HUMAN GENOME RESEARCH CENTER (HGRC)

Instituto de Biociências
Universidade de São Paulo

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REPORT - 2007

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Part 1. RESEARCH REPORT

1. SUMMARY

Our proposal for 2006 - 2008 was focused on two main projects:
a) Exploration of the causes and clinical variability of genetic disorders by the dissection of the genetics and architecture of the human genome.
b) Assessment of different approaches for future treatment and/or therapy of human genetic diseases, particularly neuromuscular disorders and craniofacial syndromes, focusing mainly on the potential of stem cells, from different sources to differentiate in specific tissues. Gene therapy approaches were also included.

2. RESULTS

I. INVESTIGATION OF GENETIC FACTORS UNDERLYING HUMAN DISEASES

I.1 IDENTIFICATION OF DISEASE GENES

One of the main goals of the CEPID project is to identify genes associated with human genetic disorders, particularly neuromuscular and developmental disorders. The general approach used to achieve this goal is linkage and positional cloning for Mendelian disorders where large families have been identified or association studies for complex disorders. Our progress in this last year regarded to this major aim is detailed below:

NEUROMUSCULAR DISORDERS

A) Mapping and identification of new genes: We mapped spastic paraplegia to a new locus on the X-chromosome, SPG34, in a family that we reported in 1976. This study was part of the Ph.D. Thesis of Inês Macedo Soares, and the article was submitted for publication. We narrowed down the candidate regions for two diseases that we had previously mapped - LGMD1G (Starling et al., 2004) and SPOAN (Macedo-Soares et al., 2005) -, but screening of candidate genes has not revealed the specific mutations. We collaborated in the identification of *KIAAO196* as the mutated gene at the SPG8 locus in patients with hereditary spastic paraplegia (Valdamis et al, 2007), and also in determining that mutation in the *Scyl1* gene causes a recessive form of spinocerebellar neurodegeneration. (Schmidt et al., 2007).

B) Intrafamilial variability in patients with the same mutation: We identified the mutation in *SPAST* gene at locus SPG4, in a family with a dominant form of spastic paraplegia that we had previously reported. This first case of a multi-exonic duplication in *SPAST* gene generated a premature stop codon, likely resulting in haploinsufficiency (Mitne-Neto et al., 2007). The penetrance was higher in men than in women and men also had earlier onset of symptoms and were more severely affected than females. Understanding these differences and, in particular, why some individuals are “protected” from the manifestation of the mutated gene could open new venues for treatment of this disorder.

C) Identification of new mutations: In central core disease (CCD), a predominantly autosomal-dominant congenital myopathy, we identified two out of nine Brazilian CCD families with the autosomal recessive form (AR) and mutations in *RYR1* gene. The patients were mildly

affected, differing from the few AR cases described previously. AR inheritance in CCD may therefore be relatively common, with implications for genetic counseling and prevention of malignant hipertermia in affected families (Kossugue et al., 2007). In addition, mutations in the Dynamin 2 gene, which was recently identified as causative of centronuclear myopathy, were found in three among six affected Brazilian families (Sell et al., 2007).

DEVELOPMENTAL DISORDERS

A) Syndromic mental retardation:

A1) A1) The detailed clinical evaluation of a family with six males affected by syndromic X-linked mental retardation led to the hypothesis that they presented Snyder-Robson syndrome. This syndrome was previously described in the literature in only one family with a causative mutation in *SMS* gene at Xp22. The analysis of this gene in the Brazilian family led to the identification of a novel missense mutation. We are currently conducting functional analysis to better characterize the effect of this mutation on the phenotype.

A2) We have previously described a *UBE2A/HR6A* mutation as the cause of a novel X-linked mental retardation syndrome. This gene encodes a conjugase in the ubiquitin proteasome pathway. We have not found mutations in this gene in 23 probands from families in which mental retardation mapped to an interval that included *UBE2A.* We are presently conducting functional studies, as described below.

B) Auriculo-condylar syndrome (ACS): It is an autosomal dominant condition that involves structures derived from the first and second branchial archs. Through linkage analysis with whole-genome markers in two large Brazilian families, we mapped the disease gene to chromosome 1 in one of the kindreds (Masotti et al., 2007). We are trying to identify additional families in order to confirm this finding and to narrow down the candidate region. Linkage analysis is in course in the family unlinked to chromosome 1.

C) Syndromic forms of craniosynostosis (SC): This is a heterogenous group of disorders in which the genetic etiology is identified in about 50% of the cases. We analyzed 47 patients with SC, by karyotyping, MLPA and comparative genomic hybridization. A total of 22 possibly pathogenic chromosomal rearrangements were identified. Eleven of these were microdeletions or duplications not detected through karyotype analysis. These results show that small chromosomal rearrangements are an important cause of SC. (Jehee et al., manuscript in preparation). We also showed that *FGF3* and *FGF4* are likely causative genes of human craniosynostosis (Jehee et al., 2007). In addition, we collaborated with the identification of the causative gene for Carpenter syndrome, another form of syndromic craniosynostosis (Jenkins et al., 2007), and contributed to a better characterization of the phenotype of patients with FGFR3 (Doherty et al., 2007).

D) Syndromic obesity: Patients with syndromic obesity were investigated with a set of probes designed for detecting subtelomeric chromosome imbalances; monosomy 1p36 and del 3p were detected, and mapping of the breakpoints (BAC-FISH) are under way. Six 1p36 deletions were characterized by MLPA and FISH analyses. Five were apparently pure <3.0 Mb terminal deletions, and, in one case, triplication and duplication of segments in the proximal 1p36 region were also present. In addition, one case presented a duplication of 1q subtelomeric region that had been translocated to the end of the short arm. These findings reveal the complexity of the rearrangements. All patients had in common the deletion of GABRD and SKI genes. Four out of six patients presented, obesity and/or hyperphagia, in some period of their life, and three were referred for Prader-Willy syndrome testing. We also found a rare 1Mb 22q11.2 deletion within the DGS/VCFS 3 MB region in a girl with obesity, hyperphagia and aggressive behavior, also present in her mother who had a major depressive disorder. This finding suggests that another gene at the

most telomeric 3Mb region is associated with the onset of neuropsychiatric disorders (D´Angelo et al., 2007)

E) Autism: This is a complex disorder, and the multifactorial model most likely explains the involvement of genetic factors. We analysed SNPs within *HTR1A HTR1B, HTR1D, HTR2A, HTR2C* genes in 200 controls, 220 patients and their mothers. We detected evidence for association between *HTR1B* markers and autism (manuscript submitted for publication).

F) Deafness: we described a family with high level of inbreeding, presenting autosomal recessive deafness and two novel *MYO15A* mutations, thus characterizing allelic heterogeneity within one pedigree (Lezirovitz et al., 2007). Linkage analysis in a large pedigree with autosomal dominant deafness indicated a novel candidate locus on chromosome 2 (manuscript in preparation). Sequencing of genes in the candidate region is underway.

G) Ectrodactily/tibial hypoplasia syndrome: In a large family with individuals affected by autosomal dominant ectrodactily associated to tibial hypoplasia, we mapped the defect to chromosome 17, the first mapped locus (manuscript in preparation). Sequencing of candidate genes in the region is under way.

H) Syndromes associated with balanced translocations: The breakpoints of two apparently balanced translocations in syndromic patients [t(1;15) and t(5;14)] were localized to BAC clones by FISH. We are narrowing down the breakpoint regions in the search for candidate genes for the clinical phenotypes.

I) Sotos syndrome: Sixty five patients with clinical diagnosis of Sotos syndrome were investigated for submicroscopic deletions. Three patients had a deletion encompassing *NSD1* and *FGFR4* genes, and in two others, the deletion encompassed the whole *FGFR4* gene, but some exons of *NSD1* gene. (Fagali et al.,2007). The search for point mutations in *NDS1* gene in the remaining patients is under way. In a patient with a Sotos-like syndrome, an entire duplication of chromosome 20 was found; his clinicall normal mother was a mosaic carrier of this duplication. (Oliveira et al., 2007).

J) Robinow syndrome: In a collaborative study with Dr. Jamie Lohr, University of Minnesota, and Dr. Han Brunner, University of Nijmegen, a point mutation in *WNT5A* gene was identified in individuals affected by the dominant form of Robinow syndrome (DRS) from the original family described in 1969, and in two other patients in a cohort of 32 (Person et al., submitted). In the other 30 patients we failed to detect large deletions or duplications. Screening of genes (*WNT5B, FZD5* and *RYK*) coding for proteins that interact with WNT5A or ROR2 (the latter mutated in the recessive form) did not reveal mutations. The majority of DRS patients remain without a causative diagnosis. Our chromosomal investigation of DRS patients, after G-banding and array CGH, revealed alterations of chromosome 1 and 15 (Mazzeu et al., 2007b, and unpublished data), thus indicating candidate genes for this heterogeneous condition, which are under investigation.

I.2 MECHANISMS MODULATING PHENOTYPIC EXPRESSION

A) Characterization of regulatory regions related to genes associated with developmental disorders:

A1) TCOF1: Treacher Collins syndrome (TCS), an autosomal dominant condition caused by haploinsufficiency of treacle, is associated with a large spectrum of clinical variability within and between families. We have not identified any important regulatory mechanism (SNPs or methylation of the CpG island at the promoter region) that could explain this clinical variability. We are currently investigating if the expression of *TCOF1* is biallelic and if the levels of TCOF1 in

lymphocytes of TCS patients differ from control individuals. We organized a *TCOF1* mutation database at our website.

A2) COL18A1: Mutations in this gene cause Knobloch syndrome (KS), an autosomal recessive condition characterized by high myopia, vitreoretinal degeneration and occipital encephalocele. Few patients have been described, and the spectrum of clinical variability is not well characterized. In this regard, we identified a pathogenic mutation in *COL18A1gene* in patients with the diagnosis of KS presenting cognitive impairment, a clinical manifestation not yet described in this syndrome (Keren et al., 2007).

COL18A1 is a molecule involved with angiogenesis and might be associated with predisposition to disorders dependent on vascular control, such as diabetic retinopathy, cancer and obesity. We found a SNP in the frizzled domain in association with obesity (manuscript in preparation). In addition, when characterizing regulatory elements in the promoter region of the *COL18A1* gene, we observed that CEBPalpha, a transcription factor associated with hepatocarcinoma, is involved in the control of expression of *COL18A1* gene. These results were obtained in a collaborative study with Dr. Musso, Inserm, France.

A3) FGFR2: We have recently shown that a gain-of-function mutation in *FGFR2* that is causative of the craniosynostotic Apert syndrome (AS), is associated with an enhanced osteogenic potential and an expression signature (Fanganiello et al., 2007). We are currently investigating the importance of some of these genes in bone differentiation.

A4) IRF6: Mutations in this gene cause Van der Woude syndrome, an autosomal dominant condition characterized by lower lip pits, cleft lip and/or palate. There is a wide spectrum of clinical variability and the full phenotype is still not characterized. We have described a patient with some classical features of this syndrome and cognitive impairment (Zecchi-Ceide et al., 2007). A novel functional SNP has been identified in the promoter region of this gene, which will be tested in the genealogies with an atypical phenotype.

B) Clinical variability in facioscapulohumeral muscular dystrophy (FSHD): FSHD is an autosomal dominant disorder characterized by inter- and intrafamilial variability ranging from severely affected to asymptomatic carriers. We collected muscle biopsies from five families in which severely affected and asymptomatic carriers occurred, and also obtained a muscle sample from one family member who did not carry the mutation. Gene expression analysis using microarrays is currently being performed by the Ph.D. student Patricia Arashiro, in collaboration with Prof. Louis M. Kunkel in Boston.

C) Clinical variability in fragile X-associated tremor ataxia syndrome *(FXTAS)* This recently described neurodegenerative syndrome is associated with the permutation of the *FMR1* (fragile X syndrome) gene. Atypical presentations of the sydrome are under study. We described a patient with severe and rapidly progressive cognitive impairment in addition to major and minor radiological signs diagnostic of FXTAS in premutations carriers This patient had no tremor or limb ataxia, thus characterizing a new course of the disease (Gonçalves et al., 2007).

I.3 PROTEIN AND FUNCTIONAL ANALYSIS

A) Proteins involved in axonal guidance: Yeast two-hybrid analysis have been used to identify proteins that might interact with collybistin, which is involved in axonal guidance. Three candidate collybistin binding partners were identified in the first screen and were further confirmed, using the yeast two-hybrid approach. More recently, interaction between collybistin and one of the candidate interacting-partner, the eIF3S3 - involved in translation control, was confirmed through co-immunoprecipitation of epitope-tagged proteins in HEK293 cells. Now, we are investigating whether these proteins interact *in vivo*, performing co-immunoprecipitation experiments involving the endogenous proteins, in newborn mouse brain extracts

B) Protein analysis in amyotrophic lateral sclerosis type 8 (ALS8): We have previously identified *VAP-B* gene as responsible for an autosomal dominant form of amyotrohic lateral sclerosis showing a great clinical variability in progression rate (ALS8). Brazilian patients identified to date have a missense mutation, P56S, in the MSP (major sperm domain) of the gene. *In vitro* analyses of the effect of this mutation on human VAP-B protein were performed, in an attempt at understanding the mechanisms responsible for ALS8. The results demonstrated that P56S mutation does not seem to be related to a modification of MSP–VAP-B's state of oligomerization, but rather with the interactions between VAP-B and other cellular proteins, mainly tubulin and GAPDH (glyceraldehyde-3-phosphate dehydrogenase). Interestingly these two proteins have been previously related to other forms of neurodegenerative diseases and are potential key points to understand ALS8 pathogenesis and other forms of Motor Neuron Disease. This investigation is part of the Ph.D. thesis of Miguel Mitne-Neto (Mitne-Neto M et al., 2007)

C) Protein in neuromuscular disorders:

C1) Characterization of protein complexes: The analyses of muscle proteins in patients with several neuromuscular diseases were reported in two new book chapters (Vainzof et al., 2007; Zatz and Vainzof, 2007). The mechanism of glycosilation of alpha-dystroglycan in the muscle of patients with mutation in the *FKRP* gene is under analysis. The study of different muscle proteins in patients with LGMD2I was submitted for publication (Yamamoto et al.). Galactins 1 and 3 were studied in muscle biopsies from patients with different forms of muscular dystrophies. The results in Duchenne patients, as compared to the mdx mouse, were presented in the last meeting of the WMS (Yamamoto et al., 2007). Sarcoglycan protein analysis identified a new patient with partial deficiency of only d-SG, suggesting that the DGC complex can be formed in spite of the deficiency of this protein (Gouveia et al., 2007).

C2) Proteins involved in muscle development: Some genes involved with the degenerative process, like *TGF-b1* and pro-collagen are under study in differet muscles (skeletal versus diafragm) from mice strains, at different ages. Strains presenting milder phenotypes (such as *mdx* or *SJL*) are compared with strains with more aggressive manifestations of the disease (like *Large myd* or *dy2j/dy2j*). Preliminary results show higher expression of both pro-collagen and TGF-b1 in the skeletal muscle of the mdx mice, when compared to age-matched normal controls (2 months of age), but a higher expresssion of only pro-collagen, in the more severely affectd diafragm muscle of the mdx mice.

C3) Functional and structural analysis of mutations at the protein level: The cloning and expression in *Escherichia coli* of several domains of FKRP is ongoing. Three fragments from the mutated, normal and C-terminal region of the protein FKRP were cloned expressed and purified. We are preparing immunization experiments in rabbits and the transfection in mammalian cells. We are also performing biochemistry and biophysics *in silico* analyses, as a basis for the structural characterization of the FKRP.

Studies in human B lymphocytes have shown that the measurement of RYR1 mediated intracellular Ca2+ release can differentiate between normal and malignant hyperthermia-susceptible individuals. The effect of the anesthetics halotane and caffeine in the viability of lymphocytes was tested in patients with different mutations in the *RYR1* gene causative of Central Core Disease and Malignant Hyperthermia. Lymphocytes were submitted to different concentrations of the anesthetics, and cell viabily was evaluated by citometry. Preliminary results showed a drastic effect of halotane, but no effect of caffeine on this cell system (Maia et al., 2007).

D) Fragile X Mental Retardation Protein (FMRP) and Pep28K: (a) *A* 28-kDa protein was identified in our investigation of FMRP isoforms. We demonstrated that this protein (provisionally named pep28K) is not derived from FMRP. We partially purified it from adult female rat brain lysates, and showed that pep28K is a protein from microtubule-organizing centers, where it co-localizes with gamma-tubulin. Immunohistochemistry analyses detected pep28K in the median

eminence and islands of Calleja from brains of pregnant rat (E19). Reticular thalamic nuclei and subfornical organ are structures with likely expression of pep28K, what remains to be confirmed. (b) We cloned rat *Fmr1* genomic segments to search for RNA motifs regulating alternative splicing of *Fmr1* exons 12 and 14. To analyze FMRP distribution in ribonucleoprotein complexes, we performed polysomal gradients of rat brain, which will be analyzed by Western blotting and RT-PCR. We established primary cultures of rat bone marrow stem cells that will be induced to differentiate into either glial or neuronal cells. This *in vitro* system may have applications for the studies on FMRP and pep28K.

E) Functional studies to evaluate oxidative stress in patients with hearing deficiency: In order to investigate the possible role of oxidative stress in hearing deficiency, the establishing of an assay to measure the levels of peroxides in plasma, serum and lymphoblastoid cell lines is under way.

F) UBE2A (ubiquitin-conjugase encoded by UBE2A mutated in a novel mental retardation syndrome): (a) Expression analysis: three *UBE2A* transcripts were found in blood cells of a carrier of the mutation and in all human embryonic and adult tissues tested from normal individuals (blood, placenta, embryonic renal cells, and brain). In murine cells a novel transcript was found. (b) Functional complementation analysis of yeast *ΔRAD6* mutation (conserved ortholog) by normal and mutated human isoforms: only normal human transcript 1 restored the normal phenotype, thus indicating that it differs functionally from the other two normal transcripts (Nascimento et al., 2007, 53th Brazilian Congress of Genetics, Prize: "Post-graduation students - Best Work presented in Human Genetics and Evolution, and Medical Genetics").

G) Tuberous sclerosis complex (TSC): We have established bi-dimensional primary cultures of rat airway smooth muscle cells to be employed in a tri-dimensional cell system to approach the molecular bases of TSC lymphangiomyomatosis.

I.4 COMPLEX DISORDERS AND GENETIC VARIATION AT THE POPULATION LEVEL

A) Genetic basis of noise induced hearing loss: In a sample of 255 individuals similarly exposed to noise (104 of them affected by noise-induced hearing loss) association studies were performed with polymorphisms in the genes *GJB2, GSTM1,GSTT1* genes. We did not find significant effects of genotypes at these **l**oci, but a significant excess of familial history of hearing loss was detected in the affected group. Sequencing of mitochondrial genes *MT-RNR1* e *MT-TS1*i indicated a significant effect of some mitochondrial haplotypes in protecting against hearing loss (manuscript in preparation).

B) Genetic factors associated to hypertension and obesity in Afro-Brazilian partially isolated populations: Presently we have a sample of 570 individuals that had been clinically evaluated for hypertension and obesity and were genotyped for 11 loci: *ACE, eNOS ,GNB3 , AGT LEP, LEPR, ADBR2, PPARG, PLIN, RETN* and *INSIG2*. Multiple regression analysis indicated significant association between genotypes at *GNB3* and *INSIG2* and blood pressure. Results were presented at national and international meetings (Kimura et al., 2007 and Angeli et al, 2007). A report on the frequency of the sickle-cell trait and its relationship with the origins of the individuals from the partially isolated Afro-Brazilian populations is in press.

C) Diabetic Retinopathy (DR): We have tested if SNPs mapped within genes in the angiogenesis and vascular pathways were involved with the diabetic retinopathy. We identified an association between a SNP in the promoter region of *VEGF* and diabetic retinopathy (Errera et al., 2007) but not with SNPs in the *MTHFR* gene (Errera et al., 2006). We have also analysed SNPs in *COL18A1*

in diabetes type 2 patients; unexpectedly we found association between one of these SNPs and obesity but not with diabetic retinopathy, as detailed above.

I.5 Genomic architecture

Clinical impact of DNA sequence copy number variation

Array-CGH was used in the identification of chromosome regions relevant for syndromes under investigation in the Center. About 100 families of syndromic patients have been analyzed this year. Among patients ascertained by mental retardation, about 15% had submicroscopic chromosomal alterations, similarly to other studies in the literature. However, this frequency was around 30% when ascertainment criteria such as deafness or Müllerian aplasia were adopted. This study uncovered candidate genes for the investigated pathologies. Results from this investigation published in 2007, some of them in collaboration with other centers: Cheroki et al. (2007), Hoffer et al. (2007), Knijnenburg et al. (2007), Kriek et al. (2007), Mazzeu et al. (2007a e b), Rodriguez-Revenga et al. (2007), Ullmann et al. (2007).

II. DEVELOPMENT OF FUTURE THERAPEUTIC APPROACHES TO GENETIC DISEASES

Studies on stem cells and other cell types are being conducted with the future aim at ameliorating the phenotypes in neuromuscular and craniofacial disorders, or to be used in therapeutic trials for induced deafness.

II.1 STEM CELL RESEARCH

During this year we have established culture conditions and characterize adult stem cells from different sources, such as umbilical cord, lipo-aspirate and dental pulp, which resulted in a number of publications.

A) Muscular disorders:

A1) Human adult Mesenchymal stem-cells (MSC) from umbilical cord blood: Preliminary results attempting to differentiate adult MSC into muscle cells *in vitro* and *in vivo* have shown that MSC from human cord blood have little potential to differentiate into muscle cells “in vitro”. However, these cells differentiated into myotubes and expressed dystrophin, when injected into the mdx mouse model, that is, only after exposure to *in vivo* muscle environment. This research was undertaken by the pos-doctoral student Viviane Nunes, and was the cover of the journal Biology of the Cell (Nunes et al., 2007).

A2) Human adult adipose stem cells: Better results were obtained with MSC obtained from human lipo-aspirate. These cells differentiated into myoblasts and myotubes and expressed dystrophin *in vitro*. This work was done by the Ph.D students Natassia Vieira and Eder Zucconi (Vieira et al., 2007).

A3) Human adult stem cells from umbilical cord: We compared the efficiency in obtaining MSCs from unrelated paired UCB and UC samples harvested from the same donors under the same culture conditions. Although MSCs from blood were obtained from only one among 10 samples, we isolated large amounts of multipotent MSCs from all UC samples, which originated different cell lineages. Since the routine procedure in UC banks has been to store the blood and discard other tissues, such as the cord and/or placenta, these results are of immediately clinical value. Furthermore, the possibility of originating different cell lines from neonates UC born with genetic defects may provide new cellular research models for understanding human malformations and genetic disorders as well as the possibility of testing the effects of different therapeutic drugs.

This work was done by the Ph.D. students Mariane Secco and Eder Zucconi and were published in stem-cells as a rapid publication (Secco et al., 2007)

A4) Human mesenchymal stem cells from dental pulp were injected into affected GRMD dogs in a collaborative project with Dr. Irina and Alexandre Kerkis, and the veterinarian group under the coordination of Dr. Maria Angelica Miglino. Different concentrations of cells, as well as local versus systemic injections are under analysis. The morphology and the differentiation potential of cells from different sources and tissues are being characterized aiming at establishing an animal cell bank.

A5) Murine Stem Cells: We tested the therapeutic potential of mesenchymal gfp-labelled stem cells and embryonic stem cells in the mdx and Large mice. The analysis of the muscles of non immuno suppressed injected mice, sacrificed after 2 days, showed the presence of injected cells. But after 30 days, there was no evidence of the presence of these cells. Surprisingly, in two injected mice with ES and using immunosuppression, the injected area presents inflammatory infiltration and necrosis (Ayub-Guerriri et al., 2007), BM stem cells and C2C12 labeled with GFP are also being injected in dy2j/dy2j mice and Large myd mice, and are being followed up.

B) Craniofacial Disorders: We have established an *in vivo* model to test the potential of adult mesenchymal cells to reconstruct cranial bone defects. We reconstructed large cranial defects in rats using dental pulp stem cell lineages (Mendonça et al., submitted for publication). In addition, we characterized a new source of stem cells from oribicularis oris muscle. The plasticity of these cells were tested *in vitro*, and we showed that they led to the reconstruction of large cranial defects in rats (manuscript in preparation; patent deposited).

C) Deafness: Potential of cultured dissociated cochlea hair cells to regenerate induced deafness in the guinea pig. We have successfully established primary cultures of dissociated organ of Corti cells, positive for markers of premature or mature neurons, glia, and cochlea support or hair epithelial cells. *In vitro* induced differentiation of cultured cells increased the relative amount of cochlea epithelial cells. Preliminary results were presented as abstracts and one publication in press (Bento et al., 2007). The aim of this approach is to study cochlear cells protein network, and differentiation, as well as developing a future therapy for deafness induced by aminoglicosides. These experiments resulted from collaboration with the Otorhynolaringology Department of the Medical School – USP**.**

II.2 MOUSE MODELS FOR MUSCULAR DYSTROPHY

The colonies of four mice models for neuromuscular disease were established in our animal house. We are now standardizing comparative clinical tests to measure strength and resistance of different muscles in these mice models. (Lopes et al., 2007). We started breeding mice with mutations in different genes to study the relationship between them. Double mutant for dystrophin/large genes was created, and is viable. We are currently analyzing their fertility and clinical course. Histological, histochemical and immunohistochemical analysis of the muscle are ongoing to elucidate the involved histopathological alterations (Martins et al., 2007). Double mutant for dystrophin and α2-laminin is in the second generation of breeding (Onofre et al., 2007).

II.3 ADENOVIRUS-MEDIATED TRANSDUCTION OF DNA REPAIR GENES RELATED TO HUMAN DISEASES

During this period we finished two reviews summarizing the theme on the use of recombinant adenovirus to study DNA Repair (Armelini et al, 2007), and on skin gene therapy perspectives (Menck et al, 2007). Using the adenovirus carrying photolyases we were able to

discriminate the roles of two UV lesions on DNA (CPD and 6-4PP) in inducing apoptosis. Clearly, the responses were different among DNA proficient or deficient cells, as lesions such as 6-4PP seem to play a role only in the latter cells. The implications of these results for skin cancer are discussed in the work recently accepted for publication (Lima-Bessa et al, DNA Repair). We have also been working, in collaboration with Dr. B. Kaina (Univ. of Mainz, Germany), in the determination of the effects of chemotherapeutic agents in cancer (glioma) cell lines. The role of p53 seems to be crucial in the control of the apoptotic responses in these cells, as the cells are more or less sensitive depending on the presence of the functional p53 protein and differ depending on the chemotherapeutic agent. For example, for TMZ p53 cells are more sensitive (as this protein is necessary for apoptosis induction), and for chloroethylating agents (ACNU and BCNU), p53 cells are more sensitive, as p53 participate in DNA repair of lesions. The data and a discussion on the possible consequences of such findings in tumor therapy are discussed in two recent publications (Roos et al, 2007, and Batista et al, in press).

3. OBJECTIVES FOR 2008

I. INVESTIGATION OF GENETIC FACTORS UNDERLYING HUMAN DISEASES

I.1 IDENTIFICATION OF DISEASE GENES

Mapping and/or identification of genes and new mutations associated with the following phenotypes: limb-girdle muscular dystrophy type 1G, SPOAN (spastic paraplegia optic atrophy and neuropathy), idiopathic scoliosis, auriculo-condylar syndrome, sindromic obesity, Sotos syndrome, autism, X-linked mental retardation, syndromic craniosynostosis, deafness and ectrodactily/tibial hipoplasia syndrome.

I.2 MECHANISMS MODULATING PHENOTYPIC EXPRESSION

1) Characterization of regulatory elements of genes involved with developmental disorders - *TCOF1* and *COL18A1*.
2) Characterization of cells from Apert patients at the cellular and molecular level in order to understand their increased osteogenic potential.
3) Analysis of a SNP in the promoter region of the IRF6 in order to evaluate its effect in clinical variability;
4) Functional analysis of pathogenic mutations in the SMS gene
5) Investigation of the functional role of COL18A1 in adipogenesis.
6) Comparison of gene expression in affected and asymptomatic FSH patients carrying the same mutation.

I.3 PROTEIN ANALYSES

1) Comparison of serum levels of VAPB protein in ALS8 patients and controls in the same family. This work will be done in collaboration with Prof. Hugo Bellen, Houston, Texas.
2) Validation of the interaction of three candidate proteins, detected by yeast two-hybrid approaches, with collybistin
3) Investigation of the contribution of galectins to the dystrophic process.
4) Analysis of the SG complex in patients with different phenotypes aiming at clarifying genotype/phenotype correlations.
5) Evaluation of the mecanism of glycosylation, by studying the temporal expression of genes involved in the glycosylation of a-DG in different mice models for NMD.

6) Genes involved in the degenerative/regenerative muscle process will continue to be studied in different mice models. This knowledge will help us in the evaluation of the therapeutic potencial of the approaches tested.
7) UBE2A (ubiquitin-conjugase 2A): (a) effect of the *UBE2A* mutation detected in an XLMR family on protein synthesis and cellular localization in lymphocytes and adipocytes; (b) activity assays of normal and mutated isoforms based on histone ubiquitination; (c) differentiation potential of adipocyte-derived stem cells from mutated patient.
8) FMRP (fragile X mental retardation protein) and pep28K: (a) To fully purify pep28K and submit it for sequencing; (b) to analyze by IHC the distribution of pep28k in skeletal muscle and in the brain of adult male and non-pregnant female rat; (c) to analyze the expression level of Fmr1 transcripts with or without exon 12 or 14 in transfected cells; (d) to identify segments harboring alternative splicing regulatory elements by deletion mutagenesis; (e) to analyze FMRP isoforms containing the segment encoded by exon 12 in human brains with or without FXTAS (fragile X-associated tremor ataxia syndrome); (e) to establish tri-dimensional cultures of rat airway smooth muscle and inner medullary collecting duct (IMCD) cell line.

I.4 COMPLEX DISORDERS AND GENETIC VARIATION AT THE POPULATION LEVEL

1) Conclusion of SNP genotyping and statistical analysis in association studies of hypertension and obesity in African-derived quilombo populations. We will follow the segregation of markers in pedigrees.
2) Investigation of the above-mentioned populations with population-specific markers of ancestry (PSAs) in order to avoid population stratification.

I.5 GENOMIC ARCHITECTURE

In our search for chromosome regions/genes involved in syndromic patients, CGH screening of selected patients will continue, extended by the use of *(a)* an array with a full coverage of the X-chromosome (tiling-path array), produced at the University of Nijmegen, Holanda, and (b) high-resolution whole-genome arrays. High-resolution arrays will also be used to investigate the genome archtecture at the breakpoint regions.

II. DEVELOPMENT OF FUTURE THERAPEUTIC APPROACHES TO GENETIC DISEASES

II.1 STEM CELL ANALYSIS AND ANIMAL THERAPEUTIC TRIALS

1) Compare the potential of dental pulp, orbicularis oris muscle and adipose stem cells to reconstruct large cranial defects in rats, using the model already developed in the pilot study.
2) Evaluate if adult stem cells obtained from umbilical cord, adipose tissue and dental pulp have the same potential of tissue regeneration *in vivo*. The potential to differentiate into muscle will continue to be tested in different mice models (mdx, dysferlin deficient, dydy, large) as well as in the GRMD dog.
3) Compare the effect of the same stem cells in different animal models and of stem cells of different origin in the same animal model.
4) Compare through microarray analysis the expression of genes in adult stem cells from different sources and in different phases of differentiation .
5) Compare the gene expression profile in different phases of bone differentiation of mesenchymal cells from patients with disorders that affect bone development.

6) Try to reprogram mesenchymal stem cells to embryonic stem cells and if successful we will compare muscle-derived stem cells obtained from natural and reprogrammed cells in animal models.
7) Analyse the immune response “in vitro” in 3 situations: xenotransplantation of human cells to animal models; animal vs animal models of the same species; human cells vc human receptor.
8) Compare the potential of regeneration of adult versus embryonic stem cells *in vivo*.
9) Double mutants for different muscle proteins will be generated and characterized.
10) Evaluate the potential of hair cells obtained from cultivated cochlea tissues to regenerate induced deafness in guinea pig.
11) Silence the expression of specific genes involved in cell cycle arrest, in cultivated organ of Corti cells and compare cell proliferation rates between treated and non-treated cells.
12) Identify new proteins that interact with Connexin 26, the product of the most frequent gene involved with non-syndromic deafness, in cultivated organ of Corti cells.

II.2 GROWTH HORMONE DEFICIENCY AND THE PROGRESSION OF MUSCULAR DYSTROPHIES

The effect of growth hormone (GH) deficiency will be tested through the generation of double mutant mice models (little-little versus muscular dystrophy models).

II.3 ADENOVIRUS-MEDIATED TRANSDUCTION OF DNA REPAIR GENES RELATED TO HUMAN DISEASES

Some of the *in vivo* experiments with adenovirus and adeno-associated vectors were performed this year, but the results were very preliminary. Unfortunately, it seems that we need an amount of virus that we cannot produce in our lab for the moment. We plan to conclude the experiments with UV - induced apoptosis signaling in cell culture in confluency and also in synchronized cells. Our perspective is also to conclude the work on the use of the virus to diagnose xeroderma pigmentosum genes defective in Brazilian patients.

PART 2. EDUCATION/PUBLIC INFORMATION

I. RESULTS

A) Education:

A1) Partnership with 13 public schools: A partnership established with 13 public high schools (Annex 6) from the Educational Directory for the northern area of the city of São Paulo at the end of 2006 was implemented and is fully operational. The main objective was to contribute to the improvement of teacher's competence and to stimulate the development of differentiated projects and activities in the classroom. A learning community was established constituted by researchers, graduated and post graduated students, teachers, and pupils. Every month, a meeting with 14 teachers from the partner schools took place, eight hours each, totaling 80 hours. We focused on Cellular and Molecular Biology, what to teach, where to get educational material to use in classes, how to prepare and teach practical classes, how to involve students in preparing models, educational games, songs with biological themes etc. There were continuing education classes. Teachers were stimulated to develop their work through projects they elaborated by them and put in practice by their students. Six different kits for practical classes were prepared and made available to the teachers after specific training for their use. The Institute of Biosciences/USP made available five microscopes and two stereomicroscopes. Considering that each of these teachers had around 700 students, this program benefited approximately 10.000 students.

A **Forum** at the CEGH web page was constructed in order to improve our communication with high school teachers (http://www.genome.ib.usp.br/forum).

On October 27th, a **Biology Fair** took place in one of the schools, with 270 expositors and 1,000 visitors (video - ANNEX 8) http://www.genoma.ib.usp.br/educacao/escolas_parceiras2007.php.

The evaluation of the partnership is still under way, but we anticipate that outcomes were positive. Teachers stated that the students became much more interested and participative in classes.

The evaluation of the partnership is still under way, but we anticipate that outcomes were positive. Teachers stated that the students became much more interested and participative in classes.

A2) High School visiting program (ANNEX 7)*:* The Center of Human Genome Study (CEGH) and the Group of Optics from the Institute of Physics, University of São Paulo at São Carlos (CEPOF) developed a collaborative project: **"A USP vai à sua escola"** (USP goes to your school). CEPOF bought a car to carry thematic exhibitions to schools, and CEGH equipped the vehicle. We set up the first exhibition focused on Stem cell and Optic, in a mall, the Iguatemi Shopping Center of São Carlos (November 9th and 10th). In February 2008 the exposition will become itinerant and will visit schools in towns surrounding São Carlos and São Paulo City. An educational CD related to the content of the exposition is in preparation and will be used in the teacher meetings.

A3) Training professionals to develop the current and future educational projects: The second part of the post graduation discipline Ensino de Genética": (BIO-5727 - Teaching Genetics, IB-USP, under the coordination of Eliana M. Belluzzo Dessen) occurred in July, and students prepared and gave the course "Revealing stem cells: from dreams to reality" to 48 high-school teachers.

A4) Difficulties in the implementation of the educational projects: The main difficulties remained the same as last year, mainly, lack of hired people to work on the projects. A far-reaching program of interaction with high-school teachers requires at least two qualified full-time persons. The monitors for the visiting program are not sufficient, and work as volunteers. This structure results in a lack of personnel and a high turnover, not compatible with the task of organizing and managing a program involving so many activities dedicated to teachers and students. Another complicating factor is the grant rules for acquiring consumables and paying personnel, which are not adaptable to the proposed activities.

B) Publications:

B1) Directed to High school teachers:

Myiaki CY, Dessen BEM, Mori L (2007) - A contribuição da genética na conservação biológica. (An contribution from genetic to conservation biology) Genética na Escola Vol 02.02; 15-24 www.sbg.org.br.

Nigro RG, Campos MCC, Dessen EMB (2007) - A Célula vai até a Escola. (The cell goes to the school) Genética na Escola Vol 02.02; 4-10. www.sbg.org.br.

B2) Science diffusion:

Menck CF - RNA interferência: a nova corrida do ouro. (RNA interference: a new race to gold). Microbiologia em Foco, 1: 17-21, 2007.

Zatz M - Dolly faz 10 anos: e as pesquisas com células-tronco no Brasil ? (Dolly is 10 years old: and stem-cell research in Brasil?)Enciclopédia Barsa, Julho de 2007

Zatz M -Ainda em foco as embrionárias. (Embryonic stem-cells still in focus) Estado de S.Paulo, Caderno Aliás, 26 de Novembro

Zatz M- Embriões inviáveis para reprodução mas fundamentais para pesquisa (embryos not viable for reproduction but important for research)- Veja com. December 13, 2007

Zatz M- Minha filha com leucemia e meu novo bebê (My daughter with leukaemia and my new baby) Veja com. November 30th, 2007

Zatz M- O que diz a lei e o que pedem os pesquisadores (What law says and what researchers ask) Veja com. December 06, 2007

Zatz M- Da pele humana às células-tronco (from human skin to stem-cells) Veja com. November 23th, 2007

Zatz M- Células-tronco embrionárias (embryonic stem-cells). Veja com. November 16th, 2007

Zatz M- O que fazer com o cordão umbilical (What should be do with the umbilical cord). Veja com. November 9th, 2007

Zatz M - Fraude, ciência e ética. (Fraud, science and ethics) **g1**.globo.com. July 6th, 2007.

Zatz M - A agressividade é genética? (Is aggressivity genetics?) **g1**.globo.com. June 22th, 2007.

Zatz M - Questionamentos versus certezas. **g1**.globo.com. June 8th, 2007.

Zatz M - Herbert Vianna e células-tronco híbridas. **(**Herbert Viana and hybrid stem cells**)** **g1**.globo.com May 25th, 2007.

Zatz M - Medicina telefônica e eletrônica. (Telephonic and electronic medicine) **g1**.globo.com. May 11th, 2007.

Zatz M - Antes de discutir o início, o que é vida? (Before discuss the beginning, what is life?) **g1**.globo.com. April 27th, 2007.

Zatz M - Idéia do tempo de Hitler. (Ideas from Hitler time) **g1**.globo.com. April 13th, 2007.

Zatz M - Pai da Dolly discute ciência brasileira.(Dolly's father discuss Brazilian science) **g1**.globo.com. March 30th, 2007.

Zatz M - Ítalo: escrevendo suas próprias páginas da vida. (Ítalo: writing it´s own life pages) **g1**.globo.com. March 16th, 2007.

Zatz M - Genético é diferente de hereditário. (Genetics is different from hereditary) **g1**.globo.com. March 2nd, 2007.

Zatz M - A maldade é genética? (Is wickedness genetics?) **g1**.globo.com. February 16th, 2007.

Zatz M - E se fosse possível clonar seres humanos? Você estaria preparado? (And if it was possible to clone human beings? Would you be prepared to?) **g1**.globo.com. February 2nd, 2007.

Zatz M - Células-tronco no líquido amniótico. (Stem cells in the amniotic fluid) **g1**.globo.com. January 19th, 2007.

C) Seminar Cycle:
Desautorizando o sofrimento - Os casos do Genoma atendidos pela psicanálise - Mayana Zatz e Jorge Forbes. Mondays, from 10:30 to 1:00 p.m., from September to December 2007.

D) Continuing Education Course:
Revealing stem cells: from dream to reality - 30 hours - July (17-20th, 2006) - participation of 48 teachers from public high schools. Eliana Maria Beluzzo Dessen and Regina Célia Mingroni Netto.

E) Debates:
Mayana Zatz - Subject: The use of embryonic stem cells in scientific studies. Café Cultura - TV Cultura - August 14th, 2007.

F) Giant Cell Exhibition:
The giant cell was has been housed in Estação Ciência (Science Station) since January 2007. It was relocated to participate in the following programs:
Microbiology Exhibit - Biomedical Science Institute - USP. April, 16 to 20th. Visitors: 1,000 students from fundamental and high schools.
National Congress of Genetics - September 5th. Águas de Lindóia, São Paulo. Programmed visitation :300 high-school teachers and students.
"The National Science and Technology Week" - Ibirapuera Park, São Paulo, SP, October 6th and 7th, 2007. - http://www.youtube.com/watch?v=xsZwtla1W-M&mode=user&search.
Biology Fair - October 27th. Escola Estadual Silva Jardim, São Paulo. 1,000 visitors.

G) Media (newspapers, magazines, TV) (Annex 10)

H) Educational activities in scientific meetings:
Dessen EMB - 53º Congresso Brasileiro de Genética (53rd Brazilian Congress of Genetics), September 2-5, 2007, Águas de Lindóia, SP. Coordination: Genética na Praça (activities for high school students and teachers).

II. PLANS FOR 2008

- Improve the high school education program in collaboration with the Educational Directory for the Northern area of the city of São Paulo. Practical classes are key events to motivate studentsnand to engage them in related activities. We applied for new microscopes from Fapesp.
- Make the produced educational material available to a larger number of high-schools teachers: availability for lending and in the web.
- Organize continuing education courses and seminars for high-school teachers.
- Implement "scientific coffee" talks – dialogues, in cultural spaces, such as bookshops, between geneticists and the general public interested in genetics and its impact on society.

PART 3. TRANSFER OF TECHNOLOGY/TECHNOLOGY APPLICATIONS

Our proposal includes genetic counseling and the set up of services, as detailed below. In addition to the services, we have done a patent deposit at the INPI on November 23rd, 2007 (inventors: Daniela F. Bueno, Irina Kerkis, Mayana Zatz and MR Passos-Bueno) and establish a partenerhsip between Petrobrás-ABDIM and CEGH.

3.1 Genetic Counseling

Most of the researchers of the CEPID are involved in genetic counseling. During this year we have attended 640 families with affected patients with neuromuscular disorders, 333 new families with mental retardation, 93 families with behavioral syndromes, 350 families with craniofacial syndromes and 80 with autism. Patients with neuromuscular disorders are seen by a multidisciplinary team including professionals of different areas, physiotherapists - motor and respiratory, neurologists and psychoanalysts, who work together to improve and extend life of affected patients. Diagnosis, carrier detection and management were done when applicable. About 1000 DNA tests, 450 karyotypes were done for diagnostic and genetic counseling purposes. In addition, about 500 protein analyses were done in muscle biopsy samples for diagnosis.

3.2 Psychoanalytic clinic: We have established a collaboration with the Institute of Lacanian psychoanalysis (IPLA-Instituto de Psicoanálise Lacaniana) directed by the psychoanalyst Jorge Forbes. Twenty-seven patients and relative members with different forms of neuromuscular disorders were attended and are being followed, since September of 2006, by a team of psychoanalysts under the direction of JF at the Human Genome Center. The aim is to evaluate the effect of a new psychoanalytic approach, *Desauthorizing the standard suffering*, on patients affected by neurodegenerative disorders. The preliminary results of this work were presented in two international congress: in Paris(Journée de l´Écoles de la cause Freudienne, September 2007) and in Italy (XII International Congress of Neuromuscular disorders).

3.3 Other Services

We are currently offering the following: DNA sequencing, microssatelite analysis, molecular diagnostic tests of genetic disorders, and scanning of cDNA microarrays. The progress of the three main services (DNA sequencing, microssatelite analysis and molecular diagnostic tests) is depicted in Figures 3.1 and 3.2. The sequencing service is under the responsibility of Vanessa Naomi, while the microssatelite and scanning activities are under the responsibility of Katia Rocha. We currently offer more than 30 genetic tests, which are being conducted at the core laboratory at the Genome Center (Drs. MR Passos-Bueno, Fernanda S. Jehee and Martha Lima) and by six research groups (Drs. Angela Vianna-Morgante, Carla Rosenberg, Célia Koiffmann, Mariz Vainzof, Regina C. Mingroni-Netto, and Mayana Zatz). Details of these services are available at http://genoma.ib.usp.br/index_exames_diagnosticos.php).

a) Development of a bioinformatic system: A software to evaluate the work flow of DNA analysis is still under development by Dr. João E. Ferreira and his team, at the Institute of Mathematics/USP in collaboration with CEPID/Genoma.

b) Diagnostic tests: We have focused on the development of parameters to a better quality control of the genetic tests performed and to a better information access to these tests by medical doctors and patients. In order to achieve these goals, we have reevaluated the tests being offered and decided to discontinue some of them based on the low number of orders in 2006 or because the costs to perform them were too high. Test protocols at the core laboratory were revised and additional controls were included whenever necessary. Quality control of samples and workflow was implemented. Sample control is performed with microssatelite analysis once a month.

Regarding our second aim, information about the tests and diseases, the site was remodelled. A contact person was designated so that either patients or doctors could reach better information. A new requisition form was prepared and the sheets for results reports reevaluated. We added new services such as genetic consultation for Trombophilia, Malignant Hyperthermia, and Infertility and Reproduction. We are in the process of validating the use of MLPA (Multiple Ligation-dependent Probe Amplification) for subtelomeric rearrangements and plan to offer it as a test in early 2008. At least 10 technicians and a post-doctoral fellow are working in this service. We will evaluate the effect of these changes next year.

3.4 Patent: We made a patent deposit for "Processo de obtenção de células tronco a partir de células do músculo orbicular do lábio, composições e usos", at INPI, November 23rd, 2007.

3.5 Establishment of a partnership between PETROBRÁS/ABDIM and CEGH: We have established a new partnership with Petrobrás and ABDIM (Brazilian Association of Muscular Dystrophy) and CEGH for supporting the service to patients with neuromuscular disorders who live out of the State of São Paulo. This patnership includes: Diagnosis and genetic counseling of families with neuromuscular diseases, follow-up incluiding clinical and physiotherapeutic treatments. This project allowed us to hire one additional physician, one physiotherapist, one technician, secretary, and administrative staff. The project also includes funds to perform molecular tests, muscle protein analysis, and clinical exames.

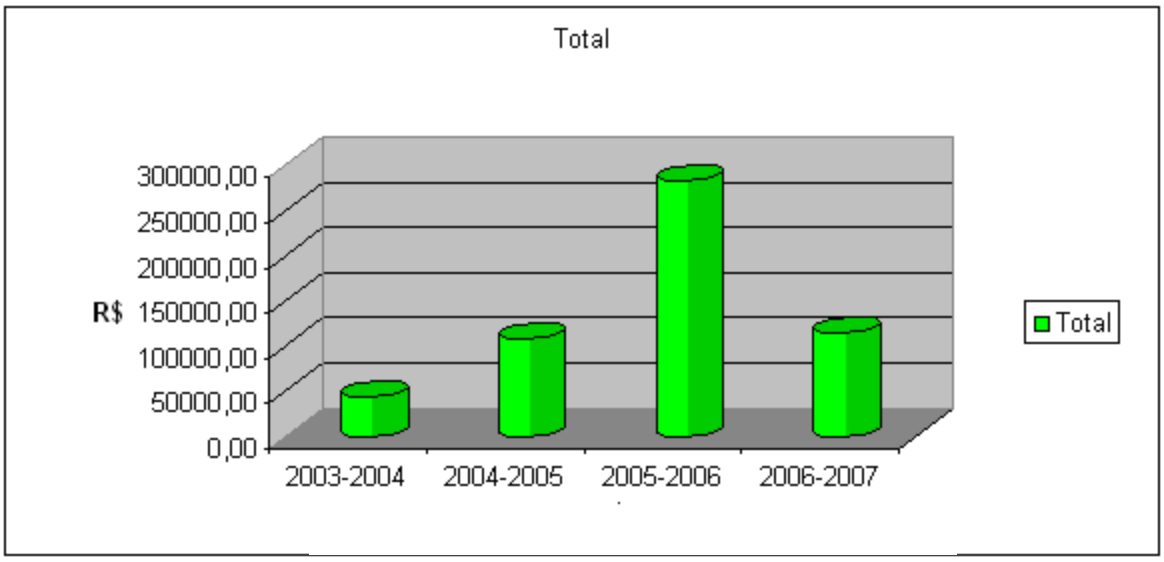

Figure 3.1: Income from genetic tests since 2003. We observe a significant decrease in the number of tests done, due to difficulties to get imported reagents and P^{32}.

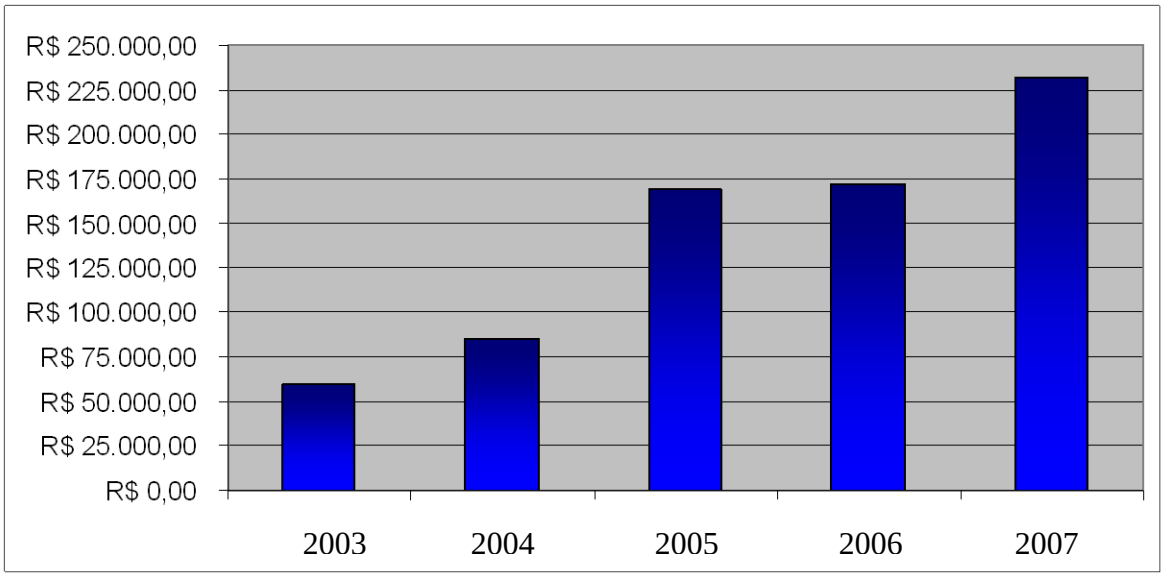

Figure 3.2: Income per year since the set up of the service for sequencing and microssatelite analysis. We observe the continuous increase of these services, thus supporting the importance of larger investments in this segment.

ANNEXES

ANNEX 1. RESEARCH TEAM 2007

1. Researchers		
Name	**Participation**	**Research Subproject**
Mayana Zatz	**Coordinator**	Neuromuscular disorders: I.1 Identification of disease genes. I.2 Mechanisms modulating phenotypic expression II.1 Stem cell research
Maria Rita Passos-Bueno	**Coordinator:** **Transfer of Technology**	I.1 Identification of disease genes: craniofacial disorders; autism. I.2 Mechanisms modulating phenotypic disorders: craniofacial disorders I.3 Protein Analysis: craniofacial disorders I.4 Complex disorders: diabetic retinopathy II.1 Stem cell research: craniofacial disorders
Eliana M. Belluzzo Dessen	**Coordinator:** **Education/Public Information**	**Education**
Angela M. Vianna-Morgante	Full-time investigator	Mental retardation/congenital anomalies: I.1 Identification of disease genes I.2 Phenotypic variability I.3 Protein and functional analysis 1.5 Genome Architecture: impact of copy-number variation; chromosomal structural abnormalities
Célia P. Koiffmann	Full-time investigator	Mental retardation/neurobehavioral diseases (obesity, overgrowth syndromes) I.1 Identification of disease genes I.2 Phenotypic variability 1.5 Genome Architecture: impact of copy number variation; chromosomal abnormalities **(cont)**

1. Researchers (cont.)		
Name	**Participation**	**Research Subproject**
Mariz Vainzof	Full-time investigator	Neuromuscular disorders: I.3. Protein and function analysis: proteins involved in muscle development II.1- Stem cells research: muscular dystrophies in mice models. Animal models
Regina Célia Mingroni-Netto	Full-time investigator	I.1 Identification of disease genes: deafness; ectrodactily I.3 Protein and Functional Analysis: deafnessI.4 Complex disorders in Afro-Brazilian "isolates": obesity and hypertension II. 1. Animal therapeutic trials: deafness
Carla Rosenberg	Full-time investigator	Mental retardation/ congenital anomalies: I.1 Identification of disease genes 1.5 Genome Architecture: impact of copy number variation
Luciana Haddad	Collaborator	Neurodevelopmental disorders: I.3. Protein and functional analysis
Fernando Kok	Collaborator	Neuromuscular and developmental disorders: clinical aspects
Carlos F. Menck	Collaborator	II.2 Adenovirus-mediated transduction of DNA repair genes related to human diseases
Maria Angélica Miglino	Collaborator	II.1 Stem cell research: animal model in neuromuscular disorders
Luis Eduardo Netto	Collaborator	I.3 Protein and functional analysis

2. Post-doctoral fellows			
Name	**Agency**	**Supervisor**	**Research Subproject**
Ambrósio,CE	FAPESP	Zatz, M	I.3 Protein analyses
Jehee, FS	FAPESP	Passos-Bueno, MR	I.2 Mechanisms modulating phenotypic expression
Krepischi-Santos, ACV	CNPq	Rosenberg, C	I.5 Genomic Architecture
Mazzeu, JF	FAPESP	Vianna-Morgante, AM	I.1 Identification of disease genes I.2 Mechanisms modulating phenotypic expression
Monteiro, G	FAPESP	Netto, LES	I.2 Mechanisms modulating phenotypic expression I.3 Protein analyses
Oliveira, MA	FAPESP	Netto, LES	I.3 Protein analyses
Sertié, AL	FAPESP	Passos-Bueno, MR	I.2 Mechanisms modulating phenotypic expression I.3 Protein analyses
Costa Silva, TJ	FAPESP	Miglino, A	II.1 Stem Cell Research
Varela, MC	FAPESP	Koiffmann, CP	I.1 Identification of disease genes I.5 Genome Architecture
Yamamoto, LU	FAPESP	Vainzof, M	I.3 Protein analyses

3. PhD Students			
Name	**Agency**	**Advisor**	**Research Subproject**
Abreu-Silva, RS	FAPESP	Mingroni-Netto, RC	I.4 Complex disorders and genetic variation at the population
Angeli, CB	FAPESP	Mingroni-Netto, RC	I.4 Complex disorders and genetic variation at the population
Arashiro, P	FAPESP	Zatz, M	I.2 Mechanisms modulating phenotypic genes
Araújo, KPC	FAPESP	Miglino, MA	II.1 Stem cell analysis and animal therapeutic trials
Armelin, L	FAPESP	Passos-Bueno, MR	I.2 Mechanisms modulating phenotypic expression
Azevedo, NF	FAPESP	Vianna-Morgante, AM	I.5 Genomic Architecture
Batissoco, AC	CNPq	Mingroni-Netto, RC	I.3 Protein analyses
Berra, CM	FAPESP	Menck, CFM	II.3 Adenovirus-mediated transduction of DNA repair genes related to human diseases
Branco,ER	CNPq	Miglino, MA	II.1 Stem cell analysis and animal therapeutic trials
Bueno, DF	CAPES	Passos-Bueno, MR	II.1 Stem cell analysis and animal therapeutic trials
Cabral,RM	CNPq	Miglino,MA	II.1 Stem cell analysis and animal therapeutic trials
Capelli, LP	FAPESP	Vianna-Morgante, AM	I.2 Mechanisms modulating phenotypic expression
Carvalho, MD	FAPESP	Zatz, M	I.3 Protein analyses
Casagrande, CF	FAPESP	Miglino, MA	II.1 Stem cell analysis and animal therapeutic trials
Catelani, ALPM	Laboratório Fleury	Rosenberg, C	I.5 Genomic Architecture
D´Angelo, CS	FAPESP	Koiffmann, CP	I.1 Identification of disease genes I.5 Genome Architecture
Fanganiello, R	FAPESP	Passos-Bueno, MR	I.2 Mechanisms modulating phenotypic expression
Gaiad, T.P.	FAPESP	Miglino, MA	II.1 Stem cell analysis and animal therapeutic trials
Gifalli-Iughetti, C	FAPESP	Koiffmann, CP	I.5 Genome Architecture
Horta, BB	FAPESP	Netto, LES	I.2 Mechanisms modulating phenotypic expression I.3 Protein analyses
Kague, E	FAPESP	Passos-Bueno, MR	I.2 Mechanisms modulating phenotypic expression

(cont)

3. PhD Students (cont)			
Kimura, L	FAPESP	Mingroni-Netto, RC	I.4 Complex disorders and genetic variation at the population level
Kohl, I	CAPES	Koiffmann, CP	I.1 Identification of disease genes
Leite, RA	FAPESP	Menck, CFM	II.3 Adenovirus-mediated transduction of DNA repair genes related to human diseases
Lezirovitz, K	FAPESP	Mingroni-Netto, RC	I.1 Identification of disease genes
Lima-Bessa, KM	FAPESP	Menck, CFM	II.3 Adenovirus-mediated transduction of DNA repair genes related to human diseases
Luppi, MMRC	CNPq	Miglino, MA	II.1 Stem cell analysis and animal therapeutic trials
Fontes, L	FAPESP	Vianna-Morgante, AM	I.2 Mechanisms modulating phenotypic expression
Magalhães, ML	FAPESP	Zatz, M	I.1 Identification of disease genes
Martins, DS	FAPESP	Miglino, MA	II.1 Stem cell analysis and animal therapeutic trials
Martins, PCM	CNPq	Vainzof, M	I.3 Protein analyses
Masotti, C	FAPESP	Passos-Bueno, MR	I.1 Identification of disease genes I.2 Mechanisms modulating phenotypic expression
Nascimento, RMP	FAPESP	Vianna-Morgante, AM	I.2 Mechanisms modulating phenotypic expression
Neto, MM	FAPESP	Zatz, M	I.1 Identification of disease genes
Orabona, G	FAPESP	Passos-Bueno, MR	I.1 Identification of disease genes
Peres, MA	FAPESP	Miglino, MA	II.1 Stem cell analysis and animal therapeutic trials
Schlesinger, D		Zatz, M	I.1 Identification of disease genes
Silva, GM	FAPESP	Netto, LES	I.2 Mechanisms modulating phenotypic expression I.3 Protein analyses
Soltys, D	FAPESP	Menck, CFM	II.3 Adenovirus-mediated transduction of DNA repair genes related to human diseases
Souza, LIM	FAPESP	Zatz, M	I.1 Identification of disease genes
Vieira, NMS	FAPESP	Zatz, M	I.3 Protein analyses
Wenceslau, CV	FAPESP	Miglino, MA	II.1 Stem cell analysis and animal therapeutic trials
Yeh, E	FAPESP	Passos-Bueno, MR	I.2 Mechanisms modulating phenotypic expression
Zucconi, E	FAPESP	Zatz, M	I.3 Protein analyses

4. MSc Students			
Name	**Agency**	**Advisor**	**Research Subproject**
Alencastro, G	FAPESP	Passos-Bueno, MR	I.3 Protein analyses
Barros, DA	FAPESP	Vainzof, M	II.1 Stem cell analysis and animal therapeutic trials
Batissoco, AC	CNPq	Mingroni-Netto, RC	I.2 Mechanisms modulating phenotypic expression
Brólio, MP	CNPq	Miglino, MA	II.1 Stem cell analysis and animal therapeutic trials
Cavaçana, N	----	Zatz,M	II.1 Stem cell analysis and animal therapeutic trials
Fagali, CQ	FAPESP	Koiffmann, CP	I.1 Identification of disease genes; I.5 Genome Architecture
Fogaça, LQ	FAPESP	Vainzof, M	I.3 Protein analyses
Jarra, J.	FAPESP	Miglino, MA	II.1 Stem cell analysis and animal therapeutic trials
Kimura, L	FAPESP	Mingroni-Netto, RC	I.4 Complex disorders and genetic variation at the population level
Mendes, M.	CAPES	Miglino, MA	II.1 Stem cell analysis and animal therapeutic trials
Mortari, AC	CAPES	Vainzof, M	I.3 Protein analyses
Oliveira, KG	CNPq	Passos-Bueno, MR	I.1 Identification of disease genes
Oliveira, MA	FAPESP	Koiffmann, CP	I.5 Genome Architecture
Oliveira, NA	FAPESP	Passos-Bueno, MR	I.2 Mechanisms modulating phenotypic expression I.1 Identification of disease genes
Onofre, PCG	FAPESP	Vainzof, M	II.1 Stem cell analysis and animal therapeutic trials
Ornelas, C	FAPESP	Passos-Bueno, MR	I.2 Mechanisms modulating phenotypic expression
Passos, J	CAPES	Miglino, MA	II.1 Stem cell analysis and animal therapeutic trials
Reis, SBA	FAPESP	Vianna-Morgante, AM	I.1 Identification of disease genes; I.5 Genome Architecture
Romanos, J	CNPq	Mingroni-Netto, RC	I.2 Mechanisms modulating phenotypic expression
Secco, M	FAPESP	Zatz, M	I.3 Protein analyses
Silva, MB	FAPESP	Miglino, MA	II.1 Stem cell analysis and animal therapeutic trials
Silva, WF	FAPESP	Miglino, MA	II.1 Stem cell analysis and animal therapeutic trials
Velloso, FJ	CNPq	Haddad, LA	I.3 Protein analyses
Vieira, LCZ	FAPESP	Vianna-Morgante, A.M.	I.1 Identification of disease genes; I.5 Genome Architecture

5. Specialization and Technical Training Students			
Name	**Agency**	**Advisor**	**Research Subproject**
Alvez, SV	Procontes	Netto, LES	I.3 Protein analyses
Costa, SS	LGH	Vianna-Morgante, AM	I.2 Mechanisms modulating phenotypic expression 1.5. Genomic Architecture
Lopes, VF	ABDIM	Vainzof, M	I.3 Protein analyses
Quayle,C	USP	Menck,CFM	II.3 Adenovirus-mediated transduction of DNA repair genes related to human disease

6. Undergraduate Students			
Name	Agency	Advisor	Research Subproject
Aguiar, RST		Mingroni-Netto	I.1 Identification of disease genes
Bonaldi, A		Vianna-Morgante, AM	I.1 Identification of disease genes
Braggio, LZ	FAPESP	Miglino, MA	II.1 Stem cell analysis and animal therapeutic trials
Coqueti, KN	FAPESP	Vianna-Morgante, AM	I.5 Genomic Architecture
Cruvinel, EM	FAPESP	Koiffmann, CP	I.5 Genome Architecture
Duarte, C.N.	FAPESP	Miglino, MA	II.1 Stem cell analysis and animal therapeutic trials
Ladenthin, ACM	FAPESP	Miglino, MA	II.1 Stem cell analysis and animal therapeutic trials
Maia, LS	CNPq (PIBIC)	Vainzof, M	I.2 Mechanisms modulating phenotypic expression
Milano, AM	FAPESP	Miglino, MA	II.1 Stem cell analysis and animal therapeutic trials
Montalbano,G	FAPESP	Zatz,M	I.1 Identification of disease genes
Rincón, D	CNPq (PIBIC)	Mingroni-Netto, RC	I.4 Complex disorders and genetic variation at the population level
Sell, K	CNPq (PIBIC)	Vainzof, M	I.2 Mechanisms modulating phenotypic expression
Uehara DT		Mingroni Netto	I.1 Identification of disease genes
Valadares,MC		Zatz,M	I.1 Identification of disease genes
Vieira, E.	FAPESP	Miglino, MA	II.1 Stem cell analysis and animal therapeutic trials
Zilberstein, D	FAPESP	Vainzof, M	I.3 Protein analyses

ANNEX 2. LIST OF PUBLICATIONS 2007

A) Directly related to the Project:

1. Armelini MG, Lima-Bessa KM, Marchetto MCN, Muotri AR, Chiganças V, Leite RA, Carvalho H and **Menck CFM.** Exploring DNA damage responses in human cells with recombinant adenoviral vectors. Hum Exper Toxicol, 2007;6: 899-906.
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ANNEX 3. ABSTRACTS IN CONGRESS - 2007

International Meetings:

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Menck CFM. Approaches for skin gene therapy of xeroderma pigmentosum patients, oral presentation (Workshop 11: 'Skin Stem cells'; 0487), at the 21st World Congress of Dermatology, Buenos Aires, Argentina, from September 30th to October 5th, 2007.

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Menck CFM. Viral vectors to explore the consequences of UV-induced DNA damage, oral esentation (Symposium 'Biological Consequences of UV damage'; IL304), at the 12th Congress of the European Society of Photobiology, Bath, England, 1st to 6th September, 2007.

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Martins PCM, Ayub-Guerrieri D, Lopes VF, Onofre PCG, Mori CMC, **Vainzof M**. Geração do camundongo duplo mutantes para os genes da Distrofina e LARGE e avaliação histológica e clínica: um novo modelo para distrofias musculares. In: Gagliardi RJ, Reimao R, Fragoso YD. Neurologia em Destaque. VI Congresso Paulista de Neurologia - Guarujá, 21-23 de junho de 2007. Assoc. Paulista de Medicina, pp. 595-596, 2007.

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Oliveira MA, Castro CI, **Koiffmann CP**. Translocações aparentmente equilibradas: detecção dos pontos de quebra e investigação de mecanismos de reparo. In: 53º Congresso Brasileiro de Genética, 2007, Águas de Lindóia. de 2 a 5 de setembro. Ribeirão Preto - SP: Zeppelini Editorial & Comunicação, 2007.

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Vainzof M, Yamamoto LU, Barros DA, Gurgel-Gianneti J, Muniz VP, Fogaça LLQ, Zilberztajn D. Expression of developmental genes in the normal and myopathic muscle. FESBE 2007.

Vainzof M, Yamamoto LU, Maia LS, Kossugue PM, Silva HC. Bases Genéticas da Hipertermia Maligna. Congresso de Anestesiologia, Curso de Hipertermia Maligna, São Paulo, 17 de maio de 2007.

Varela MC, Cruvinel EM, Zanelato RM, Fridman C, Castro CI, Kok F, Kim CA, Koiffmann CP. Síndrome de Prader-Willi: 10 anos de investigação, diagnóstico e aconselhamento genético a 142 famílias. In: 53º Congresso Brasileiro de Genética, 2007, Águas de Lindóia. 2 a 5 de setembro. Ribeirão Preto: Zeppelini Editorial & Comunicação, 2007. p. 128.

ANNEX 4. THESIS AND DISSERTATIONS RELATED TO THE CEPID PROJECT (2007)

PhD Thesis:

1. Cibele Masotti: Análise da região promotora do gene *TCOF1*. Instituto de Biociências/USP, 2007 (Scholarship: FAPESP).
   Advisor: Maria Rita Passos Bueno.
   Research Subproject: I.2 Mechanisms modulating phenotypic expression
2. Daniela Bueno: Estudo de células tronco mesenquimais na reconstrução óssea. Instituto de Biociências/USP, 2007 (Scholarship: CAPES).
   Advisor: Maria Rita Passos Bueno.
   Research Subproject: II. Stem cell analysis
3. Guilherme Orabona: Identificação de genes associados ao autismo. Interunidades Biotecnologia,USP, 2007. (Scholarship: FAPESP).
   Advisor: Maria Rita Passos Bueno.
   Research Subproject: I.1 Identification of disease genes
4. Karina Lezirovitz: Mapeamento de genes em doenças geneticamente heterogêneas: surdez e hemimelia tibial associada à ectrodactilia. Instituto de Biociências/USP, 2007 (Scholarship: FAPESP).
   Advisor: Regina Célia Mingroni Netto
   Research Subproject: I.1 Identification of disease genes
5. Leonardo Pires Capelli: Estudos da repetição CGG do gene *FMR1*: I. Caracterização de alelos propensos à instabilidade. II. A história contada pelos alelos dos macacos do novo e do velho mundo. III. A pré-mutação como causa de doença neurodegenerativa. Instituto de Biociências/USP, 2007 (Scholarship: FAPESP).
   Advisor: Angela M. Vianna-Morgante
   Research Project: I.2 Mechanisms modulating phenotypic expression
6. Lucia Armelin: Análise da região promotora do gene *COL18A1*. Instituto de Biociências/USP, 2007 (Scholarship: FAPESP).
   Advisor: Maria Rita Passos Bueno
   Research Subproject: I.2 Mechanisms modulating phenotypic expression
7. Melissa Gava Armelini, "Estudos de reparo de DNA por excisão de nucleotídeos utilizando vetores virais", Tese de Doutorado em Microbiologia, Instituto de Ciências Biomédicas, Universidade de São Paulo, SP, 2007. (Scholarship:FAPESP).
   Advisor: Carlos F Menck
   Research Subproject: II.2 Adenovirus-mediated transduction of DNA repair genes related to human diseases

MSc Dissertations:

1. André Gatti: Estudo da função glomerular em Golden Retrievers normais, portadores e afetados pela Distrofia Muscular Progressiva (GRMD). Faculdade de Medicina Veterinária e Zootecnia/USP, 2007. (Scholarship: CAPES).
   Advisor: Maria Angelica Miglino
   Research subproject: II.1 Stem cell research: animal model in neuromuscular disorders
2. Luciana Luchesi Quintanilha Fogaça: Estudo da expressão da proteína utrofina na distrofia canina. Programa de Biologia-Genética, Instituto de Biociências USP. Defesa: 03/04/2007. (Scholarship FAPESP).
   Advisor: Mariz Vainzof
   Research subproject: I.3. Protein and function analysis: proteins involved in muscle development

3. Luiz Carlos Zangrande Vieira: Os mecanismos de formação de duas deleções cromosômicas (Scholarship: FAPESP)
   Advisor: Angela M. Vianna-Morgante
   Research Project: I.5 Genome Architecture
4. Marina Pandolphi Brólio: Análise clínica e morfológica do desenvolvimento da distrofia muscular do cão Golden Retriever (GRMD). Faculdade de Medicina Veterinária e Zootecnia/USP, 2007. (Scholarship: CNPq).
   Advisor: Maria Angelica Miglino
   Research subproject: II.1 Stem cell research: animal model in neuromuscular disorders

ANNEX 5. LECTURES AND SEMINARS

Koiffmann CP. Síndrome de Angelman: diagnóstico e aconselhamento genético. III Encontro de Pais e Profissionais da Associaçao Síndrome de Angelman. Human genome Research Center, USP, June 2007.

Miglino MA. Implantação Embrionária e Placentação - Centros Pré-clínicos de Terapia Celular e Gênica, Transgenia e Clonagem Animal, Teresina, Piauí, April 2007.

Miglino MA. Placentação em Embriões produzidos in vitro. XXI Reunião Anual da Sociedade Brasileira de Tecnologia de Embriões. Costa do Sauípe, BA, August 2007.

Miglino MA. Placenta-Platform for Life. Workshop - Placental Insufficiency in Cloned Animals. Kingston, Ontário Canadá, August, 2007.

Mingroni-Netto RC. Genética das populações remanescentes de quilombos do Ribeira. Departamento de Genética e Biologia Evolutiva, IB-USP, April 2007

Mingroni-Netto RC. Genética e Surdez - Curso de Extensão Universitária em Otorrinolaringologia, Faculdade de Medicina ABD, Santo André, São Paulo, November, 2007.

Mingroni-Netto RC. Surdez neurossensorial: surpreendente heterogeneidade de genes e mutações. 53º Congresso Brasileiro de Genética, Águas de Lindóia, SP, September 2007.

Netto LE. Biomarcadores de processos oxidativos. In the 10th International Union Biochemistry and Molecular Conference - XXXVI Reunião Anual da Sociedade Brasileira de Bioquímica e Biologia Molecular, May, 2007.

Netto LE. Estrutura e função de proteínas antioxidantes e identificação de nova função de vitamina C. Departament of Genetcs and Evolutionary Biology, IB, USP, 2007.

Netto LE. New aspects related to vitamin C. Interactions with antioxidant proteins and vitamin E. Workshop on Antioxidants. ILSI - International Life Sciences Institute, 2007.

Netto LE. Functional and structural characterization of antioxidant proteins from *Xylella fastidiosa*. International Workshop on *Xylella fastidiosa*. Royal Palm Plaza Hotel Campinas/SP, Brazil, 2007

Netto LE. Functional and structural characterization of cytosolic thioredoxin system from *Saccharomyces cerevisiae*. Insights into protein-protein interactions. V meeting of the Society for Free Radical Research Biology and Medicine - South American Group, Montevideo, Uruguai.

Netto LE. Atividade ascorbato peroxidase de peroxirredoxinas: quebra de um paradigma e possível identificação de um novo processo redox. Department of Biochemistry, Institute of Chemistry, USP, 2007.

Netto LE. Peroxirredoxinas e vitamina C, parceiros de uma nova nova via antioxidante" Department of Psicobiology, UNIFESP, São Paulo SP, 2007.

Passos-Bueno MR. Craniofacial Anomalies - Orofacial Clefting and its Branchyal arch anomalies syndromes, 3rd International Conference on Birth Defects and Disabilities in the Developing World, June 2007.

Passos-Bueno MR. Debate on "Projetos da Associação Apresentados pelos Deputados Complementados por Sugestões". Hospital da Cruz Vermelha Brasileira, São Paulo, SP, July 2007.

Passos-Bueno MR. Genética nas Fissuras Lábio-Palatais e Síndromes Associadas, Seminário Fissuras LabioPalatinas, Assembléia Legislativa, São Paulo, SP, March 2007.

Passos-Bueno MR. Genética nas fissuras lábio-palatinas**,** 13º Curso continuado de Cirurgia Craniomaxilofacial, SP, September 2007.

Passos-Bueno MR. Identificação de genes associados a doenças mendelianas e complexas, Post-graduation course on Oncology, Fundação Antônio Prudente, São Paulo, SP, May 2007.

Passos-Bueno MR. Análise Genômica na elucidação de doenças genéticas**,** Department of Biochemistry, IQ-USP, October, 2007.

Passos-Bueno MR. Atualização em Autismo: Tratamento e pesquisas em genética e neurociências**,** FARN, Natal, RN, July, 2007.

Passos-Bueno MR. Genetics of Cleft Lip/Palate, Operation Smile, Norfolk, Virginia, USA, October 22007.

Rosenberg C. Alterações cromossômicas submicroscópicas como causa de retardo mental, in the Symposium "Variação no Número de Cópias (VNC) e sua Relação com Doenças Humanas". 53º Congresso Brasileiro de Genética, Águas de Lindóia, SP, September 2007.

Rosenberg C. Genomic variability and genetic diseases". 3rd Course of the Escola Latino Americana de Genética Humana e Médica, Angra dos reis, RJ, Junho, 2007.

Rosenberg C. Can recurrence risks be estimated from array CGH investigations? 3rd International DECIPHER Symposium. Wellcome Trust Conference Centre, The Wellcome Trust Genome Campus, Cambridgeshire, May 2007.

Rosenberg C. New Candidate Regions For Utero-Vaginal Defects. 3rd International GENOMIC DISORDERS 2007. Wellcome Trust Conference Centre, The Wellcome Trust Genome Campus, Cambridgeshire, March 2007

Rosenberg C. Short Course "Citogenética molecular no diagnóstico e na pesquisa".53º Congresso Brasileiro de Genética, Águas de Lindóia, SP, September 2007.

Vainzof M. "O uso da terapia celular para doenças neuromusculares", Course on em Biologia do Desenvolvimento e Células Tronco, Progrma de Pós-Graduação em Anatomia dos Animais Domésticos e Silvestres, Faculdade de Medicina Veterinária e Zootecnia ,USP. ão Paulo, May 2007.

Vainzof M. Genética da Hipertermia Maligna, UNIFESP, São Paulo, June 2007.

Vainzof M. Modelos animais em doenças genéticas. VI Congresso Paulista de Neurologia. Guarujá, June 2007.

Vainzof M. Expressão de genes de desenvolvimento muscular nas distrofias musculares. Simpósio Aspectos Celulares e Moleculares da Plasticidade Muscular Esquelética. XXII FESBE, Águas de Lindóia, SP, August 2007.

Varela M. As implicações do imprinting genômico nas síndromes de Prader-Willi e Angelman. Simpósio. Epigenética e doenças humanas: perpectivas e aplicações. 53º Congresso Brasileiro de Genética, Águas de Lindóia, SP, September 2007

Vianna-Morgante AM. Genética Humana no Brasil – Avanços e Perspectivas. Conferência "Avanços e Perspectivas da Ciência no Brasil, América latina e Caribe", Academia Brasileira de Ciências, Rio de Janeiro, December 2007.

Zatz M. Ciência no Brasil e América Latina - Cooperação Científica Brasil/América Latina e Caribe- Academia Brasileira de Ciências, Rio de Janeiro, January, 2007.

Zatz M. Audiência pública-STF: Por que defendo as pesquisas com células-tronco embrionárias, STF, Brasília, April 2007.

Zatz M. Por que defendo o direito de pesquisar células-tronco embrionárias; Fundação Getúlio Vargas, São Paulo, May 2007.

Zatz M. Célula-tronco embrionárias: usá-las ou não para pesquisas? 20 de junho de 2007, Salão Nobre da Câmara Municipal de São Paulo, June 2007.

Zatz M. Ethical Challenges in Human Genome and Stem-cell Researches, Jerusalem, Israel, June 2007.

Zatz M. Genoma Humano: Aplicações Médicas e Implicações Éticas. Congresso Nacional da Unimed , August 2007.

Zatz M. Células-tronco embrionárias: como me envolvi nessa briga política? Livraria Cultura, São Paulo, August 2007.

Zatz M. Nossa luta para aprovar as pesquisas com células-tronco embrionárias: Vii São Paulo Research Conference: Cérebro E Pensamento, São Paulo, August 2007.

Zatz M. Do genoma às células-tronco**.** Plenary Conference, 53º Congresso Brasileiro de Genética, Águas de Lindóia, SP, September, 2007.

Zatz M. Stem-cells and muscular dystrophies. International Congress on Stem Cells. Rio de Janeiro, September, 2007.

Zatz M. Pesquisas com células-tronco., CNPq, Brasília, September 2007

Zatz M What is the potential of adult stem cells from different sources to differentiate in functional skeletal muscle? XII Internactional Congress on neuromuscular disorders, Late breaking News,Taormina, Italy, October 2007

ANNEX 6. EDUCATION/PUBLIC INFORMATION

List of partner schools (13)

Teachers (14)	Partners schools
Maria da Graça Sapage Estácio Gaspar	E.E. Profa. Carmosina Monteiro Vianna Rua Antonio Palmieri, 377 Vila Medeiros
Leonardo Peres Cardoso de Andrade	EE Guilherme de Almeida Av. Parada Pinto
Daiane Danielle Bastos	EE Profa. Raquel Assis Barreiros Av General Penha Brasil
Luciana Lucas de Almeida	EE Prof. Carlos de Laet R. Albertina Vieira da Silva Gordo, 147
Márcia Herrera Garcia Antonio	EE Albino César
Hosana Corrêa Luz Pastore	EE Profa. Amenaide Braga de Queiroz R. Barra Mansa, 400
Priscila Marassi de Araújo	EE Leonidas Paiva Rua Mártires Armênios, 68
Sonia Lucia Costa Nogueira	EE Prof. Sebastião de Souza Bueno Rua Francisco Medeiros Jordão, 579
Ciderjane Aparecida º Ribeiro Soares	EE Silva Jardim Avenida Tucuruvi, 742
Emerson Pereira da Silva	EE Gabriela Mistral e EE Vitor da Santa Cunha Rua Major Baraca, 584
Alessandra Martins Silveira Secco e Maria Helena Caetano	EE Assis José Ambrosio Rua Alfarroubeiras Jardim Pery Alto
Hamilton Santos João	EE Pedro Alexandrino Rua Imbiras, 49
Alexandra G. Caramês	EE Júlio Pestana Av. Guapira, 2862

Vera Lúcia Pirrè de Castro - Pedagogic Technical assistant from Educational Directory for the Northern area (2) of São Paulo

ANNEX 7: EDUCATION/PUBLIC INFORMATION

Pictures - Program “A USP vai à sua Escola”

ANNEX 8. EDUCATION/PUBLIC INFORMATION

CD - Biology Fair.

http://www.genoma.ib.usp.br/educacao/video_feirabiologia071027.php

ANNEX 9. EDUCATION/PUBLIC INFORMATION

Post-graduation students working in the CEGH program

1. Adriana Ribeiro de Oliveira Marques
2. Ana Carolina Suzuki Dias Cintra
3. Érika Yeh
4. Fernando Nodari
5. Gustavo Alencastro
6. Karina Griesi
7. Paula Cristina Gorgueira Onofre
8. Renato Chimaso dos Santos
9. Silvio Ganiko Higa
10. Vivian Lavander Mendonça

ANNEX 10. EDUCATION/PUBLIC INFORMATION

Media: List of interviews to different communication medium

Name	Subject	Medium	Date
Dessen, E.M.B.	"Projeto celular estimula criatividade e realiza Feira de Biologia (Cellular Project stimulate creativity and realiza a Biology Fair)	Agência USP	November11th, 2007.
Dessen, E.M.B.	Exposição técnico-científica no shopping tem novidades (Thecnical-scientific exposition have novelties)	A Tribuna - São Carlos	November 8th, 2007.
Dessen, E.M.B.	Feira de Biologia em Parceria com escolas da zona norte (Biology Fair in partnership with high school from Northern área of São Paulo)	Radio USP	October 23th, 2007.
Dessen, E.M.B.	Feira de Biologia em Parceria com escolas da zona norte (Biology Fair in partnership with high school from Northern área of São Paulo)	Gazeta da Zona Norte	October 27th, 2007.
Dessen, E.M.B.	Projeto Celular – (Cellular Project)	Jornal do Silva Jardim	Ano II, No 4, May, 2007.
Netto, L.E.	Vitamina C faz faxina dupla no organismo (Vitamin C cleans the organism)	Jornal o Estado de São Paulo	April 10th, 2007.
Netto, L.E.	Brasileiro acha nova função para vitamina C (Brasilian finds a new function for Vitamin C)	Portal de Notícias da Globo g1	March 7th, 2007.
Netto, L.E.	Nova função para a vitamina C (A new function for Vitamin C)	TV Bandeirantes Jornal da Band	April 14th, 2007.
Netto, L.E.	Mais uma utilidade: identificado novo mecanismo pelo qual Vitamina C combate radicais livres (Identified a new mechanism used by vitamin C in the combate of free radicals)	Revista Fapesp	April, pg 44-45, 2007.
Netto, L.E.	Nova função da Vitmina C (A new function of vitamin C)	CNB – programa Noite Total	March 16th, 2007. **(Cont)**

Name	Subject	Medium	Date
Netto, L.E.	Nova função da Vitamina C (A new function of vitamin C)	Radio Bandeirantes – Band News	April 10th, 2007.
Zatz, M.	Célula-tronco no líquido amniótico (Stem cell in amniotic liquid)	Jornal O Estado de São Paulo	January 8th, 2007.
Zatz, M.	Célula-tronco no líquido amniótico (Stem cell in amniotic liquid)	Radio Bandeirantes	January 17th, 2007
Zatz, M.	Os 100 brasileiros mais influentes (The 100 more influent Brazilians)	Revista Isto É - Especial	January 10th, 2007
Zatz, M.	Vitória da Ciência (Science victory)	Revista Isto É	January 17th, 2007.
Zatz, M.	O desafio de ser cientista no Brasil (The chalange of being a scientist in Brazil)	Revista Cláudia	January, 2007.
Zatz, M.	Envelhecer com saúde	Rede Globo – Fantástico	February 11th, 2007
Zatz, M.	A maldade é genética?	Radio Bandeirantes	February 23th, 2007
Zatz, M.	Quando começa a vida?		
Zatz, M.	Células-tronco	Boris Casoy – Jornal do Brasil	April 18th, 2007
Zatz, M.	Audiência pública: quando começa a vida?	Jornal Nacional	April 20th, 2007
Zatz, M.	Audiência pública: quando começa a vida?	Globo on-line	April 20th, 2007
Zatz, M.	Audiência pública – Brasília – Por que defendo as pesquisas com células-tronco embrionárias	Supremo Tribunal Federal	April 20th, 2007
Zatz, M.	Debate com Alice Teixeira: Quando começa a vida?	CBN	April 23th, 2007
Zatz, M.	Quando se inicia a vida?	Radio Cultura de PA	April, 24th, 2007
Zatz, M.	Audiência pública sobre células-tronco	Radio USP	April 24th, 2007
Zatz, M.	Audiência pública sobre células-tronco	Jornal da USP	April 24th, 2007
Zatz, M.	Quando se inicia a vida	Revista do Tribunal Regional Federal	May 25th, 2007
Zatz, M.	A importância das pesquisas com células-tronco embrionárias	Radio Cultura Programa Fapesp	May 15th, 2007
Zatz, M.	Cerimônia de Premiação do Prêmio Jovem Cientista	Palácio do Planalto	May 15th, 2007 **(Cont)**

Name	Subject	Medium	Date
Zatz, M.	Sala de Notícias em Debate tema células-tronco embrionárias"	Canal Futura	May 22th, 2007
Zatz, M.	Entrevista sobre Pesquisas, avanços e inovações tecnológicas no campo da medicina que proporcionam melhores condições para pacientes enfrentarem doenças graves	TV Cultura	October 25th, 2007
Zatz, M.	Brasileiros descobrem "reservatório" de células-tronco em cordão umbilical	Jornal O Estado de São Paulo	October 25th, 2007
Zatz, M.	Parte mais rica do cordão está no lixo	Jornal Folha de São Paulo	October 25th, 2007