HUMAN GENOME AND STEM CELL RESEARCH CENTER (HUG-CELL)

Departamento de Genética e Biologia Evolutiva

Instituto de Biociências

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HUMAN GENOME AND STEM CELL RESEARCH CENTER

(HUG-CELL)

GOALS FOR THE FIRST TWO YEARS

RESEARCH

1. **Identification and characterization of novel genes associated with disease:** Our proposal anticipates the identification of six novel disease-related genes in the first two years. At least three genes associated with rare or complex diseases (craniofacial malformations, autism spectrum disorders and muscular dystrophy) should be subject to publications in the next two years. We expect three articles to be published in American Journal of Human Genetics or journals of similar impact. Further, we are investigating microdeletion/microduplication sites, which may harbor many candidate disease-associated genes. Under this strategy, two undergoing projects aim to identify genes related to obesity and neurodevelopmental diseases, with the use of *in vitro* and *in vivo* models. *In vitro* disease modeling will involve induced pluripotent stem cells (iPSCs) or adult stem cells, while *in vivo* models may include yeast, zebrafish, or mouse model organisms. We intend to establish these models in the next two years, and we estimate at least 20 iPSC lines to be derived from patients with autism spectrum disorders, Angelman syndrome, Prader-Willi syndrome, and amyotrophic lateral sclerosis.

2. **Project 80+:** Within the first two years we anticipate to collect samples from at least 1,400 elderly subjects with 60 years of age or more (including approximately 500 subjects older than 80 years of age). At least 400 of these individuals will be subjected to 3T magnetic resonance imaging (MRI) of the brain (structural and functional assessment). Our immediate goal is to obtain a genomic variability and MRI databank of the Brazilian population, including individuals with impaired or preserved cognitive capacity. Innovative research will be developed within these first two years, such as: studies on laterality through association between genomic and 3TMRI data; comparison between data obtained from individuals with cognitive loss and individuals with preserved cognition; whole genome methylation analysis of healthy elderly women. We expect to publish at least two articles in high (>5) impact journals.

3. **Stem cell therapy:** Three relevant questions will be tackled: the therapeutic contribution of the paracrine effects of stem cells, the host immune system effects on exogenous stem cells, and the tumorigenic properties of stem cells. In this line, the projects aim to **(a)** investigate the transplantation efficiency of human stem cells and factors released by these cells in preclinical neuromuscular and neurodegenerative disease models, **(b)** to investigate the effects of human stem cell transplantation in comparison to mouse stem cells in mouse models, and **(c)** to evaluate the relationship between stem cell pluripotency and tumorigenicity. Projects branched from these objectives are expected to generate two or three publications high (>5) impact journals.

TRANSFER OF TECHNOLOGY/TECHNOLOGY APPLICATIONS

1. Maintenance of already consolidated services (Sanger sequencing/genomic tests) by the Núcleo de Desenvolvimento e Análise Genômica sector (NAGEN), and inclusion of an international quality system. These actions are expected to increase service demand.
2. Course in embryonic stem cells: derived from the partnership with foreign researchers Dr. Joshua Brickmann and Dr. Jenny Nichols, from the United Kingdom.
3. Establishment of an iPSC service: in the first year, we will establish cell bank with iPSCs derived from cell populations from exfoliated deciduous teeth (5) and fibroblasts (5) from healthy subjects. In the second year, we will start accepting customized requests for iPSC generation to meet demands from CEPID, as well as external researchers.
4. Implementation of NGS technology. NGS will be employed in the diagnostic of genetic diseases and offered as a service to the CEPID community and external researchers. We anticipate that the introduction of the NGS methodology will provide competitiveness to diverse research projects within CEPID, besides reducing costs for some genetic tests. We plan to have this service available in 2013.

EDUCATION

1. Practical classes in 80 schools (40/year): in average, 700 students/school.
2. *USP vai à escola* program: approximately 10,000 students/year.
3. Didactic material: 140 teachers (70/year); 700 students/teacher.
4. High impact, main project: release of 5,000 science kits (with support from CAPES) for public school students, to be evaluated by teachers and students. Depending on the results, we plan to produce kits for public schools all over Brazil, with support from CAPES, MEC, and BNDES.

INTERNATIONALIZATION

Projects will be implemented in collaboration with important international research centers. Additionally, we will request four postdoctoral stipends to bring researchers specialized in Biostatistics, Bioinformatics, Genomics, and pluripotent stem cells. We will also organize a conference with the participation of all CEPID members, and the researchers from our international advisory committee.

PART 1 – RESEARCH

I. 1) SUMMARY OF THE PROJECTS AND 2013-2015 RESEARCH RESULTS

Our main research results from July 2013 to June 2015 are presented below, separated by our different objectives, as presented in the initial project.

a) Identification of new human genes in both simple (Mendelian) and complex disorders

Mendelian disorders

We identified and characterized seven new genes associated with rare genetic diseases, and collaborated with the identification of an additional one, as summarized below:

- **Spondylometaphyseal dysplasia** with cone-rod dystrophy is a rare autosomal recessive disorder. Exome analyses in affected individuals from two unrelated families lead to the identification of pathogenic mutations in *PCYT1A*. This gene belongs to the cholinergic pathway, which was known to be associated with muscle disorders. Our work showed for the first time the importance of this pathway to bone metabolism (Yamamoto *et al.*, 2014).

- **Richieri-Costa-Pereira syndrome** is a rare autosomal craniofacial disorder associated with limb defects, originally described by Brazilian researchers (reviewed in Favaro *et al.*, 2014). Homozygosity mapping followed by Sanger sequencing of the candidate genes led to the identification of an expansion at the promoter region of the gene *EIF4A3* as the causative mutation for this syndrome. We have also shown that the mutation led to decreased *EIF4A3* transcript levels in lymphocytes and mesenchymal stem cells. Further, *EIF4A3* knockdown in zebrafish causes craniofacial abnormalities. These data suggest that the pathophysiology of the disease is caused by deficiency of *EIF4A3* (Favaro *et al.*, 2014). We are currently studying the spectrum of variability of the phenotype associated with *EIF4A3* expansions and coding region variants. Further, we are testing the correlation between the size and pattern of the 5'UTR expansions and *EIF4A3* expression. The current state of the art related for this disorder has been recently reviewed (Lehalle *et al.*, 2015).

- The locus for the **autosomal dominant limb-girdle muscular dystrophy type 1G** (LGMD1G) had been previously mapped by our group at 4q21 in a Caucasian-Brazilian family. Subsequently, we mapped a Uruguayan family with patients displaying a similar LGMD1G phenotype at the same locus. Whole genome sequencing identified mutations in the *HNRPDL* gene in both families. *HNRPDL* is a heterogeneous ribonucleoprotein that participates in mRNA biogenesis and metabolism. *In vivo* analysis showed that

hnrpdl is important for muscle development in zebrafish, causing a myopathic phenotype when knocked down. The present study presents a novel association between a muscular disorder and a RNA-related gene and reinforces the importance of RNA binding/processing proteins in muscle development and muscle disease (Vieira *et al.*, 2014).

- We have also collaborated with the identification of a fourth gene, *PDGF-B* which was shown to cause **brain calcification** in humans and mice. This research was published in Nature Genetics (Keller *et al.*, 2013). The main author, João Ricardo de Oliveira, currently a professor at the University of Pernambuco, was previously a member of our group, while working on his doctoral dissertation.

- We have previously mapped the locus for **craniometaphyseal dysplasia** based on linkage analysis of a large Brazilian family (Iughetti *et al.*, 2000). Recently, exome sequence led to identification of a *GJA1* missense mutation as causative of this condition. The data of our family was important to confirm this finding (Hu *et al.*, 2013).

- **Noonan syndrome**, an autosomal dominant multisystemic disorder caused by dysregulation of the RAS/mitogen activated protein kinase (MAPK) pathway, is genetically heterogenous, and pathogenic variants in 10 known genes account for approximately 80% of cases. The identification of novel genes associated with this syndrome is a current challenge in the field. By the study of 50 Brazilian probands with Noonan syndrome, including familial cases, Dr. Bertola's group identified two new genes (*SOS2* and *LZTR1*) associated with the phenotype, thus expanding the molecular spectrum of RASopathies. While *SOS2* is a natural candidate due to its homology with *SOS1*, the functional role of *LZTR1* in the RAS/MAPK pathway is unknown. Further, *LZTR1* would not have been identified without the large pedigrees (Yamamoto *et al.*, 2015). We are currently studying the functional effect of *LZTR1* pathogenic variants.

- Two novel genes for **autosomal recessive intellectual disability (ID)** were identified. The first one, *MED25*, was identified with Genome-Wide Human SNP Array 6.0 (Affymetrix) microarray to determine regions of homozygosity-by-descent. Whole exome sequencing (WES) was performed in one affected individual and two regions with a lod-score > 3 were identified: one at 19q and the other at 2p. WES disclosed in the critical region of chromosome 19 a homozygous variant (c.418C>T, p.Arg140Trp) in Mediator complex subunit 25 (*MED25*), predicted to be deleterious by PolyPhen-2, Provean, Mutation Taster and Sorting Intolerant From Tolerant (SIFT). *MED25* is a component of the Mediator complex, involved in regulation of transcription of nearly all RNA polymerase II-dependent genes. Deleterious mutations in *MED12*, *MED17* and *MED23* have already been associated with ID. (Figueiredo *et al.*, 2014). The second gene was identified in a family with 9 adults descending from 4 closely related first-cousin couples

affected by severe ID associated with disruptive behavior. Homozigosity-by-descent analysis disclosed a 20.7 Mb region at 8q12.3-q21.2 (lod score: 3.11). WES identified a homozygous deleterious variant in the gene inositol monophosphatase 1 (*IMPA1*), consisting of a 5 bp duplication (c.489_493dupGGGCT) (chr8: 82,583,247) (GRCh37/hg19) leading to frameshift and premature stop codon (p.Ser165Trpfs*10). The *IMPA1* gene product is responsible for the final step of biotransformation of the second messenger inositolpolyphosphate. Despite its many physiological functions, no clinical phenotype has been assigned to dysfunction of this gene to date. Additionally, *IMPA1* is the main target of lithium, a drug that is in the forefront of treatment of bipolar disorder.

- A collection of seven large families presenting with **autosomal dominant deafness** has been previously studied using conventional mapping strategies. Linkage analysis followed by exome sequencing or copy number variation studies allowed identification of the causative genes in some of them. In two cases, mutations in two previously known genes were found (Dantas *et al.*, 2014; Dantas *et al.*, 2015). In one pedigree, a dominant mutation was found, but in a gene previously related to recessive deafness. Functional studies are underway to validate the effect of the mutation. In other cases, there are putative novel genes involved, for which functional validation is necessary before publication.

Complex disorders

- **Hypertension:** We had previously identified a 1.6 Mb region on chromosome 14 that was shared by 16 individuals affected by hypertension, from a population isolate of African ancestry. Exome sequencing was performed in 8 selected samples, and variant filtering did not reveal obvious candidates to explain the phenotype. Additional exomes from affected individuals from the same population are under analysis. We genotyped 365 samples with the Affymetrix Axiom Human Origins Array, with 600,000 SNPs. Global and local ancestry were inferred by the ADMIXTURE software and RFMix software, and admixture mapping studies were performed. Except for enrichment in African ancestry related to chromosome 6 in the MHC region, no striking deviations were observed. The candidate region on chromosome 14 showed no ancestry deviations. The same data set is under analysis, but focused on comparing hypertensive and normotensive subjects; the genotypes obtained with the Axiom Array will soon be used in other approaches, such as family-based association studies.

- Copy number variations have been investigated in several cohorts to identify genes or chromosomal regions involved in: **children born small for gestational age, deafness, mullerian aplasia, microdeletion syndromes, and cancer predisposition** (Dornelles-Wawruk *et al.*, 2013; Sandbacka *et al.*, 2013; Silva *et al.*, 2013; Freitas *et al.*, 2014; Santos *et al.*, 2014).

- **Nonsyndromic orofacial cleft** (NSOFC) is a complex disease of still unclear genetic etiology. To investigate the contribution of rare epithelial cadherin (*CDH1*) gene variants to NSOFC, we target sequenced 221 probands. Candidate variants were evaluated via *in vitro*, *in silico*, or segregation analyses. Three of the four potentially pathogenic variants identified (c.760G>A, c.1023T>G, c.2351G>A, c.387+5G>A) segregated according to autosomal dominant inheritance in four nonsyndromic cleft lip/palate (NSCL/P) families (Lod score: 5.8 at θ=0; 47% penetrance). The overall prevalence of *CDH1* candidate variants was 2% and 15.4% among familial cases. *CDH1* mutational burden was higher among probands from familial cases when compared to that of controls (P=0.002). We concluded that *CDH1* contributes to NSCL/P with mainly rare, moderately penetrant variants, and *CDH1* haploinsufficiency is the likely etiological mechanism. In addition, we are testing the missense *CDH1* candidate variants using a zebrafish model in order to understand their contribution to OFC. This project is being developed in collaboration with Dr. Eric Liao, Harvard University. We are also investigating the etiology of NSOFC through a combination of transcriptomic profiling and functional approaches. This strategy has shown that NSOFC stem cells from exfoliated deciduous teeth exhibit dysregulation of a co-expressed gene network mainly associated with DNA double-strand break repair and cell cycle control. This network included important genes for these cellular processes, such as *BRCA1*, *RAD51*, and *MSH2*, which are predicted to be regulated by transcription factor E2F1. Functional assays have supported these findings, revealing that NSOFC cells accumulate DNA double-strand breaks upon exposure to H_2O_2. Furthermore, we show that *E2f1*, *Brca1* and *Rad51* are co-expressed in the developing embryonic orofacial primordia, and may act as a molecular hub playing a role in lip and palate morphogenesis. In summary, we have shown that cellular defenses against DNA damage may take part in determining susceptibility to NSOFC (Kobayashi *et al.*, 2013). In order to understand the cause of this dysregulation we are currently testing: a) if the *BRCA1* promoter is differentially methylated; b) if epigenomic regulation is involved in the manifestation of this differential transcriptome.

- **Autism spectrum disorder (ASD)** is a complex heterogenous disorder. The clinical manifestation of about 10-20% of ASD-affected individuals is caused by private loss-of-function heterozygous mutations. We have identified a novel candidate gene, *TRPC6* (which encodes a cation channel) in a nonsyndromic autistic individual. Using multiple models, such as stem cells from exfoliated deciduous teeth, iPSC-derived neuronal cells, and mouse models, we demonstrate that *TRPC6* reduction or haploinsufficiency leads to altered neuronal development, morphology and function. The observed neuronal phenotypes could then be rescued by *TRPC6* complementation and by treatment with insulin-like growth factor-1 or hyperforin, a *TRPC6*-specific agonist, suggesting that ASD individuals with alterations in this pathway may benefit from these drugs. Genetic sequencing of *TRPC6* in 1041 ASD individuals and 2872 controls revealed loss-of-function mutations with incomplete penetrance in two additional patients. Our findings suggest that *TRPC6* is a novel susceptibility gene for ASD that may act in a multiple-hit model. We also demonstrated for the first time the use of iPSC-

derived human neurons to model non-syndromic ASD, demonstrating the potential of modeling genetically complex sporadic diseases using such cells (Griesi-Oliveira *et al.*, 2014).

- In order to further elucidate the etiological **mechanisms leading to ASD**, we are also investigating cellular and signaling pathways. Protein synthesis regulation via mammalian target of rapamycin complex 1 (mTORC1) signaling pathway has key roles in neural development and function, and its dysregulation is involved in neurodevelopmental disorders associated with autism and intellectual disability. Using iPSC-derived neural progenitor cells from a patient harboring a deletion spanning the entire Collybistin (CB) gene, we showed that CB physically interacts with mTOR and inhibits the mTORC1 signaling pathway. These findings suggest that disinhibited mTORC1 signaling may also contribute to the pathological process in patients with loss-of-function variants in CB. (Machado *et al.*, 2015). Furthermore,, through functional studies in stem cells from exfoliated deciduous teeth, we found that mTORC1 signaling is increased in nearly 25% of ASD patients, despite the lack of pathogenic variants in the main genes of this pathway. These results open new possibilities for treatment and methods for the classification of ASD patients (Suzuki *et al.*, 2015). We are currently testing other pathways in cells derived from ASD patients, such as cytoskeleton regulation, in order to better understand the pathophysiology of this group of disorders.

b) Identifying disease-modifying genes

Human genes

- The search for modifier genes or mechanisms that protect some individuals and exceptional GRMD and LRMD dogs (summarized below) from the deleterious effect of a pathogenic mutation has been of great interest, since it may open new avenues for treatment. We have identified two Duchenne muscular dystrophy (DMD) patients with nonsense mutations in the dystrophin gene who had a milder course despite the complete absence of muscle dystrophin. Exome sequencing failed to identify in these two patients any reported polymorphisms apparently associated with a milder phenotype (Zatz *et al.*, 2014; Zatz *et al.*, 2015). Additional studies were done in these patients to verify whether differences in utrophin expression could explain the milder phenotype. The same pattern of utrophin overexpression was observed in DMD patients mildly affected and more severely affected. More recently, (Castro-Gago, 2015) also reported a 34-year old DMD patient with no dystrophin and a mild course. These observations reinforce our hypothesis that it is possible to have a partially functional muscle without muscle dystrophin. The search for “protective” polymorphisms or mechanisms will continue.

- In patients with other forms of myopathies, we observed that polymorphisms in the *RYR1* gene are not modifying the phenotype of the pathogenic mutation in central core disease (Cuperman *et al.*, 2014).

Murine models

- Dystroglycanopathies are muscular dystrophies caused by defects in the glycosylation of α-dystroglycan, an important component of the dystrophin-glycoprotein complex. Recent studies involving overexpression of the glycosyltransferase LARGE protein showed clinical improvement in different mouse models for muscular dystrophy. A study was done to evaluate the endogenous expression of genes involved in glycosylation in murine models and in patients with neuromuscular disorders. The possible modifying effect of heterozygous mutations in the *Large* gene was analyzed. A mdx mouse that is also heterozygous for the *Large*^{myd} mutation showed a more severe phenotype.

- We transferred the mdx mutation to the 129/Sv strain aiming to create a more severe DMD model (mdx129). Unexpectedly, functional analysis of mdx129 showed a progressive amelioration of the phenotype. Transcriptome comparative analysis showed involvement of immune system genes and a decreased participation of the endo/exocytic pathway and homeostasis categories, and an increased participation of the extracellular matrix and enzymatic activity categories. The most significant differentially expressed genes (DEGs) exclusively expressed in mdx129, were the upregulated *Spp1* and *Il1rn* genes. *Spp1* is a known DMD prognostic biomarker, and our data indicate that its upregulation can ameliorate the phenotype. Modeling the expression of the DEGs involved with the milder course of mdx mutants should be tested as a possible therapeutic strategy for the dystrophic process.

- A new study, using electroporation as a model of degeneration/regeneration to investigate the regenerative potential in neuromuscular disorders, has been introduced. Animals' calves were electroporated and analyzed after 3, 5, 10, 15, 21 and 30 days. Normal mice and two mouse models with mutations in the dysferlin (*Dysf)* and the dynamin-2 (*Dnm2*) genes, respectively (in collaboration with the Institute of Myology of Paris) are being analyzed. The aim is to investigate the pattern of alterations along time, both through histological analysis and quantitative mRNA expression of genes involved in the degeneration/regeneration pathways. Preliminary results were presented at the American Society of Human Genetics Annual Meeting (2014).

Canine models

- The Golden-retriever muscular dystrophy (GRMD) and Labradors muscular dystrophy (LRMD) dogs represent the best models for Duchenne muscular dystrophy (DMD). These dogs have no muscle dystrophin and they show a severe course. Most of them do not survive beyond age two. We have identified in our colony two dogs (named Ringo and Suflair) with a milder course, despite the lack of muscle dystrophin. Ringo died

recently, at age 11, showing thus a normal lifespan. (Zatz *et al.*, 2015). These dogs received notorious international attention and a new colony of dystrophin-deficient LRMD dogs with a milder phenotype was identified in the United States (Vieira *et al.*, 2015).

- The search for protective variants or mechanisms to explain the milder GRMD phenotype has been the focus of important investigation in a collaborative study between our center and Harvard Medical Center (Dr. Louis Kunkel). In this study, we identified a new modifier gene, *Jagged1*, which can modulate the phenotype of the GRMD dogs. Only one gene within the mapped region showed altered expression when comparing muscle tissue from escaper and affected dogs. Through whole-genome sequencing analysis we found a variant present only in mildly affected GRMD dogs, which creates a myogenin binding site in the *Jagged1* promoter. Overexpression of *Jagged1* rescues the dystrophic phenotype in the *sapje* DMD zebrafish model and explains the clinical variability in GRMD dogs. This suggests that *Jagged1*, when highly expressed in muscle, can rescue the dystrophin deficiency phenotype in two animal models, pointing to possible new therapeutic approaches in humans.

c) Neurodegeneration and neurodevelopmental disorders

Intracellular trafficking and protein aggregation in neurodegeneration

- The association between intracellular trafficking and protein aggregation related to neurodegenerative diseases was evaluated in cultured neurons from hippocampus, substantia nigra and locus coeruleus exposed to low concentrations of rotenone, as a model of early stages of neurodegeneration. It was demonstrated that mitochondria and their motor proteins are altered before protein aggregation (Melo *et al.*, 2013; Chaves *et al.*, 2013), which can lead to inclusions associated with neurodegenerative diseases. Mitochondria traffic was also evaluated in dopaminergic neurons derived from human iPS cells from Parkinson's patients harboring three copies of the alpha-sinuclein gene. It was observed that mitochondria dynamics is impaired in dopaminergic neurons derived from Parkinson's patients, even in the absence of protein aggregates, since autophagy was increased (100%) in these neurons derived from Parkinson's patients and might resolve the excess of misfolded protein.

Synaptic plasticity in Down syndrome

- Cognitive deficit in patients with Down syndrome (DS) have been associated with macro and microstructural changes occurring during brain development. Evidence suggests that astrocytes are major players in the maturation of the nervous system, as they efficiently modulate all stages of synapse formation and maturation. We began to study the influence of astrocytes in synaptic modulation *in vitro*, using cultured neurons from DS patients as a model to investigate the signaling pathways and important factors for CNS maturation and function in these individuals. Thus far, iPS cells have been generated from fibroblasts of DS individuals using Sendai virus. Those cells are

currently under characterization and they will be used to generate both astrocytes and neurons for downstream experiments.

Genetics of Alzheimer's disease

- Apolipoprotein E (apoE, encoded by the *APOE* gene) plays an important role in lipid and cholesterol metabolism and is known to be associated with cardiovascular disease, cognitive decline and Alzheimer's disease (AD)-related pathologies. *APOE* still remains the only unequivocal genetic risk factor associated with the multifactorial form of AD, and GWAS data collectively explain only a small percentage of the heritable variation in AD risk. The relatively frequent allele ApoE4 and the minor allele ApoE2 are respectively considered factors of risk and protection to these cognitive-related conditions, although ApoE2 homozygosity is a known risk factor for cardiovascular-related disorders. We have genotyped two large elderly population-based cohorts from the city of São Paulo, Brazil: one of them composed of a census drawn sample, aged 60 and older, and the second one derived from a brain bank. Surprisingly, we observed that the frequency of the rare homozygous E2/E2 genotype was underrepresented in the first cohort and differs significantly between the two groups. Although the frequency of the allele E2 did not differ from expected, the genotype E2/E2 was significantly more frequent in the samples from the brain bank than in the elderly population suggesting that it may confer an increased risk for carriers.

- We investigated two aspects related to the multifactorial form of individuals diagnosed *post mortem* as affected by AD: (a) identification by array-CGH of rare CNVs that could contribute to the development of the disease, and (b) analysis of the DNA methylation pattern in the frontal cortex of individuals with AD. We identified 6 rare CNVs with relevant gene content to AD, in particular two microduplications in genes that encode different subunits of the same type of Ca^{2+} voltage channel, previously published (Villela *et al.*, 2013). A second paper based on the rare CNVs detected in AD was published (Villela *et al.*, 2014) wherein a subject with late-onset AD harboring a rare CNV disrupting the *NAMPT* gene is reported. *NAMPT* encodes an important enzyme that mediates nicotinamide adenine dinucleotide (NAD) biosynthesis. Recently an interesting study showed that overexpression of the gene for NAD-dependent deacetylase sirtuin-1 (*SIRT1*) reduces production of amyloid beta (Aβ) and plaques in the brain of AD mice. Disruption of *NAMPT*, therefore, is a likely mechanism for increased production of Aβ and plaques.

- Genome-wide DNA methylation changes in noncoding RNA genes have been investigated for the first time in our study on frontal cortices from individuals with AD. The methylome of 10 AD individuals and 10 age-matched controls were obtained using the Illumina 450K methylation array. A total of 2,095 among the 15,258 interrogated noncoding RNA CpG sites showed differential methylation, 161 of which were associated with miRNA genes. In particular, 10 miRNA CpG sites that were found to be hypermethylated in AD compared to control brains represent transcripts that have been previously associated with the disease. This miRNA set is predicted to target 33 coding

genes from the neuregulin receptor complex pathway, which is required for myelination of neurons. For 6 of these miRNA genes (MIR9-1, MIR9-3, MIR181C, MIR124-1, MIR146B, MIR451), the hypermethylation pattern is in agreement with previous results from the literature that show downregulation of miR-9, miR-181c, miR-124, miR-146b, and miR-451 in the AD brain. Our data suggest that DNA methylation could be involved in the dysregulation of miRNA expression in brain and may contribute to the pathogenesis of AD.

Genome instability

- Cancer, neurodegeneration and premature aging are directly linked to genome instability and DNA repair processes. Part of our group studies how DNA damage is dealt with in human cells, through the investigation of cells from subjects affected by DNA repair syndromes such as Cockayne syndrome (CS) and xeroderma pigmentosum (XP), among many others (see a complete review in (Menck e Munford, 2014)). Spontaneous DNA damage and products of oxidative stress in cells are the main candidates for decreasing the stem cell reservoir and for impairing tissue repair (reviewed in Rocha *et al.*, 2013), and the relationship between genome maintenance by DNA repair pathways and autophagy was also reviewed (Vessoni *et al.*, 2013). We obtained evidence on the participation of specific nucleotide excision repair proteins in repairing oxidative DNA damage, and this may relate to the clinically severe phenotypes of patients with neurodegeneration and premature aging (Berra *et al.*, 2013; Soltys *et al.*, 2013).

- The deleterious action of the different DNA lesions, induced by the UV component of sunlight, were also investigated with the development of sensors and evaluation of damage biological implications after removal with specific photorepair systems (Cortat *et al.*, 2013; Schuch *et al.*, 2013). More recently, we described a new system to measure the efficacy of sunlight filters to block UVB's and UVA's direct effects on human cells, employing XP cells (Schuch *et al.*, 2014). The effects of UV-induced DNA damage on cell cycle and DNA replication were dissected, and we proposed important models on how cells deal with- and respond to these lesions (Ortolan e Menck, 2013; Quinet *et al.*, 2014).

- The signaling process through which ATR regulates apoptosis and how ATR is related to the translesion synthesis pathway and other tolerance mechanisms was described in human cells (Andrade-Lima *et al.*, 2014). In collaboration with Dr. Mats Ljungman (Michigan University, USA) a genome wide methodology was employed to investigate how transcribed genes are repaired, with special insights on long genes (Andrade-Lima *et al.*, 2015). Another approach through which DNA damage can be used to fight tumor cells is being developed. By comparing 2D and 3D cell cultures of breast cancer cells, we found that 3D-cultured cells were more sensitive to treatment with the genotoxic agent doxorubicin. This study revealed that this enhanced sensitivity was due to a reduced autophagy process in 3D-cultured cells, mainly controlled by transcription factor p53 (Gomes *et al.*, 2015).

d) Project 80+

- During this period, we have collected DNA and demographic data from about 1,460 individuals older than 60, which comprise a large cohort of a population-based sample followed since year 2000 (n=1320) with comprehensive questionnaires, health measures and socioeconomic data; approximately 140 octogenarians with preserved cognitive function were also recruited. From the combined sample, we were able to enroll about 600 to the Brain Institute (Albert Einstein Hospital) where most subjects were submitted to brain MRIs and functional tests to detect complex phenotypes that are prevalent during aging such as frailty. Results on gait speed performed by subjects from this sample were recently published (Busch Tde *et al.*, 2015). Neuroimaging findings, including quantitative estimates of the lesion load in white matter, cortical thickness, cerebral connectivity and incidental findings were analysed and are currently in preparation for submission to publication in peer reviewed journals. In addition, 604 individuals had their exomes sequenced. This study is a collaborative project between our center, Faculdade de Saúde Pública (Prof. Maria Lucia Lebrão and Yeda Duarte) and Instituto de Pesquisas Albert Einstein (Prof. Edson Amaro Jr.). The results on exome data are already being used as a data bank of normal controls leading to the publication of several articles such as the identification of the LGMD1G pathogenic mutation (Vieira *et al.*, 2014). Additionally, this data bank was used to assess, through association studies, the risk of the polymorphism rs2066827 (p27-V109G) with sporadic pituitary adenomas (Sekiya *et al.*, 2014) and tumor multiplicity in patients harboring *MEN1* germline mutations (Longuini *et al.*, 2014).
- We are currently establishing an international collaboration with the Human Longevity Inc. for the whole genome sequencing of this cohort and the resulting data will open the possibility for several studies, including the association between genomic variants and brain measures, ancestry estimations, epidemiology of the pathogenic genomic burden. Members of the HUG-CELL are expected to be trained and work together with Human Longevity Inc. group.

e) Genomic imprinting disorders in human development

Angelman (AS) and Prader-Willi (PWS) syndromes are neurodevelopmental disorders which were the first examples of genomic imprinting found in humans, where a parent-specific allele is inactivated in chromosome region 15q11.2-q13.

PWS and Obesity

- We used in-house MLPA probes and whole-genome Chromosomal Microarray Analysis (CMA) in a cohort of 338 ‘non-PWS’ patients presenting obesity in association with intellectual/learning disabilities and additional features. In 23 patients, we detected clinically relevant CNVs overlapping clearly defined syndromic loci. Several have been linked to obesity, including two recently described CNVs involving regions 1p21.3 (*MIR137*) and 12p13.31 (*GNB3*) (D’angelo *et al.*, 2014). Additionally, we found that the

CNV intervals in 8 patients overlapped loci that escape syndromic classification, including a deletion of the 16p11.2 *SH2B1*-containing region that is known to be implicated in obesity, and two rarely described microduplications, 17q11.2 (*NF1*) and 17q21.31 (*MAPT*). Our results confirmed the link between CNVs and obesity and emphasize the efficacy of whole-genome CMA in clinical practice using obesity (in the presence of other anomalies) as an initial paradigm (D'angelo *et al.*, 2013; D'angelo *et al.*, 2014).

Chromosome region 15q11-q13 gene expression in neurons derived from stem cells from AS and PWS patients

- Loss of paternal copies of the cluster of *SNORD116* C/D box snoRNAs and their host transcript, *116HG*, on human chromosome 15q11-q13 imprinted region is considered to be the major mechanism responsible for PWS. The PWS-imprinting center (PWS-IC) regulates 15q11-q13 imprinting. PWS-IC is located upstream and in the exon 1 of the *SNURF-SNRPN* gene. In mice, *Zfp57* plays important role in establishment and maintenance of *Snrpn* imprinting. In humans, the ENCODE database indicates that *ZNF274* binds to *SNORD116.* Moreover, *ZNF274* is a C2H2/KRAB zinc finger protein similarly to *Zfp57*. We investigated the repression mechanism the maternal *SNORD116* and report that the *ZNF274*, in association with the histone H3 lysine 9 (H3K9) methyltransferase *SETDB1*, is part of a complex that binds to the silent maternal but not the active paternal alleles in iPSCs. Knockdown of *SETDB1* in PWS-specific iPSCs causes a decrease in the accumulation of H3K9 trimethylation (H3K9me3) at *SNORD116*. We also show that upon knockdown of SETDB1 in PWS-specific iPSCs, expression of the maternally silenced *116HG* RNA is partially restored. *SETDB1* knockdown in PWS iPSCs also disrupts DNA methylation at the PWS-IC where a decrease in 5-methylcytosine is observed in association with a concomitant increase in 5-hydroxymethylcytosine. In iPSC-derived neurons and stem cells from human exfoliated teeth (SHED) *ZNF274/SETDB1* complex binding and H3K9me3 modification occur in both alleles. These observations suggest that the *ZNF274/SETDB1* complex bound to the *SNORD116* cluster may protect the PWS-IC from DNA demethylation during early development, as indicated in iPSCs. Our findings reveal novel epigenetic mechanisms that function to repress the maternal 15q11-q13 region. The better understanding of epigenetic mechanisms provides new tools for future therapy research.

Genomic imprinting in growth disorders

- A significant number of patients with growth disturbances remains without a causative diagnosis. Alterations of genomic imprinting have been causally associated with a few growth restriction and overgrowth syndromes. In a study of patients with growth disturbances of prenatal onset and unknown etiology, we evaluated the presence of submicroscopic chromosomal alterations (through array-CGH), the expression pattern of imprinted genes (with cDNA pyrosequencing), and the global methylation pattern (with

methylation microarray). Array-CGH analysis detected causative chromosomal microimbalances in three out of the 40 patients under study. Normal monoallelic expression for six imprinted genes expressed in blood was documented in 18 growth-retarded patients. Global methylation analysis in 20 growth-retarded patients and 26 age-matched controls revealed hypermethylated segments in genes involved in cell proliferation and differentiation in 11 patients. This study is part of the PhD Project of Adriano Bonaldi; results have been presented in international meetings (2013 European Human Genetics Conference; 2014 Annual Meeting of the American Society of Human Genetics).

Mining novel candidate imprinted genes using genome-wide methylation screening

- Different strategies have been applied in the search for imprinted genes by focusing on monoallelic expression or epigenetic signatures. In this study we investigated genome-wide DNA methylation patterns in multiple human tissues, using a high-resolution microarray to uncover hemimethylated CpGs located in promoters overlapping CpG islands. Using stringent selection criteria, we recovered ~30% of the known human imprinted genes, and identified further 168 candidates, 27 of which with at least three hemimethylated CpG sites shared by three or more tissues. Seven of these genes have been already reported as candidates for imprinting. Among our candidates, *CCDC166*, *ARC*, *PLEC*, *TONSL* and *VPS28* are mapped at 8q24.3, and may constitute a novel imprinted cluster. Additionally, 34 protocadherins clustered in region 5q31.3 exhibited hemimethylated CpGs at promoter regions in multiple human tissues. In mice, *Pcdh* genes are known to have non-imprinted monoallelic randomic expression, which might be the case in humans. The screening for hemimethylated CpG sites shared by multiple tissues appears as a useful approach to reveal candidate imprinted genes.

f) Genetic mechanisms causing intellectual disability and/or congenital anomalies

The contribution of apparently balanced chromosomal rearrangements (BCRs)

- By combining aCGH and next-generation based mate-pair sequencing (MPS) to characterize BCRs in patients with developmental disorders, this study aims at (a) identifying disease-associated genes and (b) disclosing the mechanisms of BCR formation. It is part of the *International Breakpoint Mapping Consortium (IBMC)* coordinated by Prof. Niels Tommerup at the University of Copenhagen, with the objective of linking hundreds of phenotypes and diseases to specific genes and genomic regions, and of generating a unique resource for studying the effects of genomic reshuffling on epigenetic mechanisms and on the functional and structural organization of the genome in topological domains. For her training in MPS analysis, the PhD student ACS Fonseca spent a year at the Wilhelm Johannsen Centre (FAPESP grant). In our cohort of 45 BCRs, 12 (27%) were associated with imbalances as revealed by aGCH.

Breakpoint mapping by MPS expanded the number of structural variants and breakpoints; known disease genes or their regulatory regions were disrupted in 10/27 BCRs; candidate genes were disrupted by five others. The most complex BCRs (10-22 breaks) displayed hallmarks of *chromothripsis.* Analysis of breakpoint junction at the nucleotide level by Sanger-sequencing pointed to non-homologous (NHEJ) or micro-homology-mediated end joining (MMEJ) mechanisms in the formation of these BCRs. These data have been presented in international meetings, focusing on clinical impact and mechanisms of formation of BCRs (European Human Genetics Conference 2014, 2015; Annual Meeting of the American Society of Human Genetics 2014), and in the broad context of the saturation of the human genome with chromosomal breakpoints (European Human Genetics Conference, 2014; 43rd Biennial American Cytogenetics Conference, 2014).

X-chromosome mutations in intellectual disability

- At least 10% of males with intellectual disability (ID) carry X-chromosome mutations, including submicroscopic gains or losses of segments. However, known X-chromosome mutations only explain ~50% of X-linked mental impairment. We continued our search for X-linked mutations in rare families with an X-linked pattern of inheritance (XLID), using the skewed X-inactivation pattern of mothers as the inclusion criterion, in sibships with two or more affected brothers and in sporadic cases. Analysis of data generated by exome sequencing from 13 sporadic cases, and the probands of nine X-linked ID families and ten sibships is in progress. A post-doc (José Oliveira dos Santos) and an undergraduate student (Andressa CG Martins) participate in the development of this project. In 2006, we identified *UBE2A*, which encodes a ubiquitin-conjugating enzyme, a member of the ubiquitin proteasome pathway, as the mutated gene causing a novel syndromic form of ID (Nascimento et al, Am J Hum Genet 79:549, 2006); since then, *UBE2A* point mutations and deletions have been described in patients with similar phenotypes. Our group participated in a collaborative work led by Patrik Verstreken (Center for Human Genetics and Leuven Research Institute for Neuroscience and Disease, Belgium), which established a critical role for *UBE2A* in maintaining neuronal function as a regulator of the clearance of dysfunctional mitochondria (Haddad *et al.*, 2013)

g) Stem Cell for therapy in Neuromuscular disorders

Preclinical studies using human adult stem-cells

- We have compared the effect of human pericytes obtained from the same donor and different sources (adipose tissue, endometrium, muscle and fallopian tube) injected in mdx/utrophin mice. These animals are severely affected and have a lifespan of about 120-150 days. Interestingly, we observed a beneficial effect only with pericytes obtained from adipose tissue. Injected animals lived 25% more (Valadares *et al.*, 2014). These

results, which are currently being confirmed in additional experiments, may have important impact in therapeutic trials.

- We have also shown the clinical benefit of cell therapy in 3 GRMD-affected dogs, two of them born in 2008 and one in 2011. They were repeatedly transplanted with human adipose-derived mesenchymal stromal cells (hASC), derived from 4 different donors. Xenogeneic cell transplantation, which was done without immunosuppression, was well tolerated in all animals with no apparent long-term adverse effect. In the present study, the longest reported preclinical follow-up in GRMD dogs, we show that repeated heterologous stem-cell injection is a safe procedure, which is fundamental before starting human clinical trials. These results have been shown in several international meetings.

Pre-Clinical studies with murine stem cells

- Muscle satellite cells have been widely studied, especially to understand their mechanism of action in muscle regeneration and correspondent implications in the different dystrophic processes, aiming the identification of potential therapeutic targets. Two mice models for muscular dystrophies, Largemyd and Lama2dy2j/J, have a pattern of an intense and very similar degeneration, but with differences in the expression of genes involved in the regeneration cascade, as we showed in our previous work. Therefore, they are interesting models to study possible differences in the mechanism of activation and action of satellite cells in the dystrophic muscle. The main objective of this work was to evaluate the characteristics presented by satellite cells from both dystrophic mouse models as they can explain the known differences in the regeneration process. For this evaluation, we used the pre-plating technique and the different populations were then characterized by flow cytometry using markers for myogenic and mesenchymal populations. In the phenotypic characterization of cells from normal muscle, both faster (PP1) and slower (PP2) populations show similar phenotypic characteristics, which were closer to myogenic phenotype. On the other hand, the population of cells with very delayed adhesion ability (PP6) presented a mixed pattern, maintaining the myogenic characteristics, but associated to positive mesenchymal stem cell's markers, suggesting a phenotype of more immature cells. In dystrophic muscles, we could identify differences in the constitution of the original pool of cells present in the Lama2dy2j/J muscle where there is evidence of a population in proliferative and myogenic stage, while in the Largemyd strain we found very similar characteristics in both faster and slower populations, which suggests an initial pool poor of cells with myogenic potential. These observations are corroborating our previous gene expression results, suggesting that the mutation present in Largemyd mouse leads to defects in the regeneration potential of satellite cells, which does not occur in the Lama2dy2j/J model.
- Additionally, noninvasive characterization of muscle alterations have been done in different mouse models for muscle dystrophies, using magnetic resonance imaging (MRI) and micro-Computed Tomography (micro-CT). The muscle phenotypes of the double-mutant mdx/*Large*^{myd} mouse, with very severe phenotype, and of the parental

mdx (mild phenotype) and *Large*^{myd} (severe phenotype) mice were compared by MRI .These results, will be important to evaluate the effect of stem-cell therapy in preclinical studies with these murine models (Martins-Bach *et al.*, 2015).

h) Stem cells in craniofacial/bone disorders

- New strategies to regenerate craniofacial bone defects have gained attention in recent years due to the morbidity of autologous bone graft harvesting. We aimed to evaluate the *in vivo* efficacy of bone tissue engineering strategy using mesenchymal stem cells (MSCs) associated with two matrices (bovine bone mineral and α-tricalcium phosphate), compared to an autologous bone transfer. Based on the analysis of 28 adult, male, non-immunosuppressed Wistar rats, who underwent a critical-sized osseous defect of 5 mm in diameter in the alveolar region, we observed that bone defects repaired with α-tricalcium phosphate and MSCs presented the highest bone volume filling the defects, which in turn were not statistically different from autogenous bone (Raposo-Amaral *et al.*, 2014).

- Another issue in this field is the restricted self-renewal and limited cell amounts necessary for bone remodeling using cell therapy. Therefore, one of our goals is to search for molecules that can improve bone reconstruction. We have recently published two articles that contribute to this field: **a)** We have shown that employing MSCs from exfoliated dental tissue (SHED) for the generation of iPSCs (iPS-SHED cells) followed by re-differentiation to MSCs confers a higher *in vitro* osteogenic potential when compared to the originating SHED population. The higher osteogenic potential of MSCs from iPS-SHED may be due to cellular homogeneity and/or to donor tissue epigenetic memory. Our findings strengthen the rationale for the use of iPSCs in bone bioengineering (Ishiy *et al.*, 2015); **b)** In order to search for novel molecular markers predictive of osteopotential, we compared MSC populations from two sources harboring different osteogenic potentials. We show that SHED have an intrinsically higher osteogenic potential when compared with MSCs from human adipose tissue (hASCs) under the same *in vitro* controlled induction system. Transcriptome profiling revealed *IGF2* to be one of the top upregulated transcripts before and during early *in vitro* osteogenic differentiation, and exogenous IGF2 supplementation enhanced alkaline phosphatase activity and matrix mineralization, whereas IGF2 inhibition lessened these parameters, validating IGF2 as an osteogenic factor in these MSCs. Further, we showed that IGF2 upregulation in SHED is at least in part due to loss of imprinting. This study thus implies IGF2 as a potential biomarker of MSCs with higher osteopotential (Fanganiello *et al.*, 2015). We are expanding this study in order to better understand the differential osteogenic potential between SHED and hASCs, as this approach can contribute to the identification of molecules to be used in bone reconstruction.

i) Stem cells and cancer

Stem cells in tumors of the central nervous system: insights into human brain development and cancer

- The interplay between stem cell and tumor biology offers an exceptional opportunity to advance our knowledge about cancer, with potential impacts in diagnosis and therapy. Additionally, in the general rush towards implementing stem cells in many areas of tissue regeneration, a major threat limiting such applications is the risk of tumor formation, which urges studies concerning the potential oncogenic risks involved. In the first years of project, the tumorigenic properties of pluripotent cells and the involvement of pluripotency-related genes in cancer cells were investigated. The capacity of human embryonic stem cells (hESC) to form teratomas is well known but it remained unclear whether suppression of tumorigenic potential could be achieved without critically affecting pluripotency. In a study published in Stem Cells & Development (Suzuki *et al.*, 2014), we reported that knockdown of the *E2F2* gene in hESC significantly inhibited hESC proliferation and *in vivo* tumorigenicity without significantly harming stemness, providing a rationale to future protocols aiming at minimizing risks related to therapeutic applications of cells and/or products derived from human pluripotent cells. This study was also disseminated in the general press. We also found that silencing the same *E2F2* gene in highly malignant brain cancer cells (Glioblastoma - GBM) significantly inhibited tumor development in subcutaneous and orthotopic xenograft models of GBM in nude mice. This study was published in Oncology Letters (Nakahata *et al.*). Since expression of the *E2F2* gene is associated with cancer stem cells and is involved in the transformation of human astrocytes, this finding suggest that *E2F2* could be explored as a potential therapeutic target in malignant gliomas.

- The impact of DNA damage by cisplatin and temozolomide (TMZ) on glioma cells was also investigated, and the role of glutathione protecting the tumor cells was unraveled. This led to the proposal of using an inhibitor of glutathione (BSO) in combination with cisplatin and TMZ to kill tumor cells with very high efficiency, overcoming tumor resistance to chemotherapy. The preclinical experiments in animals demonstrated the high potential of this proposal (Rocha *et al.*, 2014).

- Other studies concerning the role of pluripotency-related genes in the aggressiveness of brain tumors have been presented in several international meetings (including an EMBO/EMBL Symposium, a Keystone Symposia Conference, and ISSCR congress) and generated two patent applications. The results suggest that misexpression of several pluripotency-related genes drives aggressiveness of medulloblastoma, which is the most frequent and lethal type of embryonal brain tumor. The implications of DNA repair capability to pluripotency and tumorigenicity of stem cells were discussed in a work we published in Mutation Research (Rocha *et al.*, 2013). Furthermore, we edited a special issue dedicated to the relevance of Stem Cells in Translational Cancer

Research, which was published in the journal Stem Cells International (Okamoto *et al.*, 2015).

Stem cells and the tumor microenvironment

- Studies on the contribution of stem cells to the tumor microenvironment (TME) were performed. One of the issues contemplated in such studies was the use of MSCs to treat cancer, which has shown very contradictory results in the literature. In a recent work by our group, we evaluated the clinical effect of human fallopian tube MSCs (htMSCs) in murine mammary adenocarcinoma using two different approaches: (a) coinjections of htMSCs and 4T1 murine tumor cell lineage; and (b) injections of htMSCs in mice at the initial stage of mammary adenocarcinoma development. Coinjected animals had a more severe course of the disease and a reduced survival, while tumor-bearing animals treated with 2 intraperitoneal injections of 10^{-6} htMSCs showed significantly reduced tumor growth and increased lifespan as compared with control animals. Cocultured htMSCs and 4T1 tumor cells revealed an increase in IL-8 and MCP-1 and decreased VEGF production. For the first time, we showed that MSCs isolated from a single source and donor, when injected in the same animal model and tumor, can lead to opposite results depending on the experimental protocol. Also, our results demonstrated that htMSCs can have an inhibitory effect on the development of murine mammary adenocarcinoma (Jazedje *et al.*, 2015). Another issue discussed in a work published in Stem Cells International (Ribeiro e Okamoto, 2015) was the multiple roles of pericytes in the TME. In this work, we argue that, by affecting classical hallmarks of cancer, namely, tumor angiogenesis, tumor growth, metastasis, and evasion of immune destruction, pericytes are pertinent targets for therapy, providing a rationale for cancer drugs aiming at the TME

- Collaborative studies with national and international research groups on drug development for cancer treatment were carried out. Research and development of a new monoclonal antibody targeting cancer cells in primary tumors and micrometastasis *in vivo* generated two publications (Dos Santos *et al.*, 2013; Lindegren *et al.*, 2015). This work was awarded the Prêmio Octavio Frias de Oliveira, modalidade Inovação Tecnológica em Oncologia by the Instituto do Câncer do Estado de São Paulo / Grupo Folha de S. Paulo, in 2014. Collaborations with other CEPID members on studies of cell therapy for chronic degenerative diseases (muscular dystrophy, epilepsy, and ALS) have been performed, generating three additional publications (Secco *et al.*, 2013; Araujo *et al.*, 2014; Coatti *et al.*, 2015).

2) ADDITIONAL ACTIVITIES INVOLVED WITH SCIENTIFIC PROJECTS

a) Postdoc Selection

We have selected three postdoc candidates for our project, respectively for bioinformatics, cell biology and stem cell for regenerative medicine. One of them, **Vivek Kuman** (cell biology), from India, will start in September. The other two, **David Santo Marco Antonio** (bioinformatics) and **Luiz Carlos de Caires Junior** (regenerative medicine) have already started their projects but were not awarded FAPESP fellowships and will be funded by CNPq.

b) Meeting with the International Advisory Board

The meeting with the international advisory board, respectively Prof. Gert-Jan VanOmmen from the Netherlands and Prof. Nissim Benvenisty from Israel, occurred from October 29 to 31, 2014, in Guarujá. A three-day seminar was organized with the participation of all CEPID's researchers and about 50 students. The main results of our CEPID were presented orally by the group members and all students presented their projects/results in posters, which were discussed individually with the visitor professors. At the end of the meeting we had a discussion with the international board who gave us important suggestions. A written report was sent to FAPESP and before leaving Prof. Gert-Jan and Nissim had a meeting with Hernan Chaimovich, who was the CEPID coordinator from FAPESP. The report provided by the international board of referees is annexed to this document.

3) NEXT GOALS (2015-2018)

The Human Genome Center was initiated in 2000 with the aim of improving our basic knowledge and diagnosis of prevalent genetic diseases in the Brazilian population, mainly neuromuscular, craniofacial, and mental disability. The activities were expanded in 2005, by introducing stem-cell research to understand gene expression and differentiation in complex genetic disorders and to evaluate stem cell based disease therapy. In 2013, the Human Genome and Stem-cell research center (HUG-CELL) was started and further expanded to include research on the genetics and genomic instability associated with aging and degenerative diseases, epigenetic mechanisms involved in disease manifestation, phenotypic variability between individuals with identical Mendelian disease mutations, and the 80 plus project, aiming to compare the genome variation and brain functioning (MRI) of healthy Brazilian individuals older than 80 with a cohort older than 60 that have been followed since 2000. Our goals for the first two years were accomplished and resulted in 118 peer-reviewed publications.

Our aims for the next three years are to continue novel disease-genes identification, to unravel the genetic mechanisms associated with multifactorial diseases such as cleft lip and palate, autism and hypertension, and finally the and the search for variants or mechanisms responsible for modulating the severity of the phenotype. We plan to focus more on functional studies and on the search of etiological mechanisms through the investigation of cellular and signaling pathways in particular in autism and amyotrophic lateral sclerosis. To achieve these goals at the genomic level, we will use DNA and RNA next generation sequencing technology for *in vitro* studies we will focus mainly on pluripotent stem cells derived from patients' somatic cells, while for *in vivo* models we will use yeast as well as animal models, ranging from zebrafish to canine models for muscular dystrophy. The recently acquired technology to derive IPS cells from blood samples (erythroblasts) will greatly facilitate obtaining samples from patients or subjects of interest (such as healthy octogenarians).

Healthy human aging is a growing topic of interest and understanding the complex nature versus nurture balance is one of the greatest challenges. The establishment of a collaboration project between our center and the Human Longevity Institute in S. Diego will allow us, within the next 3 years, to analyze the genome of the cohort of healthy elderly population we have collected during the first part of our CEPID project. We hope that this collaborative study will contribute to enhance our comprehension on the genetic and environment mechanisms involved in aging as well as constitute an important databank of our population. It is also our expectation that a better characterization of the variants of Brazilian exomes can provide estimates of incidence and prevalence of some rare diseases. Analysis of the microbiome is a new promise to understand human diseases, particularly the complex ones. In addition to genomic analysis of multifactorial diseases, we will invest in the analysis of microbiome to evaluate its contribution to the etiology of non syndromic cleft lip and palate.

Our pre-clinical studies on stem-cell therapy in different animal models have shown that the clinical benefits from mesenchymal stem-cells (MSCs) are based on their immunomodulatory and anti-inflamatory properties and not due to stem-cell differentiation. Based on these results we will focus on the study of stem-cell secretome. It is also our plan to start a cell therapy clinical trial in two groups of patients: a) Duchenne muscular dystrophy; b) rheumatoid arthritis. This project, planned to start in 2016, will be done in collaboration with

AACD (Associação de assistência a criança defeituosa). We have also started a new collaborative project on regenerative medicine where our first goal is to compare the potential of different stem cells to differentiate in hepatocyes.

Furthermore, a new equipment allows to prepare individual cells for genome and transcriptome analysis. Single cells isolated from a stem cell culture, normal cultures or even cells from in vivo human tumors could have the transcriptome (RNA-Seq) investigated to check for potential differences during differentiation protocols, or to identify processes that makes the tumor more aggressive and resistant to therapy. Moreover, investigating exome brings the possibility to identify induced genetic alterations (mutations) after DNA damage, or simply, how the tumor cells may evolve. It also can allow the identification of somatic mosaicism, a process that might explain clinical variability in diseases.

Therefore, if the proposal to acquire this equipment (Single cell automated system, C1 FLUIDIGM, attached invoice) is accepted by FAPESP it will benefit many potential users for many different projects from CEGH-CELL.

II. PUBLICATIONS

From June 2013 until June 2015, our group has published 122 journal articles (all listed below; reference 25 is from our group published before 2013), one book, 9 book chapters, 30 abstracts in National meetings, and 105 abstracts in International meetings. During this period, our graduate students submitted 9 Master Theses and 14 Doctoral Dissertations. Four patents were deposited in these two years. There are 99 research projects currently being developed by undergraduate (IC), graduate, and post-graduate students.

a) Articles

Referred in-text citations

1. ANDRADE-LIMA, L. C.; ANDRADE, L. N.; MENCK, C. F. M. ATR suppresses apoptosis after UVB irradiation by controlling both translesion synthesis and alternative tolerance pathways. **Journal of Cell Science,** v. 128, n. 1, p. 150-159, 2014.

2. ANDRADE-LIMA, L. C. et al. DNA repair and recovery of RNA synthesis following exposure to ultraviolet light are delayed in long genes. **Nucleic Acids Research,** v. 43, n. 5, p. 2744-2756, 2015.

3. ARAUJO, B. et al. Decreased expression of proteins involved in energy metabolism in the hippocampal granular layer of rats submitted to the pilocarpine epilepsy model. **Neuroscience Letters,** v. 561, p. 46-51, 2014.

4. BERRA, C. M. et al. Nucleotide excision repair activity on DNA damage induced by photoactivated methylene blue. **Free Radic Biol Med,** v. 61, p. 343-56, 2013.

5. BUSCH TDE, A. et al. Factors associated with lower gait speed among the elderly living in a developing country: a cross-sectional population-based study. **BMC Geriatr,** v. 15, p. 35, 2015.

6. CHAVES, R. S. et al. Dynein c1h1, dynactin and syntaphilin expression in brain areas related to neurodegenerative diseases following exposure to rotenone. **Acta Neurobiol Exp (Wars),** v. 73, n. 4, p. 541-56, 2013.

7. COATTI, G. C. et al. Stem cells for amyotrophic lateral sclerosis modeling and therapy: Myth or fact? **Cytometry Part A,** v. 87, n. 3, p. 197-211, 2015.

8. CORTAT, B. et al. The relative roles of DNA damage induced by UVA irradiation in human cells. **Photochem. Photobiol. Sci.,** v. 12, n. 8, p. 1483, 2013.

9. CUPERMAN, T. et al. Silent polymorphisms in the *RYR1* gene do not modify the phenotype of the p.4898 I>T pathogenic mutation in central core disease: a case report. **BMC Research Notes,** v. 7, n. 1, p. 487, 2014.

10. D'ANGELO, C. S. et al. Obesity with associated developmental delay and/or learning disability in patients exhibiting additional features: Report of novel pathogenic copy number variants. **American Journal of Medical Genetics Part A,** v. 161, n. 3, p. 479-486, 2013.

11. D'ANGELO, C. S. et al. Investigation of selected genomic deletions and duplications in a cohort of 338 patients presenting with syndromic obesity by multiplex ligation-dependent probe amplification using synthetic probes. **Mol Cytogenet,** v. 7, n. 1, 2014.

12. DANTAS, V. G. L. et al. Novel partial duplication of *EYA1* causes branchiootic syndrome in a large Brazilian family. **International Journal of Audiology**, p. 1-6, 2015.

13. DANTAS, V. G. L. et al. c.G2114A *MYH9* mutation (DFNA17) causes non-syndromic autosomal dominant hearing loss in a Brazilian family. **Genetics and Molecular Biology,** v. 37, n. 4, p. 616-621, 2014.

14. DORNELLES-WAWRUK, H. et al. Complex Phenotype Associated with 17q21.31 Microdeletion. **Molecular Syndromology,** v. 4, n. 6, p. 297-301, 2013.

15. DOS SANTOS, M. L. et al. Rebmab200, a Humanized Monoclonal Antibody Targeting the Sodium Phosphate Transporter NaPi2b Displays Strong Immune Mediated Cytotoxicity against Cancer: A Novel Reagent for Targeted Antibody Therapy of Cancer. **PLoS ONE,** v. 8, n. 7, p. e70332, 2013.

16. FANGANIELLO, R. D. et al. Increased In Vitro Osteopotential in SHED Associated with Higher IGF2 Expression When Compared with hASCs. **Stem Cell Reviews and Reports**, 2015.

17. FAVARO, FRANCINE P. et al. A Noncoding Expansion in *EIF4A3* Causes Richieri-Costa-Pereira Syndrome, a Craniofacial Disorder Associated with Limb Defects. **The American Journal of Human Genetics,** v. 94, n. 1, p. 120-128, 2014.

18. FIGUEIREDO, T. et al. Homozygous missense mutation in *MED25* segregates with syndromic intellectual disability in a large consanguineous family. **Journal of Medical Genetics,** v. 52, n. 2, p. 123-127, 2014.

19. FREITAS, É. L. et al. Deletion of the entire *POU4F3* gene in a familial case of autosomal dominant non-syndromic hearing loss. **European Journal of Medical Genetics,** v. 57, n. 4, p. 125-128, 2014.

20. GOMES, L. R.; VESSONI, A. T.; MENCK, C. F. M. Three-dimensional microenvironment confers enhanced sensitivity to doxorubicin by reducing p53-dependent induction of autophagy. **Oncogene**, 2015.

21. GRIESI-OLIVEIRA, K. et al. Modeling non-syndromic autism and the impact of TRPC6 disruption in human neurons. **Molecular Psychiatry**, 2014.

22. HADDAD, DOMINIK M. et al. Mutations in the Intellectual Disability Gene *Ube2a* Cause Neuronal Dysfunction and Impair Parkin-Dependent Mitophagy. **Molecular Cell,** v. 50, n. 6, p. 831-843, 2013.

23. HU, Y. et al. A Novel Autosomal Recessive *GJA1* Missense Mutation Linked to Craniometaphyseal Dysplasia. **PLoS ONE,** v. 8, n. 8, p. e73576, 2013.

24. ISHIY, F. A. A. et al. Improvement of In Vitro Osteogenic Potential through Differentiation of Induced Pluripotent Stem Cells from Human Exfoliated Dental Tissue towards Mesenchymal-Like Stem Cells. **Stem Cells International,** v. 2015, p. 1-9, 2015.

25. IUGHETTI, P. et al. Mapping of the autosomal recessive (AR) craniometaphyseal dysplasia locus to chromosome region 6q21-22 and confirmation of genetic heterogeneity for mild AR spondylocostal dysplasia. **Am J Med Genet,** v. 95, n. 5, p. 482-91, 2000.

26. JAZEDJE, T. et al. Human Mesenchymal Stromal Cells Transplantation May Enhance or Inhibit 4T1 Murine Breast Adenocarcinoma through Different Approaches. **Stem Cells International,** v. 2015, p. 1-11, 2015.

27. KELLER, A. et al. Mutations in the gene encoding PDGF-B cause brain calcifications in humans and mice. **Nat Genet,** v. 45, n. 9, p. 1077-1082, 2013.

28. KOBAYASHI, G. S. et al. Susceptibility to DNA Damage as a Molecular Mechanism for Non-Syndromic Cleft Lip and Palate. **PLoS ONE,** v. 8, n. 6, p. e65677, 2013.

29. LEHALLE, D. et al. A review of craniofacial disorders caused by spliceosomal defects. **Clinical Genetics**, p. n/a-n/a, 2015.

30. LINDEGREN, S. et al. Binding Affinity, Specificity and Comparative Biodistribution of the Parental Murine Monoclonal Antibody MX35 (Anti-NaPi2b) and Its Humanized Version Rebmab200. **PLoS ONE,** v. 10, n. 5, p. e0126298, 2015.

31. LONGUINI, V. C. et al. Association between the p27 rs2066827 variant and tumor multiplicity in patients harboring MEN1 germline mutations. **European Journal of Endocrinology,** v. 171, n. 3, p. 335-342, 2014.

32. MACHADO, C. O. F. et al. Collybistin binds and inhibits mTORC1 signaling: a potential novel mechanism contributing to intellectual disability and autism. **Eur J Hum Genet**, 2015.

33. MARTINS-BACH, A. B. et al. Quantitative T2 Combined with Texture Analysis of Nuclear Magnetic Resonance Images Identify Different Degrees of Muscle Involvement in Three Mouse Models of Muscle Dystrophy: mdx, Largemyd and mdx/Largemyd. **PLoS ONE,** v. 10, n. 2, p. e0117835, 2015.

34. MELO, T. Q. et al. Rotenone-Dependent Changes of Anterograde Motor Protein Expression and Mitochondrial Mobility in Brain Areas Related to Neurodegenerative Diseases. **Cell Mol Neurobiol,** v. 33, n. 3, p. 327-335, 2013.

35. MENCK, C. F. M.; MUNFORD, V. DNA repair diseases: what do they tell us about cancer and aging? **Genetics and Molecular Biology,** v. 37, n. 1, p. 220-233, 2014.

36. NAKAHATA, A. et al. RNAi‐mediated knockdown of E2F2 inhibits tumorigenicity of human glioblastoma cells. **Oncology Letters**, 2014.

37. OKAMOTO, O. K.; MATHEU, A.; MAGNANI, L. Stem Cells in Translational Cancer Research. **Stem Cells International,** v. 2015, p. 1-2, 2015.

38. ORTOLAN, T. G.; MENCK, C. F. M. UVB-Induced Cell Death Signaling Is Associated with G1-S Progression and Transcription Inhibition in Primary Human Fibroblasts. **PLoS ONE,** v. 8, n. 10, p. e76936, 2013.

39. QUINET, A. et al. Gap-filling and bypass at the replication fork are both active mechanisms for tolerance of low-dose ultraviolet-induced DNA damage in the human genome. **DNA Repair,** v. 14, p. 27-38, 2014.

40. RAPOSO-AMARAL, C. E. et al. Is bone transplantation the gold standard for repair of alveolar bone defects? **Journal of Tissue Engineering,** v. 5, n. 0, 2014.

41. RIBEIRO, A. L.; OKAMOTO, O. K. Combined Effects of Pericytes in the Tumor Microenvironment. **Stem Cells International,** v. 2015, p. 1-8, 2015.

42. ROCHA, C. R. R. et al. Glutathione depletion sensitizes cisplatin- and temozolomide-resistant glioma cells in vitro and in vivo. **Cell Death Dis,** v. 5, n. 10, p. e1505, 2014.

43. ROCHA, C. R. R. et al. The role of DNA repair in the pluripotency and differentiation of human stem cells. **Mutation Research/Reviews in Mutation Research,** v. 752, n. 1, p. 25-35, 2013.

44. SANDBACKA, M. et al. *TBX6*, *LHX1* and copy number variations in the complex genetics of Müllerian aplasia. **Orphanet J Rare Dis,** v. 8, n. 1, p. 125, 2013.

45. SANTOS, S. et al. As causas da deficiencia fisica em municipios do nordeste brasileiro e estimativa de custos de servicos especializados. **Ciência & Saúde Coletiva,** v. 19, n. 2, p. 559-568, 2014.

46. SCHUCH, A. P. et al. DNA damage as a biological sensor for environmental sunlight. **Photochem. Photobiol. Sci.,** v. 12, n. 8, p. 1259, 2013.

47. SCHUCH, A. P. et al. Highly Sensitive Biological Assay for Determining the Photoprotective Efficacy of Sunscreen. **Environmental Science & Technology,** v. 48, n. 19, p. 11584-11590, 2014.

48. SECCO, M. et al. Systemic Delivery of Human Mesenchymal Stromal Cells Combined with IGF-1 Enhances Muscle Functional Recovery in *LAMA2* dy/2j Dystrophic Mice. **Stem Cell Reviews and Reports,** v. 9, n. 1, p. 93-109, 2013.

49. SEKIYA, T. et al. p27 variant and corticotropinoma susceptibility: a genetic and in vitro study. **Endocrine Related Cancer,** v. 21, n. 3, p. 395-404, 2014.

50. SILVA, A. G. et al. Does germ-line deletion of the PIP gene constitute a widespread risk for cancer? **Eur J Hum Genet,** v. 22, n. 3, p. 307-309, 2013.

51. SOLTYS, D. T. et al. Novel XPG (*ERCC5*) mutations affect DNA repair and cell survival after ultraviolet but not oxidative stress. **Hum Mutat,** v. 34, n. 3, p. 481-9, 2013.

52. SUZUKI, A. M. et al. Altered mTORC1 signaling in multipotent stem cells from nearly 25% of patients with nonsyndromic autism spectrum disorders. **Molecular Psychiatry,** v. 20, n. 5, p. 551-552, 2015.

53. SUZUKI, D. E.; NAKAHATA, A. M.; OKAMOTO, O. K. Knockdown of E2F2 Inhibits Tumorigenicity, but Preserves Stemness of Human Embryonic Stem Cells. **Stem Cells and Development,** v. 23, n. 11, p. 1266-1274, 2014.

54. VALADARES, M. C. et al. Human Adipose Tissue Derived Pericytes Increase Life Span in Utrn tm1Ked Dmd mdx /J Mice. **Stem Cell Reviews and Reports,** v. 10, n. 6, p. 830-840, 2014.

55. VESSONI, A. T. et al. Autophagy and genomic integrity. **Cell Death and Differentiation,** v. 20, n. 11, p. 1444-1454, 2013.

56. VIEIRA, N. M. et al. Muscular dystrophy in a family of Labrador Retrievers with no muscle dystrophin and a mild phenotype. **Neuromuscular Disorders,** v. 25, n. 5, p. 363-370, 2015.

57. VIEIRA, N. M. et al. A defect in the RNA-processing protein HNRPDL causes limb-girdle muscular dystrophy 1G (LGMD1G). **Human Molecular Genetics,** v. 23, n. 15, p. 4103-4110, 2014.

59. VILLELA, D. et al. Germline DNA copy number variation in individuals with Argyrophilic grain disease reveals CTNS as a plausible candidate gene. **Genetics and Molecular Biology,** v. 36, n. 4, p. 498-501, 2013.

60. VILLELA, D. et al. A microdeletion in Alzheimer's disease disrupts *NAMPT* gene. **J Genet,** v. 93, n. 2, p. 535-537, 2014.

61. YAMAMOTO, G. L. et al. Rare variants in *SOS2* and *LZTR1* are associated with Noonan syndrome. **Journal of Medical Genetics,** v. 52, n. 6, p. 413-421, 2015.

62. YAMAMOTO, GUILHERME L. et al. Mutations in *PCYT1A* Cause Spondylometaphyseal Dysplasia with Cone-Rod Dystrophy. **The American Journal of Human Genetics,** v. 94, n. 1, p. 113-119, 2014.

63. ZATZ, M. Response to: Milder course in Duchenne patients with nonsense mutations and no muscle dystrophin. **Neuromuscular Disorders,** v. 25, n. 5, p. 444, 2015.

64. ZATZ, M. et al. Milder course in Duchenne patients with nonsense mutations and no muscle dystrophin. **Neuromuscular Disorders,** v. 24, n. 11, p. 986-989, 2014.

65. ZATZ, M. et al. A normal life without muscle dystrophin. **Neuromuscular Disorders,** v. 25, n. 5, p. 371-374, 2015.

Additional article publications

66. ALVES, L. U. et al. A novel c.1037C > G (p.Ala346Gly) mutation in *TP63* as cause of the ectrodactyly-ectodermal dysplasia and cleft lip/palate (EEC) syndrome. **Genetics and Molecular Biology,** v. 38, n. 1, p. 37-41, 2015.

67. AMORIM, S. et al. Nerve conduction studies in spastic paraplegia, optic atrophy, and neuropathy (SPOAN) syndrome. **Muscle & Nerve,** v. 49, n. 1, p. 131-133, 2013.

68. BECKEDORFF, F. C. et al. The Intronic Long Noncoding RNA ANRASSF1 Recruits PRC2 to the RASSF1A Promoter, Reducing the Expression of RASSF1A and Increasing Cell Proliferation. **PLoS Genetics,** v. 9, n. 8, p. e1003705, 2013.

69. BORLOT, F. et al. Mucopolysaccharidosis type IVA: Evidence of primary and secondary central nervous system involvement. **American Journal of Medical Genetics Part A,** v. 164, n. 5, p. 1162-1169, 2014.

70. CANTON, A. P. M. et al. Genome-wide screening of copy number variants in children born small for gestational age reveals several candidate genes involved in growth pathways. **European Journal of Endocrinology,** v. 171, n. 2, p. 253-262, 2014.

71. CARVALHO, CLAUDIA M. B. et al. Dosage Changes of a Segment at 17p13.1 Lead to Intellectual Disability and Microcephaly as a Result of Complex Genetic Interaction of Multiple Genes. **The American Journal of Human Genetics,** v. 95, n. 5, p. 565-578, 2014.

72. CARVALHO, E. et al. Schinzel-Giedion syndrome in two Brazilian patients: Report of a novel mutation in SETBP1 and literature review of the clinical features. **American Journal of Medical Genetics Part A,** v. 167, n. 5, p. 1039-1046, 2015.

73. CLOUTHIER, D. E. et al. Understanding the basis of auriculocondylar syndrome: Insights from human, mouse and zebrafish genetic studies. **Am. J. Med. Genet.,** v. 163, n. 4, p. 306-317, 2013.

74. COMIM, C. M. et al. Activity of Krebs cycle enzymes in mdx mice. **Muscle & Nerve**, p. n/a-n/a, 2015.

75. COMIM, C. M. et al. Behavioral Responses in Animal Model of Congenital Muscular Dystrophy 1D. **Mol Neurobiol**, 2014.

76. COTTA, A. et al. Limb girdle muscular dystrophy type 2G with myopathic-neurogenic motor unit potentials and a novel muscle image pattern. **BMC Clin Pathol,** v. 14, n. 1, p. 41, 2014.

77. CRUVINEL, E. et al. Reactivation of maternal SNORD116 cluster via SETDB1 knockdown in Prader-Willi syndrome iPSCs. **Human Molecular Genetics,** v. 23, n. 17, p. 4674-4685, 2014.

78. CUNHA, P. D. S. et al. Accurate, Fast and Cost-Effective Diagnostic Test for Monosomy 1p36 Using Real-Time Quantitative PCR. **Disease Markers,** v. 2014, p. 1-8, 2014.

79. D'ANGELO, C. S. et al. Two New Cases of 1p21.3 Deletions and an Unbalanced Translocation t(8;12) among Individuals with Syndromic Obesity. **Molecular Syndromology**, 2015.

79. DE AQUINO, S. N. et al. *MTHFR* rs2274976 polymorphism is a risk marker for nonsyndromic cleft lip with or without cleft palate in the Brazilian population. **Birth Defects Res A Clin Mol Teratol,** v. 100, n. 1, p. 30-5, 2014.

80. DE ARAÚJO, É. S. S. et al. *LINE-1* hypermethylation in peripheral blood of cutaneous melanoma patients is associated with metastasis. **Melanoma Research,** v. 25, n. 2, p. 173-177, 2015.

81. DE ARAÚJO, É. S. S. et al. Genome-wide DNA methylation profile of leukocytes from melanoma patients with and without *CDKN2A* mutations. **Experimental and Molecular Pathology,** v. 97, n. 3, p. 425-432, 2014.

82. DE CASTILHOS, R. M. et al. Spinocerebellar Ataxias in Brazil—Frequencies and Modulating Effects of Related Genes. **Cerebellum,** v. 13, n. 1, p. 17-28, 2013.

83. DE ROCKER, N. et al. Refinement of the critical 2p25.3 deletion region: the role of MYT1L in intellectual disability and obesity. **Genet Med,** v. 17, n. 6, p. 460-466, 2014.

84. DEMASI, M. et al. 20S proteasome activity is modified via S-glutathionylation based on intracellular redox status of the yeast Saccharomyces cerevisiae: Implications for the degradation of oxidized proteins. **Archives of Biochemistry and Biophysics,** v. 557, p. 65-71, 2014.

85. DEMASI, M. et al. Redox regulation of the proteasome via S-glutathionylation. **Redox Biology,** v. 2, p. 44-51, 2014.

86. DOS SANTOS, M. L. et al. Rebmab200, a Humanized Monoclonal Antibody Targeting the Sodium Phosphate Transporter NaPi2b Displays Strong Immune Mediated Cytotoxicity against Cancer: A Novel Reagent for Targeted Antibody Therapy of Cancer. **PLoS ONE,** v. 8, n. 7, p. e70332, 2013.

87. FIDALGO, F. et al. Lymphovascular invasion and histologic grade are associated with specific genomic profiles in invasive carcinomas of the breast. **Tumor Biology,** v. 36, n. 3, p. 1835-1848, 2014.

88. FIGUEIREDO, T. et al. Homozygous missense mutation in MED25 segregates with syndromic intellectual disability in a large consanguineous family. **Journal of Medical Genetics,** v. 52, n. 2, p. 123-127, 2014.

89. FONSECA, A. C. S. et al. The clinical impact of chromosomal rearrangements with breakpoints upstream of the *SOX9* gene: two novel de novo balanced translocations associated with acampomelic campomelic dysplasia. **BMC Med Genet,** v. 14, n. 1, p. 50, 2013.

90. GAMBA, B. F. et al. Cleft Lip/Palate, Short Stature, and Developmental Delay in a Boy with a 5.6-Mb Interstitial Deletion Involving 10p15.3p14. **Molecular Syndromology**, 2015.

91. HASE GRACIOSO, L. et al. Proteome Analysis of Phenol-Degrading Achromobacter sp. Strain C-1, Isolated from an Industrial Area. **Current Proteomics,** v. 9, n. 4, p. 280-289, 2012.

92. KIMURA, L. et al. Genomic ancestry of rural African-derived populations from Southeastern Brazil. **Am J Hum Biol,** v. 25, n. 1, p. 35-41, 2013.

93. KREPISCHI, A. C. V. et al. Large germline copy number variations as predisposing factor in childhood neoplasms. **Future Oncology,** v. 10, n. 9, p. 1627-1633, 2014.

94. LAURELL, T. et al. Molecular and clinical delineation of the 17q22 microdeletion phenotype. **Eur J Hum Genet,** v. 21, n. 10, p. 1085-1092, 2013.

95. LEMES, R. B. et al. Estimation of inbreeding and substructure levels in african-derived brazilian quilombo populations. **Hum Biol,** v. 86, n. 4, p. 276-88, 2014.

96. LINHARES, N. D. et al. Subtelomeric 6p25 deletion/duplication: Report of a patient with new clinical findings and genotype–phenotype correlations. **European Journal of Medical Genetics,** v. 58, n. 5, p. 310-318, 2015.

97. LINHARES, N. D. et al. Dental developmental abnormalities in a patient with subtelomeric 7q36 deletion syndrome may confirm a novel role for the *SHH* gene. **Meta Gene,** v. 2, p. 16-24, 2014.

98. MARTINS, P. C. M. et al. Dmdmdx/Largemyd: a new mouse model of neuromuscular diseases useful for studying physiopathological mechanisms and testing therapies. **Disease Models & Mechanisms,** v. 6, n. 5, p. 1167-1174, 2013.

99. MEIRELES, D. D. A. et al. A 14.7 kDa Protein from Francisella tularensis subsp. novicida (Named FTN_1133), Involved in the Response to Oxidative Stress Induced by Organic Peroxides, Is Not Endowed with Thiol-Dependent Peroxidase Activity. **PLoS ONE,** v. 9, n. 6, p. e99492, 2014.

100. MELO, U. S. et al. Strategies for genetic study of hearing loss in the Brazilian northeastern region. **Int J Mol Epidemiol Genet,** v. 5, n. 1, p. 11-21, 2014.

101. MOREIRA, D. P. et al. Investigation of 15q11-q13, 16p11.2 and 22q13 CNVs in Autism Spectrum Disorder Brazilian Individuals with and without Epilepsy. **PLoS ONE,** v. 9, n. 9, p. e107705, 2014.

102. MORETTI-ALMEIDA, G.; NETTO, L. E. S.; MONTEIRO, G. The essential gene YMR134W from Saccharomyces cerevisiae is important for appropriate mitochondrial iron utilization and the ergosterol biosynthetic pathway. **FEBS Letters,** v. 587, n. 18, p. 3008-3013, 2013.

103. NORTH, K. N. et al. Approach to the diagnosis of congenital myopathies. **Neuromuscular Disorders,** v. 24, n. 2, p. 97-116, 2014.

104. OLIVEIRA, J. et al. Reviewing Large *LAMA2* Deletions and Duplications in Congenital Muscular Dystrophy Patients. **Journal of Neuromuscular Diseases,** v. 1, n. 2, 2014.

105. ORTEGOSA, M. V. et al. Challenges in the Orthodontic Treatment of a Patient With Pycnodysostosis. **The Cleft Palate-Craniofacial Journal,** v. 51, n. 6, p. 735-739, 2014.

106. PEREIRA, T. V. et al. Multivariate meta-analysis of the association of G-protein beta 3 gene (*GNB3*) haplotypes with cardiovascular phenotypes. **Molecular Biology Reports,** v. 41, n. 5, p. 3113-3125, 2014.

107. RAPOSO-AMARAL, C. E. et al. A Subcranial Le Fort III Advancement With Distraction Osteogenesis as a Clinical Strategy to Approach Pycnodysostosis With Midface Retrusion and Exorbitism. **Journal of Craniofacial Surgery,** v. 24, n. 4, p. 1327-1330, 2013.

108. RICCI, G.; ZATZ, M.; TUPLER, R. Facioscapulohumeral Muscular Dystrophy: More Complex than it Appears. **CMM,** v. 14, n. 8, p. 1052-1068, 2014.

109. RODRIGUES, T. C. et al. Upregulated genes at 2q24 gains as candidate oncogenes in hepatoblastomas. **Future Oncology,** v. 10, n. 15, p. 2449-2457, 2014.

110. ROMANELLI TAVARES, V. L. et al. Novel variants in *GNAI3* associated with auriculocondylar syndrome strengthen a common dominant negative effect. **Eur J Hum Genet,** v. 23, n. 4, p. 481-485, 2014.

111. SANTOS, S. et al. Increased prevalence of inherited neuromuscular disorders due to endogamy in Northeast Brazil: the need of community genetics services. **Journal of Community Genetics**, 2013.

112. SANTOS, S.; MARQUES, R. S.; INFANTE-MALACHIAS, M. E. Teaching of the Biological Evolution Synthetic Theory: a case report of a didactic research experience during pre-service teacher education. **Revista de Educacion de las Ciencias**, 2013.

113. SANTOS, S. et al. As causas da deficiencia fisica em municipios do nordeste brasileiro e estimativa de custos de servicos especializados. **Ciência & Saúde Coletiva,** v. 19, n. 2, p. 559-568, 2014.

114. SCHAEFER, E. et al. Autosomal recessive *POLR1D* mutation with decrease of TCOF1 mRNA is responsible for Treacher Collins syndrome. **Genet Med,** v. 16, n. 9, p. 720-724, 2014.

115. SILVA, A. G. et al. The profile and contribution of rare germline copy number variants to cancer risk in Li-Fraumeni patients negative for *TP53* mutations. **Orphanet J Rare Dis,** v. 9, n. 1, p. 63, 2014.

116. SILVA, A. G. et al. Germline BAX Deletion in a Patient With Melanoma and Gastrointestinal Stromal Tumor. **The American Journal of Gastroenterology,** v. 108, n. 8, p. 1372-1375, 2013.

117. SILVA, A. G. et al. Array-CGH as an adjuvant tool in cytogenetic diagnosis of pediatric MDS and JMML. **Med Oncol,** v. 30, n. 4, 2013.

118. TANIKAWA, D. Y. S. et al. Fat Grafts Supplemented with Adipose-Derived Stromal Cells in the Rehabilitation of Patients with Craniofacial Microsomia. **Plastic and Reconstructive Surgery,** v. 132, n. 1, p. 141-152, 2013.

119. TOLEDO, R. A. et al. Comprehensive assessment of the disputed *RET* Y791F variant shows no association with medullary thyroid carcinoma susceptibility. **Endocr Relat Cancer,** v. 22, n. 1, p. 65-76, 2015.

120. TORRES, L. B. et al. Parvalbumin expression and distribution in the hippocampal formation of Cebus apella. **American Journal of Primatology,** v. 77, n. 4, p. 449-461, 2014.

121. VALENTE, K. D. et al. Angelman syndrome caused by deletion: A genotype–phenotype correlation determined by breakpoint. **Epilepsy Research,** v. 105, n. 1-2, p. 234-239, 2013.

122. VERNHES, M. et al. Protective effect of a Phyllanthus orbicularis aqueous extract against UVB light in human cells. **Pharmaceutical Biology,** v. 51, n. 1, p. 1-7, 2013.

123. ZATZ, M.; PAVANELLO, R. C. M. Steroids in Duchenne dystrophy. **Neuromuscular Disorders,** v. 23, n. 11, p. 952-953, 2013.

b) Books and Book Chapters

1. Lezirovitz K, Mingroni-Netto RC. Disacusias de origem Genética. In: Tratado de Otologia. 2 ed. São Paulo: Editora Atheneu, 2013, p. 235-258.
2. Mello SS, Menck CFM, Andrade LNS. Estratégias para o uso de RNAi em células de mamíferos in vitro. In: Introdução à Técnica de Interferência por RNA- RNAi. Editora SBG, 2013, Ribeirão Preto, Capítulo 9, pp 94-112.
3. Netto LES, Oliveira MA. Site-Directed Mutagenesis as a tool to characterize specificity in thiol based redox interactions between proteins and substrates In: Directed Mutagenesis.1, 2013, p. 12-. DOI 10.5772/54183
4. Oiticica J, Lezirovitz K, Batissoco AC. Etiologia da Deficiência Auditiva. In: Ricardo Ferreira Bento; Luiz Rodolpho Penna Lima Junior; Robinson Koji Tsuji; Maria Valéria Schmidt Goffi-Gomez; Danielle do Valle Silva Penna Lima; Rubens de Brito Neto (Org.). Tratado de Implante Coclear e Próteses Auditivas Implantáveis. 1ª ed. Rio de Janeiro: Thieme, 2014, v.1. p. 111-112. ISBN 978-85-67661-02-5.

5. Oiticica J, Lezirovitz K, Batissoco AC. Surdez Neonatal de Origem Genética. In: Ricardo Ferreira Bento; Luiz Rodolpho Penna Lima Junior; Robinson Koji Tsuji; Maria Valéria Schmidt Goffi-Gomez; Danielle do Valle Silva Penna Lima; Rubens de Brito Neto (Org.). Tratado de Implante Coclear e Próteses Auditivas Implantáveis. 1ª ed. Rio de Janeiro: Thieme, 2014, v.1. p. 113-133. ISBN 978-85-67661-02-5.
6. Otto PA, Mingroni-Netto RC, Otto PG. Genética Médica. São Paulo: Roca, 2013, 440pp.
7. Passos-Bueno MR, Brito LA, Kobayashi GS, Meira, JGC. A importância da genética na fissura labiopalatina. In: Coleção Tratado de Cirurgia Plástica. Vol. 5 - Cirurgia Craniomaxilofacial. Ed. Atheneu. Submetido em 2013.
8. Soltys DT, Schuch AP, Moraes MCS, Menck CFM. Instabilidade genômica, reparos de DNA e Cancer. In: Tratado de Oncologia. Editora Atheneu, 2013, São Paulo, Capítulo 16, pp 169-184.
9. Vianna-Morgante AM. X Frágil. In: Doenças Raras de A a Z. APMS e SBGM, São Paulo, 2013, p. 174-175.

c) Abstracts

National Meetings

1. Alves LU, Pardono E., Otto PA, Mingroni-Netto R. C.A novel c.1037C>G (p.Ala346Gly) mutation in TP63 as cause of EEC syndrome In: 60º Congresso Brasileiro de Genética, 2014, Guarujá.: Sociedade Brasileira de Genética, 2014. p.10 –
2. Alves LU, Thiele-Aguiar RS, Santos SC, Otto PA, Mingroni-Netto RC. Candidate Loci in chromosome 3 mapped for Santos Syndrome (OMIM613005) In: 59º Congresso Nacional de Genética, 16-19 de setembro, Águas de Lindóia, SP. 2013.
3. Auricchio MTBM, Stadulni ARP, Angrisani RG, Azevedo MF, Mesquita Neto O, Tabith-Jr A, Lewis DR, Mingroni-Netto RC. The importance of genetic studies in children with hearing loss ascertained after universal neonatal hearing screening In: 59º Congresso Nacional de Genética, 16-19 de setembro, Águas de Lindóia, SP. 2013.
4. Batissoco AC, Calizaya BJL, Henza CRML, Oiticica J, Mingroni-Netto RC, Bento RF. Otospheres obtained in vitro from mouse cochlea sensory epithelia express connexin 26. In: 12º Congresso da Fundação Otorrinolaringologia. 15-17 de agosto, Campos do Jordão, SP. 2013.
5. Batissoco AC, Lezirovitz K, Bissoli MM, Vasques LR, Zanatta D, Mingroni-Netto RC, Strauss BE, Haddad LA, Bento RF, Oiticica, J.HES-1 shRNA knocking down leads to expression of markers of supporting, hair and progenitor cells in mouse cochlea In: Advanced Topics in Genomics and Cell Biology, 2014, 4-6 de agosto. Campinas. Advanced Topics in Genomics and Cell Biology. , 2014.
6. Batissoco AC, Lezirovitz K, Bissoli MM, Zanatta D, Strauss BR, Vasques LR, Mingroni–Netto RC, Haddad LA, Bento RF, Oiticica J. Hes 1 and Coup-Tf1 shRNA knocking down give rise to new hair cells and supporting cells in organ of Corti organotypic culture. (Apresentação Oral). In: VI Congresso Iberoamericano de Implantes Cocleares e Ciências Afins – Gicca 2015, Centro de Convenções Rebouças, São Paulo –SP, 20 a 23 de maio de 2015.
7. Batissoco AC, Oiticica J, Lezirovitz K, Mingroni-Netto RC. Otospheres obtained in vitro from mouse cochlea sensory epithelia express connexin 26. In: Advanced Topics in Genomics and Cell Biology, 19-24 de maio, Campinas, SP. 2013.
8. Bernardino-Cruz D, Oiticica, Jeanne, Bittar RSM, Auricchio MTBM, Mingroni-Netto RC. Investigating Deafness genes as a cause of sudden sensorineural hearing loss In: 59º Congresso Nacional de Genética, 16-19 de setembro, Águas de Lindóia, SP. 2013.
9. Breyer CA, Kido LY, Santos MC, Netto LES, Oliveira MA. Investigating Physiological Oxidants Of Yeast Thiol-Specific Antioxidant Protein 1. In: XLII Annual Meeting of the Brazilian Society for Biochemistry and Molecular Biology (SBBq), Foz do Iguaçu, RS, 2013.
10. Capelo, L. VI BRADOO- Congresso brasileiro de densitometria, osteoporose e osteometabolismo.18-21 de abril de 2015. Periósteo: existe apenas um? Relevância do estudo do PO para a prática clínica.
11. Carnavalli JEP, Kimura L, Nunes K, Fernandes GR, Pereira AC, Mingroni-Netto R C. Association study of FTO gene with overweight and obesity in rural semi-isolated African-derived Brazilian populations In: 60º Congresso Brasileiro de Genética, 2014, Guarujá. Sociedade Brasileira de Genética, 2014. p.21 –

12. Cunha AF, Romanello KS, Lopes K, Oliveira MA, Netto LES, Malavazi I. Regulation of Peroxiredoxins Production Plays an Important Role in The Survival Of Erythroid Cells in Beta Thalassemia and Sickle Cell Disease Patients. In: XLII Annual Meeting of the Brazilian Society for Biochemistry and Molecular Biology (SBBq), Foz do Iguaçu, RS, 2013.
13. Fonseca, ACS; Antonini, S; Bonaldi, A; de Carvalho DR; Abe, KT; Bak, M; Tommerup, N; Vianna-Morgante, AM. Balanced chromosomal rearrangements, presumptively causing misregulation of genes near the breakpoints, define candidate regions for cis-regulatory elements of *IHH*, *FOXG1*, *GRIA3* and *SALL1* genes. In: 4ª Reunião Brasileira de Citogenética, 26-29 de maio, Atibaia, SP. 2015.
14. Gomes FB, Cunha TCF, Kok F, Macedo-Souza LI, Melo US, Santos SC. Estimating Of The Age Of The Spoan Syndrome Mutation Using Dmle+: Preliminary Analysis Indicate A 2625-Year-Old Mutation. In: 59º Congresso Nacional de Genética, 16-19 de setembro, Águas de Lindóia, SP. 2013.
15. Kimura L, Nunes K, Macedo-Souza LI, Auricchio MTBM, Mingroni-Netto RC. Inferring paternal history of rural African-derived Brazilian populations from Y chromosomes In: 59º Congresso Nacional de Genética, 16-19 de setembro, Águas de Lindóia, SP. 2013.
16. Kimura L, Pereira AC, Kubisch C, Mingroni-Netto RC. A putative novel locus associated with essential hypertension mapped through a genome-wide scan in a large pedigree from African-derived Brazilian population In: 60º Congresso Brasileiro de Genética, 2014, Guarujá. Sociedade Brasileira de Genética, 2014. p.15 -
17. Leme JMM, Netto LES, Barros MH, Demasi M. Analysis Of The Glutathiolated Cysteine Residues In The -Subunit Of 20s Proteasome From The Saccharomyces Cerevisiae. In: XLII Annual Meeting of the Brazilian Society for Biochemistry and Molecular Biology (SBBq), Foz do Iguaçu, RS, 2013.
18. Lemes RB, Nunes K, Meyer D, Mingroni-Netto RC, Otto P. A.Dealing with heterogeneity issues in the estimation of inbreeding and substructure levels in small samples In: 60º Congresso Brasileiro de Genética, 2014, Guarujá. Sociedade Brasileira de Genética, 2014. p.19 -
19. Lemes RB, Nunes K, Mingroni-Netto RC, Meye, D, Otto PA. Estimation of population genetic parameters in human isolates from Vale do Ribeira, São Paulo ('quilombo populations') In: 59º Congresso Nacional de Genética, 16-19 de setembro, Águas de Lindóia, SP. 2013.
20. Lopes K, Romanello KS, Bezerra MAC, Araujo AS, Oliveira MA, Netto LES, Malavazi I, Cunha AF. Analysis of Peroxiredoxins in Patients with Glucose-6-Phosphate Dehydrogenase Deficiency and Hemoglobin Sc Disease. In: XLII Annual Meeting of the Brazilian Society for Biochemistry and Molecular Biology (SBBq), 2013, Foz do Iguaçu.
21. Martins ALB, Nascimento PP, Ribeiro CM, Moreira DP, Lourenco NCV, Giunco CT, Rosan DBA, Passos-Bueno MR, Conte ACF. Análise de variação no número de cópias (CNVs) da região 15q11-13 em Transtornos do Espectro Autístico no Brasil. In: XXV Congresso Brasileiro de Genética Médica, 11-15 de junho, Florianópolis, SC. 2013.
22. Meira JGC, Brito LA, Kobayashi GS, Yamamoto GL, Ferreira SG, Alvizi L, Morales AG, Fernandes CB, Franco D, Alonso N, Passos-Bueno MR. Identificação e avaliação do impacto fenotípico de variantes raras no IRF6 em famílias com fissuras orais não sindrômicas. In: XXVI Congresso Brasileiro de Genética Médica. 13-16 de maio, Fortaleza, CE. 2014 (Aceito).
23. Moreno, NC, Garcia, CCM and Menck, CF. UVA induced DNA damage responses in Xeroderma Pigmentosum patients cells, 60° Congresso Brasileiro de Genética, de 26 a 29 de agosto de 2014, Guarujá, SP. (Award Graduation Poster for Mutagenesis).
24. Oiticica J, Bernardino-Cruz D, Cavalcante LTC, Auricchio MTBM, Mingroni-Netto RC, Bittar RSM.Investigating Deafness genes as a cause of sudden sensorineural hearing loss In: 12º Congresso da Fundação Otorrinolaringologia. 15-17 de agosto, Campos do Jordão, SP. 2013.
25. Pretell-Bocangel MA, Mingroni-Netto RC, Otto, PA. Novel mutations of PAX3, MITF and SOX10 genes found in Waardenburg syndrome Types 1 and 2 in Brazilian patients In: 59º Congresso Nacional de Genética, 16-19 de setembro, Águas de Lindóia, SP. 2013.
26. Santos A, Campagnari F, Câmara MLRC, Brasil RCEA, Krepischi ACV, Rosenberg C. Genetic Testing For Idiopathic Intellectual Disability: Use Of Dna Extracted From Saliva For Snp Genotyping. 60º Congresso Brasileiro De Genética. 26-29 de agosto, Guarujá, SP, 2014
27. Santos MC, Tairum-Jr CA, Breyer CA, Bagini RH, Netto LES, Oliveira MA. Effects of Yeast Tsa1p Thr44 Substitution Over Hydroperoxide Reactivity And Cysr Pka. In: XLII Annual Meeting of the Brazilian Society for Biochemistry and Molecular Biology (SBBq), Foz do Iguaçu, RS, 2013.

28. Schultz L, Genu V, Breyer CA, Santos VF, Netto LES, Oliveira MA. Structural and Functional Characterization of Yeast Ahp1 Peroxiredoxin: Insights in Electron Transfer. In: XLII Annual Meeting of the Brazilian Society for Biochemistry and Molecular Biology (SBBq), Foz do Iguaçu, RS, 2013.
29. Souza TACB, Moraes MAB, Giuseppe PO, Honorato RV, Oliveira PSL, Oliveira MA, Netto LES, Murakami MT. Enzymatic Ros-Scavenging System Is Regulated By Calcium in Trypanosomatids via Tryparedoxin Peroxidases. In: XLII Annual Meeting of the Brazilian Society for Biochemistry and Molecular Biology (SBBq), Foz do Iguaçu, RS, 2013.
30. Tairum-Jr CA, Netto LES, Oliveira MA. Investigation of Tsa1 D141n Substitution Over Trx Interaction and Tsa1 Over-Oxidation Process. In: XLII Annual Meeting of the Brazilian Society for Biochemistry and Molecular Biology (SBBq), Foz do Iguaçu, RS, 2013.

International Meetings

1. Almeida CF, Martins PCM, Onofre-Oliveira P, Vainzof M. Global gene expression profile in different forms of murine muscular dystrophies. 19th International Congress of the Word Muscle Society, Berlin, Alemanha, 7-11 outubro de 2014. Neurom Disord 24:791-928004, 2014
2. Almeida CF, Onofre-Oliveira PCG, Zatz M, Negrao L, Vainzof M. Why LGMD2G is rare? In: 18th International Congress of the World Muscle Society, 1-5 de outubro, Asilomar, EUA, 2013.
3. Almeida T, Valente M, Yamamoto GL, Kim CA, Passos-Bueno MR, Bertola DR. Further evidence of brain anomalies related to ALX4 mutations: possible genotype-phenotype correlation In: 63rd Annual Meeting of the American Society of Human Genetics. 22-26 de outubro, Boston, EUA, 2013.
4. Alves LU, Santos S, Thiele-Aguiar R, Otto PA, Mingroni-Netto RC. Santos syndrome is caused by homozygous mutation in WNT7A In: 64th Annual Meeting of the American Society of Human Genetics, San Diego, EUA, 2014.
5. Alvizi L, Kobayashi GS, Silva CBF, Sunaga DY, Bueno DF, Passos-Bueno MR. DNA differential methylation is observed at BRCA1 promoter but not in 8q24.21 in cleft lip and palate. In: 63rd Annual Meeting of the American Society of Human Genetics. 22-26 de outubro, Boston, EUA, 2013.
6. Alvizi, L., Kobayashi, G. S. , Rodrigues, T. , Passos-Bueno, M.R. “Methylome analysis in Cleft Lip and Palate samples reveals impairment in WNT pathway genes” no “Epigenetics & Chromatin Meeting” realizado na Cold Spring Harbor Laboratory (USA), set-2014,
7. Anschau V, Bannitz-Fernandes R, Oliveira MA, Netto LES. Characterization and Kinetic of Reduction of 1-Cys Peroxiredoxin from Aspergillus fumigatus by Ascorbate In: SFRBM's 20th Annual Meeting, 20-24 de novembro, San Antonio, EUA, 2013.
8. Assoni A, Beccari M, Mitne-Neto M, Carvalho V, Zatz M Characterization Of Mesenchymal Stem Cells Secretome From Various Tissues.. In: International Society of Stem Cell Reseach, 24-27 de junho, Estocolmo, Suécia, 2015.
9. Assoni AF. Substance P: a chemotactic factor to attract stem-cells to the dystrophic muscle In: 11th Meeting of the International Society for Stem Cell Research, 12-15 de junho, Boston, EUA, 2013.
10. Bannitz-Fernandes R, Tairum-Jr CA, Oliveira MA, Malavazi I, Netto LES. Functional and structural characterization if peroxiredoxin from the human opportunistic pathigen Aspergillus fumigates. In: VIII International Congress of the Society for Free Radical Biology and Medicine, 14-17 de outubro, Buenos Aires, Argentina, 2013.
11. Beccari M, Mitne-Neto M, Melechco Carvalho V, Venturini G, Zatz M. Evaluation of a Protein Marker for Amyotrophic Lateral Sclerosis. 62nd ASMS Conference on Mass Spectrometry and Allied Topics. *American Society for Mass Spectrometry,* June 15-19th, 2014. Baltimore Convention Center.
12. Bertola D. Osteoporosis-pseudoglioma syndrome: a novel mutation in the fourth beta-propeller domain of LRP5 associated with prominent short metacarpals and metatarsals. 28º Congresso de Displasias Esqueléticas, 28-31 de agosto, Bologna, Itália, 2013.
13. Bonaldi A, Foneca ACS, Bertola DR, Vianna-Morgante AM. Co-occurrence of 4p16.3 microdeletion and 11p15 microduplication in a boy carrying a der(4)t(4;11)(p16.3;p15.4)mat. In: European Human Genetics Conference, 8-11 de junho, Paris, França, 2013.
14. Bonaldi A, Fonseca ACS, Bertola DR, Kim CA, Otto PA, Vianna-Morgante, AM. Submicroscopic chromosomal imbalances in patients with intrauterine growth retardation and features of Silver-Russell syndrome. In: 64th Annual Meeting of the American Society of Human Genetics, 18-22 de outubro, San Diego, EUA, 2014.

15. Bonaldi A, Vasques L, Kashiwabara AY, Araujo ESSA, Paschoal AR, Andosia M, Villela D, Claudia K, Suemoto CK, Pasqualucci CA, Grinberg LT, Rosenberg C, Vianna-Morgante AM, Dirce Carraro D, Krepischi AC. Mining novel candidate imprinted genes or monoallelic expressed genes in multiple human tissues using high resolution DNA methylation microarrays In: In: European Human Genetics Conference 2015, 6-9 de junho, Glasgow, Reino Unido, 2015.
16. Bonilla X, Makrythanasis P, Santoni FA, Pellet A, Rall K, Eisenbeis S, Guipponi M, Gherig C, Rosenberg C, Lyonnet S, Antonarakis SE. Exploring somatic mosaicism in uterovaginal aplasia. 64th Congresso da American Society of Human Genetics,18-22 de outubro, San Diego, EUA, 2014.
17. Breyer CA, Kido LY, Santos MC, Netto LES, Oliveira MA. Insights of yeasttypical 2-Cys peroxiredoxin overoxidation by organic hydroperoxides. In: VIII International Congress of the Society for Free Radical Biology and Medicine, 14-17 de outubro, Buenos Aires, Argentina, 2013.
18.Brito LA, Malcher C, Yamamoto G, Ferreira S, Aguena M, Naslavsky M, Zatz M, Passos-Bueno-MR. RARE VARIANTS IN E-CADHERIN GENE UNDERLYING FAMILIAL CASES OF NONSYNDROMIC CLEFT LIP AND/OR PALATE Genomics of Common Diseases 2014 (Wellcome Trust Conference), Potomac, MA, USA.
19. Brito LA, Yamamoto G, Aguena M, Passos-Bueno MR. Implication of CDH1 in two familial cases of non syndromic cleft lip with or without cleft palate. In: 63rd Annual Meeting of the American Society of Human Genetics. 22-26 de outubro, Boston, EUA, 2013.
20. Campagnari F, Santos A dos, Pearson PL, Costa SS, Rosenberg C. Diagnostic Efficiency of intellectual disability etiology by a combination of SNP arrays and targeted gene sequencing. 2nd International Gencody Conference, 27-29 de abril, Creta, Grécia, 2015.
21. Coatti GC1; Frangini M.1; Gomes JPA1;Valadares M1; Pelatti, M1; Assoni, AF1; De Lima ACP2 and Zatz M1human Adipose Derived Pericytes Increase Survival In An Als Sod1 Mouse Model But Only In Affected Males. In: International Society of Stem Cell Reseach, 24-27 de junho, Estocolmo, Suécia, 2015.
22. Cortez BA, Okamoto OK. Hippo pathway in human medulloblastoma cancer stem cells. In: Keystone Symposia Conference: The Hippo Pathway: Signaling, Development and Disease, 17-21 de maio, Taos, Novo México, 2015.
23. Costa S, Krepischi A, Rosenberg C. Does increase in genomic microarray resolution result in increased diagnostic yield? 64th Congresso da American Society of Human Genetics,18-22 de outubro, San Diego, EUA, 2014.
24.Cuperman T, Alcântara S, Canovas M, Yamamoto LU, Pavanello RCM, Zatz M, Oliveira ASB, Vainzof M. Association of two mutations in the RYR1 gene in Central Core Disease: Recessive or modifying effect? In: 18th International Congress of the World Muscle Society, 1-5 de outubro, Asilomar, EUA, 2013.
25.Cuperman T, Alcântara S, Lourenço NCV, Yamamoto LU, Pavanello RCM, Silva HC, Gurgel-Gianneti J, Zatz M, Oliveira ASB, Vainzof M. Central core disease (CCD): improving the screening for mutations in the RYR1 gene. In: 18th International Congress of the World Muscle Society, 1-5 de outubro, Asilomar, EUA, 2013.
26.D'Angelo CS, Santos MFM, Kim CAE, Lourenço CM, Koiffmann CP. Molecular Diagnosis of Deletions and Duplications Associated with Intellectual Disability and Obesity. In: 63rd Annual Meeting of the American Society of Human Genetics. 22-26 de outubro, Boston, EUA, 2013.
27. Dos Santos MI, Yeda FP, Tsuruta LR, Horta BB, Inocêncio AL, Okamoto OK, Tuma, MC, Moro AM. Strategies for clone detection, selection and isolation in Per.C6 cells - Case for Rebmab100. In: 23rd ESACT Meeting - European Society for Animal Cell Technology, 23-26 de junho, Lille, França, 2013.
28. Fanganiello R, Ishiy FAA, Yumi D, Capelo LP, Passos-Bueno MR. Differentially expressed genes associated to higher osteogenic potential of human mesenchymal stem cells. In: 11th Meeting of the International Society for Stem Cell Research, 12-15 de junho, Boston, EUA, 2013.
29. Figueiredo T, Souto U, Pessoa A, Ribeiro P, Brandão A, Zatz M, Kok F, Santos S. Prospecting genetic disorders in a highly inbred region of Brazil: two novel genes for AR intellectual deficiency.In: The American Society of Human Genetics, 18-22 de outubro, San Diego, EUA, 2014.
30. Fonseca ACS, Bonaldi A, Bak AM, Abe KT, Vianna-Morgante AM, Tommerup N. Mate-pair sequencing analysis of karyotypically balanced chromosomal rearrangements associated with cryptic imbalances reveals additional structural variants and complex genomic reorganization typical of chromothripsis or replication mechanisms. In:The American Society of Human Genetics 2014 Annual Meeting, October 18-22, San Diego, USA, 2014.
31. Fonseca ACS, Antonini S, Bonaldi A, Abe KT, Bak M, Tommerup N, Vianna-Morgante AM. Investigating clinical impact and mechanism of formation of karyotypically balanced chromosomal

rearrangements: the power of combining breakpoint mapping by mate-pair sequencing and copy number analysis by aCGH. In: European Human Genetics Conference 2015, June 6 - 9, Glasgow, UK, 2015.
32. Fonseca ACS, Antonini S, Bonaldi A, Mehrjouy M, Bak M, Tommerup N, Vianna-Morgante AM. Signature of germline chromothripsis in a 20-break complex rearrangement associated with deletions at 7q33-q35/11p13 and *CNTNAP2* gene disruption**.** In: European Human Genetics Conference 2014, May 31 - June 3, Milan, Italy, 2014.
33. Fonseca ACS, Bonaldi A, Vianna-Morgante AM. Deletions at 18q21.1-q21.2 associated with an apparently balanced translocation t(6;18)(q13;q22.3) in a patient with developmental delay, corpus callosum agenesis and craniofacial dysmorphisms. In: European Human Genetics Conference, 8-11 de junho, Paris, França, 2013.
34.Forbes J, Genesini T, Riolfi C, et al. Psychoanalysis impact to facioscapulohumeral (FSHD) patients. In: 18th International Congress of the World Muscle Society, 1-5 de outubro, Asilomar, EUA, 2013.
35. Forbes J, Riolfi C, Viann MG, Pavanello RCM, Igreja SG, Genesini T, Zatz M. Incidental findings in next generation dna sequencing: people´ s opinion about the effects of their knowledge. In: The American Society of Human Genetics, 18-22 de outubro, San Diego, EUA, 2014
36. Furukawa G, Rodini CO, Silva PBG, Okamoto, OK. Differential Expression Of Specific Oct4 Transcripts In Brain Tumors. In: 12th Annual Meeting - International Society for Stem Cell Research, 18-21 de junho, Vancouver, Canadá, 2014.
37. Gimenez M, Verissimo-Filho S, Rosa JC, Netto LES, Lopes, LR. A Mixed Intermolecular Disulfide Bond is Generated between Reduced Protein Disulfide Isomerase and Oxidized NADPH Oxidase Regulatory Subunit p47phox. In: SFRBM's 20th Annual Meeting, 20-24 de novembro, San Antonio, EUA, 2013.
38. Gomes JPA. Comparison Between In Vitro Differentiations Of Adipose Derived Mesenchymal Stromal Cells From Two Different Sources: Outer Thigh And Abdomen. In: 11th Meeting of the International Society for Stem Cell Research, 12-15 de junho, Boston, EUA, 2013.
39. Gomes, JPA; Valadares, MC; Coatti, GC; Assoni, AF; Pelatti, M; Secco, M; Vieira, NM; Zatz, M Comparison between therapeutic potential of human adipose derived pericytes and stromal cells in a murine muscular dystrophy model. In: International Society of Stem Cell Reseach, 24-27 de junho, Estocolmo, Suécia, 2015.
40. Griesi-Oliveira K. Analysis of actin cytoskeleton dynamics in stem cells from autistic patients: a preliminary study. In: 11th Meeting of the International Society for Stem Cell Research, 12-15 de junho, Boston, EUA, 2013.
41.Griesi-Oliveira, Karina ; Suzuki, A.M. ; Sertie, A.L. ; Sunaga, D.Y. ; Passos-Bueno, Maria Rita . Analysis of actin cytoskeleton dynamics in stem cells from autistic patients. Annual meeting american society of human genetics - 2014.
42.Ishiy, FAA; Fanganiello, RD; Capelo, LP; Kuriki, PS; Morales, AG; Passos-Bueno, Mr. CD105 expression as a marker to explain osteogenic potential differences of mesenchymal stem cells of different sources. 12th international society of stem cell research. 2014. Vancouver, Canada. Poster Presentation.
43. Jazedje T, Pellati M, Ribeiro A, Zatz M Cytokines Release By Human And Murine Mesenchymal Stem Cells From Different Sources When Co-Cultured With Murine Adenocarcinoma Cells.. In: International Society of Stem Cell Reseach, 24-27 de junho, Estocolmo, Suécia, 2015.
44. Jazedje T, Ribeiro AL, Pelatti MV, Siqueira BH, Nagata GS, Treiveiler M, Rodrigues EG, Zatz M. Mesenchymal stromal cells from different sources may lead to different therapeutic results against 4T1 murine breast câncer. 12th Annual Meeting of the ISSCR, June 2014, Vancouver, Canada, pag. 165
45. Jazedje T. Human mesenchymal stromal cells may lead to opposite therapeutic results against 4T1 murine breast tumor model in different. In: 11th Meeting of the International Society for Stem Cell Research, 12-15 de junho, Boston, EUA, 2013.
46. Kaid C, Silva PBG, Rodini CO, Kuriki OS, Okamoto, O.K . Identification Of Mirna Involved In Medulloblastoma Aggressiveness. In: 12th Annual Meeting - International Society for Stem Cell Research, 18-21 de junho, Vancouver, Canadá, 2014.
47. Kobayashi GS, Alvizi L, Almada BVP, Andrade-Lima LC, Menck CF, Passos-Bueno MR. A role for IRF6 in cell cycle regulation and DNA damage response in mesenchymal stem cells. In: 63rd Annual Meeting of the American Society of Human Genetics. 22-26 de outubro, Boston, EUA, 2013.
48. Ligeiro de Oliveira AP, Silva V, Neves V et al. Effect of low level laser and Mesenchymal Stem Cells therapies on cigarette-induced lung inflammation in mice. In: 100th Annual Meeting of the American Association of Immunologists, 3-7 de maio, Honolulu, EUA, 2013.

49.Martins-Bach AB, Malheiros J, Machado PCM, Almeida CF, Sousa PL, Tannús A, Carlier PG, Vainzof M. NMR imaging comparison of dystrophic mouse models: mdx, Large, mdx/Large. In: 18th International Congress of the World Muscle Society, 1-5 outubro, Asilomar, EUA, 2013.
50. Meira JGC, Brito LA, Morales AG, Ferreira SG, Fernandes CB, Alonso N, Franco D, Passos-Bueno MR. Molecular analysis of patients affected by orofacial clefts to establish criteria for IRF6 mutational screening. In: IX Course of the Latin American School of Human and Medical Genetics. 5-11 de maio, Caxias do Sul, RS, Brasil, 2013.
51. Meireles DA, Alves SV, Alegria TGP, Netto LES. A 14.7 KDa Protein from Francisella tularensis subsp. novicida (named FTN_1133) is Involved in the Response to Oxidative Stress Induced by Organic Peroxides but It Is Not Endowed with Thiol Peroxidase Activity. In: SFRBM's 20th Annual Meeting, 20-24 de novembro, San Antonio, EUA, 2013.
52. Menck, CF, Rocha CRR. Mechanisms of resistance of glioma cells to chemotherapy, 20th International Charles Heidelberger Symposium on Cancer Research, Instituto de Alta Investigación, Universidade de Tarapaca, 08-11 de outubro, Arica, Chile, 2014.
53. Metairon S, Zamboni CB, Suzuki MF, Rizzutto MA, Bueno Jr CR, Andrade TO, Landini V, Cangussu EB, Caetano HVA, Zatz M. Determination of Ca and Fe in blood of grmd dog submited to a systemic transplantation of stromal cells (hascs) using naa and frx techniques. Global Biotechnology Congress (GBC), Boston, June 2014
54. Metairon S, Zamboni CB, Suzuki MF, Rizzutto MA, Bueno Jr CR, Andrade TO, Landini V, Cangussu EB, Caetano HVA, Zatz M. Determination of inorganic elements in biological tissues of dystrophic mice strains using naa. New Directions in Biology and Disease of Skeletal Muscle Conference. Chicago, June-July, 2014.
55. Metairon S, Zamboni CE, Suzuki MF, Andrade TO, Cangussu EB, Bueno CE, Caetano HVA, Zatz M. Investigation of Ca and Mg in blood of dystrophic animal model using NAA. In: X Latin American Symposium on Nuclear Physics and applications, 1-6 de dezembro, Montevideo, Uruguay, 2013
56. Metairon S, Zamboni CE, Suzuki MF, Andrade TO, Cangussu EB, Bueno CE, Caetano HVA, Zatz M. Investigation of Ca and Mg in blood of dystrophic animal model using NAA. X Latin American Symposium on Nuclear Physics and applications, Montevideo, Uruguay, December 1-6
57. Mingroni-Netto RC, Dantas VGL, Freitas EL, Moraes AMM, Braga MCC, Ramos SB, Rosenberg C, Della-Rosa VA. Duplication of EYA1 causes branchiootic syndrome in a Brazilian family In: 63rd Annual Meeting of the American Society of Human Genetics. 22-26 de outubro, Boston, EUA, 2013.
58. Moraes MVD, Barbirato C, Almeida MG, Belcavello L, Reboucas MRGO, Sipolatti V, Nunes VRR, Akel ANJ, Zatz M, Paula F. Identification of novel COL1A1 gene mutations in Brazilian patients with Osteogenesis Imperfecta. In: European Human Genetics Conference, 8-11 de junho, Paris, França, 2013.
59. Munford V, Menck CF. Dissecting Mutations that lead to Xeroderma Pigmentosum in a Tropical and Sunny Country. In: 16th International Congresso n Photobiology,7-12 de setembro, Córdoba, Argentina, 2014.
60. Nieves-Alvarez C, Portillo-Lodesma S, Netto LES, Ferrer-Sueta G. Influence of conserved residues in the catalysis by Tsa1. In: VIII International Congress of the Society for Free Radical Biology and Medicine, 14-17 de outubro, Buenos Aires, Argentina, 2013.
61. Nigro V, Naslavsky MS, Vieira NM, Kok F, Vainzof M, Pavanello RC, Kunkel LM , Tupler R, Zatz M Limb-girdle muscular dystrophy 1G: How frequent are mutations in this gene? In: The American Society of Human Genetics, 18-22 de outubro, San Diego, EUA, 2014
62. Nunes, K; Kimura L; Carnavalli JP; Mingroni-Netto, RC; Weir, B; Meyer D. Excess Of African Ancestry In The Mhc Region Of A Rural Brazilian Admixed Population. 2015 On The Biology Of Genomes. Cold Spring Harbor Laboratory, EUA. 2015
63. Nunes, K; Torres, MA; Piovezan, BZ; Pontes, GN; Kimura, L; Carnavalli, JEP; Mingroni-Netto, RC; Meyer, D; Moraes ME. A New HLA-C*02 Null Allele Described In Quilombo Remnants Samples From Southern Brazil. Annual Meeting of the American Society for Histocompatibility and Immunogenetics. Savanna, EUA. 2015 (accepted, to be presented).
64. Oliveira MA, Tairum-Jr CA, Netto LES. Reduction of disulfides in peroxiredoxins: a neglected step with possible relevant consequences in signaling and cell biology. In: VIII International Congress of the Society for Free Radical Biology and Medicine, 14-17 de outubro, Buenos Aires, Argentina, 2013.

65. Onofre-Oliveira P, Martins P, Lanzotti A, Calyjur P, Vainzof M. Gene expression profile of Satellite cells from Largemyd and Lama2dy2j/J. 19th International Congress of the Word Muscle Society, Berlin, Alemanha, 7-11 outubro de 2014. Neurom Disord 24:880, 2014
66. Onofre-Oliveira P, Martins P, Lanzotti A, Calyjur P, Vainzof M. Satellite cells from Largemyd and Lama2dy2j/J: Are they different in their myogenic potential? In: 13th International Congress on Neuromuscular Diseases, 5-10 de julho, Nice, França, 2014.
67. Pelatti MV, Gomes J, Perin P, Czeresnia C, Rodrigues E, Zatz M, Jazedje T. Identification of inflmatory cYtokines released by human tube mesenchymal stromal cells. 12th Annual Meeting of the ISSCR, June 2014, Vancouver, Canada, pag. 508
68. Pellati MV. Human Tube Mesenchymal Stromal Cells As Feeder-Layers For Human Embryonic Stem Cells. In: 11th Meeting of the International Society for Stem Cell Research, 12-15 de junho, Boston, EUA, 2013.
69. Pereira MCL, Secco M, Rodini CO, Torres LB, Araujo AG, Cavalheiro EA, Zatz M, Okamoto OK. Single injection of mesenchymal stem cells provides long term protection against dopaminergic neurodegeneration in an experimental model of Parkinson s disease. In: 11th Meeting of the International Society for Stem Cell Research, 12-15 de junho, Boston, EUA, 2013.
70. Pereira, Marcia C. L. ; SECCO, M. ; Rodini, Carolina O. ; Torres, Layla B. ; Araujo, A.G. ; Cavalheiro, E.A. ; Zatz, Mayana ; Oswaldo K. Okamoto . Single injection of mesenchymal stem cells provides long term protection against dopaminergic neurodegeneration in an experimental model of Parkinson s disease.. In: 11th meeting of the International Society for Stem Cell Research, 2013, Boston. Abstract compilation, 2013.
71. Quinet A,Menck CF. Unraveling the pathways by which 6-4PP or CPD are bypassed in the human genome, Gordon Research Conference on Mammalian DNA Repair, 8-13 de fevereiro, Ventura, Califórnia, EUA, 2015.
72. Rasmussen MB, Schlechter CL, Mehrjouy MM, Bache I, Lind-Thomsen A, Silahtaroglu A, Hansen C, Kjaergaard S, Brøndum-Nielsen K, Jensen PKA, Fagerberg C, Krogh LN, Hansen J, Fonseca ACS, Vianna-Morgante AM, Abe KT, Halgren C, Bak M, Jacky P, Tommerup N. Saturation of the Human Genome with Chromosomal Breakpoints - 43rd Biannual American Cytogenetics Conference, 4-7 de maio, Asheville, Carolina do Norte, EUA, 2014.
73. Ribeiro CM, Martins ALB, Takahashi VNVO, Moreira DP, Griesi-Oliveira K, Rosenberg C, Vasdaz E, Passos-Bueno MR. Glutamatergic Pathway and Axonal Guidance Signaling Genes As Candidate for ASD Etiology. In: International Meeting for Autism Research, 2013, 2-4 de maio, Donostia/San Sebastián, Espanha, 2013.
74. Ribeiro CM, Moreira ES, Martins ALB, Morales AG, Ferreira SG, Takahashi VN, Moreira DP, Griesi-Oliveira K, Conte ACF, Rosenberg C, Vadasz E, Passos-Bueno MR. Use of a custom-designed array-CGH to identify small CNVs in nonsyndromic autism spectrum disorders In: 63rd Annual Meeting of the American Society of Human Genetics. 22-26 de outubro, Boston, EUA, 2013.
75. Rodini CO, Silva PBG, Okamoto OK. Mesenchymal Stem Cell-Mediated Enhancement Of Glioblastoma Cell Proliferation. In: 12th Annual Meeting - International Society for Stem Cell Research, 18-21 de junho, Vancouver, Canadá, 2014.
76. Rodini, CO, Silva PBG, Okamoto OK. Mesenchymal Stem Cells Enhance Glioblastoma Cell Aggressiveness And Tumorigenesis. In: The EMBO/EMBL Symposium: Frontiers in Stem Cells & Cancer, 29-31 de março, Heidelberg, Alemanha. 2015.
77. Romanell K, Lopes K, Bezerra MAC, Hatzhofer BLD, Domingos IF, Araujo AS, Oliveira MA, Netto LES, Costa FF, Malavazi I, Cunha A. FPRDX1, PRDX2 and PRDX6 are differentially expressed in sickle cell and beta thalassemia patients and could be involved in the severity. In: VIII International Congress of the Society for Free Radical Biology and Medicine, 14-17 de outubro, Buenos Aires, Argentina, 2013.
78.Romanelli Tavares, Vanessa Luiza ; Gordon C.T. ; Zechi-Ceide, Roseli Maria ; Kokitsu-Nakata, Nancy Mizue ; Voisin, N. ; Tan, T. Y. ; Heggie, A. A. ; Vendramini-Pittoli, Siulan ; Propst, E. J. ; Papsin, B. C. ; Torres, T. T. ; Buermans, H. ; Capelo, L. P. ; den Dunnen, J. T. ; Guion-Almeida, Maria Leine ; Lyonnet, S. ; Amiel, J. ; Passos-Bueno, M. R. . Novel mutations in GNAI3 associated with Auriculocondylar Syndrome strengthen a common dominant negative effect. In: American Society of Human Genetics, 2014, San Diego - CA. American Society of Human Genetics, 2014.
79. Rueda AV, de Souza RR, Kobayashi GS, Camarini R. Ethanol-Induced Behavioral Sensitization Is Blocked By Environmental Enrichment: Effects On Micro-RNAs Targeting BDNF. In: First Joint Meeting on Alcohol and other Drugs of Abuse. 16-19 de outubro, Concepción, Chile, 2013.

80. Santos MCT, Silva PBG, Pohl F, Penalva LO, Okamoto OK. LIN28 interacts with specific OCT4 transcript variants in medulloblastoma cells. In: 11th Meeting of the International Society for Stem Cell Research, 12-15de junho, Boston, EUA, 2013.
81. Sarges KS, Franco EC, Pereira WLA, Silva LEC, Torres LB, Araujo BHS. Cabral FR. Cebus Apella: A New Model For The Study Of Parkinson´ S Disease Histopathological Changes Induced In Substantia Nigra By Mptp. 2013.
82. Secco M. Beneficial effect of systemic delivery of human mesenchymal stromal cells combined with growth factors in dystrophic mice. In: 11th Meeting of the International Society for Stem Cell Research, 12-15 de junho, Boston, EUA, 2013.
83. Sertie A, C. O. F. Machado1,K. GriesiOliveira2,C. Rosenberg2, F. Kok2,3, S. Martins1, M. R. Passos Bueno An emerging role for the RhoGEF Collybistin in neuropathological mTORC1mediated protein translation. In: 64th Congresso da American Society of Human Genetics,18-22 de outubro, San Diego, EUA, 2014.
84. Silva KSM, Cabral FR, Silva WB, Torres LB, Araujo BHS. Haematological Evaluation Of A New Model Of Parkinson Disease (Sapajus Apella). 2015.
85. Silva PBG, Rodini CO, Kaid C, Furukawa G, Okamoto OK. Dose Dependent Effect Of Oct4a On Brain Tumor Agressiveness. . In: 12th Annual Meeting - International Society for Stem Cell Research, 18-21 de junho, Vancouver, Canadá, 2014.
86. Silva PBG, Rodini CO, Kaid C, Pereira MCL, Okamoto OK. Oct4a Enhances Invasive Growth And Metastasis Of Medulloblastoma Cells In: The EMBO/EMBL Symposium: Frontiers in Stem Cells & Cancer, 29-31 de março, Heidelberg, Alemanha. 2015.
87. Silva PBG, Santos MCT, Cruz DSG, Oliveira KG, Okamoto OK. OCT4A isoform enhances agressiveness of medulloblastoma cells. In: 11th Meeting of the International Society for Stem Cell Research, 12-15 de junho, Boston, EUA, 2013.
88.Silva, Isabela M. W. ; Moreira, Eloisa S.; Lourenço, Naila; Moreira, Danielle P.; Ribeiro, Cintia M.; Martins, Ana Luiza B.; Griesi-Oliveira, Karina; Lazar, Monize; Costa, Silvia S. ; Rocha, Kátia M.; Aguena, Meire; Fett-Conde, Agnes C; Rosenberg, Carla ; Bertola, Débora R.; Vadasz, Estevão; Passos-Bueno, Maria Rita. Contribution of Small Copy Number Variations (CNVs) to Autism Spectrum Disorder (ASD) - International Meeting for Autism Research (IMFAR, 13-16 de Maio).
89. Silva, KS, Franco EC, Silva LEC, Oliveira E, Souza M, Imbeloni A. Tobelem A, Torres LB, Araujo BHS, Cabral FR. Clinical Evaluation Of A New Model Of Pd (Sapajus Apella) Treated With Mesenchymal Stem Cells. 2015.
90. Souza JS, Ferreira DR, Torres LB, Araujo BHS, Carromeu C, Maciel RMB, Muotri A, Giannocco G. Evaluation Of Th Transporters During Differentiation Of Induced Pluripotent Stem Cell Until Neuronal Cell Of Rett Syndrome And Control Patients. 2015.
91. Souza JS, Torres LB, Araujo BHS,; Carromeu C, Cugola F, Muotri A, Maciel RMB, Giannocco G. Characterization Of Thyroid Hormone (Th) Action In Human Induced Pluripotent Stem Cell (Ipsc) Until Neuron Differentiation. 2014.
92. Suzuki DE, Nakahata AM, Okamoto OK. E2F2 silencing inhibits expression of oncogenes and suppresses proliferative capacity of human embryonic stem cells. In: 11th Meeting of the International Society for Stem Cell Research, 12-15 de junho, Boston, EUA, 2013.
93. Tairum-Jr CA, Santos MC, Breyer CA, Bagini RH, Netto LES, Oliveira MA. Thr, member of the catalytic triad of Peroxiredoxins, is involved Tsa1 reduction by thioredoxin and reactive cysteine overoxidation. In: VIII International Congress of the Society for Free Radical Biology and Medicine, 14-17 de outubro, Buenos Aires, Argentina, 2013.
94. Tommerup N, Jacky P, Bache I, Lind-Thomsen A, Rasmussen MB, Mehrjouy MM, HansenC, Fonseca ACS, Vianna-Morgante AM, Abe KT, Christina Halgren C, Bak M & The International Breakpoint Mapping Consortium - Saturation of the human genome with chromosomal breakpoints. In:The European Human Genetics Conference, 31 de maio a 3 de junho, 2014, Milão, Itália, 2014.
95.Vainzof M, Calyjur P, Otaduy MCG, Almeida CF, Martins-Bach A, Carlier RY, Gurgel-Giannetti J, Amaro Jr E, Carlier PG Muscle NMR imaging helping to define the pathogenicity of a new mutation in the DNM2 gene in a centronuclear myopathy patient. In: 18th International Congress of the World Muscle Society, 1-5 de outubro, Asilomar, EUA, 2013.
96.Vainzof M, Lazar M, Yamamoto GL, Almeida CF, Onofre-Oliveira P, Nogueira L, Yamamoto LU, Zatz M, Pavanello RCM, Silva HCM. X-linked myopathy with excessive autophagy (XMEA): NGS identifies a

new in/del in the critic splicing region of the VMA21 gene. In: 13th International Congress on Neuromuscular Diseases, 5-10 de julho, Nice, França, 2014.
97. Vainzof M, Lazar M, Yamamoto GL, Almeida CF, Onofre-Oliveira P, Nogueira L, Yamamoto LU, Zatz M, Pavanello RCM, Silva HCM. A new in/del in the critic splicing region of the VMA21 gene causing X-linked myopathy with excessive autophagy (XMEA). 19th International Congress of the Word Muscle Society, Berlin, Alemanha, 7-11 outubro de 2014. Neurom Disord 24:791-792, 2014
98. Vainzof M. The genetic approach to muscle diseases. 18th International Congress of Neuropathology Local: Rio de Janeiro, BRAZIL 14-18 setmbro, 2014 BRAIN PATHOLOGY Volume: 24: 14, 2014
99. Valadares MC, Gomes J, Castello G, Assoni A, Pelatti M, Vainzof M, Zatz M. Comparison of different tissues from the same donor shows that only human adipose derved pericytes increased significantly life span in mdx/utr-. 12th Annual Meeting of the ISSCR, June 2014, Vancouver, Canada, pag. 496
100. Vianna-Morgante AM, Fonseca ACS, Bonaldi A, Kok F Bertola DR and Otto PA. Imbalances in apparently balanced chromosomal rearrangements. In: Genomic Disorders 2013 - From 60 years of DNA to human genomes in the clinic. A Wellcome Trust Scientific Conference, 10-12 de abril, Cambridge, Inglaterra, 2013.
101. Vianna-Morgante AM, Oliveira-Santos J, Costa SS, Bonald A, Krepischi ACV, Rosenberg C. X-chromosome microimbalances in boys with intellectual disability and maternal completely skewed inactivation. In: Gencodys Conference, 14-17 de abril, Paphos, Chipre, 2013.
102. Vieira NM, Naslavsky MS, Licinio L, Kok F, Schlesinger D, Vainzof M, Sanchez N, Kitajima JP, Gal L, Cavaçana N, Serafini PR, Chuartzman S, Vasquez C, Mimbacas A, Nigro V, Pavanello RCM, Schuldiner M, Kunkel LM, Zatz M. A defect in the RNA-processing protein HNRPDL causes limb-girdle muscular dystrophy 1G (LGMD1G). 19th International Congress of the Word Muscle Society, Berlin, Alemanha, 7-11 outubro de 2014. Neurom Disord 24:851, 2014
103. Yeda FP, dos Santos ML, Tsuruta LR, Horta BB, Inocencio AL, Okamoto OK, Tuma MC, Moro AM. Strategies for clone detection, selection and isolation in Per.C6 cells - case for Rebmab100. In: 23rd European Society for Animal Cell Technology (ESACT) Meeting, 23-26 de junho, Lille, França, 2013.
104. Zatz M, Pavanello RCM, Lazar M, Lourenço NCV, Cerqueira A, Nogueira L, Vainzof M. Milder course in patients with nonsense mutations and no muscle dystrophin. In: 63rd Annual Meeting of the American Society of Human Genetics. 22-26 de outubro, Boston, EUA, 2013.
105. Zatz M, Vieira N, Secco M, et al. Human adipose mesenchymal stem-cells injections in golden retriever muscular dystrophy (GRMD) dogs: a four-year follow-up. In: 18th International Congress of the World Muscle Society, 1-5 de outubro, Asilomar, EUA, 2013.

d) Theses and Dissertations

1. Ayub-Guerrieri D. Avaliação da via de glicosilaçao da alpha-distroglicana na formação e manutenção do complexo distrofina-glicoproteinas-associadas, e sua relação com o músculo normal e distrófico. Orientador: Mariz Vainzof. Tese de Doutorado, 2013.
2. Calyjur PC. Avaliaçao do efeito da mutação no gene da distrofina do camundongo mdx (C57Bl), no background do camundongo 129". Orientador: Mariz Vainzof. Dissertaçao de mestrado, 2015.
3. Cavaçana N. Estudo genético-molecular de pacientes discordantes de Paraplegia Espástica Hereditária do tipo 4. Orientador: Mayana Zatz. Tese de Doutorado, 2014
4. Cruvinel EM. Estudo da expressão diferencial de genes localizados no segmento cromossômico 15q11-13 em pacientes com as síndromes de Angelman e Prader-Willi. Orientador: Celia P Koiffmann. Tese de Doutorado, 2015.
5. Dantas VGL. Estudos moleculares na perda auditiva de herança autossômica dominante. Orientador: Regina Célia Mingroni-Neto. Tese de Doutorado, 2013.
6. Dávila, CK. Expressão de hsa-miR-367 e agressividade de meduloblastoma humano. Orientador: Oswaldo Keith Okamoto. Dissertação de Mestrado, 2015.
7. dos Santos, MFM. Pesquisa de genes associados à obesidade. Orientadora: Célia P. Koiffmann. Dissertação de Mestrado, 2014.

8. Fernandes RB. Caracterização funcional e estrutural de AfPrxA, uma tiól peroxidase do fungo patógeno humano Aspergillus fumigatus, um potencial alvo para desenvolvimento de droga. Orientador: Luis Eduardo Soares Netto. Tese de Doutorado, 2013.
9. Gomes, JP. Comparação entre células-tronco mesenquimais e pericitos injetadas em camundongos mdx/utr. Orientadora: Mayana Zatz. Dissertação de Mestrado, 2014.
10. Malcher C. Investigação do papel de SNVs (*single nucleotide variants*) na etiologia da fissura lábio-palatina não sindrômica. Orientador: Maria Rita Passos-Bueno. Dissertação de Mestrado, 2013.
11. Martins Bach AB. Aplicação de Espectroscopia e Imageamento por Ressonância Magnética Nuclear no estudo de Distrofias Musculares. Orientador: Mariz Vainzof. Tese de doutorado em co-tutela com a Universidade Paris-Sud, 2015.
12. Meira JGC. Estudo clínico e molecular em pacientes com fissuras orais para avaliação do efeito fenotípico de variantes do IRF6 e estimativa da contribuição genética nas fissuras palatinas. Orientador: Maria Rita Passos-Bueno. Dissertação de Mestrado, 2014.
13. Melo US. Estudo epidemiológico e genético da surdez em dois municípios do estado da Paraíba, Brasil. Orientador: Regina Célia Mingroni-Neto. Dissertação de Mestrado, 2013.
14. Nonose RW. Estudos moleculares em surdez de herança autossômica recessiva: o papel do gene *SLC26A4*. Orientador: Regina Célia Mingroni-Neto. Dissertação de Mestrado, 2013.
15. Onofre PCG. Caracterização e estudo da capacidade regenerativa de células-satélite de camundongos distróficos Lama2dy-2J/J, com deficiência de α2-laminina, e Largemyd, com deficiência de glicosiltransferase Large. Orientador: Mariz Vainzof. Tese de Doutorado, 2013.
16. Pereira, MCL. Estudo de terapia celular em modelo experimental de Doença de Parkinson. Orientador: Oswaldo Keith Okamoto. Tese de Doutorado, 2013.
17. Ribeiro CM. Estudos de genes candidatos aos Transtornos do Espectro Autista. Orientador: Maria Rita Passos-Bueno. Tese de Doutorado, 2013.
18. Rodrigues MG. Em busca da etiologia das displasias frontonasais. Orientador: Maria Rita Passos-Bueno. Dissertação de Mestrado, 2013.
19. Rodrigues TC. Avaliação de fatores genéticos e epigenéticos envolvidos no tumor embrionário hepatoblastoma e correlação com a morfogênese hepática. Orientadora: Carla Rosenberg. Tese de Doutorado, 2015
20. Santos JO. Estudo da Deficiência Mental de Herança Ligada ao Cromossomo X. Orientador: Angela M. Vianna-Morgante. Tese de Doutorado, 2013.
21. Suzuki DE. Fator de transcrição E2F2 e propriedade tumorigênica de células-tronco embrionárias humanas. Orientador: Oswaldo Keith Okamoto. Tese de Doutorado, 2013.
22. Valadares M. Avaliação comparativa do potencial miogênico de células tronco mesenquimais adultas obtidas de diferentes fontes. Orientador: Mayana Zatz. Tese de Doutorado, 2014
23. Villela D. Alterações Genômicas e Epigenômicas nas Manifestações Anatomopatológicas e Cognitivas da Doença de Alzheimer. Orientadora: Carla Rosenberg. Tese de Doutorado, 2014.

e) Conferences, Symposia, Round Tables, Lectures

1. Bertola D. Lecture: “Aspectos Clínicos e Diagnósticos Diferenciais das Crianças com DNPM (Deficiência Neuro Psico Motora)”
2. Bertola D. Lecture: “Cariótipo e Hibridização Genômica Comparativa (a-CGH array/ CMA) - Painéis genéticos, Exoma e Genoma”
3. Fonseca ACS – Lecture: “Investigating clinical impact and mechanisms of formation of balanced chromosomal rearrangements by array-based genomic hybridization and next generation sequencing” – Round Table: Da citogenética a citogenômica: aplicações relevantes. 4a. Reunião Brasileira de Citogenética, Atibaia, SP. May 26-29, 2015.
4. Menck CF. Lecture: “Carcinogênese induzida pela irradiaçãoo UV da luz solar”. XXXI Jornada Norte-Nordeste da Dermatologia, Manaus, Amazônia. 21/06/2013.
5. Menck CF. Lecture: “Deficiências em reparo de DNA e pacientes xeroderma pigmentosum no Brasil: Câncer e envelhecimento”. Tópicos Avançados em Biologia e Tópicos Especiais, Pós Graduação em Genética, IBB-UNESP, Botucatu. 22/08/2013.
6. Menck CF. Lecture: “Desvendando mutações em *xeroderma pigmentosum* no Brasil: perguntas científicas e perspectivas

7. Menck CF. Lecture: “DNA repair and cancer therapy”. SPSAS, Advances in Molecular Oncology, Translationg Molecular Biology into Cancer treatment, Faculdade de Medicina, Universidade de São Paulo. 07/02/2013.
8. Menck CF. Lecture: “DNA repair diseases: what do they tell us about carcinogenesis and aging processes?”. 59º Congresso Brasileiro de Genética, 18/09/2013.
9. Menck CF. Lecture: “Genética e Mutagênese”. IX Course of the Latin American School of Human and Medical Genetics, Caxias do Sul, RS, 07/05/2013
10. Menck CF. Lecture: “O Curso de Ciências Biomédicas no ICB, USP”. Comissão de Graduação, Instituto de Ciências Biomédicas, Universidade de São Paulo. 25/02/2013.
11. Menck CF. Lecture: “Origem da Vida” Seminários Gerais do Instituto de Ciências Biomédicas, Universidade de São Paulo. 13/03/2013.
12. Menck CF. Lecture: “Origem e Evolução da vida na Terra”. II Semana de Inovações Biológicas Biotecnológicas Aplicadas a Saúde, Instituto de Ciências Biomédicas, Universidade de São Paulo. 23/04/2013.
13. Menck CF. Lecture: “Seminários Gerais do Depto de Bioquímica, Instituto de Química. 21/03/2013.
14. Mingroni- Netto RC. Lecture: Diagnóstico molecular da síndrome do X frágil. Conferencista no(a) Fórum sobre o teste molecular de DNA, a síndrome do X frágil e projeto de lei 139/2014 de, 2014, na Assembléia Legislativa do Estado de São Paulo.
15. Mingroni-Netto RC Lecture. Heterogeneidade Genética da Surdez Hereditária, 2013. Round Table: Análises e diagnósticos biomoleculares: desafios das análises genômicas. 21º Congresso de Biólogos do CRBio-01 - 15/07/2013, Santos, SP.
16. Mingroni-Netto RC Lecture; Conferencista no(a) A formação de profissionais de saúde para atuar em Aconselhamento Genético. 60o Congresso Brasileiro de Genética, 2014. Guarujá .Sociedade Brasileira de Genética (Congresso) -
17. Mingroni-Netto RC, Melo US. Genética da Surdez em Populações Humanas do Nordeste Brasileiro, 2014. Curso de curta duração ministrado durante o Encontro de Genética do Nordeste, Campina Grande, PB.
18. Mingroni-Netto RC. Lecture Aconselhamento Genético da Surdez. II Congresso Internacional de Surdez, Implante Coclear, Próteses auditivas 2013. (Congresso), São Paulo, S.P.
19. Mingroni-Netto RC. Simposya: Os biólogos e a reserva de mercado: Formação do profissional para atuar em aconselhamento genético. no(a) 17a Semana Temática da Biologia, 2014, Instituto de Biociências da USP
20. Okamoto OK. “Estratégias para o desenvolvimento de terapia-alvo em câncer”. Reunião científica, CIPE-A.C. Camargo Cancer Center. São Paulo, SP, 2015.
21. Okamoto OK. “Stem-like cells in primitive neuroectodermal tumors”. New Advances in Stem-Cell Research, i-STEM / HUG-Cell Meeting, IB-USP, 2013.
22. Okamoto OK. Células-tronco no câncer. II Simpósio de Biotecnologia e Medicina Regenerativa. Faculdade de Medicina, Universidade Federal da Bahia. Salvador, BA, 2015.
23. Okamoto OK. Lecture: “Expression of stem cell related genes in tumors of the central nervous system. Simpósio Internacional - Stem Cells in Developmental Biology and Cancer. A. C. Camargo Cancer Center. 2012.
24. Rosenberg,C (Lecture) - Array CGH e Deficiência Intelectual - XXVII CONGRESSO BRASILEIRO DE GENÉTICA MÉDICA 03 - 06 de junho: Ribeirão Preto – SP, 2015
25. Rosenberg,C (Lecture): Arrays genômicos como ferramenta no diagnóstico citogenético de deficiência intelectual 4ª Reunião Brasileira de Citogenética, 26-29 de maio, Atibaia, SP,2015.
26. Vainzof M. Lecture: Animal models for muscular dystrophies helping to understand proteins function and for testing therapies. School Biological Sciences, University of Reading, Reading, UK. Outubro de 2014.
27. Vainzof M. Lecture: “Diagnóstico molecular na prática diária: até onde podemos chegar?”. IX Congresso Paulista de Neurologia. Guarujá, 27 de junho de 2013.
28. Vainzof M. Lecture: “Métodos de fenotipagem de animais geneticamente modificados portadores de alterações musculares” disciplina BTC 5805 - Métodos utilizados para a fenotipagem de animais geneticamente modificados, FMVZUSP. São Paulo, 19 de março de 2013.

29. Vianna-Morgante AM. Lecture: “Perdas e ganhos de segmentos genômicos e sua associação com doenças genéticas” – Round Table: Análises e diagnósticos biomoleculares: desafios das análises genômicas. 21º Congresso de Biólogos do CRBio-01 - 15/07/2013, Santos, SP.
30. Vianna-Morgante AM. Short course: “Aconselhamento Genético” - 21º Congresso de Biólogos do CRBio-01, Santos, SP. Julho 2013.
31. Zatz M. **Women Changing Brazil: A Barnard College Global Symposium.** March 18, 2013, São Paulo, Brazil .
32. Zatz M. **Stem-cells from and for neuromuscular disorders**- Symposium INSERM- Genome Center, S. Paulo, Março, 2013.
33. Zatz M**. Terapia celular em doenças degenerativas neurológicas** */ Cellular therapy for degenerative neuromuscular diseases. Simposio internaciona,, Inst. De Pesquisas , Hospital Albert Einstein- S. Paulo, março de 2013*
34. Zatz M ***. Felicidade: Genético ou Ambiental;*** *Casa do Saber, Rio de Janeiro, Abril de 2013*
35. Zatz M. ***Genética: quais são os limites?*** *II Forum da Saude e Bem Estar, Campinas, Maio de 2013*
36. Zatz M. ***Genoma Pessoal****: Tópicos Avançados em Genômica e Biologia Celular, Campinas, maio de 2013*
37. Zatz M. ***Genética e envelhecimento Cerebral: Conferência Magna****. Congresso Brasileiro de Neuropsiquiatria Geriátrica, Sào Paulo, 05 de setembro*
38. Zatz M. ***Jornalismo científico:*** *Focas do Estadão, 10 de setembro, S. Paulo*
39. Zatz M. ***Limb-girdle muscular dystrophies****. Internacional Congress of Neurology. Vienna, 23 de setembro*
40. Zatz M. ***Ethical Aspects of next generation sequencing****. Symposium on complex disorders. São Paulo, 16 de outubro*
41. Zatz M. ***Nossas pesquisas e compromissos com esclerose lateral amiotrófica (ELA).*** *Simpósio de doenças raras, Brasília, 7 de novembro*
42. Zatz M. ***Genética e Psicanálise****: Escola Brasileira de Psicanálise. São Paulo, 8 de novembro*
43. Zatz M. ***GenËTICA****- II Forum internacional de doenças neuromusculares, Instituto Paulo Gontijo, São Paulo, 8 d novembro*
44. Zatz M. ***GenÉtica e Genoma****: Como isso impacta nossas vidas? Livraria Cultura, São Paulo, 25 d enovembro*
45. Zatz M. *GenEtica e Genoma: Como isso influencia nossas vidas? Aula inaugural, Instituto de Ciências Biomédicas, fevereiro , S. Paulo*
46. Zatz M. **Genética do envelhecimento**. III Congresso de Clínica Psiquiátrica. 25 de abril, Centro de Convenções Rebouças, São Paulo
47. Zatz M. **Jornalista Científico:** Auditório da Folha de S.Paulo, 7 de maio, São Paulo
48. Zatz M. Diagnóstico molecular e GenÉtica- III Summer School LASID, 16 de maio, Campinas, São Paulo
49. Zatz M. Next generation sequencing and incidental findings: what should be revealed? Global Summit on Regulatory Sciences, Montreal, Canada, Agosto de 2014
50. Zatz M. Células-tronco em doenças neuromusculares: dos e para os pacientes. Congresso Nacional da Sociedade Brasileira de Genética, Guarujá, agosto de 2014
51. Zatz M. A defect in the RNA-processing protein HNRPDL causes limb-girdle muscular dystrophy 1G (LGMD1G). XIV Congresso internacional da world muscle society, Berlin, outubro de 2014
52. Zatz M. Cell therapy in preclinical models off neuromuscular. :what are we learning? III IPG Forum on ALS research, S. Paulo, Novembro, 2014
53. Zatz M. Células-tronco: Aplicações, realizações e dúvidas. XXVI Congresso brasileiro de neurologia, Curitiba, novembro de 2014
54. Zatz M. Células-tronco nas doenças neurodegenerativas: o que é ilusão e o que é realidade. XXVI Congresso brasileiro de neurologia, Curitiba, novembro de 2014
55. Zatz M. Terapia celular em doenças neuromusculares: o que aprendemos? Seminários da Bioquímica, Novembro de 2014
56. Zatz M. Terapia celular em doenças neuromusculares: Encontro latino americano de miopatias, Salvador, dezembro de 2014

f) Development of Instructional Material

1. Kobayashi GS, Brito LA, Meira JGC, Alvizi L, Passos-Bueno MR. Você sabe o que é síndrome de van der Woude?. (produção em vídeo) 2014. http://www.youtube.com/watch?v=O0uqJ4MPwGQhttp://www.youtube.com/watch?v=O0uqJ4MPwGQ
2. Kobayashi GS, Brito LA, Meira JGC, Alvizi L, Passos-Bueno MR. Você sabe o que é síndrome velocardiofacial?. (produção em vídeo) 2014. http://www.youtube.com/watch?v=_-veUyBgwC0http://www.youtube.com/watch?v=_-veUyBgwC0
3. Kobayashi GS, Brito LA, Malcher C, Alvizi L, Rodrigues MG, Meira JGC, Bassi CF, Passos-Bueno MR. Você sabe o que é lábio leporino? (produção em vídeo) 2013. http://www.youtube.com/watch?v=2g2AP3jHkykhttp://www.youtube.com/watch?v=2g2AP3jHkyk
http://www.youtube.com/watch?v=2g2AP3jHkyk
http://www.youtube.com/watch?v=2g2AP3jHkyk

III. PATENTS

1. Oiticica J, Bento RF, Lezirovitz K, Batissoco AC, Vasques LR; Salomone R. Retrovírus recombinante compreendendo um vetor para a transcrição de um shRNA no interior de uma célula, no qual o shRNA substancialmente inibe a expressão de um gene-alvo, uma composição compreendendo o retrovírus recombinante e o método de inibição da expressão de um gene-alvo em uma célula". Patente: Privilégio de Inovação. Número do registro: BR1020140199292, data de depósito: 12/08/2014, Instituição de registro: INPI - Instituto Nacional da Propriedade Industrial.
2. Okamoto OK, Rodini CO, Silva PBG, Furukawa G. Método De Prognóstico Da Agressividade De Tumores E Kit. 2014, Brasil. Patente: Privilégio de Inovação. Número do registro: BR1020140155775, data de depósito: 17/06/2014, título: "Método De Prognóstico Da Agressividade De Tumores E Kit" , Instituição de registro:INPI - Instituto Nacional da Propriedade Industrial.
3. Okamoto OK, Silva PBG, Santos MCT . Composições Farmacêuticas Para Eliminação De Células-Tronco Tumorais E Uso Das Mesmas. 2015, Brasil. Patente: Privilégio de Inovação. Número do registro: BR1020150030169, data de depósito: 11/02/2015, título: "Composições Farmacêuticas Para Eliminação De Células-Tronco Tumorais E Uso Das Mesmas" , Instituição de registro:INPI - Instituto Nacional da Propriedade Industrial.
4. Ribeiro CM, Passos-Bueno MR. Sequência para detecção de mutações associadas a Transtornos do Espectro Autista e lâmina de microarranjo. 2013, Brasil. Patente: Privilégio de Inovação. Número do registro: BR10201301319, data de depósito: 28/05/2013, título: "Sequência para detecção de mutações associadas a Transtornos do Espectro Autista e lâmina de microarranjo", Instituição de registro: INPI - Instituto Nacional da Propriedade Industrial. Instituição(ões) financiadora(s): FAPESP.

IV. AWARDS

1. Batissoco AC, Lezirovitz K, Bissoli MM, Zanatta D, Strauss BR, Vasques LR, Mingroni–Netto RC, Haddad LA, Bento RF, Oiticica J. Hes 1 and Coup-Tf1 shRNA knocking down give rise to new hair cells and supporting cells in organ of Corti organotypic culture. Segundo Lugar no Prêmio de Melhor Trabalho Científico. In: VI Congresso Iberoamericano de Implantes Cocleares e Ciências Afins, Centro de Convenções Rebouças, São Paulo –SP, 2015
2. Carnavalli, JEP, Kimura L, Nunes K, Fernandes GR, Pereira AC, Mingroni-Netto R C. Association study of FTO gene with overweight and obesity in rural semi-isolated African-derived Brazilian populations. Menção Honrosa no Prêmio Newton Freire-Maia pelo trabalho Sociedade Brasileira de Genética, In: 60º Congresso Brasileiro de Genética, 2014, Guarujá. Sociedade Brasileira de Genética
3. Salazar-Silva, R.; Batissoco A.C., Haddad L.A. Bernardino-Cruz, D. Oiticica J. ; Mingroni-Netto, R.C. "Imunofluorescência da cóclea como ferramenta de estudo de expressão de genes de surdez", In Simpósio de Incentivo à Pesquisa Científica “Oswaldo Frota-Pessoa”, Departamento de Genética e Biologia Evolutiva, Instituto de Biociências da Universidade de São Paulo, São Paulo-SP, 12 de dezembro . Prêmio de melhor trabalho de iniciação científica.
4. Lopes dos Santos M, Yeda FP, Tsuruta LR, Horta BB, Pimenta AA Jr, Degaki TL, Soares IC, Tuma MC, Okamoto OK, Alves VA, Old LJ, Ritter G, Moro AM. “Rebmab200, a humanized monoclonal antibody targeting the sodium phosphate transporter NaPi2b displays strong immune mediated

cytotoxicity against cancer: a novel reagent for targeted antibody therapy of cancer." Prêmio Octavio Frias de Oliveira, modalidade Inovação Tecnológica em Oncologia, Instituto do Câncer do Estado de São Paulo / Grupo Folha de S. Paulo, 2014.

5. Kimura L. Inferring paternal history of rural African-Derived Brazilian Populations. Menção Honrosa no Prêmio Francisco Mauro Salzano. In: 59º Congresso Nacional de Genética da Sociedade Brasileira de Genética, Águas de Lindóia, SP, 2013.

6. Oiticica J, Bernardino-Cruz D, Cavalcante LTC, Auricchio MTBM, Mingroni Netto RC, Bittar RSM. Investigating deafness genes as a cause of sudden sensorineural hearing loss. 3º Lugar no prêmio de trabalhos científicos apresentação oral em Otorrinolaringologia. In: 12º Congresso da Fundação Otorrinolaringologia. Campos do Jordão, SP, 2013.

V. PERSONNEL

a) Students with Current Projects

Name	Level	Supervisor
Andressa Cristina G. Martins	IC	Angela M. Vianna-Morganti
Andreza Caieiro	IC	Regina C. Mingroni-Netto
Artur Berselle	IC	Maria Rita Passos-Bueno
Camila Lovaglio Santos	IC	Maria Rita Passos-Bueno
Gabriella Hsiya	IC	Maria Rita Passos-Bueno
Carolina de Seixas Couto Leite	IC	Oswaldo Keith Okamoto
Daniel Fredy Vargas Teran	IC	Mariz Vainzof
Davi Jardim Martins	IC	Carlos F. Menck
Davi Mendes	IC	Carlos F. Menck
Eduardo Tsuchida	IC	Luis Eduardo Soares Netto
Erika Ramos	IC	Maria Rita Passos-Bueno
Gabriel Monteiro do Carmo	IC	Mayana Zatz
Gabriela Furukawa	IC	Oswaldo Keith Okamoto
Joana Guiro Carvalho da Rocha	IC	Oswaldo Keith Okamoto
Lucas Vecchiato de Melo	IC	Maria Rita Passos-Bueno
Maíra Fessardi	IC	Luis Eduardo Soares Netto
Marina Garcia Ribeiro	IC	Mariz Vainzof
Natalia Pereira	IC	Mayana Zatz
Niara Régia F. de Souza	IC	Angela M. Vianna-Morganti
Rodrigo Salazar da Silva	IC	Regina C. Mingroni-Netto
Rosanna Miki Kimura Cerioni	IC	Oswaldo Keith Okamoto
Stephanie de Alcântara Fernandes	IC	Mariz Vainzof
Alexsandro Santos	Master	Carla Rosenberg
Aline Lopes Ribeiro	Master	Oswaldo Keith Okamoto
Amanda Aparecida Cardoso Coimbra	Master	Célia P. Koiffmann
Amanda Faria Assoni	Master	Mayana Zatz
Antonio Fernando Ribeiro Junior	Master	Mariz Vainzof
Dayane Bernardino da Cruz	Master	Regina C. Mingroni-Netto
Fernanda Marchetto da Siva Kanno	Master	Debora Romeo Bertola
Humberto Cezar Marcolino	Master	Regina C. Mingroni-Netto
Isabela Mayá Wayhs Silva	Master	Maria Rita Passos-Bueno
Joanna Goes Castro Meira	Master	Maria Rita Passos-Bueno
Juliana Emilia Prior Carnavalli	Master	Regina C. Mingroni-Netto
Juliana Plat de Aguiar Gomes	Master	Mayana Zatz
Livia Moura	Master	Carlos F. Menck
Mauren Fernanda Moller dos Santos	Master	Célia P. Koiffmann
Mayra Pelatti	Master	Mayana Zatz

Melinda Santos Beccari	Master	Mayana Zatz
Stephanie de Alcântara Fernandes	Master	Mariz Vainzof
Renata Ishiba	Master	Mariz Vainzof
Thaise Nayane	Master	Carla Rosenberg
Thiago Rosa Olávio	Master	Mayana Zatz
Vanessa Simões	Master	Luis Eduardo Soares Netto
Adriano Bonaldi	Doctorate	Angela M. Vianna-Morgante
Alexandre Vessoni	Doctorate	Carlos F. Menck
Ana Carolina dos Santos Fonseca	Doctorate	Angela M. Vianna-Morgante
Camila de Freitas Almeida	Doctorate	Mariz Vainzof
Carolina de Oliveira Rodini	Doctorate	Oswaldo Keith Okamoto
Carolina Malcher	Doctorate	Maria Rita Passos-Bueno
Carolini Kaid Dávila	Doctorate	Oswaldo Keith Okamoto
Clarissa R. Ribeiro Rocha	Doctorate	Carlos F. Menck
Danielle de Paula Moreira	Doctorate	Maria Rita Passos-Bueno
Estela Mitie Cruvinel	Doctorate	Célia P. Koiffmann
Felipe Augusto André Ishiy	Doctorate	Maria Rita Passos-Bueno
Fernando Gomes	Doctorate	Luis Eduardo Soares Netto
Flávio Romero Palma	Doctorate	Luis Eduardo Soares Netto
Francine Campagnari	Doctorate	Carla Rosenberg
Gerson Shigeru Kobayashi	Doctorate	Maria Rita Passos-Bueno
Giuliana Coatti	Doctorate	Mayana Zatz
Guilherme Lopes Yamamoto	Doctorate	Debora Romeo Bertola
Leandro Ucela Alves	Doctorate	Regina C. Mingroni-Netto
Leonardo Carmo de Andrade Lima	Doctorate	Carlos F. Menck
Letícia Koch Lerner	Doctorate	Carlos F. Menck
Ligia Pereira de Castro	Doctorate	Carlos F. Menck
Lucas Alvizi Cruz	Doctorate	Maria Rita Passos-Bueno
Luciano Abreu Brito	Doctorate	Maria Rita Passos-Bueno
Michel Satya Naslavsky	Doctorate	Mayana Zatz
Natale Cavaçana	Doctorate	Mayana Zatz
Natália C. Moreno	Doctorate	Carlos F. Menck
Patrícia Benites Gonçalves da Silva	Doctorate	Oswaldo Keith Okamoto
Renata Bannitz Fernandes	Doctorate	Luis Eduardo Soares Netto
Renato Domingos	Doctorate	Luis Eduardo Soares Netto
Rodrigo Atique	Doctorate	Maria Rita Passos-Bueno
Silvia Costa	Doctorate	Carla Rosenberg
Tatiana Almeida	Doctorate	Maria Rita Passos-Bueno
Valesca Anschau	Doctorate	Luis Eduardo Soares Netto
Vanessa Luiza Romanelli	Doctorate	Maria Rita Passos-Bueno
Wagner Antonio da Rosa Baratela	Doctorate	Debora Romeo Bertola
Ana Carla Batissoco	Post Doctorate	Regina C. Mingroni-Netto
Beatriz de Araujo Cortez	Post Doctorate	Oswaldo Keith Okamoto
Bruno Henrique Silva Araujo Torres	Post Doctorate	Esper Abrão Cavalheiro
Carla Sustek D'Angelo	Post Doctorate	Célia P. Koiffmann
Clarice Savastano	Post-Doctorate	Maria Rita Passos-Bueno
Cristiani Gifalli Iughetti	Post Doctorate	Célia P. Koiffmann
Danielle Ayub-Guerrieri	Post Doctorate	Mariz Vainzof
Darine Villela	Post Doctorate	Carla Rosenberg
Diogo de Abreu Meireles	Post Doctorate	Luis Eduardo Soares Netto
Eder Zucconi	Post Doctorate	Mayana Zatz
Huma Asif	Post Doctorate	Carlos F. Menck
José Oliveira dos Santos	Post Doctorate	Angela M. Vianna-Morganti

Karina Griesi Oliveira	Post Doctorate	Maria Rita Passos-Bueno
Kelly Nunes	Post Doctorate	Regina C. Mingroni-Netto
Lilian Kimura	Post Doctorate	Regina C. Mingroni-Netto
Luciana Rodrigues Gomes	Post Doctorate	Carlos F. Menck
Márcia Cristina Teixeira dos Santos	Post Doctorate	Oswaldo Keith Okamoto
Maria Cristina Mingues Spinola	Post Doctorate	Luis Eduardo Soares Netto
Mariane Secco	Post Doctorate	Mayana Zatz Zatz
Miriam Frangini	Post Doctorate	Mayana Zatz
Monica Castro Varela	Post Doctorate	Célia P. Koiffmann
Roberto Dalto Fanganillo	Post Doctorate	Maria Rita Passos-Bueno
Rosa Estela Caseira Cabral	Post Doctorate	Carlos F. Menck
Poliana Cristina de Melo Martins	Post Doctorate	Mariz Vainzof
André Luís Fernandes dos Santos	Post Doctorate	Mariz Vainzof
Luciane Portas Capelo	Visiting Researcher	Maria Rita Passos-Bueno

b) Laboratory Technicians and Assistants

Name	Supervisor	Funding source
Andressa Gois Morales	Maria Rita Passos-Bueno	INCT-USP
Simone Gomes Ferreira	Maria Rita Passos-Bueno	USP
Vanessa Naomi	Maria Rita Passos-Bueno	CEPID-USP
Kátia Maria da Rocha	Maria Rita Passos-Bueno	CEPID-USP
Monize Lazar Magalhães	Maria Rita Passos-Bueno	CEPID-USP
Meire Aguena	Maria Rita Passos-Bueno	CEGH-CELL-FUSP
Guilherme Lopes Yamamoto	Maria Rita Passos-Bueno	CEGH-CELL-FUSP
Suzana Andreoli Marques Ezquina	Maria Rita Passos-Bueno	DTI-INCT-CNPq
Monica Castro Varela Rodrigues da Silva	Maria Rita Passos-Bueno	CEGH-CEL-FUSP
Antonia Cerqueira	Mayana Zatz	USP
Naila Cristina V. Lourenço	Maria Rita Passos-Bueno	INCT-USP
Roberto Rivelino de Camargo	Maria Rita Passos-Bueno	CEPID-USP
Marta Canovas	Mayana Zatz	CEPID-USP
Heloísa Maria de Siqueira Bueno	Mayana Zatz	FUSP
Patricia Semedo Kuriki	Oswaldo Keith Okamoto	INCT-USP
Maria Raimunda Lisboa Santana Pinheiro	Angela M. Vianna-Morganti	USP
Laurinda de Fátima P. Cally Baptista	Angela M. Vianna-Morganti	USP
Maria Teresa Balester de Mello Auricchio	Regina C. Mingroni-Netto	USP
Paulo Rogério de Souza	Regina C. Mingroni-Netto	USP
Andressa Yurie Sakugawa	Luis Eduardo Soares Netto	USP
Simone Vidigal Alves	Luis Eduardo Soares Netto	USP
Thiago Geronimo Alegria	Luis Eduardo Soares Netto	USP
Marta Rita Celestino de Macedo	Eliana M B. Dessen	CEPID-USP
Letícia Nogueira Feitosa	Mariz Vainzof	CEGH-CELL-FUSP
Thais Oliveira de Andrade	Mayana Zatz	AACD
Vivian Palmeira Landini e Silva	Mayana Zatz	FUSP-AACD
Erica Baroni Cangusu	Mayana Zatz	FUSP-AACD
Silvia Costa	Carla Rosenberg	USP
Tatiana Rodrigues Nahas	Eliana M B. Dessen	FUSP
Thatyane Sereia Terci	Maria Rita Passos-Bueno	CEGH-CELL-FUSP

c) Administrative

Name	Supervisor	Funding source
Wagner Falciano	Mayana Zatz	CEPID-I-USP

Vanessa Yumiko Sato de Jesus	Mayana Zatz	AACD-CEGH-CELL
Márcia Góes Teixeira	Mayana Zatz	AACD
Bernadete Morelli Soares	Mayana Zatz	AACD
Luciana Cristina A. Oliveira	Mayana Zatz	CEPID-USP
Leandro Pereira Leirião	Mayana Zatz	CEPID-II-USP
Constancia Urbani Gotto	Mayana Zatz	AACD
Maraisa de Castro Sebastião	Angela M. V. Morgante	USP
Luceleni da Silva	Celia P. Koiffmann	USP

d) IT

Name	**Supervisor**	**Funding source**
Fernando Luis Molina	Mayana Zatz	CEGH-CELL-FUSP
Daniel Bozoklian do Amaral	Mayana Zatz	CEGH-CELL-FUSP

PART 2 - TRANSFER OF TECHNOLOGY/TECHNOLOGY APPLICATIONS

a) Genetic Tests

Before 2013, our service provided 56 genetic diagnostic tests: 23 were based on Sanger sequencing, 10 were performed with amplicon-specific PCR, 21 were performed with MLPA (Multiplex Ligation-dependent Probe Amplification), and 2 were performed with Southern Blotting. All these different tests are still offered, but the Sanger sequencing methodology was replaced by Next-Generation Sequencing (NGS; refer to item **f**), and currently only 1 test is carried out through Southern Blotting. During the period of 2013-2015, we performed about 2000 genetic tests using different techniques, including MLPA, Triple (TP)-PCR, Southern Blotting and NGS (see **item f** for details).

We are revising the information about genetic testing on our website. Our next step is to create a dedicated website for the genetic tests, as the amount of information has significantly increased. Additionally, we expect that this website will bring about more visibility to our center.

b) International Quality Assessment

In the beginning of 2014, our genetic testing services were submitted to a quality evaluation by the EMQN (The European Molecular Genetics Quality Network; http://www.emqn.org/) external quality assessment schemes. Quality assessment schemes are designed to test the whole analytical process of molecular genetics laboratories; the ability to interpret data in the light of clinical information supplied with a referral, and to produce a clear and accurate report. The tests evaluated were: spinocerebellar ataxias, muscular spinal atrophy, and Duchenne/Becker muscular dystrophy, in addition to Sanger sequencing. We achieved the maximum score (2.0) for all the schemes in which we participated.

c) Establishment of an iPSC bank/service

To date, 63 iPSC lines (20 cell lines from healthy individuals and 43 cell lines from subjects affected by a genetic disorder) have been established. In the last year, we also implemented the methodology for somatic cell reprogramming using episomal vectors. Besides the fact that this type of vector does not integrate in genome (in contrast to the retroviral vectors previously used), this protocol allows for the reprogramming of peripheral blood cells with relatively high efficiency. The use of these cells represents a great achievement as it facilitates iPSC generation from somatic cells from almost any patient of interest, without carrying out invasive procedures. The implementation of this new protocol in our laboratory was the result of a technology transfer from a collaboration project funded by CNPq (I-stem: CEGH-CELL). One technician and a postdoc from our group spent one month training at the Institute for Stem Cell Research in France, under the supervision of Dr. Marc Peschanski.

d) Implementation of Next-Generation Sequencing (NGS)

During the CEPID-I term, our center established a core facility for sequencing and microsatellite genotyping, serving all CEPID researchers as well as external clients. In the period of 2013-2015, with the exception of services provided for the CEPID community, we performed about 51,000 sequencing reactions and 22,100 genotyping analyses for external researchers.

In 2013, we started a training program for our technicians, enabling them to prepare human DNA libraries from patients with rare genetic disorders to be analyzed through Next-Generation Sequencing (NGS) in a MiSeq equipment (Illumina) or using an outsourced HiSeq 2000 (Illumina) at LaCTAD (Laboratório Central de Tecnologias de Alto Desempenho em Ciências da Vida) - UNICAMP. In 2015, we set up an EMU (Equipamento Multiusuário/Multiuser Equipment) - FAPESP, comprised by a HiSeq 2500 (Illumina), in addition to our previous MiSeq and ABI 3730 DNA Analyser sequencer (Applied Biosystems). We have also acquired three new servers: two for data processing (with 16 computers with 1544Gb/RAM and 300Gb/HD) and one for data storage (36Tb capacity), in addition to CLOUD at USP. These servers allow us to process and store (with a backup) big data being generated by our facility. We established a workflow for DNA library construction, sequencing, and initial data processing to fulfill the demands of CEPID researchers. Rules and guidelines regarding the EMU are available at http://genoma.ib.usp.br/servicos. Two committees for running this NGS EMU were created: ***a)*** *Managing committee*, responsible for discussing rules for the use of this equipment as well as the best choice of reagents. It is constituted by three Professors and two technicians. ***b)*** *User committee*, responsible for providing suggestions directed at improving the management of the equipment; these suggestions, when necessary, may be addressed to the CEPID coordinator. This committee is currently composed by 4 members who have submitted samples for NGS in the first two years. Preferentially, these users will be from different units of USP, and not necessarily from CEPID. This committee will be renewed biannually. The current rosters of these committees are available at http://genoma.ib.usp.br/servicos. A first report of the user committees is here included: “During 2014, great effort was done in order to standardize techniques related to massive parallel sequencing using MiSeq and HiSeq (Illumina) in our Center. Because of serious problems related to maintenance of the computational apparatus, it was not possible to keep a routine of exome by NGS or to offer such services to researchers. However, since October 2014, after solving computational difficulties, NGS could be performed and interpreted regularly. Since then, in average, within 8 weeks after sending samples the researcher receives spreadsheets containing results of all candidate variants, after proper bioinformatics analyses performed by technicians of the Center. This service, regularly delivered, has provided researchers with a fast access to the NGS methodology, of which the results have already greatly contributed to the conclusion of many publications. This is very important to keep our research group competitive, when compared to similar research groups abroad.”

Up to now, we have conducted exome sequencing of about 600 individuals. The results generated have been important for ongoing research projects, and part of these data were included in several original publications (Yamamoto et al., 2014; Yamamoto et al., 2015;

Cuperman et al., 2014; Zatz et al., 2014 and more which are described in the research results).

NGS is being used for diagnosis under two services: **a)** *targeted sequencing:* a customized panel with genes relevant for 5 groups of disorders (item f); **b)** *exome clinical analysis*, which we have recently made available (as of June, 2015), currently with 8 samples under analysis.

e) Customizing a NGS panel for molecular diagnosis

In 2013, we customized a NGS gene panel that enabled us to offer molecular diagnosis for 5 groups of disorders:

- Group I: Neuromuscular/neurodegenerative disorders (95 genes)
- Group II: Craniofacial disorders/skeletal dysplasias (132 genes)
- Group III: Cognitive deficit syndromes, autism, or other developmental abnormalities (36 genes)
- Group IV: Congenital disorders with available treatment, including inborn metabolic deficits, hearing loss and others (121 genes)
- Group V: Hereditary cancer syndromes (46 genes)

This panel has already been validated, and the molecular diagnosis for 23 disorders previously done with the use of Sanger sequencing is already being performed through this gene panel. In the last two years we sequenced 966 samples including individuals from research protocols and patients referred to our diagnostics and clinical services. Of these, 329 samples were from patients affected by neuromuscular diseases, cancer, skeletal dysplasias and neurodevelopmental diseases. We were able to find the causative mutation in 219 cases (~67%). Although point mutations and small deletions or duplications comprised the majority of these cases, we were also able to identify large deletions or duplications in patients affected by Duchenne muscular dystrophy, and also in those affected by CMT1A, Sotos, Lynch or Saethre-Chotzen syndromes. Part of these findings was shown at the 2014 American Society of Human Genetics meeting (Targeted massively parallel sequencing in molecular diagnosis: a Brazilian report**.** *M. Lazar, K. M. Rocha, G. L. Yamamoto, M. Aguena, V. Takahashi, N. Lourenço, M. Varela, S. Ezquina, D. R. Bertola, R. Pavanello, M. Vainzof, M. Zatz, M. R. Passos-Bueno*).

This clinical gene panel is also being used for the development of a noninvasive prenatal diagnosis test for genetic disorders, which is part of a PhD project (FAPESP-2013/14996-0). Initially, we will focus on the diagnosis of trisomy 18 and trisomy 21. To achieve this goal, 166 probes for chromosome 18 and 199 probes for chromosome 21 have been included, which allows us to interrogate at least 600 probes on each of these chromosomes. Methodology regarding cell-free DNA extraction, library preparation, and capture and sequencing has already been standardized. We collected samples from 28 pregnant women and samples from 4 duos (mother+affected child) for the proof-of-concept of the test (3 with trisomy 21/Down's syndrome and 1 with trisomy 18/Edwards syndrome). Sequencing of these samples is scheduled for the 2nd semester of 2015.

f) Course in Bioinformatics

Dr. Tatiana Torres has offered additional spots for CEPID's students in the course "Introduction to computational programming for Biology students" (August 18th to December 1st, 2014). Besides the 31 students regularly enrolled, 5 post-graduate or post-docs working at CEPID attended the course.

g) Next Goals

Based on the above reports, nearly all of our proposed aims for the first two years have been achieved. For the third year, we have the following goals:

- To create a website for the genetic tests;
- To initiate a partnership with Fundação Faculdade de Medicina, to be able to provide services for clinical analysis laboratories of the healthcare system;
- To validate the mutation screening assay for congenital disorders with available treatment;
- To implement noninvasive prenatal diagnosis;
- To train students and technicians of USP to analyse NGS data through courses or informal courses organized by each lab according to their needs.

PART 3 - EDUCATION/ SCIENCE DISSEMINATION

a) Projects

Our High School Support Program offered a 40-hour course on basic concepts of Genetics (**Courses project**) to 34 high school teachers. As a result of partnerships with Educational Directories of Osasco and Itapecerica da Serra (**School laboratory classes project**), we provided 120 hours of technical and pedagogical support to 134 high school teachers (annexes 1 to 7). Every three weeks (term by which the lab, microscopes and experimental kits remained in a given school), an average of 700 students per school were involved in the teaching program. 90 high schools were visited from July/2013 to June/2015 and more than 60,000 students benefited from these partnerships. 146 high school students were trained to be monitors during the time the laboratory was installed in their schools. To overcome some of the teaching and learning difficulties presented by the abstract nature of some Genetics concepts, we provided instructional support material to facilitate the teaching and learning processes for 197 high school teachers (**Instructional support material project –** annexes 8 to 11). We established three loan centers, which currently provide instructional material to about 100 teachers each year. Our center also participates in the reactivation of a previously successful program “Great Scientists” (**Adventures in Science project)** to produce and distribute Science kits enabling young people to understand scientific concepts through hands-on experimentation. An evaluation of the kits was performed all over Brazil, through support from CAPES, and now the Ministry of Education (MEC) intends to distribute kits to 22,000 high schools around the country in conjunction with online training of the teachers involved. The **Giant Cell Project**, a scenic cell amplified 130,000 times and a set of complementary activities designed to facilitate the understanding of cell concepts, and the scientific exhibition “Light and Life” (**USP goes to your school project**) had over 4,000 visitors (annex 12).

In the **Sowing the seed of knowledge project**, we distributed posters with provocative questions in subways (lines green and blue) and 250 buses (Metra company) of São Paulo, and also in all 3,775 public schools within the state of São Paulo. The posters refer to a hot site that can be instantly accessed with a smartphone. Two campaigns were performed: “Similar, but different” (from October to December, 2014 - http://www.ib.usp.br/biologia/projetosemear/diferentes/ - in 3 months, more than 3 thousand users accessed the hot site) and “Is it in the DNA?” (from May to June, 2015 - http://www.ib.usp.br/biologia/projetosemear/estanodna/). A videoconference was delivered to all pedagogical nuclei coordinators (PCNPs) of the state of São Paulo (August, 2014). A second one, related to the “Is it in the DNA?” campaign will be delivered in August, 2015. An evaluation of the effect of this project within schools is being performed in 116 schools from different regions of São Paulo: Guarulhos, Osasco, Itapecerica da Serra and the eastern part of the capital. The Sowing the Seed of knowledge, which was launched by our CEPID, will involve 10 CEPIDs that will present their research projects, under our coordination.

b) Proposal of a novel Master's degree course

During the years 2014-2015, several principal investigators and collaborators were involved in the preparation and proposal of a new Master's degree course: "Professional Master's in Genetic Counseling and Human Genomics". The aim of the course is to train professionals to act as genetic counselors or to act in laboratory work related to human molecular genetics and cytogenetic/cytogenomics. The theoretical and practical approaches will help the postgraduate students to be approved in Specialist Exams and to fulfill legal requirements related to the profession. The course was approved and recommended by the Ministry of Education (CAPES) and the first group of students will start activities in August 2015. It is of note that this represents the first course in Brazil to train health professionals in genetic counseling.

c) Interviews in the Media and Science Dissemination Articles

The interaction with the media to discuss, translate and disseminate new scientific discoveries to the general public was achieved through 55 interviews and articles of science dissemination (annex 13).

PART 4 - CONTINGENCY FUNDS AND OTHER BENEFITS

a) Expenditure of Contingency Funds

Permanent material – R$ 12,007.90

- Expenses with permanent material such as: biological microscopes, router, vacuum pump, refrigerator, computer desk, nobreak, equipment to maintain the project's workflow at HUG-CELL.

Consumables – R$ 27,282.49

- Acquisition of office supplies, informatics, cleaning, electrical supplies, autoclave filters, decontamination kits for incubators, rats and mice to maintain the project's workflow at HUG-CELL.

Services – R$ 54,373.25

- Expenses with equipment maintenance: -80ºC freezers, microscopes, CO2 incubators, plotters, centrifuges, sequencers, DNA extraction automated system, air conditioning, cold chamber, pippete calibration, veterinarian services, veterinary laboratory analyses.

Publications

- Publication of article: "Knockdown of E2F2 inhibits tumorigenicity but preserves stemness of human embryonic stem cells" - Researcher: Oswaldo Keith Okamoto.
- Payment of color figures in the publication: "Knockdown of E2F2 inhibits tumorigenicity but preserves stemness of human embryonic stem cells" - Researcher: Oswaldo Keith Okamoto.
- Payment of color figures in the publication: "A defect in the RNA-processing protein HNRPDL causes limb-gurdle muscular dystrophy 1G (LGMD1G) - Researcher: Mayana Zatz

b) Expenditure of Complementary Benefits

Subscriptions – R$ 7,806.09

- Subscription in Conference: "59º Congresso Brasileiro de Genética", placed in Águas de Lindóia, September 16th to 19th, 2013 to Eliana Maria Beluzzo Dessen
- Travel insurance to collaborative project visit to Harvard Medical School Teaching Hospital – Mayana Zatz
- Subscription in "63rd Annual Meeting – The American Society of Human Genetics (ASHG 2013)", placed in Boston, October 22nd to 26th, 2013 – Maria Rita dos Santos e Passos-Bueno.
- Subscription in "63rd Annual Meeting – The American Society of Human Genetics (ASHG 2013)", placed in Boston, October 22nd to 26th, 2013 – Regina Célia Mingroni Netto
- Subscription in "63rd Annual Meeting – The American Society of Human Genetics (ASHG 2013)", placed in Boston, October 22nd to 26th, 2013 – Célia Priszkulnik Koiffmann
- Subscription to Conference "13th International Congress in Neuromuscular Diseases (ICNMD 2014)", placed in France, July 5th to 10th, 2014 – Mariz Vainzof
- Subscription to Conference "5th Biennial Meeting of the Human Variome Project Consortium", in France, May 20th - 22nd, 2014 – Peter Lees Pearson.

Airfare – R$ 26,422.51

- Ticket for Mayana Zatz, route São Paulo / Miami / Boston / New York / São Paulo for participation in collaborative projects. Havard Medical School Teaching Hospital
- Ticket for Regina Célia Mingroni Netto, route São Paulo / Newark / Boston / Newark / São Paulo for attendance in conference "63rd Annual Meeting – The American Society of Human Genetics (ASHG 2013)".
- Ticket for Maria Rita dos Santos e Passos-Bueno, route São Paulo / New York / Boston / New York / São Paulo for attendance in conference "63rd Annual Meeting – The American Society of Human Genetics (ASHG 2013)".
- Ticket for Mariz Vainzof, route São Paulo / Houston / São Francisco / Washington / São Paulo for attendance in conference "18th International Congress of the World Muscle Society (WMS 2013)" and meeting of Consórcio de Miopatia Nemalínica.
- Ticket for Célia Priszkulnik Koiffmann, route São Paulo / Newark / Boston / Newark / São Paulo for attendance in conference "63rd Annual Meeting – The American Society of Human Genetics (ASHG 2013)".
- Ticket for Mayana Zatz, route São Paulo / Dallas / Vancouver / Dallas / São Paulo for conference attendance "12th Annual Meeting – International Society for Stem Cell Research (ISSCR 2014)"
- Ticket for Maria Rita dos Santos e Passos-Bueno, route São Paulo / Italy / Pisa / Italy / São Paulo for attendance in "Gordon Research Conferences Frontiers of Science"
- Ticket for Peter Lees Pearson, route São Paulo / Paris / São Paulo for attendance in "5th Biennial Meeting of the Human Variome Project Consortium"

Daily grants – R$ R$ 33,202.00

- To Mayana Zatz for participation in collaborative projects. Harvard Medical School Teaching Hospital
- To Eliana Maria Beluzzo Dessen for participation in conference. Congresso: "59º Congresso Brasileiro de Genética"
- To Maria Rita dos Santos e Passos-Bueno for participation in conference. "63rd Annual Meeting – The American Society of Human Genetics (ASHG 2013)
- To Célia Priszkulnik Koiffmann for participation in conference. "63rd Annual Meeting – The American Society of Human Genetics (ASHG 2013)
- To Regina Célia Mingroni Netto for participation in conference. "63rd Annual Meeting – The American Society of Human Genetics (ASHG 2013)
- To Mayana Zatz for participation in conference. "63rd Annual Meeting – The American Society of Human Genetics (ASHG 2013)
- To Peter Pearson for participation in collaborative projects and visit to LUMC.
- To Mayana Zatz for participation in collaborative projects at ISTEM.
- To Peter Pearson for participation in conference. "5th Biennial Meeting of the Human Variome Project Consortium"

Annex 1
School Laboratory Classes Project - 16 High Schools from Educational Directory of Osasco attended from August to November, 2013.

High Schools
E E Prof. José Jorge
E E Prof. José Liberatti
E E Prof. Luiz Lustoza da Silva
E E Prof. Orlando Geríbola
E E Prof.Eloi Lacerda
E E Profa. Luci Anna Latorre
E E Profa. Rosa Bonfiglioli
E E Profa.Heloisa de Assumpção
E E São Paulo da Cruz
E E Tarsila do Amaral
EE Carlos de Laet
EE Irmã Gabriela Maria Elizabeth Wienkem
EE Prof. Claudnei Garcia
EE Prof. Francisca Lisboa Peralta
EE Prof.José Maria Rodrigues Leite
ETEC Uirapuru

Annex 2
School Laboratory Classes Project
46 High Schools from Educational Directories of Osasco and Itapecerica da Serra attended in 2014.

High Schools	**Educational Directories**
E E Prof. José Jorge E E Major Telmo Coelho Filho E E Prof. José Liberatti	Osasco
E E Prof. Francisco Lisboa Peralta E E Profa. Julia Lopes E E Prof. Neusa de Oliveira Prévide	Osasco
E E Prof. Gastão Ramos E E Pof. Heloisa Assunpção E E Deputado Guilherme de Oliveira Gomes	Osasco
E E Irmã Gabriela E E Prof. Benedito Caldeira E E Francisco Matarazzo Sobrinho	Osasco
E E Glória Azedia Bonetti E E Leonardo Villas Boas	Osasco
E E Prof. Francisco Casabona E E Antonio Carlos da Trindade	Osasco
E E Prof.Alice Velho Teixeira E E Profa. Fanny Monzoni Santos	Osasco
E E Matilde Maria Cremm E E Salvador de Leone	Itapecerica da Serra

E E Jardim Cipava II E E Antonio Raposo Tavares	Osasco
E E Prof. Josué Benedito Mendes E E Dr. Americo Marco Antonio	Osasco
E E Profª Marianinha Queiroz E E Gov. André Franco Montoro	Itapecerica da Serra
E E Jardim santa Maria E E. Prof. José Ribeiro de Souza	Osasco
E E Prof. Orlando Geríbola E E Cel. Antonio Paiva de Sampaio	Osasco
E E Joaquim Fernando Paes de B. Neto E E Benevides Beraldo	Itapecerica da Serra
E E Prof. Maria Augusta Siqueira E E Prof. Lucy Anna Carroso Latorre	Osasco
E E Sebastião de M. Cardoso E E Gertrudes Eder	Itapecerica da Serra
Fundação Casa E E Prof. Oguiomar Ruggieri	Osasco
E E Prof. Vicente Peixoto E E Educador Paulo Freire	Osasco
E E Jd. Sonia Maria E E Eduardo Roberto Daher	Itapecerica da Serra
E E.Prof. Dr. Luiz Lustosa E E Rosa Bonfiglioli	Osasco
E E Donizetti Ap. Leite E E Olivia de Faria Nogueira	Itapecerica da Serra

Annex 3
School Laboratory Project
28 High Schools from Educational Directory of Osasco attended from February to June, 2015.

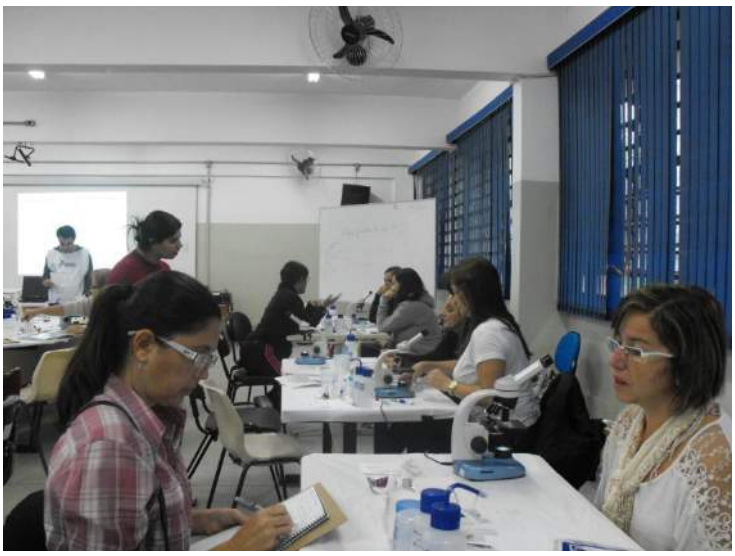
High Schools	**Educational Directories**
EE Prof. Alcyr Oliveira Porciuncula E E Antonio Raposo Tavares	Osasco
E E Profa. Julia Lopes E E Prof. José Jorge	Osasco
E E Jardim Cipava II E E Leonardo Villas Boas	Osasco
E E Prof. Newton Espirito Santo Ayres E E Prof. Maria Augusta Siqueira	Osasco
E E Joaquim Fernando Paes de Barros Neto E E Jornalista Paulo de Castro Jr.	Itapecerica da Serra
E E Prof. Gastão Ramos EE Dr. Aureliano Leite	Osasco
EE Prof. Heloisa de Assunpção E E Jardim Santa Maria III	Osasco
E E Jardim Montesano E E Salvador de Leone	Itapecerica
E E Prof. João Batista de Brito EE Dep. Guilherme de Oliveira Gomes	Osasco
EE Prof. Fanny Monzoni Santos EE Tarsila do Amaral	Osasco
E E Gertrudes Eder	Itapecerica da

E E Sebastião de M . Cardoso	Serra
E E São Paulo da Cruz EE Prof. Francisca Lisboa Peralta	Osasco
E E Ernesto Thenn de Barros E E Irmã Gabriela	Osasco
E E Maria Olimpia de S. Q. Maciel E E Jardim do Carmo	Itapecerica da Serra

Annex 4
School Laboratory Classes Project - Technical and Pedagogical support to 32 High School teachers from Educational Directory of Itapecerica da Serra (April 14th , 2014) and 38 teachers from Educational Directory of Osasco (April 15th , 2014)

High Schools	**High Schools teachers**	**Educational Directories**
EE Donizetti Ap. Leite	Janaina da Luz Andrade Barbosa	Itapecerica da Serra
	Ana Helena Souza de Abreu Barros	Itapecerica da Serra
	Keila Rocumback Flose	Itapecerica da Serra
EE Olivia de Faria Nogueira	Miriam de melo Fabre	Itapecerica da Serra
	Marli Ruiz	Itapecerica da Serra
EE Gov. André Franco Montoro	Ivaneusa de Moraes Soares	Itapecerica da Serra
	Gleice de Lima Takeda	Itapecerica da Serra
	Rafael Moranga Gonçalves	Itapecerica da Serra
EE Profª Marianinha Queiroz	Viviane Domingues Rodrigues	Itapecerica da Serra
EE Jd. Sonia Maria	Ana Emília Costa da Silva Rosa	Itapecerica da Serra
	Dirce de Souza Cleim	Itapecerica da Serra
EE Joaquim Fernando Paes de B. Neto	Eder Basílio Pereira	Itapecerica da Serra
	Rodrigo Mendes Aguiar	Itapecerica da Serra
	George Magalhães Gomes	Itapecerica da Serra
	Camila Sales de Sousa	Itapecerica da Serra
	Claudineia Lisboa Daitx	Itapecerica da Serra
EE Benevides Beraldo	Elias Adelino Framesqui	Itapecerica da Serra
	Ana Lucia Rodrigues Perri Luchini	Itapecerica da Serra
	Delina Bispo dos Santos	Itapecerica da Serra
EE Eduardo Roberto Daher	Rúbia Bolognesi Ferreira	Itapecerica da Serra
EE Salvador de Leone	Vanessa Ferreira da Silva	Itapecerica da Serra
	Cristiane Aparecida dos Santos	Itapecerica da Serra
	Andréia Martinelli Lvinholli	Itapecerica da Serra
EE Sebastião de M. Cardoso	Eliane Gomes Diniz	Itapecerica da Serra
	Geizane Rosa de Souza	Itapecerica da Serra
	Higino Jose de Andrade JR	Itapecerica da Serra
	Jessica Cesar Elias	Itapecerica da Serra
EE Gertrudes Eder	Lucinao Barbosa da Silva	Itapecerica da Serra

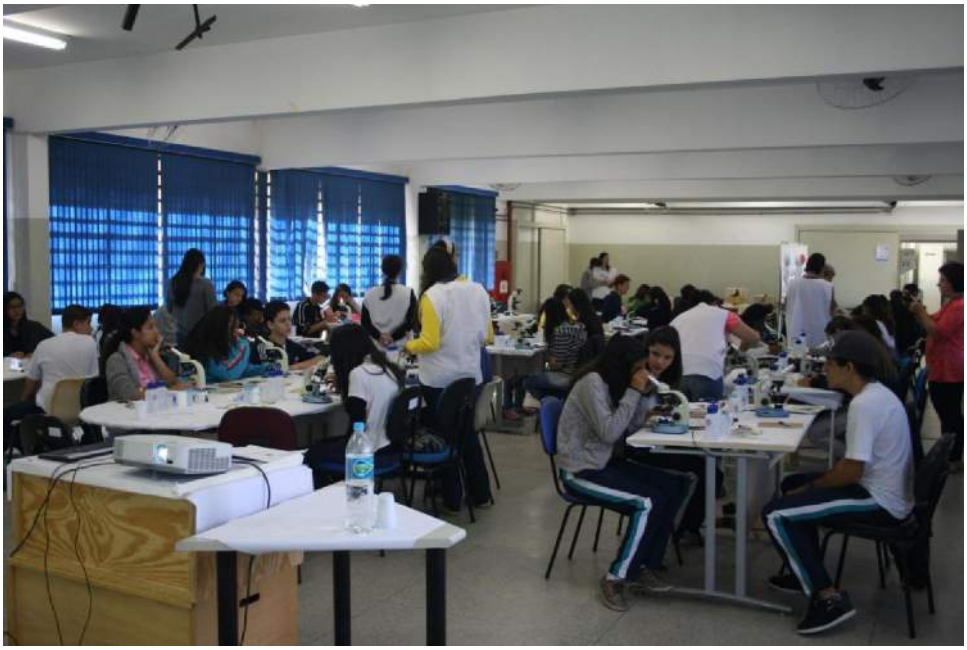
	Regina Célia de Castro Azevedo	Itapecerica da Serra
	Leandro Matias da Silva	Itapecerica da Serra
EE. Matilde Maria Cremm	Solange Emy Iwano	Itapecerica da Serra
	Francisco Alex de Freitas	Itapecerica da Serra
EE Prof. Alice Velho Teixeira	José Afonso de Souza Neto	Osasco
EE Dr. Américo Marco Antonio	Ivanildes Silva Cangussu	Osasco
EE Antonio Carlos da Trindade	Adriana Aguiar Vasconcelos	Osasco
EE Cel Antonio Paiva de Sampaio	Ivone Luzia Simões Santos	Osasco
EE Antonio Raposo Tavares	Maria Helena F Damasceno	Osasco
EE Prof. Benedito Caldeira	Elita Sgarbi Beluco Cintia Rocini	Osasco
EE Jardim Cipava II	Jucélia Aguilar Pereira	Osasco
EE Prof. Eloi Lacerda	Suzana de Souza Silva	Osasco
EE Prof. Ernesto Thenn de Barros	Yoshiko Wakabayashi Rebolças	Osasco
EE Prof. Fernando Buonaduce	Joyce de Almeida Brito	Osasco
EE Prof. Francisco Lisboa Peralta	Roseli Cristina Laranjeira	Osasco
EE Prof. Francisco Casabona	Ariene da Silva Pereira	Osasco
EE Prof. Gastão Ramos	Alessandra Brito Santos	Osasco
EE Glória Azedia Bonetti	Isabel L. De R. Muniz	Osasco
EE Graciliano Ramos	Carla Carloto Araujo	Osasco
EE Dep. Guilherme de Oliveira Gomes	Gislaine Gomes Martins Gueteri	Osasco
EE Prof. Heloisa Assunpção	Carolina Assaf	Osasco
EE Jardim Santa Maria III	Alline Ramos Pereira do Nascimento Lucimar Rodrigues	Osasco
EE Prof. José Jorge	Benedita de Souza	Osasco
EE Prof. José Liberatti	Adriana Martins Souza Lima Lucilene C. Souza Leticia Tartarini Ramires	Osasco
EE José Ribeiro de Souza	Bianca Chaves Meirelles	Osasco
EE Prof. Josué Benedito Mendes	Tânia Regina Bottaro Arantes	Osasco
EE Julia Lopes de Almeida	Rebeca Laino Gama	Osasco
EE Leonardo Vilas Boas	Carlos Alberto Ramos	Osasco
EE Lucy Anna Latorre	Fernanda Vitorino	Osasco
EE Prof. Dr. Luiz Lustosa da Silva	Neide Maria de Campos Borges	Osasco
EE Prof. Maria Augusta Siqueira	Rogério Soares dos Santos	Osasco
EE Prof. Neusa de Oliveira Prévide	Stephani Oliveira Santos	Osasco
EE Prof. Oguiomar Ruggeri	Silmara Borges da Silva Santos Eliane Cristina Borelli Damasceno	Osasco
EE Prof. Orlando Geríbola	Giane Conceição Campos	Osasco
EE Educador Paulo Freire	Douglas de Souza Silva	Osasco
EE Rosa Bonfiglioli	Ingrid Garcia Martins P. da Silva	Osasco
EE Prof. Vicente Peixoto	Bruna Gabriele Aguiar da Silva	Osasco



Annex 5
School Laboratory Classes Project – training of 68 High School students to act as monitors in their schools during the time the Laboratory is installed in the school. Educational Directory of Osasco (April 16th and 17th, 2014)

High Schools	High School Students
EE Prof.Alice Velho Teixeira	Mylena Vitoria Lima Ferreira Sabrina Souza Calixto Juliane Helen Silva Santos
EE Cel. Antonio Paiva de Sampaio	Karina Santos de Oliveira Heloisa Camile dos Santos
EE Jardim Cipava II	Esteffane Caetano da Silva Matheus Rocha Silva Sabrina Amorim Souza
EE prof. Claudinei Garcia	Adriane Gonçalves de Souza Giovanna Mazoni Zago
EE Prof. Eloi Lacerda	Luana dos Anjos Santos Neuton Nunes Ribeira Junior
EE Leonardo Vilas Boas	Mirella Vitalino de Souza Eliane Santos Santana
EE Prof. Fanny Manzoni Santos	Anny Kethilyn dos Santos Jeniffer Kiss Rodrigues Martins Joao Vinicius Sanches
EE Prof. Francisco Lisboa Peralta	Carlos Henrique Gomes Meira
EE Prof. Francisco Matarazzo Sobrinho	Thais Kelly da silva Cunha Rômulo Laerte Alves Bastos
EE Irmã Gabriela Maria Elizabeth Wienkem	Brendon Eric Gonçalves da Silva Mario Dourado dos Santos Victoria Manuela Alexandre Silva Santos
EE Prof. Gastão Ramos	Natany Nayume da Silva Sabrina Maia Duarte Soniele Costa Silva

EE Deputado Guilherme de Oliveira Gomes	Daniela Santos da Silva Bruna Gabriella Teles Graciano Jade Ferraz Maximo
EE Prof. Heloisa Assunpção	Victor de Angelo Ferreira Erika Camelo dos Santo
EE Jardim Santa Maria III	Amanda Sandy Arianne Campos
EE Prof. Fernando Buonaduce	Sara de Souza Francelino Rafaella de Souza Carvalho
EE Prof. José Jorge	Gabriel Correa Soares Gabrielle Lopes Ruiz
EE Prof. José Liberatti	Jean Gabriel Hanashiro Judice Fabíola Emilly Dutra Silva Vitória Manfré Baldassi
EE Prof. José Ribeiro de Souza	Maria Eduarda dos santos Araújo Michelly Gomes da Silva Thiago Araujo da Costa Silva
EE Prof. Josué Benedito Mendes	Roberto Jesus Amaral Ivanelly Vieira de Negreiros
EE Julia Lopes de Almeida	Luiz Felipe de Araujo Alessandra Ribeiro da Silva Fabiana Santos de Queiroz
EE Prof. Lucy Anna Latorre	Paola Dromenech Dyulia Bojar Sutto
EE Prof. Luiz Lustosa da Silva	Romildo do Nascimento Coelho Jéssica Souza da Silva
EE Prof. Maria Augusta Siqueira	Erivânia Tobias de Oliveira Paloma Rocha Costa Yasmim Lucas Flores Moraes
EE Prof. Neuza de Oliveira Prévide	Iva Jane Alexander França Oliveira Lucas Peres Pereira
EE Prof. Orlando Geríbola	Vitória Magrini c de Paula Chirley Santos de Jesus Giovanna B. Cruz Magalhaes
EE Educador Paulo Freire	Jamile Aparecida de Oliveira Amaral Samuel Araujo
EE Rosa Bonfiglioli	Roberto Maciel Joyce Victoria Leite Aquendo Bruna Costa Gomes
EE Prof. Vicente Peixoto	Richard Cristopher Amanda Silva Vital Sardila de Sousa Silva



Annex 6
School Laboratory Classes Project - Technical and Pedagogical support to 39 High School teachers from Educational Directory of Osasco (February 25th to 27th, 2015) and 78 High School students. The students act as monitors in their schools.

High Schools	High Schools teachers	High Schools students
EE Prof. Alcyr Oliveira Porciuncula	Antonio Pedro de Castro	Emily Castelhano Saraiva Thamires Leite Siqueira

EE Antonio Raposo Tavares	Hayrton Avelino Monteiro	Bruno Vinicius Oliveira Santos Amanda Gutierres de Souza Ramos Bruna Gabrielly Arruda dos Santos
EE Dr. Aureliano Leite	Jennifer Caroline de Sousa	Thyergue Candido
EE Prof. Benedito Caldeira	Celina Setsuko Kussano de Castro	
EE Jardim Cipava II	Mildre Pinto da Silva Cardoso	Suzana M de S Ferreira Aldo Victor Angelo de Mendonça
EE Claudinei Garcia	Maria Neuza de Souza Carvalho	
EE Prof. Eloi Lacerda	Suzana de Souza Silva	Sabrina da Silva Teixeira Martins Nubia Mangueira do Carmo Karina Mendes Gomes
EE Prof. Ernesto Thenn de Barros	Claudio Victorino Leite Ramos	Ivana Aparecida dos Santos Silva Sander de Souza Cordeiro Rafael Sobreira Alves
EE Prof. Francisca Lisboa Peralta	Reginaldo dos Santos Tiago Alves de Oliveira	Alexandro Uchoa Silva Esthefany Caroliny Marquezin da Silva Wemerson Lima Krygsman
EE Irmã Gabriela Maria Elizabeth Wienken	Reginaldo dos Santos Tiago Alves de Oliveira	Brendon Eric Gozales da Silva Mario Dourado dos Santos Miqueias dos Santos Bispo
E E Prof. Gastão Ramos	Alessandro Brito Santos de Freitas	Lauanny Nayara Carlos Viana Bianca de Souza Araujo Bruna de Paula Oliveira
EE Prof. Fanny Monzoni Santos	Edelson da Silva Nascimento	Jennifer Lais Ferreira Lucas Guerreiro Bianca Lacerda Costa
EE Dep. Guilherme de Oliveira Gomes	Gislaine Gomes Martins Guethi	Vitoria Fernandes Callejon Nayra Benetelo Alves Carolina Romão de Moura
EE Prof. Heloisa de Assunpção	Carolina Assaf	Marilia Regina Alves da Cruz Victor de Oliveira Barbosa Kaique de Moraes Urbano Oliveira
EE Jardim Santa Maria III	Ester Alves Correia	Ana Aparecida Rodrigues da Silva Joice Gouveia dos Santos João Pedro de França
EE Prof. João Batista de Brito	Ezilda Oliveira Aves	
EE José Geraldo Vieira	Carmen Cinira Teixeira	Sarah Espinosa Pintos João Victor Maciel Dantas Vitória Bispo de Jesus Eliel Dutra Silva
EE Prof. José Jorge	Benedita de Souza	Breno Barbieri Silva Adriele Cristina Voichicovski Santos Milene Utiama Paulo
EE Prof. Jose Liberatti	Lucilene Costa de Souza	Isabela Mendes de Lima Julia Agara de Castro Lima Gabriela Samara Santucci Garcia
EE Prof. Josué Benedito Mendes	Tânia R. Botaro Arantes	Camila Bezerra da Silva Maryanne Ladeia de Oliveira Karistem Oshei dos S. Mendonça
EE Julia Lopes de Almeida	Francisco Antonio Silva Alves	Rodrigo Jesus de Sousa Daniel Felipe de Menezes Romao

EE Leonardo Vilas Boas	Maria Angela S Gomes Luiz E S Beluco	Vitoria Gabrielle de Paula Santos Jéssica Santos Buzzo Patrick Swayse Santos Alves
EE Prof. Lucy Anna Latorre	Marcos Viana da Silva	Keren Martins dos Santos Rayanne Vitoria daSilva Leonardo Silva dos Anjos
EE Prof. Dr Luiz Lustosa Da Silva	Reginete Santana	
EE Prof. Maria augusta Siqueira	Luciana Cardoso Romeiko	Emily Rayssa Ferreira Borges Amanda Pacheco dos Santos Danielle Santos Gonçalves
EE Prof. Neuza de Oliveira Prévide	Guilherme Thiago Brandt Mazzini	Maria Vitoria da silva Pereira Mikael Dias da Silva Thassila Coreolano da Silva
EE Prof. Newton Espirito Santo Ayres	Elias Tavares	
EE Prof. Oguiomar Ruggieri	Natalia Rosa Sciaani	Igor Gregório Emilly Almeida
EE Educador Paulo Freire	Flavia Garcia Borges	
EE Rosa Bonfiglioli	Lucilene costa de Souza Maria de Fátima G. F dos Santos	Mariana Yasmin deBarros Ferreira Vitoria Vieira Dourado Kauan Lima Inácio
EE São Paulo da Cruz	Renata Aparecida de Oliveira Maino	Andressa Parra Sanches Beatriz Victoria Cabral Ascêncio
EE Tarsila do Amaral	Denise ER F Santana	Ana Beatriz Silva dos Santos Yasmin Ferreira de Sousa João Pedro Martins
EE Prof. Vicente Peixoto	Bruna Gabriele Aguiar da Silva	Isabella de Mello da Silva Viviane Bonifácio de Oliveira
EE Graciliano Ramos	Raquel Vettore Oliveira	Thais Rodrigues deSousa Niviani oliveira de Mello Maika Quirino Muller
EE Jose Ribeiro de Souza	Daniela Azevedo Brito	Leticia Roldão do Nascimento
E E Asa Branca da Serra	Roseneide de L.C . Assis Érica C. dos Santos Fabio Batista Pangardi	Itapecerica da Serra

Annex 7
School Laboratory Classes Project - Technical and Pedagogical support to 25 High School teachers from Educational Directory of Itapecerica da Serra (March 26th , 2015)

High Schools	**High School teachers**
E E Eduardo Roberto Daher	Viviane B. Barbosa
E E Gertrudes Eder	Jorge Henrique Silva Bueno Cinthya Cândida Miguel
E E Jardim do Carmo	Darlene Melo de Oliveira
E E Jardim Montesano	Gilbert Kisser Jr.
E E Joaquim Fernando Paes de Barro Netto	Deoclecia A. S de Oliveira
E E Jornalista Paulo de Castro Jr.	Maria Aparecida Oliveira Benedita Juliana Zigart
E E Julia de Castro Carneiro	Reinaldo Constancio da Silva

	Antonio Flavio Segato Carlos Alberto Vedelago
E E Maria Olimpia de S.Q. Maciel	Irene de Oliveira Santos Sheila Pereira de Souza
E E Matilde Maria Cremm	Leticia de Camargo Rosa Moura
E E Olivia de Faria Nogueira	Gislene Julia Benelli Roni A. S. Alves
E E Prof. Donizetti Aparecido Leite	Carlos Palermo
E E Prof. Gastão Ramos	Alessandro Brito Santos de Freitas
E E Prof. Marianinha de Queiroz	Eduardo Pimentel Juliana Buffon Bruno Tadeu Lopes
E E Prof. Natercia Crem de M. Pedro	Vanusa Alves da Cunha Carlos Alberto Vedelago Nanci oliveira Carvalho
E E Sebastião de M Cardoso	Raquel Ribeiro Schimidt

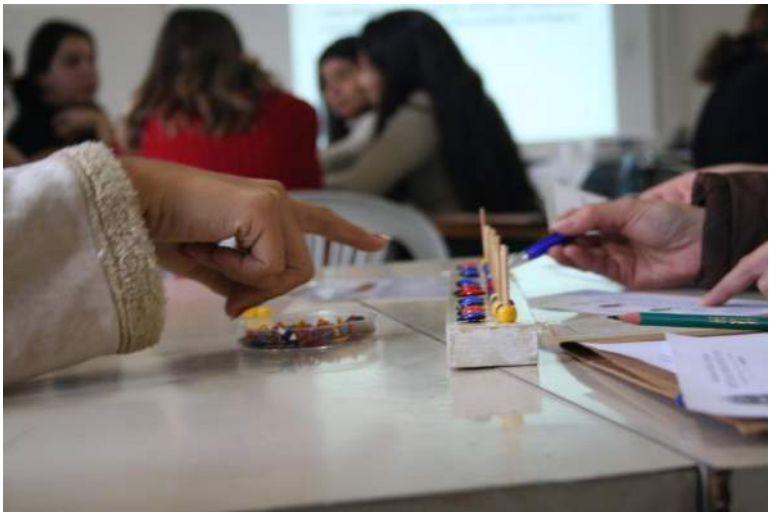
Annex 8
Instructional support material project
Training of 102 High School teachers to use Instructional material. Educational Directories of Osasco (May 27th and 28th, 2014) and of Itapecerica da Serra (June 3th and 4th, 2014)

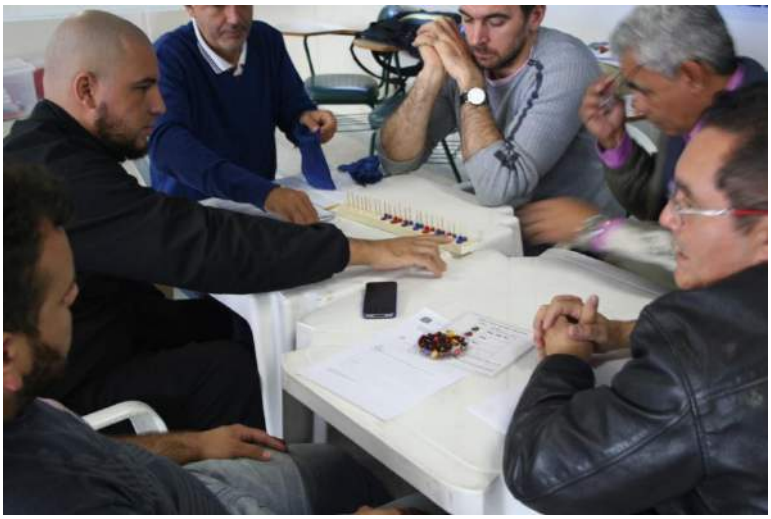
High Schools	**High School teachers**	**Educational Directories**
E E Alexandre Rodrigues Nogueira	Herminio C. Nunes	Itapecerica da Serra

E E Antonio Florentino	Rúbia B. Ferreira	Itapecerica da Serra
E E Asa Branca da Serra	Ricardo Martins de Oliveira	Itapecerica da Serra
E E Asdrubal do Nascimento Queiroz	Elisangela Aparecida Borges Souza	Itapecerica da Serra
E E Bairro da Palmeirinha	Elisangela Aparecida Borges Souza	Itapecerica da Serra
E E Bairro das Palmeiras	Edcarlos Marques	Itapecerica da Serra
E E Bairro das Senhorinhas	Josefina M. Almeida	Itapecerica da Serra
E E Bairro dos Penteados	Alberto Carlos A. Gimenez	Itapecerica da Serra
E E Carlos Alberto Pereira	Célia Lino de Jesus	Itapecerica da Serra
E E Eduardo Roberto Daher	Rúbia B. Ferreira	Itapecerica da Serra
E E Gertrudes Eder	Luciano Barbosa da Silva	Itapecerica da Serra
E E Gov. André Franco Montoro	Rafael Moranga Gonçalves	Itapecerica da Serra
E E Jardim Jacira	Marcelo Aparecido Correia Ribeiro	Itapecerica da Serra
E E Jardim Sônia Maria	Dirce de Souza Clein	Itapecerica da Serra
E E João Baptista de Oliveira	Maria de Fátima Ferreira Aguiar	Itapecerica da Serra
E E Joaquim Mendes Feliz	Pamela Bonetti	Itapecerica da Serra
E E Júlia de Castro Carneiro	Reinaldo C. da Silva	Itapecerica da Serra
E E Marianinha de Queiroz	Gizele de C. Rodrigues	Itapecerica da Serra
E E Mario Francisco Amorim	Tainan Rosa de Moura	Itapecerica da Serra
E E Massako Higashioka	Raquel Ribeiro Schimdt	Itapecerica da Serra
E E Matilde Maria Cremm	Francisco Alex de Freitas	Itapecerica da Serra
E E Oredo Rodrigues da Cruz	Bruno Ladeira Lopes	Itapecerica da Serra
E E Paulo de Castro	Juliana V Zigart	Itapecerica da Serra
E E Paschoal Carlos Magno	Regiane Aparecida B. Brandão	Itapecerica da Serra
E E Pedra Branca	Francisco Alex de Freitas	Itapecerica da Serra
E E Poeta Angenor de Oliveira	Julio Cesar de Oliveira	Itapecerica da Serra
E E Salvador de Leone	Andreia M. Lavanholi	Itapecerica da Serra
E E Sebastião de M Cardoso	Adriana Domingues Ferreira	Itapecerica da Serra

E E Seminário	Ana Helena S. Abreu Barros	Itapecerica da Serra
EE Alice Velho Teixeira	Sabrina Pareico Neves	Osasco
EE Américo Marco Antonio	Ivanildes Silva Cangussu	Osasco
EE Antonio Carlos Trindade	Rosimeire Cássia da Silva	Osasco
EE Antonio Almeida Junior	Daniela C. da Palma Luciana Aparecida Monteiro Gabriela Genari	Osasco
EE Antonio Paiva Sampaio	Ivone Luzia Simões Santos Lucila Miglioni Rodrigues	Osasco
EE Armando Gaban, Prof	Marilin Fernandes Brandão Luis Antonio Miussi	Osasco
EE Benedito Caldeira	Elita Sgarbi Beluco Cintia Rocini	Osasco
EE Jardim Cipava II	Jucélia Aguilar Pereira	Osasco
EE Claudinei Garcia	Patrícia Ap. M. Maia Rogério Augusto Sena	Osasco
EE Eloi Lacerda	Suzana de Souza Silva Erika Hirome Ikeda Cristiane de L. Potença	Osasco
EE Ernesto Thenn de Barros, prof	Claudio Vitorino Leite Ramos Yosaahiko Wakabayashi Rebolças	Osasco
EE Fanny Monzoni Santos, prof	Juliana Fonseca Caetano Edelson da Silva Nascimento Tania da Silva Nascimento Jardim Somine Alvarenga da Cunha	Osasco
EE Fernando Buonaduce, prof	Eneida Domingues Fernandes Denise dos Santos Averra Jorge Isac de Almeida	Osasco
EE Francisca Lisboa Peralta, profa	Roseli Cristina Laranjeira	Osasco
EE Francisco Casabona, prof	Ariene da Silva Pereira	Osasco
EE Gabriela M. E. Wienkem, irmã	Ruth Nonato da Silva Nagabe	Osasco
EE Gastão Ramos, prof	Alessandra Brito Santos Josilaine Ribeiro de Barros André Henrique A. Duarte	Osasco
EE Glória Azedia Bonetti	Aline Ribeiro Del Negro	Osasco
EE Graciliano Ramos	Carla Carloto Araujo	Osasco
EE Guilherme de Oliveira Gomes, deputado	Gislaine Gomes Martins	Osasco
EE Heloisa Assunpção, profa	Carolina Assaf	Osasco
EE João Batista de Brito, prof	Isis Furtado Mantovanelli	Osasco
EE José Edson Martins Gomes, prof	Lucila Magioni Rodrigues	Osasco
EE José Geraldo Vieira	Carlos Alberto da Silva Valter Pina Macea	Osasco
EE José Jorge, prof	Benedita de Souza Cesar de Morais Renata Osório R. Zanetti	Osasco

	Guilherme Augusto de Oliveira Rebelo	
EE José Liberatti, prof	Lucilene Costa de Souza	Osasco
EE José Maria Rodrigues Leite, prof	Maria Cada Cardoso Danielle Monique do Nascimento Luiz Beluco	Osasco
EE José Ribeiro de Souza	Bianca Chaves Meirelles	Osasco
EE Josué Benedito Mendes, prof.	Tania Regine B. Arantes	Osasco
EE Júlia Lopes de Almeida	Rebeca Laino Gama	Osasco
EE Leonardo Vilas Boas	Natália Silvia de Freitas Silva Carlos Alberto Ramos	Osasco
EE Lucy Anna Latorre, prof	Katia Guerreiro Carraro Cristiane Aparecida Bori	Osasco
EE Luiz Lustosa da Silva, prof Dr.	Neide Maria de Campos Borges Reginete Santana Bispo	Osasco
EE Maria Augusta Siqueira, profa.	Leticia da Silva Martinez Rogério Soarez dos Santos	Osasco
EE Neuza de Oliveira Prévide, profa	Alessandra Paula de Andrade Luz	Osasco
EE Newton Espírito Santo Ayres, prof	Elias Tavares	Osasco
EE Oguimar Roggeri, prof	Renata Aparecida de Oliveira Maino Silmara Borges da Silva Franco	Osasco
EE Orlando Geríbola, prof	Giane Coração Campos Miriam Santana S. Aparecida	Osasco
EE Paulo Freire, Educador	Aparecida Lira Aparecido Francisco Galdino Renato Policarpo da Silva	Osasco
EE Rosa Bonfiglioli	Maria de Fatima G. F. dos Santos	Osasco
EE São Paulo da Cruz	Aline Ribeiro Delnegro	Osasco
EE Tarcila do Amaral	Adriana Martins Soares	Osasco
EE Telmo Coelho Filho, Major	Carla Rocha Fernandes Uehara	Osasco
EE Vicente Peixoto, prof	Bruna Gabrieli A. da Silva	Osasco
EE Walter Negrelli	Eunice Santana de Melo	Osasco





Annex 9
Instructional support material project
Training of 28 High School teachers to use Instructional material. Educational Directories of Itapecerica da Serra (June th, 2014)

High Schools	High School teachers
E E Alexandre Rodrigues Nogueira	Herminio C. Nunes
E E Antonio Florentino	Rúbia B. Ferreira
E E Asa Branca da Serra	Ricardo Martins de Oliveira
E E Asdrubal Queiroz	Elisangela Aparecida Borges Souza
E E Bairro da Palmeirinha	Elisangela Aparecida Borges Souza
E E Bairro das Palmeiras	Edcarlos Marques
E E Bairro das Senhorinhas	Josefina M. Almeida
E E Bairro dos Penteados	Alberto Carlos A. Gimenez
E E Carlos Alberto Pereira	Célia Lino de Jesus

E E Eduardo Roberto Daher	Rúbia B. Ferreira
E E Gertrudes Eder	Luciano Barbosa da Silva
E E Gov. André Franco Montoro	Rafael Moranga Gonçalves
E E Jardim Jacira	Marcelo Aparecido Correia Ribeiro
E E Jardim Sônia Maria	Dirce de Souza Clein
E E João Baptista de Oliveira	Maria de Fátima Ferreira Aguiar
E E Joaquim Mendes Feliz	Pamela Bonetti
E E Júlia de Castro Carneiro	Reinaldo C. da Silva
E E Marianinha de Queiroz	Gizele de C. Rodrigues
E E Mario Francisco Amorim	Tainan Rosa de Moura
E E Massako Higashioka	Raquel Ribeiro Schimdt
E E Matilde Maria Cremm	Francisco Alex de Freitas
E E Oredo Rodrigues da Cruz	Bruno Ladeira Lopes
E E Paulo de Castro	Juliana V Zigart
E E Paschoal Carlos Magno	Regiane Aparecida B. Brandão
E E Pedra Branca	Francisco Alex de Freitas
E E Poeta Angenor de Oliveira	Julio Cesar de Oliveira
E E Salvador de Leone	Andreia M. Lavanholi
E E Sebastião de M Cardoso	Adriana Domingues Ferreira
E E Seminário	Ana Helena S. Abreu Barros

Annex 10
Instructional support material project
Training of 51 High School teachers to use Instructional material. Educational Directory of Osasco
(March 3th, 2015)

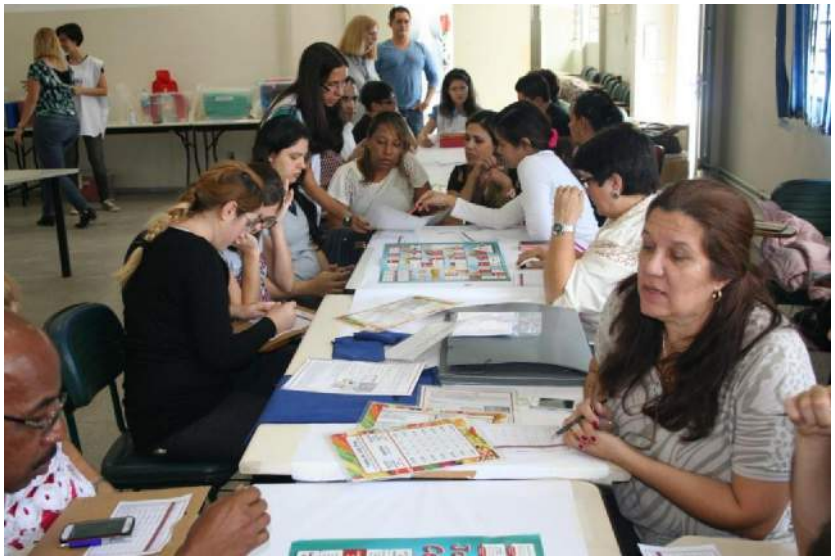
High School	**High School Teacher**
E E Dr. Antonio Braz Gambarini	Fernanda Gageti
E E Prof. Antonio de Almeida Junior	Luciana Aparecida Monteiro Gabriela Genari Crespo
E E Cel. Antonio Paiva de Sampaio	Lucila M. Rodrigues
E E Antonio Raposo Tavares	Hayrton Avelino Monteiro
E E Prof. Armando Gaban	Marina Santos Barbosa Marilin Fernandes Brandão
E E Dr. Aureliano Leite	Jennifer Caroline de Sousa
E E Prof. Benedito Caldeira	Celina Setsuko Kussano de Castro Elita Sgarbi Belucco
E E Jardim CipavaII	Denise Eduarda Roberto F de Santana
E E Claudinei Garcia	Mara Regina Senna Maria Neuza de Carvalho
E E Prof. Eloi Lacerda	Adriana Medeiros Bueno Suzana de Souza Silva
E E Prof. Ernesto Thenn de Barros	Yoshiko Wakabayashi Rebolças Marcos Viana da Silva
E E Prof. Fanny Monzoni Santos	Edelson da Silva Nascimento
E E Prof. Fernando Buonaduce	Erica dos Santos Moura Joyce Isaac de Almeida
E E Prof. Francisca Lisboa Peralta	Reginaldo dos Santos
E E Irmã Gabriela Ma. Elizabeth Wienken	Carlos Alberto Ramos

E E Prof. Gastão Ramos	Josilaine Ribeiro de Barros
E E Dep. Guilherme de Oliveira Gomes	Gislaine Gomes Martins Guethi
E E Graciliano Ramos	Raquel Vettore Oliveira Carla Carloto Araujo
E E Prof. Heloisa de Assunpção	Sergio Seixas de Barros
E E Jardim Santa Maria III	Ester Alves Correia
E E José Edson Martins Gomes	Mirian Alves Aversa
E E José Geraldo Vieira	Carmen Cinira Teixeira
E E Prof. José Jorge	Renata Osorio Rosa Zanetti
E E Prof. Jose Maria Rodrigues Leite	Danielle Monique Nascimento Luiz Emilio Sgarbi Beluco
E E José Ribeiro de Souza	Daniela Correa Azevedo
E E Prof. Josué Benedito Mendes	Nilda Aparecida Maximo de Matos Tânia Regina Botaro Arantes
E E Julia Lopes de Almeida	Rebeca Laino Gama
E E Leonardo Vilas Boas	César Jose de Moraes
E E Prof.Lucy Anna Latorre	Marcos Viana da Silva
E E Prof. Dr Luiz Lustosa Da Silva	Reginete Santana Gislene Mariano da Costa
E E Prof. Maria augusta Siqueira	Luciana Cardoso Romeiko
E E Prof. Newton Espirito Santo Ayres	Elias Tavares Fatima R.Gomes Silva
E E Prof. Oguiomar Ruggieri	Natalia Rosa Sciaani
E E Prof. Orlando Geríbola	Elaine Dias dos Santos Giane Coração Campos
E E Rosa Bonfiglioli	Maria de Fátima G. F dos Santos
E E São Paulo da Cruz	Renata Aparecida de Oliveira Maino
E E Tarsila do Amaral	Divina Maria de Camargo
E E Prof. Vicente Peixoto	Bruna Gabriele Aguiar da Silva

Annex 11
Instructional support material project
Training of 16 High School teachers to use Instructional material. Educational Directory of Itapecerica da Serra (April 10th, 2015)

High Schools	**High School teachers**
E E Abrahão de Moraes	Patrícia Lima Sales
E E Antonio Florentino	Rubia Bolognese Ferreira
E E Asa Branca	Roseneide de Lourdes Colombo
E E Asdrubal do Nascimento Queiroz	Celso Nunes Cocharro
E E Carlos Alberto Pereira	Célia Lino de Jesus
E E Instituto Maria Imaculada	Gilbert Kisser Junior
E E Isabel A redentora	Maria Esther Lima Gonçalves
E E Jardim do Carmo	Darlene Melo de Oliveira
E E Jardim Montesano	Luciana Cabral de Almeida Prado
E E João Batista de Oliveira	Izaura A.Creem R.Oliveira

E E Joaquim Fernando P. B. Neto	Rute Gomes Felício
E E Maria Olímpia de Souza Q. Maciel	Dirce de Souza Clein
E E Matilde Maria Cremm	George M. Gomes
E E Natercia C. M. Pedro	Vanuza Alves da Cunha
E E Paulo de Castro	Maria Aparecida O. dos Santos
E E Salvador Leone	Cristiane A. dos Santos



Annex 12
Projects Giant Cell Project and USP goes to your school

- Exhibition in the Osasco Plaza Shopping – October 7th to 11th, 2013.
- Professions Fair, UNIP, Santos, São Paulo – November 4th to 8th, 2013.
- Scientific Turn of University of São Paulo, São Paulo – October 11th , 2014.
- Colégio Caiçara – III Science Fair , Bertioga, São Paulo – October 29th to 30th, 2014.

Annex 13
Interviews in the Media and Science Dissemination Articles

2013

1. Okamoto OK. O avanço que chegou atrasado. Revista BioAtivo, 13ª Edição, pg. 11-13, 2013.
2. Okamoto OK. "O avanço que chegou atrasado". Revista BioAtivo, 01/10/2013.
3. Zatz M. Células Tronco em doenças genéticas. Programa Poli, TV Cultura 14/07/2013.
4. Zatz M. Descoberta mutação por trás de calcificações no cérebro - Pesquisa Fapesp 04/08/2013.
5. Zatz M. Gene da mãe pode acelerar processo de envelhecimento - Jornal O Globo 21/08/2013.
6. Zatz M. Chega ao país teste de paternidade feito durante a gestação - Jornal Folha de São Paulo - Saúde+Ciência-Entrevista 25/08/2013.
7. Zatz M. Filhos não são brinquedos - Ciência+ Saúde-Jornal Folha de São Paulo 04/10/2013.
8. Zatz M -Pesquisa genética ajuda famílias com histórico de doenças raras-Estadão- 07/11/2013.
9. Zatz M. Familiares de pacientes pedem mais investimentos para pesquisas da Esclerose lateral Amiotrófica - Extra online 08/11/2013.
10. Zatz M-O DNA dos mais de 80-O Globo 23/11/2013.
11. Zatz M. FDA manda suspender teste que sequencia DNA humano -Veja.com 02/12/2013.
12.

2014

1. Dessen, E. Metrô de São Paulo terá painéis com perguntas sobre genética. Folha de São Paulo. 03/07/2014.
2. Dessen, E. Centro de Pesquisa leva informações sobre genética a usuários do metrô em SP. Agencia Fapesp, 18/08/2014.
3. Dessen, E. Projeto espalha cartazes sobre genética em metrô e escolas. 21/08/2014.
4. Okamoto OK. "Alteração em gene reduziu índices de tumor em células-tronco". Agência USP de Notícias, 27/02/2014.
5. Okamoto OK. "Descoberto gene que regula potencial de formação de tumores das células-tronco embrionárias". Agência FAPESP, 12/02/2014.
6. Okamoto OK. "Descoberta da USP pode representar avanço no uso de células-tronco". TV Brasil, 13/02/2014.
7. Okamoto OK. "A construção de um medicamento". Revista Pesquisa FAPESP, 01/09/2014.
8. Zatz M. Células-tronco têm efeito positivo no tratamento de distrofia muscular - Jornal Hoje 16/01/2014.
9. Zatz M. Gigante, USP é pouco ágil em mudanças-Folha de São Paulo – Cotidiano 19/01/2014.
10. Zatz M. A força da pesquisa -"Tecnologia de ponta na genética"- Jornal da USP 20/01/2014.
11. Zatz M. Mão na Massa-"Examinando a velhice" Revista Galileu 21/01/2014.
12. Zatz M. Espiral infinita - O desenrolar da geometria do DNA- Jornal Folha de São Paulo 26/01/2014.
13. Zatz M. Ciência sem fronteiras-Programa prevê 21 mil bolsas para o exterior em 2014-Jornal Folha de São Paulo 26/01/2014.
14. Zatz M. Livro detalha a descoberta da estrutura do DNA- Jornal Folha de São Paulo 26/01/2014.
15. Zatz M. Japoneses desenvolvem técnica mais simples para produção de células-tronco, sem embriões nem manipulação genética - Jornal O Estado de São Paulo 29/01/2014.
16. Zatz M. Método facilita obtenção de células-tronco - Jornal O Estado de São Paulo 30/01/2014.
17. Zatz M. Geneticista critica regra que restringe aconselhamento genético a médicos - Programa Bem Estar –Rede Globo 17/02/2014.
18. Zatz M. Nova Regra limita atendimento em genética médica - Jornal Folha de São Paulo 21/02/2014.
19. Zatz M. Aconselhamento genético chega ao SUS, mas política enfrenta críticas - Revista Época 22/02/2014.
20. Zatz M. Excelência científica no feminino - Brasil Post 20/03/2014.
21. Zatz M, Forbes J, Caruana R, Pitanguy I. Prolongamento da vida CPFL Cultura 13/03/2014.
22. Zatz M. A revolução nos testes genéticos- Folha de S. Paulo, junho de 2014 http://www1.folha.uol.com.br/opiniao/2014/06/1465149-mayana-zatz-revolucao-nos-testes-geneticos.shtml.
23. Zatz M. A revolução nos testes genéticos- Jornal Folha de São Paulo 05/06/2014.

24. Zatz M. ELA não é de brincadeira – Estado de S. Paulo (caderno Aliás), agosto de 2014 http://m.estadao.com.br/noticias/aliás,ela-nao-e-de-brincadeira,1548231,0.htm.
25. Zatz M. Estado deve bancar apenas curso estratégico, afirma ex-ministro-Folha de São Paulo Caderno Educação 03/06/2014.
26. Zatz MNext generation sequencing and incidental findings: what should be revealed? Global Summit on Regulatory Sciences, Montreal, Canada, Agosto de 2014.
27. Zatz M. Células-tronco em doenças neuromusculares: dos e para os pacientes. Congresso Nacional da Sociedade Brasileira de Genética, Guarujá, agosto de 2014.
28. Zatz M. A defect in the RNA-processing protein HNRPDL causes limb-girdle muscular dystrophy 1G (LGMD1G). XIV Congresso internacional da world muscle society, Berlin, outubro de 2014.
29. Zatz M :what are we learning? III IPG Forum on ALS research, S. Paulo, Novembro, 2014.
30. Zatz M Células-tronco: Aplicações, realizações e dúvidas. XXVI Congresso brasileiro de neurologia, Curitiba, novembro de 2014.
31. Zatz M Células-tronco nas doenças neurodegenerativas: o que é ilusão e o que é realidade. XXVI Congresso brasileiro de neurologia, Curitiba, novembro de 2014.
32. Zatz M Terapia celular em doenças neuromusculares: o que aprendemos? Seminários da Bioquímica, Novembro de 2014.
33. Zatz M Terapia celular em doenças neuromusculares: Encontro latino americano de miopatias, Salvador, dezembro de 2014.

2015

1. Dessen, E. Campanha da USP ensina genética por meio de cartazes no metrô de SP. Folha de São Paulo, 25/05/15.
2. Dessen, E. Noções de Genética para todos. Jornal da USP, junho, 15/06/2015.
3. Okamoto OK. “O dramático controle da linhagem humana”. Jornal da USP, 14/04/2015.
4. Okamoto OK. “Pesquisadores discutem ganhos e riscos da alteração do DNA humano”. USP Online Destaque. 24/04/2015.
5. Zatz M. Angelina Jolie: Escolhas que nossos avós não faziam. Carta a VEJA, 8 de abril de 2015.
6. Zatz M. Cancer de mama: Quem deve ser testado? Carta ao Jornal Estado de S. Paulo, 24 de março.
7. Zatz M. O gene da dúvida- Estado de S. Paulo (caderno Aliás), 29 de março, 2015.
8. Zatz M Impressionante! Pitbull gigante dos Estados Unidos pesa 79 kg- Domingão do Faustão 20/03/2015.
9. Zatz M Brasil vai fazer parte de pesquisa sobre esclerose lateral amiotrófica- Jornal Nacional 30/04/2015.
10. Zatz M Células-Tronco I:Conceitos e Possibilidades- http://vidatroncocelular.blogspot.com.br/ 14/04/2015.
11. Zatz M Bebê com três pais está prestes a ser legal no Reino Unido- Conteúdo Estadão 04/02/2015.

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Evaluation Report

It is a pleasure to submit a report on the research performed at the Human Genome and Stem Cell Research Center at USP during the first year of research funded by CEPID.

The program has three arms: A. Research, B. Education/science dissemination, and C. Transfer of technology.

Research:

The research performed at the Human Genome and Stem Cell Research Center focuses on genetic aspects of human disorders. The center is aimed at the analysis of genetic disorders with Mendelian inheritance, on complex disorders and on chromosomal aberrations. On monogenic disorders the center is extremely fruitful identifying 12 new genes related to genetic disorders on neuro-muscular diseases, skeletal disorders and more. 4 of the newly identified genes were already published by the respective groups, often in collaboration with international scientists who recognize the strength of the centers' groups, and the remaining are at different stages of their publication. Complex disorders are a true challenge in genetic research, and the center embarked on this topic with studies on the genetic basis of hypertension and obesity, and also by studying a very interesting topic related to the wellbeing of individuals over 80 years old. The third topic is related to chromosomal aberrations, and here the research focuses on small chromosomal aberrations and translocations and their relation to intellectual impairment.

The basis of the research relies on the richness of clinical cases that the center diagnose and treat, and on the outstanding expertise of the investigators in the center. In addition, the center has state of the art sequencing facilities that enable sophisticated analysis of the human samples. In addition, in many cases the research aims on understanding the mechanism of action of the disorders, and on the understanding of the genotype-phenotype relationship, and thus animal models are used. In their study the investigators use mammals such as rodents and dogs, and vertebrates such as zebra fish. In addition to animal models, the researchers are using stem cells, and especially human induced pluripotent stem (iPS) cells to model and study the various disorders. The combination of using animal and cellular models is very impressive.

In the past year the center published 59 papers, and in most of them the researchers from the center are the principle investigators, and their students are the first authors. These manuscripts were published in the excellentjournals in the field, among them are "American Journal of Human Genetics", and "Human Molecular Genetics".

Education/science dissemination:

The educational outreach programme, led by Eliana Dessen and assisted by Rodrigo Mendes, is one of the crown jewels of the CEPID programme and can be considered as world leading, at the same level and in some respects exceeding the success of similar efforts by NIH (USA) and Wellcome Trust (UK). It

has both breadth, not only covering biology and benetics/life sciences, but even, collaborating with the Physics center, expanding into other beta-science.

We were greatly impressed by the engaging formats. On one hand including classes and kits for high school, (identifying also the need of educating the teachers themselves – even enlisting interested students for monitoring this) and on the other hand public exhibitions like the 'Giant cell' and posters in bus terminals and underground, in the 'Sowing the seeds of knowledge' programme. This cleverly attracts the fascination of the public at large, notably the young, with provocative questions, enticing them to visit the website providing understandable but yet in-depth answers.

The high school programme has benefited 57.000 students and 70 teachers. The exhibits drew ca 40.000 visitors, while the buses and underground poster programme will reach millions of people daily. The Federal ministry has seen the value of this effort and supported the spreading of this programme in 22.000 schools, allowing the training of 132 teachers in two years. It is almost inconceivable that this has been set up and overseen by such a modest group of people and – especially given the importance of the life sciences in the 21st century – we would strongly recommend that this programme, reaching far beyond the scope of the Genetics and Genomics, can be expanded and ultimately made sustainable into the Brazilian educational system.

Transfer of technology:

The genetics field coming from small-scale and labour-intensive diagnostics in rare diseases with little progress in insights into common diseases, is in a phase of tremendous growth. This is due to the advent of high throughput, large-scale genomics technologies,. The first phase first applied array technologies and the second phase involves Next Generation Sequencing (NGS) and requires substantial grip on IT technology and Bio-Informatics. While rewarding in terms of extending services for the public this is a demanding time for institutions which need to combine research and diagnostic services. The SP Genome Center has managed to follow this transition. It played a role at the front of this field in the 'classical times, contributing to the discovery and diagnostics of many disease genes in different areas (initially the neuromuscular field and gradually expanding, by DrsZatz, Passos-Bueno and Vainzof), significantly advanced array-based diagnostics notably in cytogenetics (Dr Rosenberg) - even attracting biotech industry collaboration - , and culminating in the custom design of a NGS-based diagnostics of a gene panel not only covering an largenumber of relevant genes for neurodevelopmental, neuromuscular, skeletal and craniofacial diseases as well as genes implicated inautism and other complex diseases and hereditary cancer. The panel is currently being expanded with genes and markers for supernumerary chromosomes 21, 18 and 13. Provided that insurance or statefunding of these services is increasedto a more widely accessible level, this technology has the potential to greatly contribute to public health by early diagnosis of hereditary disease and syndromes using a universal, nationally standardized approach. At short notice this technology transfer will increase the volume of research into disease mechanisms and therapy as well as reduce the cost of the service itself. Ultimately the build-up of this expertise for Brazil will also reduce the burden of disease management to patients and parents and caretakers, as well as the state, allowing to focus expenditure on a smaller fraction of affected patients, improving the quality of life of their caretakers.

Scientific meeting:

The site visit at the Human Genome and Stem Cell Research Center at USP, and the three days meeting with members of the center were very productive. The center has state of the art sequencing and genomic equipment, and it has started renovations to add another 600 sq. meters to the center. The meeting was very productive as details of the research were presented by the investigators followed by intensive discussions. In addition, the students presented about 40 posters, and each of them discussed their own research in details. The level of insight of the students into their topic was very convincing and it was also clear that the research in the center is shared between the different PIs, as each of them not only presented one topic related to his/her research, but also discussed the research performed by other investigators in the center on the same topic. The meeting demonstrated the strength of the center and its high standard of research.

Discussion and recommendations:

In our discussion with the investigators several topics were raised on ways to advance the already excellent research performed at the center. One topic that was discussed is the need for more bioinformatics analysis, andhow to educate the students in this field, which is increasingly central given the data volume generated by today equipment. Another topic was related to the need for central bio-repository for the different cellular models established in the center. Initial steps in creating such a bio-repository are on the way. The level of collaboration with international investigators was highlighted, and the need for collaboration with biotechnology companies was discussed. In addition, it was mentioned that the center should also have facilities for drug screening, once it aims at identifying potential therapies using their cellular models.

We recommend that special attention would be devoted to bioinformatics analysis, and education of graduate and post-graduate students in this field of research. That will require hiring an expert in bio-information, and a special budget should be devoted for a competitive salary. In addition, a special course should be established for the students.

To maintain the expertise in operating the infrastructure and the complex novel methodologies, there is a clear need for more continuity of experienced technical support at different levels of the research than can be provided by students and postdocs, who leave after completion of their research project. We recommend that a mechanism should be worked out to devote part of the budget for such technical assistance.

Unfortunately, agreed matching funding from USP failed to arrive, thus it is important to keep the use of the FAPESPbudget as flexible as possible, and propose that FAPESP requires from USP that the center will be able to direct the spending of the funds that goes to USP as a result of the new grant.

The meeting was very successful and we suggest that such a scientific meeting with external advisors will be held every other year, alternating with center retreats to further advance institutional networking, disseminate innovative technologies and timely react to the rapid pace of this field.

Sincerely.

Prof. Gert-Jan van Ommen

Prof. Nissim Benvenisty

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Orçamento N°: 012736

Moeda: US$

ACM - ANA CRISTINA MAGLIANO
Fone: (11) 98389-0347
E-mail: ana.cristina@ambriex.com.br