mazzeu JF, Costa SS, Bertola DR, Kim CA, Vianna-Morgante AM. Estudo genético da síndrome de Silver-Russell. 2010. 56º Congresso Brasileiro de Genetica. Guarujá, SP.
5. Calvacante LS, Monteiro G, Netto LES. Structural and Functional Characterization of the Amino acids Involved in 1-Cys Peroxiredoxins Ascorbate-Peroxidatic Activity. 2010. XXXIX Reunião Anual da Sociedade Brasileira de Bioquímica e Biologia Molecular (SBBq). Foz do Iguaçu, PR.

6. Cruvinel EM, Secco M, Almeida CAN, Zatz M, Cassola AC, Koiffmann CP. Diferenciação neuronal de células-tronco derivadas de dentes deciduos de pacientes com a síndrome de Angelman. 2010. 56º Congresso Brasileiro de Genetica. Guarujá, SP.

7. Cruz LA, Sunaga DY, Bueno DF, Kobayashi GS, Aguena M, Ferreira S, Amaral CER, Brito L, Passos- Bueno MR. Identificação de vias de sinalização associadas à predisposição às fissuras lábio-palatinas não sindrômicas. 2010. 56º Congresso Brasileiro de Genetica. Guarujá, SP.

8. Fonseca ACS, Vianna-Morgante AM. Desequilíbrios cromossômicos submicroscópicos em translocações aparentemente equilibradas associadas a sinais clínicos. 2010. 56º Congresso Brasileiro de Genetica. Guarujá, SP.

9. Freitas EL, Bertola DR, Krepischi AC, Rosenberg C. Deleção da região crítica DGS2 em uma paciente com translocação t(1;10)(p22;p11.2) aparentemente balanceada. 2009. 10º simpósio nacional de biologia molecular aplicado à Medicina. Ribeirão Preto, SP.

10. Griesi-Oliveira K, Davis N, Sanders S, Mason CE, Rose K, Vadasz E, Takahashi VNO, Muotri AR, Passos-Bueno MR, State MW. Mapping reciprocal translocation breakpoints in an autistic patient: identification of TRPC6 gene as a novel candidate gene for Autism and modeling neuronal development in vitro using the patient's cells. XXXIV Congresso Anual da SBNeC. Caxambu, MG.

11. Kido LY, Netto LES, Oliveira MA. New possibilities to study the interaction between cTPxI and TrxIC33S: stable protein complexes linked by mixed disulfide. 2010. XXXIX Reunião Anual da Sociedade Brasileira de Bioquímica e Biologia Molecular (SBBq). Foz do Iguaçu, PR.

12. Kimura L, Angeli CB, Pereira AC, Auricchio MTB, Cotrim, NH, Pereira TV, Mingroni-Netto RC. Associação entre sete polimorfismos em genes candidatos e a hipertensão arterial em afro-brasileiros. 2010. XVIII Congresso da Sociedade Brasileira de Hipertensão. Goiânia, GO.

13. Kobayashi GS, Sunaga DY, Bueno DF, Cruz LA, Ferreira SG, Passos-Bueno MR. Efeito da sincronização celular na análise do transcriptoma de culturas celulares de pacientes portadores de fissura lábio-palatina. 2010. 56º Congresso Brasileiro de Genética. Guarujá,SP.

14. Lanzotti A, Onofre-Oliveira P, Vainzof M. Geração do novo modelo murino SJL/MDX, duplo-mutante para as proteínas disferlina e distrofina. 2010. SIICUSP. São Paulo, SP.

15. Mingroni-Netto RC, Batissoco, AC, Auricchio MTBM, Otto PA. Deafness recurrence risks in families excluded for Connexin mutations. 2010. 56º Congresso Brasileiro de Genética. Guarujá, SP.

16. Nakamatsu EH, Monteiro G, Discola KF, Murakami MT, Netto LES. Enzymatic and structural analysis of thioredoxin reductase 2 from Saccharomyces cerevisiae. 2010. XXXIX Reunião Anual da Sociedade Brasileira de Bioquímica e Biologia Molecular (SBBq). Foz do Iguaçu, PR.

17. Nascimento CC, Netto LES, Oliveira MA. Site-directed Mutagenesis, Expression and Purification of Saccharomyces cerevisiae Cytosolic Thioredoxin Peroxidase II C170S. 2010. XXXIX Reunião Anual da Sociedade Brasileira de Bioquímica e Biologia Molecular (SBBq). Foz do Iguaçu, PR.

18. Naslavsky MS, Schlesinger D, Mendes TAB, Forbes JF, Amaro Jr E, Zatz M. Estudo 80+: identificação de genes associados à dominância motora em idosos cognitivamente saudáveis. 2010. 56º Congresso Brasileiro de Genetica. Guarujá, SP.

19. Netto LES, Nascimento RM, Demasi M, Monteiro G. Characterization of YCL047C, a Putative Phosphocholine Cytidylyltransferase Involved in Lipid Reposition during Oxidative Stress in Saccharomyces cerevisiae. 2010. XXXIX Reunião Anual da Sociedade Brasileira de Bioquímica e Biologia Molecular (SBBq). Foz do Iguaçu, PR.

20. Oiticica J, Barboza-Junior LCM, Batissoco AC, Mingroni-Netto RC, Haddad LA, Bento RF. Comparable in vitro phenotypes of otospheres from guinea pig and mouse cochleas. 2010. Simpósio de Avanços em Pesquisas Médicas dos Laboratórios de Investigação Médica do Hospital das Clínicas na FMUSP. São Paulo, SP.

21. Oiticica J, Barboza-Junior LCM, Batissoco AC, Mingroni-Netto RC, Haddad LA, Bento RF. Comparable fenotypes for Otospheres from Guinea Pig and Mouse Cochlea. 2010. V Congresso Brasileiro de Células Tronco e Terapia Celular. Gramado, RS.

22. Pelatti, M, Secco M, Zatz M, Jazedje T. Estudo comparativo de linhagens celulares do aparelho reprodutor feminino como Feeder-layers de células tronco embrionárias humanas. 2010. 56º Congresso Brasileiro de Genetica. Guarujá, SP.

23. Pereira MCL, Secco M, Suzuki DE, Janjoppi L, Rodini CO, Zatz M, Okamoto OK. Terapia celular em doença de parkinson: uma avaliação pré-clínica do transplante de células-tronco mesenquimais de cordão umbilical humano. 2010. XXXIV Congresso Anual da SBNeC. Caxambu, MG.

24. Pimenta MV, Horta BB, Discola KF, Netto LES. Investigation on Amino Acids Residues Involved in AhpF NADH-Oxidase Activity. 2010. XXXIX Reunião Anual da Sociedade Brasileira de Bioquímica e Biologia Molecular (SBBq). Foz do Iguaçu, PR.

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31. Suzuki DE, Ariza CB, Porcionatto MA, Okamoto OK. Expression of E2F1 during post-natal brain development: a possible role in cerebellar neuroprogenitor cell proliferation. 2010. XXXIX Reunião Anual da Sociedade Brasileira de Bioquímica e Biologia Molecular (SBBq). Foz do Iguaçu, PR.
32. Tairum-JR CA, Horta BB, Guimarães BG, Oliveira MA, Netto LES. Identification of structural and functional changes in an important alpha helix related to active site in mutant Thioredoxin peroxidase I (cTPxI) of Saccharomyces cerevisiae. resumo em congresso nacional. 2010. XX Reunião Anual dos Usuários do Laboratório Nacional de Sincronton. Campinas, SP.
33. Tairum-JR CA, Horta BB, Zara JF, Oliveira MA, Netto LES. Structural and Functional Characterization of Yeast Thiol Specific Antioxidant Protein 1 (Tsa 1): Investigating the RedoxStructural Transitions. 2010. XXXIX Reunião Anual da Sociedade Brasileira de Bioquímica e Biologia Molecular (SBBq). Foz do Iguaçu, PR.
34. Ursi S, Dessen EMB, Towata N. Descobrindo o mundo microscópico: programa para o novo Laboratório de microscopia da estação ciência (USP). 2010. III Encontro Regional de Ensino de Biologia (III ENEBIO)/IV Encontro Regional de Ensino de Biologia – NE (IV EREBIO- NE)/V Congreso Iberoamericano de Educación en Ciencias. Fortaleza, CE.
35. Vaquero AR, D'Angelo CS, Koiffmann CP. Pesquisa de mutações no Gene *RAI1*. 2010. 56º Congresso Brasileiro de Genética. Guarujá,SP.

d) Theses and Dissertations

1. Camila de Freitas Almeida. Células-tronco embrionárias murinas: indução para linhagem miogênica e caracterização. Trabalho de Iniciação Científica. Instituto de Biociências, USP, 2010.
2. Daniela Uehara. Pesquisa de microrrearranjos em genes candidatos a surdez sindrômica e não-sindrômica. Master dissertation. Instituto de Biociências, USP, 2010.
3. David Schlesinger. Ancestralidade da população de São Paulo e correlação com alterações neuropatológicas no idoso. PhD thesis. Instituto de Biociências, USP, 2010.
4. Ilana Kohl. Pesquisa de genes e/ou segmentos cromossômicos em pacientes com obesidade, hiperfagia e atraso do desenvolvimento neuropsicomotor e/ou deficiência mental. PhD thesis. Instituto de Biociências, USP, 2010.
5. Lilian Kimura. Fatores Genéticos associados à hipertensão essencial em populações remanescentes de quilombos do Vale do Ribeira – São Paulo. PhD thesis. Instituto de Biociências, USP, 2010.

6. Nabila Scabine Pessotti. Diferenciação miogênica “in vitro” de células tronco mesenquimais murinas de diferentes origens. Trabalho de Conclusão de Curso. Instituto de Biociências da Unesp – Campus de Botucatu. 2009.
7. Poliana Cristina de Melo Martins. Caracterização in vitro da Proteína FKRP (fukutin-related protein) e investigação do mecanismo de hipoglicosilação em pacientes com Distrofia Muscular congênita. Trabalho de Conclusão de Curso. Programa de biotecnologia, 2010.
8. Rafaella MP Nascimento. O gene *UBE2A* (*Ubiquitin conjugating enzyme 2A*) e a deficiência mental: triagem de mutações e estudos funcionais. Instituto de Biociências, USP, 2010.

AWARDS AND HONORS

Célia P Koiffmann- Prêmio pela dedicação, empenho e valorização do curso de Pós-Graduação em Biologia/Genética, Instituto de Biociências, USP, 2010.

Maria Rita Passos Bueno- Ordem Nacional de Mérito Cientifico, na classe Grã Cruz da Ordem.

Student Awards:

Tatiane Jazedje da Costa Silva, Daniela Franco Bueno, Carlos Eduardo Czeresnia, Paulo Marcelo Perin, Mariangela Maluf, Silvio Halpern, Maria Rita Passos-Bueno e Mayana Zatz. Prize SAÚDE, CATEGORIA SAÚDE DA MULHER, Editora ABRIL, December 2010 for the work: “Perspectivas de um futuro tratamento para osteoporose ou outras doenças ósseas com base em células-tronco”.

Lilian Kimura – Prize, 3rd place, for the work “Associação entre sete polimorfismos em genes candidatos e a hipertensão arterial em afro-brasileiros. Kimura L, Angeli CB, Pereira AC, Auricchio MTB, Cotrim, NH, Pereira TV, Mingroni-Netto RC. In XVIII Congresso da Sociedade Brasileira de Hipertensão. Goiânia, 5-7 August 2010.

PART 2. EDUCATION/PUBLIC INFORMATION

I. High School Visiting Program

a) USP goes to your School (A USP vai à sua Escola)
http://genoma.ib.usp.br/educacao/projetos_usp_escola.html.

In a partnership action, the CEGH (Center of Human Genome Study) and CEPOF (Group of Optic from Physic Institute of São Paulo University, São Carlos) elaborated an itinerant exhibition focused on Stem Cell and Optics. In São Paulo, 26 schools were visited in the second semester of 2010 (Annex 1), each of them during 2 to 5 days. The mediation was performed by 4 undergraduates or graduated students from USP, during 4.5 hours in the morning and 4 hours in the evening, 4 days a week. Sixty-eight biology and physics teachers were capacitated to be able to carry on activities related with the exhibited subjects, since we supplied educational material and follow-up (Annex 1). Around 20.800 students were contemplated with this action.

b) Partnership with Educational Directories North 2 and Osasco

b.1) "Practical classes at school" - The main objective of the partnership with these Educational Directories is to contribute to the improvement of teacher's competence and to stimulate the development of differentiated projects and activities in the classroom. During 2010, CEGH supplied microscopes and 5 different types of kits for practical classes for 26 schools. Thirty-six teachers from these schools were previously capacitated do deal with the educational material (Annex 2). The equipment for the practical classes remains at each school for 2 weeks and four schools were contemplated at the same time. Around 15.000 students were contemplated. http://genoma.ib.usp.br/educacao/projetos_dir_ensino_norte.html.

b.2) Instructional material - Two loan stations were installed at the Educational Directories Norte 2 and Osasco and 54 teachers were capacitated to deal with the instructional kits during their classes**.** (Annex 3)
http://genoma.ib.usp.br/educacao/materiais_didaticos.html.

II. Giant Cell
http://genoma.ib.usp.br/educacao/projetos_celula_gigante.html

An installation of an eukaryotic cell, amplified 130,000 times, allows people to immerse into cell organelles and have an idea of the structure and the function of a living cell. The Giant Cell participated in three events:

- **a.** 34th Annual Meeting of ANPOCS (Associação Nacional de Pós-Graduação e Pesquisa em Ciências Sociais), in Caxambú, from 25th to 29th October. Attendance was 1.600 people, mainly students from fundamental education. (Annex 4).
- **b.** 56º Brazilian Congress of Genetics, in Guarujá, São Paulo, on September 16th. Attendance was 400 visitors.
- **c.** Feira das Profissões da UNIP, Santos, October 5th to 7th.- 700 visitors.

The table bellow summarizes the efforts of CEGH in improving the knowledge of genetics of high school students and their teachers, as well as professionals.

Outreach work in 2010	Number of hours of the activity	Audience	Annex number
Exposition USP goes to your school	442	20.800 students	1A and 1B
Practical classes	1.872	15.000 students	2A and 2B
Teacher's training	16	122 teachers	3

III- <u>Other Activities</u>

a) Science Divulgation Articles

1. Zatz M. ELA: Como estão as pesquisas? VEJA.COM. 7 de janeiro
2. Zatz M. O que protege algumas pessoas de doenças respiratórias- VEJA.COM. 14 de janeiro
3. Zatz M. Laser, células-tronco, odontologia e câncer- VEJA.COM. 21 de janeiro
4. Zatz M. Hormônio de crescimento: os ensinamentos de um menino muito especial- VEJA.COM. 27 de janeiro
5. Zatz M. Distrofias musculares e meu reencontro com Julio- VEJA.COM. 04 de fevereiro
6. Zatz M. Células-tronco e terapia gênica- VEJA.COM. 11 de fevereiro
7. Zatz M. Células-tronco e regeneração óssea- VEJA.COM. 18 de fevereiro
8. Zatz M. Cérebro masculino versus feminino- VEJA.COM. 27 de fevereiro
9. Zatz M. Como dar uma má noticia? Pessoalmente ou por Internet? VEJA.COM. 5 de março
10. Zatz M. Mulheres na ciência- VEJA.COM. 11 de março
11. Zatz M. Novo banco público de sangue de cordão umbilical- VEJA.COM. 18 de março
12. Zatz M. Oswaldo Frota-Pessoa- VEJA.COM. 25 de março
13. Zatz M. Células-tronco em tratamentos estéticos. Não compre gato por lebre. VEJA.COM. 1 de abril
14. Zatz M. Esclerose lateral amiotrófica: ensasios clínicos com células-tronco estão começando- VEJA.COM. 9 de abril
15. Zatz M. O que são xenotransplantes: VEJA.COM. 16 de abril
16. Zatz M. Transferência de núcleos entre óvulos humanos- VEJA.COM. 22 de abril
17. Zatz M. Esclerose lateral amiotrófica: falta mais ousadia- VEJA.COM. 29 de abril
18. Zatz M. Os 20 anos do diagnóstico pré-implantação- VEJA.COM. 3 de maio
19. Zatz M. Células IPS: o que são? VEJA.COM. 10 de maio
20. Zatz M. Testes genéticos em farmacia- VEJA.COM. 17 de maio
21. Zatz M. Craig Venter e a ovelha Dolly- VEJA.COM. 24 de maio
22. Zatz M. Zatz M. Testes genéticos: a minha experiência pessoal- VEJA.COM. 3 de junho
23. Zatz M. Aprovado o primeiro teste clínico para tratar tumores cerebrais com células-tronco- VEJA.COM. 10 de junho
24. Zatz M. Califórnia inicia proejto gigante de pesquisa genômica- VEJA.COM. 17 de junho
25. Zatz M. Células-tronco em S. Francisco- VEJA.COM. 24 de junho

26. Zatz M. Pesquisadores identificam genes da longevidade- VEJA.COM. 3 de julho
27. Zatz M. O projeto Genoma Humano completa dez anos: Avanços ou decepções? Revista Cara@Coroa- julho de 2010
28. Zatz M. Genes para traços comuns ou genes da futilidade- VEJA.COM. 10 de julho
29. Zatz M. DNA pode ser usado sem o consentimento do doador? VEJA.COM. 17 de julho
30. Zatz M. Progeria- VEJA.COM. 23 de julho
31. Zatz M. Bancos de células tronco: polpa dentária e cordão umbilical – VEJA.COM. 29 de julho
32. Zatz M. As pesquisas clínicas com células-tronco embrionárias estão começando- VEJA.COM. Folha de S.Paulo- 30 de julho
33. Zatz M. Células-tronco virou palavra mágica- Jornal da Ciência, agosto de 2010
34. Zatz M. Informações contidas no DNA: a quem pertencem? VEJA.COM. 10 de agosto
35. Zatz M. Fibrose cística: por que é importante divulgar? VEJA.COM. 17 de agosto
36. Zatz M. Células-tronco se transformando em músculo. Gordura é melhor que cordão- VEJA.COM. 25 de agosto
37. Zatz M. Ainda as adultas- Estado de S.Paulo, Caderno Aliás, 29 de agosto
38. Zatz M. As células-tronco têm memória- VEJA.COM. 2 de setembro
39. Zatz M. Um novo dilema:quando a incerteza é mais tolerável que a certeza- VEJA.COM. 10 de setembro
40. Zatz M. Qual das vontades prevalece- VEJA.COM. 17 de setembro
41. Zatz M. Prêmio Jovem mulheres -Cientistas- VEJA.COM. 24 de setembro
42. Zatz M. Novo método para reprogramar células-tronco- VEJA.COM. 1 de outubro
43. Zatz M. A caminho de uma cura bilionária- VEJA.COM. 7 de outubro
44. Zatz M. Células-tronco ajudam a entender os genes que causam palato-fendido- VEJA.COM. 14 de outubro
45. Zatz M. Por que defendo as pesquisas com animais. VEJA.COM. 21 de outubro
46. Zatz M. Uma outra face das células-tronco- VEJA.COM. 27 de outubro
47. Zatz M. Podemos ser processados- VEJA.COM. 4 de novembro
48. Zatz M. Uma tarde no genocão- VEJA.COM. 12 de novembro
49. Zatz M. Células-tronco ensinando a tratar a doença de Rett- VEJA.COM. 18 de novembro
50. Zatz M. Um novo ensaio clínico com células-tronco embrionárias- VEJA.COM. 22 de novembro
51. Zatz M. O que emperra nossas pesquisas- VEJA.COM. 27 de novembro
52. Zatz M. Os protegidos- VEJA.COM. 2 de dezembro

b) Lectures

1. Mingroni-Netto RC. Aconselhamento Genético. IV Semana da Biologia, Universidade Federal de São Carlos, SP. October 1st, 2010.
2. Vainzof M. Modelos animais para doenças neuromusculares ajudando a entender mecanismos e testar terapias. Depto de Anatomia, ICB/USP. 29/06/2010
3. Vianna-Morgante AM. A Citogenética Humana no Brasil: Caminhos Trilhados e Perspectivas - Curso de Aperfeiçoamento em Genética Geral e Citogenética, Laboratório Hermes Pardini, Belo Horizonte, MG, 4/12/2010.

4. Vianna-Morgante AM. FMR1 premutation and ovarian insufficiency - II International Symposium Sindrome X Fragil y Autismo, Santiago, Chile, 7/10/2010.
5. Vianna-Morgante AM. Intellectual disability: what the pattern of X-inactivation in mothers of affected boys can tell us about the mode of inheritance – II International Symposium. Sindrome X Fragil y Autismo, Viña de Mar, Chile, 5/10/2010.
6. Vianna-Morgante AM. Aspectos Genéticos del Retardo Mental Ligado al Cromosoma X - XIV CONGRESO LATINOAMERICANO DE GENÉTICA (ALAG), Viña del Mar, Chile, 3/10/2010.
7. Vianna-Morgante AM. Array-CGH en el Diagnóstico de Enfermedades Genéticas - Curso ACTUALIZACIONES EN CITOGENÉTICA, Viña del Mar, Chile, 1/10/2010.
8. Vianna-Morgante AM. Oswaldo Frota-Pessoa: Fazendo e divulgando ciência e ensinando a ensinar. Simpósio em Homenagem a Oswaldo Frota-Pessoa, 56º Congresso Brasileiro de Genética, Guarujá, SP, 16/9/2010.
9. Zatz M. Pesquisas inovadoras em células-tronco. Hospital Sirio-libanês, 03/2010.
10. Zatz M. Avanços nas pesquisas com células-tronco-Recife, 03/2010.
11. Zatz M. Publicações de alto impacto- Instituto de Pesquisas do Hospital Albert Einstein- 04/2010.
12. Zatz M. NAPGENOMA- Faculdade de Ciências Farmacêuticas, USP, 06/2010.
13. Zatz M. Células Tronco: Potencialidades, Implicações Éticas e Perspectivas na Área da Saúde"- FMUSP, 13/08/2010.
14. Zatz M. Stem-cells and genome – Mexico, 06/09/2010
15. Zatz M. Bioethics- Mexico, 07/09/2010
16. Zatz M. Stem-cells researches: what can we expect? Mexico, 08/09/2010.
17. Zatz M. Neuromuscular disorders: from gene identification to preclinical studies. Mexico, 09/09/2010.
18. Zatz M. Advances in muscular dystrophy research- . Mexico, 10/09/2010.
19. Zatz M. Células-tronco em doenças neurológicas- Congresso Nacional de Neurologia, Rio de Janeiro, 09/2010.
20. Zatz M. Células-tronco em nefrologia- Congresso Nacional de nefrologia, Rio de Janeiro, 09/2010.
21. Zatz M. Como o conhecimento do genoma irá modificar a sua vida? Colégio Santa Cruz, 09/2010.
22. Zatz M. Perspectives of stem-cells- Instituto de Bioquímica, 09/2010.
23. Zatz M. Genética e ética- Curso Medicina, FMUSP
24. Zatz M. Pesquisas em células-tronco- Curso Medicina, FMUSP
25. Zatz M. National Institute of stem-cells in genetic disorders- Brasilia, 11/2010.
26. Zatz M.Células-tronco em doenças neuromusculares- Academia Brasileira de Ciências, 01/12/2010.

c) Training courses and exchange research experiences among labs:

Karina Griese-Oliveira: is doing part of her doctorate at University of California, at Dr. A Muotri's laboratory November-December 2010.

ANNEX 1A

USP goes to your School (A USP vai à sua Escola) - Visited High Schools and capacitated teachers

Schools	Capacitated teachers	Educational Directory
EE Alcyr Oliveira Porciúncula, Prof.	Jair Bezerra de Menezes Júnior – Física Antonio Pedro de Castro – Biologia	Osasco
EE Américo Marco Antonio. Dr.	Willian Camargo Aires Maranhão – Física Ivanildes da Silva Cangussu – Biologia Mara Regina Senna - Biologia	Osasco
EE Antônio Carlos da Trindade	Reginaldo Silva de Oliveira - Física Mariluci Severino Pereira – Biologia Gisele Bonilha Nogueira - Biologia	Osasco
EE Antonio de Almeida Júnior	Eder Cardoso Leão – Física Fátima do Rosário Gomes da Silva - Biologia	Osasco
EE Armando Gaban, Prof.	Ricardo Pataro – Física Marilim Fernandes Brandão - Biologia	Osasco
EE Elói Lacerda	Thiago Aparecido Ferraz Vidal – Física Erica Ikeda Nidelcia Perpétua da Silva Oliveira- Biologia Renata Aparecida de Oliveira - Biologia Maria Aparecida Lucas - Biologia Adriana A. Vasconcelos - Biologia	Osasco
EE Francisca Lisboa Peralta, Prof.	Sandra Maria Polli Casarin –Física Aparecido Francisco Galdino – Biologia Reginaldo dos Santos - Biologia	Osasco
EE Heloisa de Assumpção, Profª.	Willian Camargo Aires Maranhão – Física Carmem Cinira Teixeira -Biologia	Osasco
EE José Edson Martins	Eliel Gonçalves dos Santos – Física Andrea Ferreira da Silva – Biologia Carlos Alberto Ramos - Biologia	Osasco
EE Jardim Santa Maria III	Maria Ângela da Silva – Biologia	Osasco
EE José Geraldo Vieira	Cláudia Sales Noda – Física Pedro Lobas Neto - Biologia	Osasco
EE José Jorge, Prof.	Dulcilene Eloy Firmino – Física Benedita de Souza – Biologia	Osasco
EE José Liberatti, Prof.	Vicenti Galli - Física Francisco Alves Pereira – Física Alice Nagai – Biologia Kátia Cristina Guerreiro Carraro – Biologia Carlos Siomar Menoli – Biologia	Osasco
EE José Maria Rodrigues Leite, Prof.	Cristina Della Matta - Física Carlos Jiro Tani Inoue – Física	Osasco
EE José Ribeiro de Souza	Sonia Silva Ribeiro – Física Diogo Jorge dos Santos Silva – Biologia	Osasco

EE Leonardo Vilas Boas	Everton Almeida de Oliveira – Física	Osasco
EE Josué Benedito Mendes, Prof.	Josefa Cristina V. da Silva – Biologia Vagner Roberto Gentil – Biologia Walquiria Marques dos Reis – Biologia	
EE Luci Anna Latorre, Profª.	Ronaldo Gonzaga Moraes - Física Osny Vieira - Biologia	Osasco
EE Luiz Lustosa da Silva, Prof. Dr.	Letícia Silva dos Santos – Física Márcia dos Santos Marçal - Biologia	Osasco
EE Neuza de Oliveira Prévide, Profª	José Valdir e Silva - Fisica Iracy Vieira de Araujo – Biologia	Osasco
EE Newton Espírito Santo	Alessandra Domingues Andrade – Física Elias Tavares – Biologia Telma Satomi Maekaawa - Biologia	Osasco
EE Educador Paulo Freire	Silvia Maria Semensato - Física Milena Rodrigues Furtado – Biologia Guilherme Thiago Brandt Mazzini – Biologia Cícero Vanderlei da Silva – Biologia Shirlei Aparecida de Oliveira – Biologia	Osasco
EE Tarsila do Amaral	Daci Rodela Pretel - Biologia	Osasco
EE Telmo Coelho Filho, Major.	Rosana Helena da Silva – Física Silvio Eduardo Fogaça – Biologia Vinicius Oliveira de Almeida - Biologia	Osasco
EE Leonidas Paiva	João Roberto Teodoro – Física Adjair Pedroso – Biologia Monica Aparecida Correia - Biologia	Norte 2
PCOP Física	Ediana Barp – Física	Norte 2
EE Pastor Paulo Leivas Macalão	Roberto Lima do Prado – Física Natália Felipe Gonçalves Moreira – Biologia Patrícia Fernandes Patta - Biologia	Norte 2
PCOP Biologia	Vera Lúcia Pirré de Castro	Norte 2

ANNEX 1B

USP goes to your School (A USP vai à sua Escola)

ANNEX 2A

Practical classes in public high schools from Educational Directories North 2 and Osasco attended in 2010

Schools	Teachers	Educational Directory
EE Alberto Cardoso de Mello Neto	Andréa Valete Machado	Norte 2
EE Alfredo Inácio Trindade	Maria Lúcia dos Santos	Norte 2
EE Amenaíde Braga de Queiróz	Hosana Correa Luz Pastore	Norte 2
EE Assis José Ambrósio	Marcela Monges Silva	Norte 2
EE Carmosina Monteiro Viana	Maria da Graça Sapage Estácio	Norte 2
EE Ministro Dilson Funaro	Ana Maria Rodrigues Lima dos Santos Aline C Lima Santos	Norte 2
EE Guilherme de Almeida	Mariana Pereira	Norte 2
EE Justino Cardoso	Rosecler da Rocha Tomé Sônia Lucia Costa Nogueira	Norte 2
EE Pedro de Moraes Victor	Angela Consuelo Blanco Carmosina Aguiar	Norte 2
EE Philomena Baylão	Ana Maria Marcondes de Jesus	Norte 2
EE Antonio Carlos da Trindade	Mariluci Seberino	Osasco
EE Francisco Casabona	Maria Tereza da Silva Galvão	Osasco
EE José Liberatti	Enrique Angel S Queralt Alice Nagai Davi Kiyoshi	Osasco
EE Aureliano Leite	Maria Helena Belomo Maria Salete Montolim	Osasco
EE Jose Jorge	Benedita de Souza Maria de Lourdes Mendonça	Osasco
EE Eloi Lacerda	Maria Aparecida Lucas	Osasco
EE Antonio Raposo Tavares	Rúbia Rodrigues Nelson Takamitsu Regina Cely Feres Hadad	Osasco
EE Irmã Gabriela	Ivanildes da Silva Cangussu	Osasco
EE Neusa de Oliveira Prévide	Iraci Vieira de Araujo	Osasco
EE Deputado Guilherme de Oliveira Gomes	Luciana de Camargo Crê	Osasco
EE Prof. Dr.Luis Lustoza da Silva	Marcia dos Santos Marçal	Osasco
EE Jardim Cipava II	Cassia M Nabarro Kátia Cristina Guerreiro Carraro	Osasco
EE Julia Lopes de Almeida	Jaredes domingos da Silva	Osasco
EE Prof. João Batista de Brito	Lenice Maria Silva Kobayashi	Osasco
EE Tarsila do Amaral	Daci Rodella Pretel	Osasco
EE Prof. Ernesto Thenn de Barros	Vania Dias Flauzino Rosemeire Cássia da Silva	Osasco

ANNEX 2B
Practical classes in public high schools from Educational Directories North 2 and Osasco attended in 2010

ANNEX 3

Teacher's capacitation (10/04/2010) to handle the instructional kits

Schools	Teachers	Educational Directory
EE Francisco Casabona	Maria Teresa da silva Galvão Nazato Rebeca Laino Gama	Osasco
EE Gastão Ramos	Vilma Aparecida Venerruchi Lucilaine Braite Leite	Osasco
EE Irmã Gabriela	Ivanildes da Silva Cangussu	Osasco
EE Neuza de Oliveira Prévide	Iracy Vieira de Araujo	Osasco
EE Antonio Raposo Tavares	Claudia Regina Perazzolo Rubia Rodrigues	Osasco
EE Deputado Guilherme de Oliveira Gomes	Luciana de Camargo Crê	Osasco
EE Newton Espírito Santo	Renata Aparecida Oliveira	Osasco
EE Prof. Dr.Luis Lustoza da Silva	Marcia dos Santos Marçal	Osasco
EE Almeida Junior	Fátima R Gomes	Osasco
EE Jardim Cipava II	Cassia M Nabarro	Osasco
EE Orlando Geríbola	Vânia Maria Garcia	Osasco
EE Francisco Matarazzo Sobrinho	Adriana Santana Rocha Roseli Cristina Laranjeira	Osasco
EE Jardim Cipava II	Kátia Cristina Guerreiro Carraro	Osasco
EE Lucy Anna Carrozo Latorre	Anilton Vaz Ferreira Luciana Batelli de Mello Osny Vieira	Osasco
EE Antonio Carlos da Trindade	Mariluci Seberino Carla Rocha Ferreira	Osasco
EE Fanny Monsoni	Juliana Fonseca Caetano	Osasco
EE Francisco Casabona	Maria Tereza da Silva Galvão Alexandre Pires Correia	Osasco
EE Rosa Bonfiglioli	Maria de Lourdes Silva Seródio	Osasco
EE Graciliano Ramos	Circe Cavalcanti de Albuquerque	Osasco
EE José Liberatti	Enrique Angel S Queralt Alice Nagai Davi Kiyoshi	Osasco
EE Aureliano Leite	Maria Helena Belomo Maria Salete Montolim	Osasco
EE Jose Jorge	Benedita de Souza Maria de Lourdes Mendonça	Osasco
EE Gloria Azedia Bonetti Letícia	Tartarini Ramires	Osasco
EE Heloisa Assumpção	Carmem Cinira Teixeira	Osasco
EE Eloi Lacerda	Adriana Medeiros B Ramalho	Osasco
EE Philomena Baylão	Ana Maria Marcondes de Jesus	Norte 2
EE Alfredo Inácio Trindade	Maria Lúcia dos Santos	Norte 2

EE Assis José Ambrósio	Daianne Danielle Bastos Janina dos Passos Braga	Norte 2
EE Alberto Cardoso de Mello Neto	Andréa Valete Machado	Norte 2
EE Carlos de Laet	Luciana Lucas de Almeida	Norte 2
EE Albino Cesar	Cristina Marçal da Silva Braga	Norte 2
EE Antônio Jose Leite	Andrea S Garcia	Norte 2
EE Sebastião de Souza Bueno	Cristina Tortorelli	Norte 2
EE Eurico Figueiredo	Silvana Leite do Amaral	Norte 2
EE Ministro Dílson Funaro	Ana Maria Rodrigues Lima dos Santos	Norte 2
EE Pastor Paulo Leivas Macalão	Aline Cristina Lima dos Santos	Norte 2
EE Pedro Alexandrino	Claudia Cherice Fontes de Souza	Norte 2
EE Angelo Bortolo	Claudia Cherice Fontes de Souza Paula Galvão Alves	Norte 2
EE Gabriela Mistral	Ana Claudia Pereira	Norte 2
EE Ruy Barbosa	Viviane Regina Fernandes	Norte 2

ANNEX 4

34º Encontro Anual da ANPOCS (Associação Nacional de Pós-Graduação e Pesquisa em Ciências Sociais), TEM – Circuito de Ciência e Tecnologia –Caxambú, October 25th to 29th

PART 3. TRANSFER OF TECHNOLOGY/ TECHNOLOGY APPLICATIONS

This section will include the main activities done in the last year regarding Genetic Counseling (GC), genetic testing, sequencing and microsatellite analysis services. These activities involve the participation of all the seven main researchers of the CEPID project, as follows: Angela Vianna-Morgante, Carla Rosenberg, Célia Koiffmann, Maria Rita Passos-Bueno, Mariz Vainzof, Regina C. Mingroni-Netto, and Mayana Zatz. Also, the neurologist Fernando Kok, and clinical geneticists Rita de Cassia Pavanello and Debora Bertola, all collaborators of CEPID, contribute to these activities. Prof. Paulo A. Otto, from the Department of Genetics and Evolutionary Biology, also collaborates to the Genetic Counseling service.

a) Genetic Counseling at CEGH

We offer this service for 6 main groups of disorders: neuromuscular (M Zatz, M Vainzof, F Kok, RC Pavanello), mental retardation - syndromic and non-syndromic forms (A Vianna-Morgante, C Rosenberg, PA Otto), developmental disorders associated with behavior disturbances and/or obesity (C Koiffmann), hearing diseases (RC MingroniNetto), craniofacial syndromes (MR Passos-Bueno) and autism (MR Passos-Bueno). The average number of families seen by our group (~2000) in 2010 was similar to the previous year. Genetic testing was offered in all necessary cases, as their results are critical for estimation of genetic recurrence risks, management and follow up of patients, while Genetic Counseling was offered to all of them.

b) Genetic Counseling at other regions of the country

We have maintained our partnership with Operation Smile, which offers surgery repair for clefting patients in different regions of the country. This year, we have evaluated and offered GC for more than 400 families with cleft lip and palate patients ascertained in 3 different regions of the country (Maceio - AL, Fortaleza and Barbalha - CE and Santarém - PA).

c) Database of the Genome Center

Some members of the CEGH are currently using the Laboratory Management Information System (LIMS) software developed by IME-USP to input clinical and laboratory data (http: zen.genoma.ib.usp.br). The control of exams, workflow of DNA genetic tests and cell bank have been implemented throughout this past year, and the first two topics are already in use. We are planning to do a larger training in March/2011 in order to have additional groups using this LIMS. Besides, we will develop during 2011 better tools for search. This LIMS software is being developed by Dr. João E. Ferreira and his team, at the Institute of Mathematics/USP in collaboration with CEPID/CEGH-USP.

d) Other activities and interactions

Our Center also interacts with patients/parents associations such as the Brazilian Muscular Dystrophy Association (ABDIM), Fragile X, Prader-Willi, Angelman, and Cleft lip/palate Associations. Through ABDIM we established an important partnership with the Secretaria da Saúde de São Paulo to support genetic tests aiming diagnosis and genetic counseling as well as management to families with affected members by neuromuscular disorders. Through this program we evaluated 500 patients from the state of Sao Paulo,

and performed about 300 molecular tests for the diagnosis of NMD. Additionally, a second partnership with AACD-ABDIM, consisting in the PAF-GEN project, allowed us to evaluate patients from other states of Brazil, including clinical, physiotherapy and diagnosis of neuromuscular disorders (about 80 molecular tests and 20 muscle biopsies per year).

We also have established a collaboration since 2007 with the Institute of Lacanian psychoanalysis (IPLA-Instituto de PsicoanáliseLacaniana) directed by the psychoanalyst Jorge Forbes, in order to evaluate the effect of a novel psychoanalytic approach and treatment to families with affected members by neuromuscular disorders. The team which includes 21 psychoanalists performs about 30 consultations per week.

We have introduced this year a support to the families with autism, which is leaded by a research group of the Psychology Institute (Dr. M. Hubner).

At last, we have a significant interchange of information about genetic tests and genetic counseling with the general public through e-mails.

e) Sequencing service and diagnostic tests for the general community

In 2010, the income from our sequencing service doubled (21.338 sequencing injections and 21.063 microsatellite injections), while the number of genetic tests ordered by clinicians outside the CEGH was similar (about 300). The income obtained from our service has been used to pay salaries for technicians and secretarial assistants, and also for equipment maintenance.

f) Implementation of a Quality System in the DNA Diagnostic Lab

We are working towards the implementation of a Quality System for the DNA Diagnostics Lab. In this past year, we have prepared all the necessary Standard Operation Protocols (SOPs) for the exams that will be contemplated under the Quality System. These exams are: Cystic Fibrosis, Spinocerebellar Ataxia (SCA1, SCA2, SCA3 and SCA6), Spinal Muscular Atrophy, Dechenne/Becker Muscular Dystrophy, Rett syndrome and Velocardiofacial syndrome.

We have established and implemented a protocol for in-house quality control of tests. We also contracted the European Molecular Genetics Quality Network as an external quality control for assessment of test quality and reliability.

The protocols for general lab operations, equipment operation, software operation, test methodology, test background information, and individual disease test protocols are already written and undergoing a final round of review and correction.

Some of the technicians responsible for performing the tests were substituted during this past year. Once all the protocols are finished, and the new technicians have been properly trained, we will hire an external audit to access our quality program for the DNA diagnostics lab. We expect to be able to accomplish this step by June 2011.

Main Proposals for 2011

- Maintenance of the three mains services: genetic counseling, genetic testing and sequencing/microsatellite services.
- Finish writing the documentation and get audit evaluation.
- Train a larger number of users for the LIMS software to include clinical, lab and genetic test results.