REPORT

July 2021 to June 2022

FAPESP/CEPID 2013/08028-1

Coordinator: Mayana Zatz

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

Universidade de São Paulo

Instituto de Biociências

GROUP MEMBERS

Coordination

MayanaZatz - General coordinator

Maria Rita Passos-Bueno - Transfer of Technology

Eliana M. BelluzzoDessen - Education/Outreach

Principal investigators since 2016

Esper Cavalheiro

Mariz Vainzof

Merari de Fátima Ramires Ferrari

Oswaldo Keith Okamoto

Regina Célia Mingroni Netto

Ana Cristina Krepischi

Eliana Maria Beluzzo Dessen

Invited principal investigator

Debora Romeo Bertola

Active associate Investigators since 2019

Andrea L. Sertie

Angela M. Vianna Morgante

Carla Rosenberg

Carlos Frederico Menck

Célia P. Koiffmann

Edson Amaro Jr.

Fernando Kok

Guilherme Yamamoto

Luis Eduardo Netto

Maria Vibranovski

Michel S.Naslavsky

Miguel Mitne-Neto

Valdemir Melechco Carvalho

Yeda Duarte

ABSTRACT

Since July 2020 our group published 75 articles in peer-review journals. Most of the articles involved the collaboration of students and PIs from HUG-CELL. On line activities included about 18 conferences, lectures and symposia which were presented by our team as well as 129 Interviews to the Media and Science Dissemination Articles.

In addition to our regular projects, we were involved in new projects related to the coronavirus pandemic. We established a new rapid diagnostic test (LAMP-RT) which can be done in saliva with a much lower cost. For this initiative, Maria Rita Passos-Bueno who developed the test with her team, received an award : TRAJETÓRIA PELA INOVAÇÃO USP 2022 on June 7. Furthermore, the possibility of having our group tested routinely for COVID-19 allowed us to return to presencial activities earlier.

We published some of our research in high-impact journals such as Nature communication (IF=14.919) and Molecular Psychiatry (IF=15.992). In addition, our research on COVID-19 was the subject of interviews in international vehicles for lay people, such as: The New York Times[1] or STAT[2]. Besides the identification of SARS-Cov-2, the saliva test showed interesting results which were published and are detailed in the present report. In collaboration with the group of immunologists from FMUSP, and the team of bioinformaticians from UNESP, we are investigating possible genetic variants associated to COVID-19 resistance and reinfection.

The applications of technology transfer included genetic counseling for about 1.140 families. Despite the difficulties imposed by the coronavirus pandemia, in the last year a total of 22.213 genetic tests and about 7000 COVID tests were performed at HUG-CELL EMU, as detailed in the report. All the NGS is being performed in the Ilumina NovaSeq 6000TM, acquired in December of 2019 with Federal Funds (transfer of “verba parlamentar” from Senator Mara Gabrilli).

The service to High Schools was resumed in 2022 concomitantly with the return, on a regular basis, of face-to-face activities in schools. 84 High School teachers were trained to work on our projects directed to public Schools and 17,000 High School students were benefited. The team produced scientific dissemination content for the public: 27 videos (8,875 views), 5 chapters of a podcast (3,214 views), 3 live broadcasts (1,873 views) on Youtube. On Instagram were produced 61 posts, 8 reels and 374 Stories and on Facebook, 117 posts

1. “Why the Most Unusual Covid Cases Matter”, The New York Times. 12/07/2021. https://www.nytimes.com/2021/07/12/opinion/covid-unusual-cases-study.html

2. “A lucky seem ‘resistant’ to Covid-19. Scientists want to know why”, by Amitha Keaichandran. **Stat.**23/08/2021.<https://www.statnews.com/2021/08/23/lucky-few-seem-resistant-to-covid19-scientists-want-to-know-why-2/

CONTENTS

PART 1- RESEARCH

Our main research results from **July 2021 to June 2022**, classified by our main objectives are:

A. Gene Identification and Mechanisms in Genetic Disorders

A1. Identification of new human genes in Mendelian and complex disorders

A1.1. Mendelian Disorders

Craniofacial syndrome: Auriculocondylar syndrome (ARCND) is a rare genetic disease that affects structures derived from the first and second pharyngeal arches, mainly resulting in micrognathia and auricular malformations. To date, pathogenic variants have been identified in three genes involved in the EDN1-DLX5/6 pathway (*PLCB4*, *GNAI3* and *EDN1*) and some cases remain unsolved. Here we studied a large unsolved four-generation family. We performed linkage analysis, resequencing and Capture-C to investigate the causative variant of this family. To test the pathogenicity of the CNV found, we modeled the disease in patient craniofacial progenitor cells, including induced pluripotent cell (iPSC)-derived neural crest and mesenchymal cells. Results: This study highlights a fourth locus causative of ARCND, represented by a tandem duplication of 430 kb in a candidate region on chromosome 7 defined by linkage analysis. This duplication segregates with the disease in the family (LOD score=2.88) and includes *HDAC9*, which is located over 200 kb telomeric to the top candidate gene *TWIST1*. Notably, Capture-C analysis revealed multiple cis interactions between the *TWIST1* promoter and possible regulatory elements within the duplicated region. Modeling of the disease revealed an increased expression of *HDAC9* and its neighboring gene, *TWIST1*, in neural crest cells. We also identified decreased migration of iPSC-derived neural crest cells together with dysregulation of osteogenic differentiation in iPSC-affected mesenchymal stem cells. Our findings support the hypothesis that the 430 kb duplication is causative of the ARCND phenotype in this family and that deregulation of *TWIST1* expression during craniofacial development can contribute to the phenotype. Romanelli Tavares et al., 2021.

PI: Maria Rita Passos-Bueno -HUGH-CEL
Co-PI: Steve Twigg - University of Oxford, UK
Master student: SL Guimarães-Ramos
Publication: Romanelli Tavares VL, et al., 2021, J Med Genet Nov 8;jmedgenet-2021-107825.doi: 10.1136/jmedgenet-2021-107825. Online ahead of print.

Challenges in molecular diagnosis of admixed individuals: Diagnosis of individuals affected by monogenic disorders was significantly improved by next-generation sequencing targeting clinically relevant genes. Whole exomes yield a large number of variants that require several filtering steps, prioritization, and pathogenicity classification. Among the criteria recommended by ACMG, those that rely on population databases critically affect analyses of individuals with underrepresented ancestries. Population-specific allelic frequencies need consideration when characterizing potential deleteriousness of variants. An orthogonal input for classification is annotation of variants previously classified as pathogenic as a criterion that provide supporting evidence widely sourced at ClinVar. We used a whole-genome dataset from a census-based cohort of 1,171 elderly individuals from São Paulo, Brazil, highly admixed, and unaffected by severe monogenic disorders, to investigate if pathogenic assertions in ClinVar are enriched with higher proportions of European ancestry, indicating bias. Potential loss of function (pLOF) variants were filtered from 4,250 genes associated with Mendelian disorders and annotated with ClinVar assertions. Over 1,800 single nucleotide pLOF variants were included, 381 had non-benign assertions. Among carriers (N = 463), average European ancestry was significantly higher than noncarriers (N = 708; p = .011). pLOFs in genomic contexts of non-European local ancestries were nearly three times less likely to have any ClinVar entry (OR = 0.353; p <.0001). Independent pathogenicity assertions are useful for variant classification in molecular diagnosis. However, European overrepresentation of assertions can promote distortions when classifying variants in non-European individuals, even in admixed samples with a relatively high proportion of European ancestry. The investigation and deposit of clinically relevant findings of diverse populations is fundamental improve this scenario

PI: Mayana Zatz
This study involved several members from HUGH-CEL
Publication: Michel S Naslavsky, et.al. Biased pathogenic assertions of loss of function variants challenge molecular diagnosis of admixed individuals. American Journal of Medical genetics, June 2021

Genetic etiology of Mendelian syndromic obesity: Syndromic obesity (SO) refers to cases with other phenotypes besides obesity, including intellectual disability (ID)/developmental delay (DD), dysmorphic features, or organ-specific developmental abnormalities. SO is rare, it has high phenotypic variability and frequently follows a monogenic pattern of inheritance. However, most cases do not have their genetic etiology elucidated. We investigated SO patients by whole-exome sequencing (WES) analyses to identify causal genetic variants. Pathogenic/likely pathogenic SNVs/indels were detected in five patients (involving AHDC1, EHMT1, MYT1L, MED13L, and GRIA3), while five patients carried inherited VUS. In addition, pathogenic/likely pathogenic CNVs were observed in three patients (involving MEIS2, SATG2, and KIAA0442). All eight pathogenic/likely pathogenic variants involved genes already known to lead to syndromic

ID/DD. However, for only two of the genes, the underlying mechanism leading to obesity were already well-established (EHMT1 and MYT1L). The combination of analysis of CNVs, SNVs and indels from NGS data allowed us to achieve a high diagnostic yield (40%), illustrating the efficiency of WES in the diagnosis of SO (DOI : 10.1038/s41366-022-01149-5). In particular, we described two novel pathogenic variants in MED13L detected by whole genome sequencing (one familial and one isolated case). Genetic variants involving the MED13L gene can lead to an autosomal dominant syndrome characterized by intellectual disability/developmental delay and facial dysmorphisms. Further, we performed a literature review about clinical and molecular aspects of MED13L gene and syndrome. The two pathogenic variants identified have not been previously reported. Importantly, this is the first report of a familial case of MED13L nonsense mutation. Although the parents of the affected children were no longer available for analysis, their apparently normal phenotypes were surmised from familial verbal descriptions corresponding to normal mental behavior and phenotype. In this situation, the familial component of mutation transmission might be caused by gonadal mosaicism of a MED13L mutation in a gonad from either the father or the mother. A variant on AHDC1 presented by another patient from the SO cohort originated functional studies using iPS cellular model. Four different iPS cell lines with AHDC1 loss-of-function variants were already generated, three of them derived from unrelated patients and one produced by CRISPR. Characterization of the cell lines and functional studies are ongoing.

PIs: Carla Rosenberg, Célia Koiffmann and Ana Krepischi
Graduate student: Laura Carvalho
Publications: Carvalho et al, 2022. PMID: 34713510 DOI: 10.1111/jir.12891
Carvalho et al, 2022: DOI : 10.1038/s41366-022-01149-5

A1.2. Complex disorders

Autism Spectrum Disorder (ASD): ASD is a complex genetic neurodevelopmental disorder. Autism can be the main clinical sign or be a part of a genetic disorder (for example, about 20% of boys with Duchenne muscular dystrophy (DMD), also present ASD). One of our aim is to contribute to the genetic architecture of ASD. Below two publications that contributed to: a) strengthening the evidence of ASD candidate CNVs and, b) the relevance of the oligogenic model for ASD in patients with Duchenne Muscular Dystrophy (DMD).

ASD CNVs:Prediction of pathogenicity of rare copy number variations (CNVs), a genomic alteration known to contribute to the etiology of autism spectrum disorder (ASD), represents a serious limitation to interpreting genetic tests, particularly for genetic counseling purposes. Chromosomal microarray analysis (CMA) was conducted in a unique collection of 144 Brazilian individuals with ASD of strong European and African ancestries. Rare CNVs were detected in 39 patients: 41 of unknown significance (VUS), four pathogenic and one likely pathogenic CNVs (clinical yield of 4.1%; 5/122). Based on gene content and recurrence in three large cohorts [a Brazilian neurodevelopmental

disorder cohort, the autism MSSNG cohort, and the Canadian-based Centre for Applied Genomics microarray database], this work strengthened the pathogenicity of 14 genes (FAT1, CAMK4, BIRC6, DPP6, CSMD1, CTNNA3, CDH8/CDH11, CDH13, OR1C1, CNTN6, CNTNAP4, FGF2 and PTPRN2) within 14 CNVs. Notably, enrichment of cell adhesion proteins to ASD etiology was identified ($p < 0.05$), highlighting the importance of these gene families in the etiology of ASD (Costa ISC et al.,. 2022).

ASD and DMD:Loss-of-function variants in the dystrophin gene, a well-known cause of muscular dystrophies, have emerged as a mutational risk mechanism for autism spectrum disorder (ASD), which in turn is a highly prevalent (~1%) genetically heterogeneous neurodevelopmental disorder. Although the association of intellectual disability with the dystrophinopathies Duchenne (DMD) and Becker muscular dystrophy (BMD) has been long established, their association with ASD is more recent, and the dystrophin genotype-ASD phenotype correlation is unclear. We therefore present a review of the literature focused on the ASD prevalence among dystrophinopathies, the relevance of the dystrophin isoforms, and most particularly the relevance of the genetic background to the etiology of ASD in these patients. Four families with ASD-DMD/BMD patients are also reported here for the first time. These include a single ASD individual, ASD-discordant and ASD-concordant monozygotic twins, and non-identical ASD triplets. Notably, two unrelated individuals, which were first ascertained because of the ASD phenotype at ages 15 and 5 years respectively, present rare dystrophin variants still poorly characterized, suggesting that some dystrophin variants may compromise the brain more prominently. Whole exome sequencing in these ASD-DMD/BMD individuals together with the literature suggest, although based on preliminary data, a complex and heterogeneous genetic architecture underlying ASD in dystrophinopathies, that include rare variants of large and medium effect. The need for the establishment of a consortia for genomic investigation of ASD-DMD/BMD patients, which may shed light on the genetic architecture of ASD, is discussed. Passos-Bueno et al.., 2022.

PIs: Maria Rita Passos-Bueno, Ana Krepischi , Carla Rosenberg,
Mayana Zatz - HUGH-CEL, USP
Collaborator: Mehdi Zarrei, SW Scherer - University of Toronto, Canada

PhD Student: Claudia I.S. Costa (Msc), da Silva Montenegro

Publication: Costa CIS, et al Clin Genet. 2022 Jan;101(1):134-141.
doi: 10.1111/cge.14072. Passos-Bueno MR, Costa CIS, Zatz M. 2022.
Discovery Mental Health, Volume 2, article 4.

HLA- worldwide Genetic diversity: HLA-G is a promiscuous immune checkpoint molecule. The HLA-G gene presents substantial nucleotide variability in its regulatory regions. However, it encodes a limited number of proteins compared to classical HLA class I genes. We characterized the HLA-G genetic variability in 4640 individuals from 88 different population samples across the globe by using a state-of-the-art method to characterize polymorphisms and haplotypes from high-coverage next-generation

sequencing data. We also provide insights regarding the HLA-G genetic diversity and a resource for future studies evaluating HLA-G polymorphisms in different populations and association studies. Despite the great haplotype variability, we demonstrated that: (1) most of the HLA-G polymorphisms are in introns and regulatory sequences, and these are the sites with evidence of balancing selection, (2) linkage disequilibrium is high throughout the gene, extending up to HLA-A, (3) there are few proteins frequently observed in worldwide populations, with lack of variation in residues associated with major HLA-G biological properties (dimer formation, interaction with leukocyte receptors). These observations corroborate the role of HLA-G as an immune checkpoint molecule rather than as an antigen-presenting molecule. Understanding HLA-G variability across populations is relevant for disease association and functional studies.

PI: Mayana Zatz
This study is a collaboration between the group of Prof. Erck Castelli and our group
Publication: Erick C Castelli, et.al. HLA-G genetic diversity and evolutive aspects in worldwide populations. Scientific Reports volume 11, Article number: 23070 (2021).

Genetic and epigenetic alterations affecting cancer development and aggressiveness of embryonal cancers: several lines of evidence indicate that childhood and adult cancers are distinct entities. Despite intensive efforts, genetic factors remain difficult to be captured in rare cancers, mainly embryonal tumors, which represents a heterogeneous group supposedly derived from undifferentiated cells, with histological features that resemble tissues of origin during embryogenesis. This key observation suggests that pediatric tumorigenesis might begin during early fetal or child life due to the errors in growth or pathways differentiation.

Hepatoblastoma, the embryonal cancer of liver

Hepatoblastoma is a very rare embryonal liver cancer supposed to arise from the impairment of hepatocyte differentiation during embryogenesis. We have previously shown a low mutational background, and a novel set of candidate genes for hepatoblastoma biology, including involvement of the *CX3CL1/CX3CR1* chemokine signaling pathway in progression. We have provided an accurate cytogenomic profile of this type of cancer (PMID: 34956867 PMCID: PMC8692715 DOI: 10.3389/fonc.2021.741526), for which information in cancer databases is lacking. We performed an extensive literature review of cytogenetic studies on HBs disclosing that the most frequent copy number alterations (CNAs) are gains of 1q, 2/2q, 8/8q, and 20; and losses at 1p and 4q. Furthermore, the CNA profile of a Brazilian cohort of 26 HBs was obtained by array-CGH; the most recurrent CNAs were the same as shown in the literature review. Importantly, HBs from female patients, high-risk stratification tumors, tumors who developed in older patients (> 3 years at diagnosis) or from patients with metastasis and/or deceased carried a higher diversity of chromosomal alterations, specifically chromosomal losses at 1p, 4, 11q and 18q. In addition, we distinguished

three major CNA profiles: no detectable CNA, few CNAs and tumors with complex genomes. Tumors with simpler genomes exhibited a significant association with the epithelial fetal subtype of HBs; in contrast, the complex genome group included three cases with epithelial embryonal histology, as well as the only HB with HCC features. A significant association of complex HB genomes was observed with older patients who developed high-risk tumors, metastasis, and deceased. Moreover, two patients with HBs exhibiting complex genomes were born with congenital anomalies. Together, these findings suggest that a high load of CNAs, mainly chromosomal losses, particularly losses at 1p and 18, increases the tendency to HB aggressiveness. Additionally, we identified six hot-spot chromosome regions most frequently affected in the entire group: 1q31.3q42.3, 2q23.3q37.3, and 20p13p11.1 gains, besides a 5,3 Mb amplification at 2q24.2q24.3, and losses at 1p36.33p35.1, 4p14 and 4q21.22q25. An *in silico* analysis using the genes mapped to these six regions revealed several enriched biological pathways such as ERK Signaling, MicroRNAs in Cancer, and the PI3K-Akt Signaling, in addition to the WNT Signaling pathway; further investigation is required to evaluate if disturbances of these pathways can contribute to HB tumorigenesis. The analyzed gene set was found to be associated with neoplasms, abnormalities of metabolism/homeostasis and liver morphology, as well as abnormal embryonic development and cytokine secretion. In conclusion, we have provided a comprehensive characterization of the spectrum of chromosomal alterations reported in HBs and identified specific genomic regions recurrently altered in a Brazilian HB group, pointing to new biological pathways, and relevant clinical associations.

Epigenetic regulation of gene expression plays a critical role in the development of liver cancer, as we have previously demonstrated for hepatoblastomas; however, the molecular mechanisms of epigenetic-driven liver cancers are not well understood. During the BEPE of the PhD student Maria Prates Rivas, we collaborate in a study in which the molecular mechanisms that cause the dedifferentiation of hepatocytes into cancer cells in aggressive hepatoblastoma were investigated and the inhibition of these mechanisms was tested (doi: 10.1016/j.jcmgh.2021.06.026). This study revealed that HDAC1-mediated repression of markers of hepatocytes is an essential step for the development of HBL, providing background for generation of therapies for aggressive HBL by targeting HDAC1 activities.

Although HB risk is related to a few rare syndromes, the molecular bases of HB predisposition remain elusive for most cases. We investigated the burden of rare damaging germline variants in 30 Brazilian patients with HB and the presence of additional clinical signs (DOI: 10.3389/fgene.2022.858396). A high frequency of prematurity (20%) and birth defects (37%), especially craniofacial (17%, including craniosynostosis) and kidney (7%) anomalies, was observed. Putative pathogenic or likely pathogenic monoallelic germline variants mapped to 10 cancer predisposition genes (CPGs: *APC, CHEK2, DROSHA, ERCC5, FAH, MSH2, MUTYH, RPS19, TGFBR2* and*VHL*) were detected in 33% of the patients, only 40% of them with a family history of cancer. These findings showed a predominance of CPGs with a known link to gastrointestinal/colorectal and renal cancer risk. A remarkable feature was an enrichment of rare damaging variants affecting different classes of DNA repair genes, particularly those known as Fanconi anemia genes. Moreover, several potentially

deleterious variants mapped to genes impacting liver functions were disclosed. To our knowledge, this is the largest assessment of rare germline variants in HB patients to date, contributing to elucidate the genetic architecture of HB risk.

PIs: Ana Krepischi, Carla Rosenberg
Students: Juliana Sobral de Barros, Maria Prates Rivas
Posdocs: Talita Aguiar, Anne Barbosa
Publications:a)Barros et al 2021 - doi: 10.3389/fonc.2021.741526; b)Rivas et al 2021 - doi: 10.1016/j.jcmgh.2021.06.026; c) Aguiar T, Teixeira A, et al 2022.
doi: 10.3389/fgene.2022.858396

A2. Elucidation of mechanisms to explain phenotype, clinical variability, and non-penetrance in genetic disorders

A2.1. Neuromuscular disorders

Sarcoglycanopathies- an update: This is an invited revision, based on our large experience in the field. Sarcoglycanopathies are the most severe forms of autosomal recessive limb-girdle muscular dystrophies (LGMDs), constituting about 10–25% of LGMDs. The clinical phenotype is variable, but onset is usually in the first decade of life. Patients present muscle hypertrophy, elevated CK, variable muscle weaknesses, and progressive loss of ambulation. Four subtypes are known: LGMDR3, LGMDR4, LGMDR5 and LGMDR6, caused, respectively, by mutations in the SGCA , SGCB , SGCG and SGCD genes. Their four coded proteins, α-SG, ß-SG, λ-SG and δ-SG are part of the dystrophin-glycoprotein complex (DGC) present in muscle sarcolemma, which acts as a linker between the cytoskeleton of the muscle fiber and the extracellular matrix, providing mechanical support to the sarcolemma during myofiber contraction. Many different mutations have already been identified in all the sarcoglycan genes, with a predominance of some mutations in different populations. The diagnosis is currently based on the molecular screening for these mutations. Therapeutic approaches include the strategy of gene replacement mediated by a vector derived from adeno-associated virus (AAV). Pre-clinical studies have shown detectable levels of SG proteins in the muscle, and some improvement in the phenotype, in animal models. Therapeutic trials in humans are ongoing.

PI: Mariz Vainzof
PhD Student: Lucas Santos e Souza, PhD. And the clinical group of the HUG-CEL.
Publication: Vainzof M, Souza LS, Gurgel-Giannetti J, Zatz M. Sarcoglycanopathies: an update.Neuromuscul Disord. 2021 Oct;31(10):1021-1027.
doi: 10.1016/j.nmd.2021.07.014. Epub 2021 Jul 28.

Congenital fiber type disproportion myopathy due to mutation in the SPEG gene: Congenital myopathies are a heterogeneous group of conditions diagnosed based on

the clinical presentation, muscle histopathology and genetic defects. Recessive mutations in the SPEG gene have been described in recent years and are primarily associated with centronuclear myopathy with cardiomyopathy. In this report, we describe two Brazilian siblings, aged 13 and 6 years, with a novel homozygous mutation (c.8872 C>T:p.Arg2958Ter) in the SPEG gene leading to a congenital myopathy. In the older sibling, the muscle biopsy showed fiber size disproportion. The mean diameter of type 2 fibers (119 µm) was significantly higher than type 1 (57 µm) (P < 0,001) with a 72% prevalence of type 1 fibers. The patient also had progressive cardiomyopathy treated with heart transplantation. The present report expands the muscle histopathological findings related to mutations in the SPEG gene, including fiber size disproportion without central nuclei. Additionally, this report describes the first case of heart transplantation in a patient with SPEG mutations.

PI: Mariz Vainzof
Colaboration with Dr. Juliana Gurgel-Gianneti, UFMG.
Publication: Gurgel-Giannetti J, et.al. A Novel SPEG mutation causing congenital fiberty pedisproportion myopathy and dilated cardiomyopathy with heart transplantation. NeuromusculDisord. 2021 Nov;31(11):1199-1206.

Malignant hyperthermia phenotype-genotype correlations: In a long term collaboration with Dr. Helga C. Almeida Silva, from the Federal University of SP, we have been studing several aspects in families with malignant hyperthermia susceptibility. A new international collaborative study, " Functional consequences of RYR1 mutations on the human immune system".wasstabelished this year with Prof. Susan Treves of the Department of Biomedicine, Basel University Hospital. Malignant hyperthermia (MH) is a hypermetabolic syndrome occurring in genetically susceptible individuals exposed to halogenated anesthetics and succinylcholine. Spinal Cord Injury (SCI) above the sixth thoracic (T6) vertebra is associated with acute effects on sympathetic/parasympathetic nervous pathways and dysfunction of systems such as the thermoregulatory. This dysregulation can be expressed by poikilothermia (hypothermia in cold environments) that could mitigate an MH episode. We recently identified a SCI patient presenting obesity and a fatal development of a delayed MH crisis. Clinicaly, this 27-year-old male patient (140kg/180cm/ASA3), with an SCI after a fracture of the sixth cervical vertebra, was submitted to spinal arthrodesis. Anesthesia was performed with remifentanil, propofol, succinylcholine, rocuronium, and isoflurane. Muscular contractures were noted after surgery beginning and pancuronium successfully was administered. He evolved with hypotension/tachycardia and metabolic acidosis. After 4 hours, he presented hyperthermia, hypercarbia, hypotension, muscle rigidity, arrhythmia, and cardiogenic shock, with metabolic/respiratory acidosis. MH was suspected and the treatment was started, but he developed cardiopulmonary arrest and died 1.5 hours after. Both parents had normal CK levels and positive in vitro contracture tests. His mother presented a described variant in the ryanodine (RYR1) gene (c.14918C>T), associated to MH. We concluded that the thermoregulatory impairment in SCI patients can mask the onset/development of the MH crisis and must raise diagnostic awareness.

PI: Mariz Vainzof and geneticist responsible for the MH group.
Colaboration with Dr. Helga Cristina Almeida da Silva, Malignant Hyperthermia Unit - Discipline of Anesthesiology, Pain and Intensive Care - Federal University of Sao Paulo
Publication: Andrade PV, et al. Spinal cord injury-related thermoregulatory impairment masks a fatal malignant hyperthermia crisis. A Case Report. Can J Anaesth. 2021 Dec 13. doi: 10.1007/s12630-021-02170-4. Online ahead of print

Central Core Disease: Facial Weakness Differentiating Biallelic from Monoallelic Forms: Our long term studies and collaboration with several neuromuscular Center include the genetic study of patients from the SARAH Network of Rehabilitation Hospitals. Central Core Disease (CCD) is a genetic neuromuscular disorder characterized by the presence of cores in muscle biopsy. The inheritance has been described as predominantly autosomal dominant (AD), and the disease may present as severe neonatal or mild adult forms. Here we report clinical and molecular data on a large cohort of Brazilian CCD patients, including a retrospective clinical analysis and molecular screening for RYR1 variants using Next-Generation Sequencing (NGS). We analyzed 27 patients from 19 unrelated families: four families (11 patients) with autosomal dominant inheritance (AD), two families (3 patients) with autosomal recessive (AR), and 13 sporadic cases. Biallelic RYR1 variants were found in six families (two AR and four sporadic cases) of the 14 molecularly analyzed families (~43%), suggesting a higher frequency of AR inheritance than expected. None of these cases presented a severe phenotype. Facial weakness was more common in biallelic than in monoallelic patients ($p = 0.0043$) and might be a marker for AR forms. NGS is highly effective for the identification of RYR1 variants in CCD patients, allowing the discovery of a higher proportion of AR cases with biallelic mutations. These data have important implications for the genetic counseling of the families.

PI: Mariz Vainzof
Colaboration with Dr. Ana Cotta, from The Sarah Network of Rehabilitation Hospitals, Belo Horizonte, MG.
Publication: Cotta, et.al. Central Core Disease: Facial Weakness Differentiating Biallelic from Monoallelic Forms. Genes 2022, *13*, 760. https://doi.org/10.3390/genes13050760

Muscle regeneration in spastic muscles of children with cerebral palsy: After early brain injury, patients with Cerebral Palsy (CP) experience several musculoskeletal changes including contractures and reduced force, secondary to both central and peripheral factors. Four mechanical/structural reasons for this force reduction are suggested: (1) reduced muscle size; (2) reduced contractile tissue, with replacement by fibrosis and/or fat; (3) over-stretched sarcomeres, associated with a great loss of isometric force; and (4) loss of sarcomeric titin, resulting in a decreased passive force. Epigenetic factors related to impaired muscle growth and production of sarcomeres in

CP were also proposed, based on DNA hypermethylation of myoblast gene promotor regions. The decreased muscle volumes have been associated with several causative factors, including impaired muscle growth and regeneration. Also, muscle contractures in CP were associated with a decrease in the number and the loss satellite cell myogenic potential. However, it is still not known if the reduced number of satellite cells is the cause or a consequence of the inhibited muscle structural proteins production. In this respect, muscle impairment and muscle regeneration processes, and the role of satellite cells in spastic CP, have received increased attention, as this knowledge could be used as strategies for treatment of spastic muscles. An invited commentary about this topic has been published in the Journal Development Medicina e Child Neurology.

PIs: Mariz Vainzof and Juliana GurgelGiannetti
Publication: Vainzof M, Gurgel-Giannetti J. Muscle regeneration in spastic muscles of children with cerebral palsy. Dev Med Child Neurol. 2021 Oct;63(10):1137. doi: 10.1111/dmcn.14953A2.2.

Modelling Craniofacial syndromes in a dish: Neural crest cells (NCCs) are a multipotent and transient cell population that gives rise to many important tissues during human embryogenesis. Disturbances that occur during NCCs development may lead to numerous types of diseases and syndromes, which are called neurocristopathies. NCCs in vitro modeling enables the access to cellular, genetic, and biochemical information about the neural crest development and its derivatives. By using cells derived from patients with neurocristopathies it is possible to study the cellular and genetic mechanisms behind each disease in a specific and trustworthy manner, as well as to contribute to the development of prospective treatments. Here, we describe a protocol of 19 days, capable of efficiently generating NCCs from human induced pluripotent stem cells (hiPSCs). This differentiation process recapitulates the intermediate stage of neural plate border-like cells (NBCs), the epithelial to mesenchymal transition (EMT), and enables further generation of NCCs derivatives, such as Schwann cells, smooth muscle cells, melanocytes, peripheral neurons, adipocytes, osteoblasts, and chondrocytes (Nani et al., 2022).

PI: Maria Rita Passos-Bueno, HUGH-CEL
Master Student: Diogo A. Nani
PhD Student: Gabriella SP Hsia
Pos-Doc: Gerson S. Kobayashi
Publication: Diogo A. Nani, Gabriella Shih Ping Hsia, Maria Rita Passos-Bueno, Gerson Shigeru Kobayashi. Methods Mol Biol . 2022 Mar 31.

Autism Spectrum disorder (ASD): *TRPC6* gene: Autism Spectrum Disorder (ASD) is characterized by impaired social communication, restricted interests, and repetitive and stereotyped behaviors. The TRPC6 (transient receptor potential channel 6) represents

an ASD candidate gene under an oligogenic/multifactorial model based on the initial description and cellular characterization of an individual with ASD bearing a de novo heterozygous mutation disrupting TRPC6, together with the enrichment of disruptive TRPC6 variants in ASD cases as compared to controls. Here, we perform a clinical re-evaluation of the initial non-verbal patient, and also present eight newly reported individuals ascertained for ASD and bearing predicted loss-of-function mutations in TRPC6. In order to understand the consequences of mutations in TRPC6 on nervous system function, we used the fruit fly, Drosophila melanogaster, to show that null mutations in transient receptor gamma (trpγ; the fly gene most similar to TRPC6), cause a number of behavioral defects that mirror features seen in ASD patients, including deficits in social interactions (based on courtship behavior), impaired sleep homeostasis (without affecting the circadian control of sleep), hyperactivity in both young and old flies, and defects in learning and memory. Some defects, most notably in sleep, differed in severity between males and females and became normal with age. Interestingly, hyperforin, a TRPC6 agonist and the primary active component of the St. John's wort antidepressant, attenuated many of the deficits expressed by trpγ mutant flies. In summary, our results provide further evidence that the TRPC6 gene is a risk factor for ASD. In addition, they show that the behavioral defects caused by mutations in TRPC6 can be modeled in Drosophila, thereby establishing a paradigm to examine the impact of mutations in other candidate genes (Palacios-Munoz et al., 2022).

PI: Maria Rita Passos-Bueno -HUGH-CEL, and John Ewer- Universidade de Val Paraiso , Chile
Graduation Student: Gabriele Campos
PostDoc: Danielle P. Moreira
Publication: Palacios-Munoz et al. Mol Psychiatry. 2022 May 2.

Complement in neuronal cells of autistic patients: In recent years, accumulating evidence has shown that the innate immune complement system is involved in several aspects of normal brain development and in neurodevelopmental disorders, including autism spectrum disorder (ASD). Although abnormal expression of complement components was observed in post-mortem brain samples from individuals with ASD, little is known about the expression patterns of complement molecules in distinct cell types in the developing autistic brain. In the present study, we characterized the mRNA and protein expression profiles of a wide range of complement system components, receptors and regulators in induced pluripotent stem cell (iPSC)-derived neural progenitor cells, neurons and astrocytes of individuals with ASD and neurotypical controls, which constitute in vitro cellular models that recapitulate certain features of both human brain development and ASD pathophysiology. We observed that all the analyzed cell lines constitutively express several key complement molecules. Interestingly, using different quantification strategies, we found that complement C4 mRNA and protein are expressed in significantly lower levels by astrocytes derived from ASD individuals compared to control astrocytes. As astrocytes participate in synapse elimination, and diminished C4 levels have been linked to defective synaptic pruning, our findings may contribute to an increased understanding of the atypically enhanced brain connectivity in ASD.(Mansur et al., 2021).

PI: Andrea Sertie and Maria Rita Passos-Bueno
Publication: Mansur F, et.al. Int J Mol Sci. 2021 Jul 15;22(14):7579.
doi: 10.3390/ijms22147579

Molecular and cellular basis of hyperassembly and protein aggregation driven by a pathogenic mutation in DDX3X: In a previous publication of our group (doi: 10.2147/TACG.S165799) a *DDX3X* missense mutation (L556S) was identified in a female patient with intellectual disability. 1-3% of females with unexplained intellectual disability (ID) present *de novo* splice site, nonsense, frameshift, or missense mutations in the DDX3X protein (DEAD-Box Helicase 3 X-Linked). However, the cellular and molecular mechanisms by which *DDX3X* mutations impair brain development are not fully comprehended. In a collaboration with the Brazilian Biosciences National Laboratory (LNBio), it was shown that the ID-linked missense mutation L556S renders DDX3X prone to aggregation. By using a combination of biophysical assays and imaging approaches, it was demonstrated that this mutant assembles solid-like condensates and amyloid-like fibrils. Although we observed greatly reduced expression of the mutant allele in a patient who exhibits skewed X inactivation, this appears to be enough to sequestrate healthy proteins into solid-like ectopic granules, compromising cell function. Therefore, data suggest ID-linked *DDX3X* L556S mutation as a disorder arising from protein misfolding and aggregation.

PIs: Carla Rosenberg and Ana Krepischi
Publications: PMID:34381968 - PMCID:PMC8335631 - DOI: 10.1016/j.isci.2021.102841

STRUCTURAL VARIATION IN GENETIC DISORDERS: CNVs and complex balanced and unbalanced genomic rearrangements are known to contribute to human normal variation and disease. We have investigated during past two decades the causal association of rare genomic imbalances with several phenotypes. We recently contributed to the molecular characterization of complex genomic rearrangements, related to *MECP2* duplication syndrome (doi: 10.1016/j.ejmg.2021.104367), an apparently balanced complex chromosome rearrangement involving seven breaks and four chromosomes in a healthy female and segregation/recombination in her affected (doi: 10.1159/000516323), and a supernumerary Xp marker (*doi: 10.1159/000517085*).

Chromoanagenesis is a descriptive term that encompasses classes of catastrophic mutagenic processes that generate localized and complex chromosome rearrangements in both somatic and germline genomes. We describe a 5-year-old female presenting with a constellation of clinical features consistent with a clinical diagnosis of Coffin-Siris syndrome 1 (CSS1). Initial G-banded karyotyping detected a 90-Mb pericentric and a 47-Mb paracentric inversion on a single chromosome. Subsequent analysis of short-read whole-genome sequencing data and genomic optical mapping revealed additional inversions, all clustered on chromosome 6, one of them disrupting ARID1B for which

haploinsufficiency leads to the CSS1 disease trait (MIM:135900). The aggregate structural variant data show that the resolved, the resolved derivative chromosome architecture presents four de novo inversions, one pericentric and three paracentric, involving six breakpoint junctions in what appears to be a shuffling of genomic material on this chromosome (doi: 10.3389/fgene.2021.708348). Each junction was resolved to nucleotide-level resolution with mutational signatures suggestive of non-homologous end joining. The disruption of the gene ARID1B is shown to occur between the fourth and fifth exon of the canonical transcript with subsequent qPCR studies confirming a decrease in ARID1B expression in the patient versus healthy controls. Deciphering the underlying genomic architecture of chromosomal rearrangements and complex structural variants may require multiple technologies and can be critical to elucidating the molecular etiology of a patient's clinical phenotype or resolving unsolved Mendelian disease cases.

PIs: Ana Krepischi, Debora Bertola, and Carla Rosenberg
Publications: Grochowski et al - doi: 10.3389/fgene.2021.708348

A2.3. Neurodegeneration

TBCK encephalopathy (TBCKE or IHPRF3): Biallelic pathogenic variants in TBCK cause encephaloneuropathy, infantile hypotonia with psychomotor retardation, and characteristic facies 3 (IHPRF3). The molecular mechanisms underlying its neuronal phenotype are largely unexplored. In this study, we reported two sisters, who harbored biallelic variants in TBCK and met diagnostic criteria for IHPRF3. We provided evidence that TBCK may play an important role in the early secretory pathway in neuroprogenitor cells (iNPC) differentiated from induced pluripotent stem cells (iPSC). Lack of functional TBCK protein in iNPC is associated with impaired endoplasmic reticulum-to-Golgi vesicle transport and autophagosome biogenesis, as well as altered cell cycle progression and severe impairment in the capacity of migration. Alteration in these processes, which are crucial for neurogenesis, neuronal migration, and cytoarchitecture organization, may represent an important causative mechanism of both neurodevelopmental and neurodegenerative phenotypes observed in IHPRF3. Whether reduced mechanistic target of rapamycin (mTOR) signaling is secondary to impaired TBCK function over other secretory transport regulators still needs further investigation.

PI: Maria Rita Passos-Bueno, Debora Bertola, Merari Ferrari.
PhD Students: Angela M. Suzuki and Elisa Varella-Branco
PosDoc: Gerson Kobayashi
Publication: Moreira DP et al., Front Cell Neurosci. 2022 Jan 13;15:803302.
doi: 10.3389/fncel.2021.803302.

Trying to understand clinical variability in amyotrophic lateral sclerosis: Amyotrophic lateral sclerosis (ALS) stands out as a highly heterogeneous condition. Patients affected by ALS commonly start manifesting symptoms such as weakness in

the upper or lower limbs, difficulty in climbing stairs, fasciculations and loss of muscular mass. As the disease progresses, patients become wheelchair-bound and bulbar signs such as dysarthria and dysphagia become more pronounced. Here, we describe different aspects of amyotrophic lateral sclerosis type 8 (ALS8) clinical variability, both in terms of clinical manifestations and in rate of disease progression. We were able to rule out well-described genetic modifiers, such as *EPHA4* and *UNC13A*, and potential copy number variation alterations. Interestingly, both cell death rates and energetic metabolism appeared to be different among the severe ALS8, mild ALS8 and controls, suggesting an attenuation of pathological process in the less affected patients. Whole transcriptomic analysis of induced pluripotent stem cells (iPSCs)-derived motor neurons pointed that both “mild patients” presented 43 upregulated and 66 downregulated genes, when compared to controls and the “severe” group. Interestingly, most of the identified genes were associated with protein synthesis and protein targeting to endoplasmic reticulum (ER). Expression of protein translation markers’ pMTOR, 4EBP1 and RPS6 were found to be high in the mild ALS8 individuals, when compared to both controls and the severe group. To sum up, our data point that mitigating factors are most likely preventing neurodegeneration in ALS8 through maintenance of protein synthesis. Further studies, assessing the relationship among these potential genetic modifiers and the pathophysiology in ALS8, are fundamental. They might shed light on venues for treatment of this devastating disease.

PI- Mayana Zatz
Pos-Doc Danyllo Oliveira
Publication: Danyllo Oliveira. et.al. Phenotypic heterogeneity in amyotrophic lateral sclerosis type 8 and modifying mechanisms of neurodegeneration. Neural Regen Res.2021 Sep; 16(9): 1776–1778.

Impaired neurogenesis and intellectual disability: A homozygous mutation in the inositol monophosphatase 1 (*IMPA1*) gene was recently identified in nine individuals with severe intellectual disability (ID) and disruptive behavior. These individuals belong to the same family from Northeastern Brazil, which has 28 consanguineous marriages and 59 genotyped family members. IMPA1 is responsible for the generation of free inositol from de novo biosynthesis and recycling from inositol polyphosphates and participates in the phosphatidylinositol signaling pathway. To understand the role of IMPA1 deficiency in ID, we generated induced pluripotent stem cells (iPSCs) from patients and neurotypical controls and differentiated these into hippocampal dentate gyrus-like neurons and astrocytes. IMPA1-deficient neuronal progenitor cells (NPCs) revealed substantial deficits in proliferation and neurogenic potential. At low passage NPCs (P1 to P3), we observed cell cycle arrest, apoptosis, progressive change to a glial morphology and reduction in neuronal differentiation. These observations were validated by rescuing the phenotype with myo-inositol supplemented media during differentiation of patient-derived iPSCs into neurons and by the reduction of neurogenic potential in control NPCs-expressing shIMPA1. Transcriptome analysis showed that NPCs and neurons derived from ID patients have extensive deregulation of gene expression affecting pathways

necessary for neurogenesis and upregulation of gliogenic genes. IMPA1 deficiency did not affect cell cycle progression or survival in iPSCs and glial progenitor cells or astrocyte differentiation. Therefore, this study shows that the *IMPA1* mutation specifically affects NPC survival and neuronal differentiation.

PI: Mayana Zatz
Posdoc Thalita Figueiredo,was a pos-doc under MZ supervision
Publication: Thalita Figueiredo, et.al. Inositol monophosphatase 1 (*IMPA1*) mutation in intellectual disability patients impairs neurogenesis but not gliogenesis. Molecular Psychiatry volume 26, pages3558–3571 (2021)

The importance of *in vitro* studies to recapitulate multiple sclerosis: Astrocytes play a significant role in the pathology of multiple sclerosis (MS). Nevertheless, for ethical reasons, most studies in these cells were performed using the Experimental Autoimmune Encephalomyelitis model. As there are significant differences between human and mouse cells, we aimed here to better characterize astrocytes from patients with MS (PwMS), focusing mainly on mitochondrial function and cell metabolism.

We obtained and characterized induced pluripotent stem cell (iPSC)-derived astrocytes from three PwMS and three unaffected controls, and performed electron microscopy, flow cytometry, cytokine and glutamate measurements, gene expression, in situ respiration, and metabolomics. We validated our findings using a single-nuclei RNA sequencing dataset. We detected several differences in MS astrocytes including: (i) enrichment of genes associated with neurodegeneration, (ii) increased mitochondrial fission, (iii) increased production of superoxide and MS-related proinflammatory chemokines, (iv) impaired uptake and enhanced release of glutamate, (v) increased electron transport capacity and proton leak, in line with the increased oxidative stress, and (vi) a distinct metabolic profile, with a deficiency in amino acid catabolism and increased sphingolipid metabolism, which have already been linked to MS. Our findings recapitulate several disease features described in patients and provide new mechanistic insights into the metabolic rewiring of astrocytes in MS, which could be targeted in future therapeutic studies.

PI- Mayana Zatz
This research was a collaboration between our group and Prof. Niels from ICB.
Publication: Bruno Ghirotto, et.al. MS-Driven Metabolic Alterations Are Recapitulated in iPSC-Derived Astrocytes, Annals of Neurology, 91: 652-669, 2022

A2.4. The search for modifier variant

Protective variants in Duchenne muscular dystrophy: Duchenne Muscular Dystrophy (DMD) is a X-linked genetic muscle disease with no effective treatment. The

identification of disease protective mechanisms is of great relevance for future therapeutic approaches. Our group has identified in 2015 the Notch ligand *Jagged1* as a genetic modifier in DMD canine model. This finding opened new questions about Notch pathway role in DMD progression. In this project, we extended the search for genetic modifiers based on two rare human patients with extremely mild phenotype (mild). We identified they have two similar rare variants in *NOTCH3*, a Notch receptor important for muscle stem cell fate and muscle regeneration. iPSCs from these DMD patients and controls were differentiated in muscle progenitors and myofibers (iMuSCs). The goal is to uncover molecular pathways responsible for their mild phenotype. During this period, the project had the following outcomes: (1) We confirmed dystrophin absence in mild iPSCs-derived skeletal muscles; (2) completed the sampling, quality control, RNA sequencing and analysis of over 100 samples from primary myoblasts and iMuSCs; (3) Using CRISPR-Cas9 technology, we produced: 2 iPSCs lineages with DMD gene correction, 2 iPSCs with NOTCH3 gene knockout (KO), and several PAX7 reporter lineages from patients iPSCs. These lineages were further differentiated and characterized; Transcriptome of isogenic PAX7+ cells was also analyzed, as well as their proliferative behavior; (4) We performed luciferase assay using *NOTCH3* with wild type sequence or missense variants from the mild patients (collaboration with Dr. Stephen Blacklow, from Harvard Medical School). The results suggest that variants cause a reduction in NOTCH3 signaling, indicating they generate a hypomorphic protein; (5) We characterized the growth pattern of iPSCs-derived myoblasts from mild, severe patients and NOTCH3 KO lineages. Lineages with NOTCH3 variant and KO have greater cell proliferation compared to controls; (6) We established a 3D myogenic differentiation protocol and compared among different DMD and control lineages; (7) We produced a mice model with NOTCH3 variant. It will be crossed with *mdx5cv*, a DMD severe mice model, to produce a dystrophic animal carrying the variant for functional studies.

PI: Mayana Zatz
PosdocFelipe de Souza Leite
Students: Joyce Esposito de Souza (PhD), Igor Neves Barbosa (Master's student), Tatiana Jazedje (PhD), Thaís Martins (PhD), Márcia Pereira (PhD), Mayana Pardo (Msc) and Giovanna Olberg.
Project: Muscular Dystrophies: new therapeutic strategies based on protective mechanisms

A3. Epigenetics and diseases

How DNA damage and Genome Instability can be implicated in human disease?: Several DNA syndromes are related with deficiencies with DNA damage repair. This is the case of patients with xeroderma pigmentosum (XP), Cockayne's syndrome (CS) and trichothiodystropy (TTD). These syndromes are deficient in nucleotide excision repair

(NER) and as consequences they have symptoms related to increased frequency of cancer (in the case of XP, skin tumors, due to sunlight induced DNA lesions). One of the aspects it is to perform molecular diagnosis of Brazilian XP patients. During the last year, we identified another XP genetic cluster in the Northeast of Brazil. Curiously, despite of the rare frequency of XP mutations, that genetic cluster involves two different families, and two different genes mutated (POLH and XPC). (Published in Frontiers in Genetics, Castro et al, 2022).

We also continued studies evaluating induced mutations in DNA repair deficient cells in vitro, using exome NGS sequencing. Thus, in UVB-irradiated XP-C human cells (defective in global genome repair), we detected that most of the mutations were C>T transitions in regions of dipyrimidine, due to pyrimidine dimers, but also C>A transversions were also significantly detected, possibly due to lesions induced by oxidative stress. Interestingly, the mutation signature observed in this “in vitro” experiment was very similar to the mutation signatures of human skin tumors in the general (NER proficient) population (published in Photochemistry & Photobiology-Quintero-Ruiz et al, 2022). Another important aspect of these syndromes is that many patients develop neurological problems and premature aging symptoms, especially CS and TTD patients (Menck and Munford, 2014; Marteijn et al, 2014). During this period, we concluded the work investigating several phenotypic aspects of the CSA-/-/XPA-/- (CX) mice, in collaboration with the laboratory of Sarah and James Mitchel (from Harvard University, Boston, USA). The work was led by the PhD student Gustavo S. Kajitani. The CX mice have severe progeroid symptoms, recapitulating the clinical phenotypes of CS patients. Surprisingly, no evidence for endothelial damage was observed in these mice: in vitro endothelial cells have normal growth and aorta did not show signs of senescence or reduced angiogenesis capacity. On the other hand, the blood brain barrier was disrupted in the CX mice, and neuroinflammation was detected (published in the journal Aging, Kajitani et al, 2021). A second work using mice defective in NER pathway is the result of a collaboration with the group of the Erasmus University, the Netherlands (led by Dr. J. Hoeijmakers and Dr. G. van der Horst), who provided us with the XPA-/- mice (completely unable to perform the removal of bulk DNA lesions by NER) expressing the CPD or 6-4PP photolyases controlled by a keratinocyte specific (K14) promoter. These photolyases specifically remove one of these two main DNA lesions of UVB radiation, and thus the mice were investigated for the effects of each of these lesions in the skin of these NER deficient mice. The results of this work indicate that photoremoval of CPDs completely suppressed epidermal thickness and skin cell proliferation after UVB exposure, while the photoremoval of 6-4PPs just attenuated these effects. Moreover, a novel approach was used to detect cell death by apoptosis and inflammatory responses in the skin of these animals, which were observed after UVB irradiation, but photoremoval of any of these two lesions within the keratinocytes promoted a strong reduction of these UV-B induced effects (Published in the journal Frontiers of Immunology (Kajitani et al, 2022). Also, in a collaboration project with Dr. Ana Maria Castrucci and Dr. Leonardo Assis (IB, USP), we participated in a publication reporting the effects of melanopsin receptor (OPN4) loss on cell cycle progression and growth, in the journal Curr Issues Mol Biol (Assis et al, 2021). Finally, we published a book chapter in a traditional Photobiology book (in DNA photodamage: From light absorption to cellular

responses and skin cancer) reviewing how DNA damage induced by sunlight is replicated by translesion synthesis (Moreno et al, 2021). And a didactic book chapter on the use of mutation signatures and Next Generation Sequencing (NGS) was recently published in Portuguese, in a book sponsored by Mutagen-Brasil Society (de Souza et al, 2021).

PI: Carlos F. Menck
Postdocs: Andre Uchimura Bastos, Giovana Leantro
PhD students: Matheus Molina Silva, Livia Luz Nascimento, Davi Jardim Martins, Davi Mendes, Marcela Latância, Camila Corradi
Collaboration: Dr. Clarissa RR Rocha- UNIFESP; Dr. Gustavo Satoru Kajitani –UFOP; Dr. Leonardo Assis and Dr. Ana Maria Castrucci – IB-USP; Dr. Tirzah Petta - UFRN, Br;, Dr. Jan Hoeijmakers and Dr. Gilbert van der Horst - Erasmus University, the Netherlands; Dr. Sarah and James Mitchel from Harvard University, Boston, USA.

B.The 80plus Project

Whole genome sequencing of the largest cohort of elderly from Latin America: Whole-genome sequencing (WGS) of a large number of individuals can reveal rare variants in known disease genes, improve identification of novel genes and pathways associated with phenotypes and identify genomic regions not represented on reference genomes. Most importantly, ancestry diversity is critical to elucidate differences in disease's genomic architecture and improve signals detected by previous studies, since non-European and admixed populations harbor specific variants, which are still vastly underrepresented in genomic studies. The lack of diversity leads to a significant bias on the primary resource for precision medicine and consequently less accurate tests on non-European descent individuals, potentially increasing health disparities (Naslavsky et al., 2021 – American Journal of Medical Genetics Part C). Knowledge about allelic frequencies from multiple populations is also crucial when prioritizing candidate clinical variants. For rare Mendelian disorders, the frequency in any given population cannot be higher than expected for disease incidence. Moreover, the penetrance of variants may vary across backgrounds. For variants associated with monogenic late-onset disorders, unaffected elderly individuals serve as a proper control group to improve diagnosis accuracy. A highlight study in this research line is the peer-reviewed publication in Nature Communications journal of the first high-coverage WGS of a Latin American census-based cohort composed of 1,171 unrelated elderly from São Paulo, Brazil's largest metropolis (Naslavsky et al., 2022 – Nature Communications). These individuals aged 60 or older have been comprehensively phenotyped by the longitudinal Health, Well-Being, and Aging (SABE - Saúde, Bem- estar e Envelhecimento) study. By carrying out WGS on this population-based cohort, we identified genomic variation absent from public databases, including single nucleotide substitutions, insertion/deletion variants (indels), chromosomal haplotypes, accurate HLA variant calls, mobile element insertions, and non-reference sequences (NRS). Additionally, we explored pathogenicity assertions in

disease-related genes of clinical relevance and GWAS performance for selected phenotypes. We also created new reference imputation panels for the whole-genome and HLA alleles, which improved imputation accuracy. Lastly, we provide variants and respective allelic frequencies in a public resource, ABraOM <https://abraom.ib.usp.br>. In addition, individual level data from the same study were deposited in the European Genome-phenome Archive <https://ega-archive.org/studies/EGAS00001005052>where users can request data access.

PIs: Mayana Zatz and Michel S. Naslavsky
The following groups are participating in this multicenter effort: Pedro Galante and Thiago Miller (Instituto de Pesquisa Sírio-Libanês), Victor Guryev and Stepanka Zverinova (ERIBA, Groningen), Erick Castelli (UNESP Botucatu), Diogo Meyer and Kelly Nunes (IBUSP), Eduardo Tarazona, Wagner Magalhães, Nathalia Matta, Victor Borda (UFMG).
Data collaborators: Heinner Guio (Instituto Nacional de Salud, Lima, Peru and Universidad de Huánuco, Huánuco, Peru), Mauricio L. Barreto (UFBA and Center for Data and Knowledge Integration for Health, Institute Gonçalo Muniz, Fundação Oswaldo Cruz, Salvador, Brazil), Maria Fernanda Lima-Costa (Instituto de Pesquisas René Rachou, Fundação Oswaldo Cruz and UFMG, Belo Horizonte, MG, Brazil), Bernardo L Horta (UFPel, Pelotas, Brazil).
Publication: Michel S Naslavsky, et.al. Whole-genome sequencing of 1,171 elderly admixed individuals from, Brazil. Nature Communications volume 13, Article number: 1004 (2022)

The 90plus and COVID-19 resistant individuals

This was an invited paper where we reviewed the literature on longevity and showed new data on our cohort of individuals older than 90 who recovered from COVID-19.

The world population is getting older and studies aiming to enhance our comprehension of the underlying mechanisms responsible for health span are of utmost interest for longevity and as a measure for health care. In this review, we summarized previous genetic association studies (GWAS) and next-generation sequencing (NGS) of elderly cohorts. We also present the updated hypothesis for the aging process, together with the factors associated with healthy aging. We discuss the relevance of studying older individuals and build databanks to characterize the presence and resistance against late-onset disorders. The identification of about 2 million novel variants in our cohort of more than 1000 elderly Brazilians illustrates the importance of studying highly admixed populations of non-European ancestry. Finally, the ascertainment of nonagenarians and particularly of centenarians who were recovered from COVID-19 or remained asymptomatic opens new avenues of research aiming to enhance our comprehension of biological mechanisms associated with resistance against pathogens.

PI: Mayana Zatz and Michel Naslavasky
Undergraduate student: Monize Silva
PosDoc: Mateus Ca28stro

Publication: Mayana Zatz, et.al. The 90 plus: longevity and COVID-19 survival. Molecular Psychiatry, vol. 27, pages 1936–1944 (2022)

Gut microbiota: Genetic or environment?

Researches in healthy elderly suggest an association between gut microbiota and aging. However it still unknown how much our gut *microbiota* depends on the environment andor host genetics. Moreover, the question of whether host genetics plays a role in the development of the infant *gut microbiota* does not, as yet, have a clear answer. In order to throw additional light on this question, we have analyzed a rare set of triplets , composed of two identical twins and one dizygotic twin. Since these triplets share the same environment, our hypothesis was that if the gut microbiota depends only on environment, all three would be vey similar. However, if host genetics would play a role, the identical twins would be more similar that the dizygotic twin. We have analyzed 16S rRNA *amplicon* sequences from 99 valid fecal samples of five sets of dichorionic triplet babies born by C-section from 1 to 36 months of age. Beta diversity analysis showed that *monozygotic twins* were more similar to each other than their dizygotic siblings.

Monozygotic twins also tended to share more amplicon sequence variants between them. *Heritability* analysis showed that the genera *Bacteroides* and *Veillonella* are particularly susceptible to host genetics. We conclude that infant gut microbiota development is influenced by host genetics, but this effect is subtle and may affect only certain bacterial taxa during a limited time period early in life.

This study was a collaboration between our group, Prof. João Setubal from IQUSP
PosDoc: Larissa RB Matos, Ondina Palmeira, MSC student
Publication: Ondina Palmeira, et.al. Longitudinal 16S rRNA gut microbiota data of infant triplets show partial susceptibility to host genetics. iScience, Volume 25, Issue 3, 18 March 2022, 103861

C. Therapies in Genetic Disorders

C1. Pre-Clinical studies with murine stem cells

Pre-Clinical studies with murine stem cells Skeletal muscle injury by electroporation – a model to study degeneration/regeneration pathways in muscle – post-injury muscle regeneration in the elderly: Skeletal muscle has a remarkable capacity to regenerate after injuries mainly due to a reservoir of precursor cells named satellite cells (SCs), which are responsible for after-birth growth and response to lesions, either by exercise or disease. Upon injury, the regenerative response includes SCs exit of quiescence, activation, proliferation and fusion to repair or form new myofibers. This process is accompanied by inflammation, with infiltration of immune cells, primarily macrophages. Every phase of regeneration is highly regulated and orchestrated by manymolecules and

signaling pathways. The elucidation of players and mechanisms involved in muscle degeneration and regeneration is of extreme importance, especially for therapeutic strategies for muscle diseases. We recently developed a model of muscle injury induced by electroporation, which is an efficient method to induce muscle damage in order to follow the steps involved in degeneration and regeneration. This methodology is an easy and simple alternative to induce muscle lesion. It can be employed to study alterations in gene expression and the process of satellite cell recruitment, both in healthy and dystrophic/myopathic animal models for muscular dystrophy (Almeida and Vainzof, 2020). This methodology is being used now for the study of muscle regeneration with age. The process of muscle degeneration with subsequent poor regeneration is the primary cause of muscle loss and weakness seen in dystrophies muscle. Recent studies have identified tubular aggregates (ATs) in muscle fibers of elderly male mice, in an event dependent on the age of the animal. In human ATs have been observed in some types of dystrophic muscles, but with evidence of a relation with senescence. Myogranules are another type of myo-aggregate that has been currently related to muscle regeneration. In a pathological situation, however, an abnormal accumulation of this type of aggregate was observed, which remains accumulated in the fibers, impacting the regeneration. Now, we are evaluating muscle regeneration in elderly mice normal and with different forms of dystrophies, trying to point out the role of myo-aggregates (ATs and myogranules). Understanding the mechanistic differences in muscle regeneration between young and old muscles elderly, with and without muscular dystrophies, may be important in aiming future therapies

C2. Safety-related concerns in cell therapy

C2.1. Clinical Application of Human Induced Pluripotent Stem Cell-Derived Organoids as an Alternative to Organ Transplantation

Safety-related concerns in cell therapy: Mesenchymal stem cells (MSCs) are multipotent cells found in various tissues and are easily cultivated. For use in clinical protocols, MSCs must be expanded to obtain an adequate number of cells, but a senescence state may be instituted after some passages, reducing their replicative potential. In this study, we report a case where MSC derived from an elderly donor acquired a senescence state after three passages. The bone marrow was aspirated from a female patient submitted to a cell therapy for the incontinency urinary protocol. Controls were established using BM-MSC from healthy donors and used for senescence and gene expression assays. The patient's MSC expansion using AS displayed an early senescence state. In order to understand the role of AS in senescence, MSCs were then submitted to two different culture conditions: 1) with AS or 2) with FBS supplementation. Senescence state was assessed after 24 h, and no statistical differences were observed between the two conditions. However, patients' cells cultured with AS displayed a higher number of senescence cells than FBS medium after 48 h ($p = 0.0018$). Gene expression was performed in both conditions; increased expression of KLF4 was observed in the

patient's cells in comparison to healthy controls (p = 0.0016); reduced gene expression was observed for NANOG (p = 0.0016) and SOX2 (p = 0.0014) genes. Telomere length of the patient's cells was shorter than that of a healthy donor and that of a patient of similar age. Osteocyte differentiation seemed to be more diffuse than that of the healthy donor and that of the patient of similar age. MSCs could enter a senescence state during expansion in early passages and can impact MSC quality for clinical applications, reducing their efficacy when administered.

PI: Oswaldo Keith Okamoto. Collaboration with the groups of Dr. M.A. T. Bortolini & Dr. R. Castro (Federal University of São Paulo) and Dr. J.M. Kutner (Albert Einstein Hospital).
Publication: Alves-Paiva RM. et al. Senescence State in Mesenchymal Stem Cells at Low Passages: Implications in Clinical Use. Frontiers in Cell and Developmental Biology, v. 10, p. 1-10, 2022.

C2.2. New neonatal diagnosis protocol for SMA

New neonatal diagnosis protocol: Spinal muscular atrophy is an autosomal recessive disorder for which new therapies are underway. However it is known that the efficiency of such therapies depends on an early diagnosis. Therefore we have developed a new neonatal protocol as summarized below: Since the approval of modifying therapies for Spinal Muscular Atrophy (SMA), several protocols aiming to screen SMN1 homozygous deletion in a neonatal context have been published. However, no work has compared different methodologies along with detailed implementation costs for centers where the neonatal screening of SMA has not yet been implemented. Therefore, our work compared different qualitative real-time PCR approaches for SMA screening and the estimated costs of test implementation. Using Brazilian blood samples, the presence and absence (P/A) and melt curve protocols were analyzed. MLPA was used as a confirmatory test. The costs were calculated for the simplex and multiplex tests plus equipment. The test workflow was based on the present experience and literature report. The accuracy of the P/A protocol was 1 (95% CI 0.8677−1) using dried blood spots (DBS). The melt curve protocol also achieved 100% concordance. The consumable costs ranged from USD 1.68 to 4.42 and from USD 2.04 to 12.76 per reaction, for the simplex and multiplex tests, respectively. The equipment acquisition costs ranged from USD 44,817.07 to 467,253.10, with several factors influencing this value presented. Our work presents a framework for decision-making, with a project demonstration of the different assays that will be useful in dealing with the issues of cost and availability of reagents. Moreover, we present a literature review and discussion of important concerns regarding treatment policies. We take the first step towards a future SMA NBS pilot program where it is not yet a reality.

PI: Mayana Zatz
Vanessa Luiza Romanelli Tavares - posdoc – Mayana Zatz supervision
Publication: Romanelli Tavares VL, et.al. Newborn screening for 5q spinal muscular atrophy: comparisons between real-time PCR methodologies and cost estimations for future implementation programs.
International journal of neonatal screening, september, 2021

C3. Other therapeutic approaches

New insights in mice bearing human brain tumors injected with zika virus: The Zika virus (ZIKV) has shown a promising oncolytic effect against embryonal CNS tumors. However, studies on the effect of different administration routes and the ideal viral load in preclinical models are highly relevant aiming for treatment safety and efficiency. Here, we investigated the effect and effectiveness of different routes of administration, and the number of $ZIKV^{BR}$ injections on tumor tropism, destruction, and side effects. Furthermore, we designed an early-stage human brain organoid co-cultured with embryonal CNS tumors to analyze the $ZIKV^{BR}$ oncolytic effect. We showed that in the mice bearing subcutaneous tumors, the $ZIKV^{BR}$ systemically presented a tropism to the brain. When the tumor was located in the mice's brain, serial systemic injections presented efficient tumor destruction, with no neurological or other organ injury and increased mice survival. In the human cerebral organoid model co-cultured with embryonal CNS tumor cells, $ZIKV^{BR}$ impaired tumor progression. The gene expression of cytokines and chemokines in both models suggested an enhancement of immune cells recruitment and tumor inflammation after the treatment. These results open new perspectives for virotherapy using the $ZIKV^{BR}$ systemic administration route and multiple doses of low virus load for safe and effective treatment of embryonal CNS tumors, an orphan disease that urges new effective therapies.

PI: Mayana Zatz
Student Phd: Raiane Oliveira
PosDoc: Carolini Kaid
Publication: Raiane Oliveira Ferreira, et. al. Effect of Serial Systemic and Intratumoral Injections of Oncolytic ZIKVBR in Mice Bearing Embryonal CNS Tumors.
Viruses 2021, *13*(10), 2103, October 2021 ; https://doi.org/10.3390/v13102103

Placental zika-virus infection and maternal age: In pregnant women, Zika virus (ZIKV) is associated with a congenital syndrome, most frequently involving damage to embryo brain formation and the development of microcephaly. The mechanism (s) by which ZIKV enters the maternal-fetal interface and is transmitted to the fetus remains incompletely determined. We sought to evaluate histologic changes in the placenta of ZIKV-infected pregnant women and to determine if this varied by maternal age. Placental samples were obtained from 66 women, 33 of whom were positive for ZIKV. Histologic evaluations were performed on 4 areas of the placenta: fetal surface, maternal surface, umbilical cord, and membranes. Samples were analyzed by the tissue microarray technique and tested for CD4, CD8, CD20, CD68, FOXP3, and cyclooxygenase-2 expression. Data were evaluated using Fisher exact test. ZIKV infection was more frequent in women less than 18 yr of age (9/11, 81.8%) than in women above 18 yr old (24/55, 43.6%)(P= 0.0440). ZIKV detection was associated with neutrophilic chorioamnionitis (P= 0.0332) and with septal (P= 0.0244) and villous (P= 0.0534) calcification. Hofbauer cell hyperplasia (P= 0.0260) and cyclooxygenase-2 expression (P= 0.0346) were more prevalent in ZIKV-

positive women aged 18 yr and below than in the older ZIKV-positive women. ZIKV infection during pregnancy occurs more frequently in adolescents and induces higher rates of damage at the maternal-fetal interface than in older women.

Publication: Geovane R Santos, et.al. Differences in Placental Histology Between Zika Virus-infected Teenagers and Older Women. International Journal of Gynecological Pathology: Official Journal of the International Society of Gynecological Pathologists (a 2021, august)

Oncolytic effects of Zika Virus against Brain Tumors: In a previous study, we have shown that Zika virus (ZIKV) has a promising oncolytic effect against embryonal CNS tumors. However, studies on the effect of different administration routes and the ideal viral load in preclinical models are highly relevant aiming for treatment safety and efficiency. Here, we investigated the effect and effectiveness of different routes of administration, and the number of ZIKV injections on tumor tropism, destruction, and side effects. Furthermore, we designed an early-stage human brain organoid co-cultured with embryonal CNS tumors to analyze the ZIKV oncolytic effect. We showed that in the mice bearing subcutaneous tumors, the ZIKV systemically presented a tropism to the brain. When the tumor was located in the mice's brain, serial systemic injections presented efficient tumor destruction, with no neurological or other organ injury and increased mice survival. In the human cerebral organoid model co-cultured with embryonal CNS tumor cells, ZIKV impaired tumor progression. The gene expression of cytokines and chemokines in both models suggested an enhancement of immune cells recruitment and tumor inflammation after the treatment. These results open new perspectives for virotherapy using the ZIKVBR systemic administration route and multiple doses of low virus load for safe and effective treatment of embryonal CNS tumors, an orphan disease that urges new effective therapies.

PIs: Mayana Zatz, Oswaldo Keith Okamoto
Postgraduate studet: Raiane Oliveira Ferreira and Rodolfo Sanches Ferreira.
Undergrad student: Isabela Granha.
Postdoc: Carolini Kaid.
Publication: Ferreira RO. et al. Effect of Serial Systemic and Intratumoral Injections of Oncolytic ZIKV^{BR} in Mice Bearing Embryonal CNS Tumors. Viruses-Basel, v. 13, p. 2103, 2021.

Novel immunotherapy with CAR-like Natural Killer cells to treat Hematological Malignancies

Novel immunotherapy with CAR-T cells to treat cancer: The therapy with genetically modified T cells to express chimeric antigen receptors (CAR) is a promising strategy for immunotherapy against cancer. CAR-T cells can specifically recognize antigens on the surface of tumor cells and then effectively kill those cells. Several researchers have presented the development of CAR-T cells for various hematological targets and the treatment of solid tumors. Manufacturing of customized gene or cell therapy products

such as CAR-T cells is complex and depends on release tests and exams that can attest to a consistent quality standard for each product. The quality of CAR-T cell products is subject to donor variation, but also includes the manufacturing environment, as well as the quality and availability of materials and reagents. Quality must be carefully monitored and integrated into the manufacturing process. In addition to quality control, preclinical evaluation of these products are essential to demonstrate their safety and efficacy and allow development to the clinical trial phase. In a series of three papers, we have published technical guidelines concerning GMP production, quality testing, and preclinical validation of CAR-T cell products for therapeutic use in humans.

PI: Oswaldo Keith Okamoto – PhD student: Lucila N. Kerbauy. Collaboration with the groups of Dr. J.M. Kutner (Albert Einstein Hospital).
Publications: a)Godoy JAP et al. CAR-T cell production. Journal of Bone Marrow Transplantation and Cellular Therapy, v. 3, p. 155, 2022. b) Godoy JAP et al. Advanced Cell Therapy product release containing CAR-T cells. Journal of Bone Marrow Transplantation and Cellular Therapy, v. 3, p. 156, 2022. c) Godoy JAP et al . Preclinical studies using CAR-T cells. Journal of Bone Marrow Transplantation and Cellular Therapy, v. 3, p. 154, 2022.

C4. Tissue engineering

Hepatic bioengineering technologies aiming the future of human organs transplantation: The liver is the most important metabolic hub of endo and xenobiotic compounds. Pre-clinical studies using rodents to evaluate the toxicity of new drugs and cosmetics may produce inconclusive results for predicting clinical outcomes in humans, moreover being banned in the European Union. Human liver modeling using primary hepatocytes presents low reproducibility due to batch-to-batch variability, while iPSC-derived hepatocytes in monolayer cultures (2D) show reduced cellular functionality. Here we review the current status of the two most robust in vitro approaches in improving hepatocyte phenotype and metabolism while mimicking the hepatic physiological microenvironment: organoids and liver-on-chip. Both technologies are reviewed in design and manufacturing techniques, following cellular composition and functionality. Furthermore, drug screening and liver diseases modeling efficiencies are summarized. Finally, organoid and liver-on-chip technologies are compared regarding advantages and limitations, aiming to guide the selection of appropriate models for translational research and the development of such technologies.

PI: Mayana Zatz
Student Phd: Kayque Alves
Undergraduate Students: Lara Pacheco and Sabrina Komatsu
PosDoc: Luiz Carlos Caires-Junior and Ernesto Goulart
Publication: Kayque Alves Telles-Silva, et.al. Applied hepatic bioengineering: Modeling the human liver using organoid and liver-on-a-chip technologies. Frontiers in Bioengineering and Biotechnology, February, 2022.

D. The Covid 19 Pandemic

Our group undertook different studies related to COVID-19 as well as a collaboration in an international consortium: COVID HUMAN GENETIC EFFORT

D1. Increased susceptibility or resistance to COVID-19

COVID-19 recurrence and reduced T-cell response: Recurrence of COVID-19 in recovered patients has been increasingly reported. However, the immune mechanisms behind the recurrence have not been thoroughly investigated. The presence of neutralizing antibodies (nAbs) in recurrence/reinfection cases suggests that other types of immune response are involved in protection against recurrence. Here, we investigated the innate type I/III interferon (IFN) response, binding and nAb assays and T-cell responses to severe acute respiratory distress syndrome coronavirus 2 (SARS-CoV-2) with IFN gamma (IFN*γ*) enzyme-linked spot assay (ELISPOT) in three pairs of young adult monozygotic (MZ) twins with previous confirmed COVID-19, one of them presenting a severe recurrence four months after the initial infection. Twin studies have been of paramount importance to comprehend the immunogenetics of infectious diseases. Each MZ twin pair was previously exposed to SARS-CoV-2, as seen by clinical reports. The six individuals presented similar overall recovered immune responses except for the recurrence case, who presented a drastically reduced number of recognized SARS-CoV-2 T-cell epitopes on ELISPOT as compared to her twin sister and the other twin pairs. Our results suggest that the lack of a broad T-cell response to initial infection may have led to recurrence, emphasizing that an effective SARS-CoV-2-specific T-cell immune response is key for complete viral control and avoidance of clinical recurrence of COVID-19.

PI: Mayana Zatz
Pos-Doc: Mateus Castro
Publication: Mateus V De Castro, et.al. Recurrence of COVID-19 associated with reduced T-cell responses in a monozygotic twin pair. 02 February 2022, Open Biology https://doi.org/10.1098/rsob.210240

The risk of COVID-19 and I IFN auto-antibodies: SARS-CoV-2 infection fatality rate (IFR) doubles with every ve years of age from childhood onward. Circulating autoantibodies neutralizing IFN-α, IFN-ω, and/or IFN-β are found in~ 20% of deceased patients across age groups. In the general population, they are found in~ 1% of individuals aged 20-70 years and in> 4% of those> 70 years old. With a sample of 1,261 deceased patients and 34,159 uninfected individuals, we estimated both IFR and relative risk of death (RRD) across age groups for individuals carrying autoantibodies neutralizing type I IFNs, relative to non-carriers. For autoantibodies neutralizing IFN-α2 or IFN-ω, the RRD was 17.0 [95% CI: 11.7-24.7] for individuals under 70 years old and 5.8 [4.5-7.4] for individuals aged 70 and over, whereas, for autoantibodies neutralizing

both molecules, the RRD was 188.3 [44.8-774.4] and 7.2 [5.0-10.3], respectively. IFRs increased with age, from 0.17%[0.12-0.31] for individuals< 40 years old to 26.7%[20.3-35.2] for those≥ 80 years old for autoantibodies neutralizing IFN-α2 or IFN-ω, and from 0.84%[0.31-8.28] to 40.5%[27.82-61.20] for the same two age groups, for autoantibodies neutralizing both molecules. Autoantibodies against type I IFNs increase IFRs, and are associated with high RRDs, particularly those neutralizing both IFN-α2 and-ω. Remarkably, IFR increases with age, whereas RRD decreases with age. Autoimmunity to type I IFNs appears to be second only to age among common predictors of COVID-19 death.

PI: Mayana Zatz
Pos-Doc: Mateus Castro
Publication: Jeremy Manry, et.al. The risk of COVID-19 death is much greater and age-dependent with type I IFN autoantibodies. Res Sq. 2022 Jan 14;rs.3.rs-1225906. doi: 10.21203/rs.3.rs-1225906/v1. Preprint

Men are the main transmitters of COVID-19: COVID-19 has affected millions of people worldwide. Clinical manifestations range from severe cases with lethal outcome to mild or asymptomatic cases. Although the proportion of infected individuals does not differ between sexes, men are more susceptible to severe COVID-19, with a higher risk of death than women. Also, men are pointed out as more lax regarding protective measures, mask wearing and vaccination. Thus, we questioned whether sex-bias may be explained by biological pathways and/or behavioral aspects or both. Between July 2020 and July 2021, we performed an epidemiological survey including 1744 unvaccinated adult Brazilian couples, with there was at least one infected symptomatic member, who were living together during the COVID-19 infection without protective measures. Presence or absence of infection was confirmed by RT-PCR and/or serology results. Couples were divided into two groups: (1) both partners were infected (concordant couples) and (2) one partner was infected and the spouse remained asymptomatic despite the close contact with the COVID-19 symptomatic partner (discordant couples). Statistical analysis of the collected data was performed aiming to verify a differential transmission potential between genders in couples keeping contact without protective measures. The combination of our collected data showed that the man is the first (or the only) affected member in most cases when compared to women and that this difference may be explained by biological and behavioral factors. The present study confirmed the existence of gender differences not only for susceptibility to infection and resistance to COVID-19 but also in its transmission rate.

PI: Mayana Zatz
Undergraduate studentMonize Silva
Pos-Doc: Mateus V. de Castro
Publication:Monize VR Silva, et. al. Men are the main COVID-19 transmitters: behavior or biology? Discover Mental Health, Vol 2. Pág 1-7. 2022

X- linked recessive TLR7 deficiency and COVID-19: COVID international consortium. Age and male sex are two prominent risk factors for developing life-threatening COVID-

19 after SARS-CoV-2 infection. Asano *et al*. analyzed 1202 critical male COVID-19 patients to examine whether non-synonymous variants in genes on the X chromosome are a risk factor for developing COVID-19 pneumonia. Toll-like receptor 7 (TLR7) variants resulting in TLR7 deficiency occurred in 16 unrelated males, most of which were under age 60. Plasmacytoid dendritic cells (pDCs), primary producers of type I interferon (IFN-I), from TLR7-deficient patients were unresponsive to TLR7 stimulation and displayed impaired production of IFN-I in response to SARS-CoV-2. These results identify X-linked recessive TLR7 deficiency as a genetic risk factor for COVID-19 pneumonia in males and demonstrate a key role for intact pDC IFN-I in protective immunity against SARS-CoV-2.

This study was a collaboration between our group and Prof Jean Casanova
Publication: Bastard P et al., and COVID-19 consortium . X-linked recessive TLR7 deficiency in 1% of men under 60 years old with life-threatening COVID-19.Science Immunology**,** 20 Aug 2021, Vol 6,Issue 62,doi 10.1126/sciimmunol.abl4348

Autoantibodies neutralizing type I IFNs and COVID-19: Type I interferons are potent antiviral cytokines induced promptly after human respiratory exposure to SARS-CoV-2 virus. Either genetic or acquired defects in type I interferon signaling can increase host vulnerability to developing severe COVID-19 (coronavirus disease 2019) disease. Bastard *et al*. used sensitive immunoassays and neutralization testing to detect presence of autoantibodies to α, β, or ω type I interferons in plasma samples from a large cohort of patients with COVID-19 and prepandemic controls. The incidence of neutralizing autoantibodies to type I interferon increased with age in the control cohort, increasing sharply after the age of 70. These findings indicate that autoantibodies targeting type I IFNs represent a not uncommon type of acquired immunodeficiency that contributes to about 20% of all COVID-19 fatalities

This study was a collaboration between our group and Covid-19 consortium
Publication: Bastard P and Covid-19 consortium. Autoantibodies neutralizing type I IFNs are present in ~4% of uninfected individuals over 70 years old and account for ~20% of COVID-19 deaths. Science Immunology, 20 Aug 2021, Vol 6,Issue 62, DOI: 10.1126/sciimmunol.abl4340

D2. Immunogenetics of resistance to SARS-CoV-2 infection in discordant couples

MHC variants associated with symptomatic versus asymptomatic SARS-CoV-2 infection in highly exposed individuals - Despite the high number of individuals infected by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) who develop coronavirus disease 2019 (COVID-19) symptoms worldwide, many exposed individuals remain asymptomatic and/or uninfected and seronegative. This could be explained by a combination of environmental (exposure), immunological (previous infection), epigenetic, and genetic factors. Aiming to identify genetic factors involved in immune response in symptomatic COVID-19 as compared to asymptomatic exposed individuals, we analyzed 83 Brazilian couples where one individual was infected and symptomatic

while the partner remained asymptomatic and serum-negative for at least 6 months despite sharing the same bedroom during the infection. We refer to these as “discordant couples”. We performed whole-exome sequencing followed by a state-of-the-art method to call genotypes and haplotypes across the highly polymorphic major histocompatibility complex (MHC) region. The discordant partners had comparable ages and genetic ancestry, but women were overrepresented (65%) in the asymptomatic group. In the antigen-presentation pathway, we observed an association between *HLA-DRB1* alleles encoding Lys at residue 71 (mostly DRB1*03:01 and DRB1*04:01) and DOB*01:02 with symptomatic infections and *HLA-A* alleles encoding 144Q/151R with asymptomatic seronegative women. Among the genes related to immune modulation, we detected variants in *MICA* and *MICB* associated with symptomatic infections. These variants are related to higher expression of soluble MICA and low expression of MICB. Thus, quantitative differences in these molecules that modulate natural killer (NK) activity could contribute to susceptibility to COVID-19 by downregulating NK cell cytotoxic activity in infected individuals but not in the asymptomatic partners.

This study was a collaboration between our group, Prof. Jorge Kalil and Prof. Erick Castelli
Publication: Erick C Castelli, et.al. MHC Variants Associated With Symptomatic Versus Asymptomatic SARS-CoV-2 Infection in Highly Exposed Individuals. Front. Immunol., 28 September 2021 | https://doi.org/10.3389/fimmu.2021.742881

PART 2 - TRANSFER OF TECHNOLOGY/ TECHNOLOGY APPLICATIONS

As transfer of technology, our proposal is to translate scientific and technological advances into services, as follows:

Sequencing Facility (EMU/ Equipamento Multiusuário /Multiuser Equipment-FAPESP): HUG-CELL EMU <http://genoma.ib.usp.br/servicos> contains four sequencing apparatus: ABI 3730 DNA Analyser sequencer - (Applied Biosystems), NovaSeq, MiSeq and HiSeq 2500 (Illumina). In the year of 2022, we were able to expand our infrastructure for storage and data processing to approximately 1.5 petabytes by acquiring a new storage server (Storage Infortrend Gen2 with redundant controllers, 8 10GbE SFP+ ports, 256GB Cache, and 72 x 16 TB disks (net capacity after RAID6: 900 TB. This represents an increase of 150% of our previous storage capacity, adequate for holding whole-exome sequences on the routine diagnosis, research and ready to implement whole-genome sequencing for both research and diagnosis purposes. As mentioned in the previous report, this sequencing facility is registered at the multi-user facility at USP (http: uspmulti.prp.usp).

Genetic tests and sequencing services: We have updated the web page of the non-profit laboratory for genetic tests <http://laboratorio.genoma.usp.br> with the inclusion of Genetic Counseling. Two new upcoming tests should be added: detection of pathogenic expansion in *C9orf72*, previously associated with neurodegenerative phenotypes, and expansion at *EIF4A3*, associated with the autosomal recessive craniofacial disorder Richieri-Costa-Pereira syndrome. We have had a significant delay to complete validation of these tests due to postponed reagents shipping. We are constantly checking the quality of our pipelines and improving them as necessary. In 2022, we have incorporated two pipelines for CNV detection in exome analysis. These pipelines are used not only for the genetic tests in our routine, but also in HUG-CELL research.

During the last year (july2021 to june2022), we have performed 22.213 genetic tests (MLPA/disease specific CNVs, fluorescent PCR, Triple-PCR for expansion, NGS panels, NGS exome, aCGH, RNAseq, and Sanger sequencing). NGS service have been done for different research Institutes, such as FIOCRUZ, FMUSP, UNICAMP and UNIFESP. The quality and reliability of our genetic tests have been certified yearly by the European Molecular Genetics Quality Netwok (EMQN).

Except for aCGH test, which is done in the cytogenetic facility coordinated by two of our PIs (C Rosenberg, AC Krepischi), all the others were performed at the HUG-CELL facilities.

Genetic counseling service: Genetic counseling of families with affected patients includes diagnosis, testing the patients and when appropriate “at-risk carriers”, orientation about prognosis and management and genetic counseling. About 1.134 consultations were performed by our team. A written report, including results of genetic tests, were provided for most of the attended individuals.

DATABASES: We have developed, and hosted in our servers, a public access website <http://abraom.ib.usp.br> - ABraOM - Arquivo Brasileiro Online de Mutações) to provide information on the frequency of variants in 1171 Brazilian healthy individuals that are part of the Sao Paulo city elderly cohort studied at our center (SABE cohort; dataset 1 = 609 whole exome sequence; dataset 2 = 1171 whole genome sequencing). These datasets have provided valuable information for the interpretation of pathogenicity of variants identified in genetic tests in Brazil and around the world. The corresponding paper has recently been published in Nature Communications (Naslavsky et al., 2022). In addition to the aggregate datasets provided by open access ABraOM, the individual-level data (BAM and gVCF files) from the 1171 WGS are available for researchers who can access under request both datasets at the European Genome-phenome Archive:<https://ega-archive.org/studies/EGAS00001005052>.

DesBraVar is a software that is being developed since 2018. However, we did not anticipate a fast change on the use of NGS gene panels to whole genomes, which imply the need of large storage and processing space. Therefore, the ideal is to have a system to be assessed at the cloud space. We are currently looking for some alternatives to achieve this goal.

RT-LAMP for COVID-19: We have standardized the amplification of SARS-CoV-2 through RT- LAMP (Reverse Transcription Loop-mediated Isothermal Amplification) direct in saliva samples (Kobayashi et al., 2021;doi: 10.3390/diagnostics11081400). We have been doing SARS-CoV2 testing as a service at HUG-CELL since December 2020. Up to now, nearly 7.000 individuals were tested and a written report was sent to each tested individual less than 24 hrs after saliva collection. The availability of this test to students and employees at the Instituto de Biociências, USP, has been essential for a better control of the spread of SARS-CoV-2, even after vaccination.

Income resources administration: The income of the paid services is used to pay for activities not supported by our current grants or the University, such as payment of technicians**,** equipment maintenance, reagents for the genetic tests and building maintenance. The income of the paid services has been carried out by Fundação Faculdade de Medicina USP (FFM) and Fundação Universidade de São Paulo (FUSP).

PART 3 - EDUCATION OUTREACH

High School Support Program – The service to schools was resumed in 2022 concomitantly with the return, on a regular basis, of face-to-face activities in schools.

A.1. Project: Laboratory classes at school

https://genoma.ib.usp.br/laboratorio-nas-escolas/42.

We establish laboratory classes within individual schools for periods of 3 weeks, and assist the teachers in leading laboratory classes related to the cellular basis of Genetics, including the use of microscopes and 6 different practical kits. 16 hours of technical and pedagogical support to 37 High School teachers were delivered (**Annex 4 - table 1**). Twenty-fourHigh schools were attended until the beginning of June and nearly 17,000 students were benefited.

A.2. Instructional support project

https://genoma.ib.usp.br/materiais-didaticos/43

The objective of the project is to help teachers to over-come 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 and established three loan centers, which currently provide instructional material to more than 100 teachers each year. Fourty seven new teachers were trained on May 2nd, 2022 and May 3th, 2022 (**Annex 4 - table 2**).

B. Projects having the public as target

The main objective of the scientific dissemination actions continued to approach the public that seeks knowledge and quality information, also creating proximity between the public, science and scientists. During the period of this report, the education and diffusion activities of HUG-CELL were kept on its online platforms. On social networks, HUG-CELL is known as GenomaUsp and is present on **YouTube**, **Facebook** and **Instagram**. The outreach team produced scientific dissemination content for the public, remaining attentive to High School teachers as a target audience of the posts. It is possible to use several of posts contents as didactic material and they were collected on our site to facilitate there use by High School teachers (https://genoma.ib.usp.br/posts-educativos-em-pdf/82).

On **YouTube**<https://www.youtube.com/genomausp>, between July/2021 and June 2020, the scientific dissemination team designed videos in 4 formats:

"ABC Genoma" brings a series of videos about specific topics relevant to the public and unveiled by the HUG-CELL research team. Four different topics were covered in the video series: Genetic counseling, Cancer and Virus, the Central Dogma of Molecular Biology and Ancestry, totaling 27 videos that generated 8,875 views,

“Family Secrets” podcasts, which cover fictitious cases, nevertheless inspired by the center's genetic counseling service, were addressed and brought up discussions about genetics, ethics and genetic of the counseling dilemmas to the public (3,214 views);

“Decoding DNA - Radio USP” reproduces a series of short radio programs in which the director of HUG-CELL addresses current issues on human genetics (2,338 views);

"CINEgenoma" presents live broadcasts of roundtables composed by guests from different areas who discuss, having a film as starting point, issues related to genetics, science, medicine, society, ethics, education and cinematography. Three live broadcasts were produced in the period to which the report refers, which generated 1,873 views. The best moments of CINEgenoma were summarized in another format (The Best Moments/CINE Genome), generating 906 views;

On **Instagram**<https://www.instagram.com/genoma.usp/> the same videos as YouTube were released and also others related to HUG-CELL research or educational subjects. These posts bring enlightening illustrations, in carousel format, language suitable for the public and references to popular culture, without giving up scientific rigor. In the period to which the report refers were elaborated 61 posts, 63 videos on IGTV, 8 Reels and 374 Stories.

On **Facebook**<https://www.instagram.com/genoma.usp/> there is also the release of videos deposited on **YouTube** and content about HUG-CELL research subjects that appear in journalistic media, including those related to Instagram posts on Instagram (117 posts).

The number of GenomaUSP media followers continues to grow and, until May 2022, corresponds to 11,900 on Facebook, 17,700 on Instagram and 6,600 on YouTube. Between June 2021 and May 2022, the YouTube channel had 142,000 views, 6,500 hours assisted and 2.6 thousand new subscribers. Detailed data are summarized in the **Annex 4 - table 3**.

Annex 1 - Publications in peer reviewed journals, books and patente

From July 2021 until June 2022, our group has published 82 journal articles (all listed below), 13 abstracts in National meetings, and 21 abstracts in International meetings. During this period, our graduate students submitted 6 Master Theses and 6 Doctoral Dissertations. About 18 conferences, lectures and symposia were presented done by our team

1.1. Book and book Chapters

1. **Zatz M** and França, MSJ. O legado dos genes: O que a ciência pode nos ensinar sobre o envelhecimento, July, 2021, São Paulo, **Editora Objetiva**

2. Moreno NC, Latancia MT, Oliveira AP, Padilha E, Martins DJ, Munford V and **Menck CFM.**How do Translesion Polymerases Deal With Photodamage? In: *DNA photodamage: From light absortion to cellular responses and skin cancer*, Ed. R Improta and T Douki, Royal Society of Chemistry, 2021, London, UK, Chapter 14, pp 307-338.

3. de Souza TA, Moreno NC, Quintero-Ruiz N, Corradi C e **Menck CFM**. Toxicogenômica: uso da genômica em estudos de mutagênese e carcinogênese. In Da Toxigenética à Toxigenômica, Ed. DMF Salvadori, CS Takahashi, CK Grisolia, RA dos Santos. Ed. Atheneu, 2021, São Paulo, Brazil, Capítulo 10, pp 227-250.

4. **Mingroni-NettoRC**. The Human Mitochondrial DNA In: Human Genome Structure, Function and Clinical Considerations.1 ed.: Springer International Publishing, 2021, p. 301-328.

1.2. Articles

1. Abdala BB, Gonçalves AP, Dos Santos JM, Boy R, de Carvalho CMB, Grochowski CM, **Krepischi ACV**, **Rosenberg C**, Gusmão L, Pehlivan D, Pimentel MMG, Santos-Rebouças CB. Molecular and clinical insights into complex genomic rearrangements related to MECP2 duplication syndrome. Eur J Med Genet. 2021 Dec;64(12):104367. doi: 10.1016/j.ejmg.2021.104367. Epub 2021 Oct 19. PMID: 34678473

2. Aguiar T, Teixeira A, Scliar MO, Sobral de Barros J, Lemes RB, Souza S, Tolezano G, Santos F, Tojal I, Cypriano M, Caminada de Toledo SR, Valadares E, Borges Pinto R, Pinto Artigalas OA, Caetano de Aguirre Neto J, Novak E, Cristofani LM, Miura Sugayama SM, Odone V, Cunha IW, Lima da Costa CM, **Rosenberg C**, **Krepischi A**. Unraveling the Genetic Architecture of Hepatoblastoma Risk: Birth Defects and Increased Burden of Germline Damaging Variants in Gastrointestinal/Renal Cancer Predisposition and DNA Repair Genes. Front Genet. 2022 Apr 12;13:858396. doi: 10.3389/fgene.2022.858396. eCollection 2022. PMID: 35495172 Free PMC article.

3. Ali TM, Linnenkamp BDW, **Yamamoto GL**, Honjo RS, Cabral de Menezes Filho H, Kim CA, **Bertola DR**. The recurrent homozygous translation start site variant in CCDC134 in an individual with severe osteogenesis imperfecta of non-Morrocan ancestry. Am J Med Genet A. 2022 May;188(5):1545-1549. doi: 10.1002/ajmg.a.62651.

4. Alves-Paiva RM, do Nascimento S, de Oliveira D, Coa L, Alvarez K, Hamerschlak N, **Okamoto OK**, Marti LC, Kondo AT, Kutner JM, Bortolini MAT, Castro R, Preto de Godoy JA. Senescence State in Mesenchymal Stem Cells at Low Passages: Implications in Clinical Use. Frontiers in Cell and Developmental Biology, v. 10, p. 1-10, 2022.

5. Andrade PV, Souza LS, Santos JM, Alves JFF, Lutke C, Amaral JLG, **Vainzof M**, Silva HCA. Spinal cord injury-related thermoregulatory impairment masks a fatal malignant hyperthermia crisis. A Case Report. Can J Anaesth. 2021 Dec 13. doi: 10.1007/s12630-021-02170-4. Online ahead of print.

6. Barros JS, Aguiar TFM, Costa SS, Rivas MP, Cypriano M, Toledo SRC, Novak EM, Odone V, Cristofani LM, Carraro DM, Werneck da Cunha I, Costa CML, **Vianna-Morgante AM**, **Rosenberg C**, **Krepischi ACV**. Copy Number Alterations in Hepatoblastoma: Literature Review and a Brazilian Cohort Analysis Highlight New Biological Pathways. Front Oncol. 2021 Dec 8;11:741526. doi: 10.3389/fonc.2021.741526. eCollection 2021. PMID: 34956867 Free PMC article.

7. Bastard P, et al. Vidigal M, **Zatz M**, et al. Autoantibodies neutralizing type I IFNs are present in ~4% of uninfected individuals over 70 years old and account for ~20% of COVID-19 deaths. Sci Immunol. 2021 Aug 19;6(62):eabl4340. doi: 10.1126/sciimmunol.abl4340

8. Campos AE, **Rosenberg C**, **Krepischi ACV**, França M, Lopes V, Nakano V, Vertemati T, Cochak M, Migliavacca M, Milanezi F, Sousa AC, Silva J, Vieira L, Monfredini P, Palumbo AC, Fernandes J, Perrone E. An Apparently Balanced Complex Chromosome Rearrangement Involving Seven Breaks and Four Chromosomes in a Healthy Female and Segregation/Recombination in Her Affected Son. Mol Syndromol. 2021 Aug;12(5):312-320. doi: 10.1159/000516323. Epub 2021 Jul 15. PMID: 34602959 Free PMC article.

9. Carvalho LML, da Costa SS, Campagnari F, Kaufman A, **Bertola DR**, da Silva IT, **Krepischi ACV**, **Koiffmann CP**, **Rosenberg C**. Two novel pathogenic variants in MED13L: one familial and one isolated case. Intellect Disabil Res. 2021 Dec;65(12):1049-1057. doi: 10.1111/jir.12891.

10. **Castelli EC**, de Almeida BS, Muniz YCN, Silva NSB, Passos MRS, Souza AS, Page AE, Dyble M, Smith D, Aguileta G, Bertranpetit J, Migliano AB, **Duarte YAO**, Scliar MO, Wang J, **Passos-Bueno MR**, **Naslavsky MS**, **Zatz M**, Mendes-Junior CT, Donadi EA. HLA-G genetic diversity and evolutive aspects in worldwide populations. Scientific Reports, Sci Rep. 2021 Nov 29;11(1):23070. doi: 10.1038/s41598-021-02106-4.

11. Castelli EC, de Castro MV, **Naslavsky MS**, Scliar MO, Silva NSB, Andrade HS, Souza AS, Pereira RN , Castro CFB, Mendes-Junior CT, Meyer D, Nunes K, Matos LRB, Silva MVR, Wang JYT, Esposito J, Coria VR, Bortolin RH, Hirata MH, Magawa JY, Cunha-Neto E, Coelho V, Santos KS, Marin MLC, Kalil J, **Mitne-Neto M**, Maciel RMB, **Passos-Bueno MR**, **Zatz M.** MHC Variants Associated With Symptomatic Versus Asymptomatic SARS-CoV-2 Infection in Highly Exposed Individuals. Front Immunol. 2021 Sep 28;12:742881. doi: 10.3389/fimmu.2021.742881.

12. Castro LP, Batista-Vieira D, de Souza TA, Timoteo ARS, Coutinho JDL, Pinheiro de Almeida IC, Henriques SRM, de Azevedo FM, Rosa RCA, Kannouche PL, Sarasin A, **Menck CFM**, Petta TB. XPC and POLH/XPV Genes Mutated in a Genetic Cluster of

Xeroderma Pigmentosum Patients in Northeast Brazil. Front Genet. 2022 Jan 17;12:784963. doi: 10.3389/fgene.2021.784963.

13. Castro MAA, Dos Santos JHV, Honjo RS, **Yamamoto GL**, **Bertola DR**, Hurst AC, Chorich LP, Layman LC, Kim CA, Kim HG. Twenty-year follow-up of the facial phenotype of Brazilian patients with Sotos syndrome. Am J Med Genet A. 2021 Dec;185(12):3916-3923. doi: 10.1002/ajmg.a.62454.

14. Castro MV, Silva MVR, **Naslavsky MS**, Santos KS, Magawa JY, Neto EC, **Passos-Bueno MR**, **Zatz M**. COVID-19 in twins: What can we learn from them? MedRxiv, doi**:** https://doi.org/10.1101/2021.09.29.21263145.

15. Castro MV, Santos KS, Apostolico JS, Fernandes ER, Almeida RR, Levin G, Magawa JY, Nunes JPS, Bruni M, Yamamoto MM, Lima AC, Silva MVR, Matos LRB, Coria VR, Castelli EC, Scliar MO, Kuramoto A, Bruno FR, Jacintho LC, Nunes K, Wang JYT, Coelho VP, **MitneNeto M**, Maciel RMB, **Naslavsky MS**, **Passos-Bueno MR**, Boscardin SB, Rosa DS, Kalil J, **Zatz M**, Cunha-Neto E. Monozygotic twins discordant for severe clinical recurrence of COVID-19 show drastically distinct T cell responses to SARS-Cov-2. MedRxiV doi: https://doi.org/10.1101/2021.03.26.21253645

16. Castro MV, Santos KS, Apostolico JS, Fernandes ER, Rafael R Almeida RR, Levin G, Magawa JY, Nunes JPS, Bruni M, Yamamoto MM, Lima AC, Silva MVR, Matos LRB, Coria VR, Castelli EC, Scliar MO, Kuramoto A, Bruno FR, Jacintho LC, Nunes K, Wang JYT, Coelho VP, **Mitne-Neto M**, Maciel RMB, **Naslavsky MS**, **Passos**-**Bueno MR**, Boscardin SB, Rosa DS, Kalil J, **Zatz M**, Cunha-Neto E. Recurrence of COVID-19 associated with reduced T-cell responses in a monozygotic twin pair. Open Biology, 02 Feb 2022, 12(2):210240 DOI: 10.1098/rsob.210240

17. Comim CM, Soares JA, Alberti A, Freiberger V, Ventura L, Dias P, Schactae AL, Grigollo LR, Steckert AV, Martins DF, Junior RJN, **Vainzof M**, Quevedo. Effects of low-intensity training on the brain and muscle in the congenital muscular dystrophy 1D model.J.Neurol Sci. 2022 Feb 19. doi: 10.1007/s10072-022-05928-w. Online ahead of print.

18. Costa CIS, da Silva Montenegro EM, Zarrei M, de Sá Moreira E, Silva IMW, de Oliveira Scliar MO, Wang JYT, Zachi EC, Branco EV, da Costa SS, Lourenço NCV, **Vianna-Morgante AM**, **Rosenberg C**, **Krepischi ACV**, Scherer SW, **Passos-Bueno MR**. Copy number variations in a Brazilian cohort with autism spectrum disorders highlight the contribution of cell adhesion genes. Clin Genet. 2022 Jan;101(1):134-141. doi: 10.1111/cge.14072. Epub 2021 Nov 15.

19. Cotta A, Souza LS, Carvalho E, Feitosa LN, Cunha AJr, Navarro MM, Valicek J, Menezes MM, Neves SVN, Xavier-Neto R, Vargas AP, Takata RI, Paim JF, **Vainzof M**. Central Core Disease: Facial Weakness Differentiating Biallelic from Monoallelic Forms. Genes 2022, 13, 760. https://doi.org/10.3390/genes13050760

20. da Rocha LA, Pires LVL, **Yamamoto GL**, Magliocco Ceroni JR, Honjo RS, de Novaes França Bisneto E, Oliveira LAN, **Rosenberg C**, **Krepischi ACV**, **Passos**-**Bueno MR**, Kim CA, **Bertola DR**. Congenital limb deficiency: Genetic investigation of 44 individuals presenting mainly longitudinal defects in isolated or syndromic forms. Clin Genet. 2021 Nov;100(5):615-623. doi: 10.1111/cge.14041.

21. de Assis LVM, Moraes MN, Mendes D, Silva MM, **Menck CFM**, Castrucci AML. Loss of Melanopsin (OPN4) Leads to a Faster Cell Cycle Progression and Growth in Murine Melanocytes. Curr Issues Mol Biol. 2021 Oct 4;43(3):1436-1450. doi: 10.3390/cimb43030101

22. de Castro Fonseca M, de Oliveira JF, Araujo BHS, Canateli C, do Prado PFV, Amorim Neto DP, Bosque BP, Rodrigues PV, de Godoy JVP, Tostes K, Filho HVR, Nascimento AFZ, Saito A, Tonoli CCC, Batista FAH, de Oliveira PSL, Figueira AC, Souza da Costa S, **Krepischi ACV**, **Rosenberg C**, Westfahl H Jr, da Silva AJR, Franchini KG. Molecular and cellular basis of hyperassembly and protein aggregation driven by a rare pathogenic mutation in DDX3X. iScience. 2021 Jul 10;24(8):102841. doi: 10.1016/j.isci.2021.102841. eCollection 2021 Aug 20. PMID: 34381968 Free PMC article.

23. de Castro MV, Santos KS, Apostolico JS, ..., **Naslavsky MS**, **Passos-Bueno MR**, Boscardin SB, Rosa DS, Kalil J, **Zatz M**, Cunha-Neto E. Recurrence of COVID-19 associated with reduced T-cell responses in a monozygotic twin pair. Open Biol. 2022 Feb;12(2):210240. doi: 10.1098/rsob.210240. Epub 2022 Feb 2

24. Dias VL, de Oliveira Braga KA, Nepomuceno NA, Ruiz LM, Perez JDR, Correia AT, Caires-Junior LC, Goulart E, **Zatz M**, Pêgo-Fernandes PM. Soluble factors of mesenchimal stem cells (FS-MSC) as a potential tool to reduce inflammation in donor's lungs after hypovolemic shock. J Bras Pneumol. 2021 Aug 9;47(4):e20200452. doi: 10.36416/1806-3756/e20200452.

25. Ferreira RO, Granha I, Ferreira RS, Bueno HS, **Okamoto OK**, Kaid C, **Zatz M** . Effect of Serial Systemic and Intratumoral Injections of Oncolytic ZIKVBR in Mice Bearing Embryonal CNS Tumors. Viruses. 2021 Oct 19;13(10):2103. doi: 10.3390/v13102103.

26. Fidalgo F, Torrezan GT, Sá BCS, Barros BDF, Moredo LF, Valieris R, de Souza SJ, Duprat JP, **Krepischi ACV**, Carraro DM. Family-based whole-exome sequencing identifies rare variants potentially related to cutaneous melanoma predisposition in Brazilian melanoma-prone families. PLoS One. 2022 Jan 27;17(1):e0262419. doi: 10.1371/journal.pone.0262419.
.

27. Figueiredo T, Mendes APD, Moreira DP, Goulart E, Oliveira D, Kobayashi GS, Stern S, **Kok F**, Marchetto MC, Santos R, Gage FH, **Zatz M**. Inositol monophosphatase 1 (IMPA1) mutation in intellectual disability patients impairs neurogenesis but not gliogenesis. Mol Psychiatry. 2021 Jul;26(7):3558-3571. doi: 10.1038/s41380-020-00862-9. Epub 2020 Aug 24.

28. Freitas JLGS, Silva JMM, Nóbrega JCL, Simões RFM, Medeiros JB, Alves RO, Santos JLF, **Duarte YAO**, **Zatz M**, Matheson D, de Menezes TN, Santos S. Health-Related Quality of Life and Associated Factors: Regional Differences Among Oldest-Old in Brazil. Inquiry. Jan-Dec 2022; 59:469580221086922. doi: 10.1177/00469580221086922.

29. Galisa ALG, Jacob PL, de Farias AA, Lemes RB, Alves LU, Nóbrega JCL, **Zatz M**, **Santos S**, Mathias Weller. Haplotypes of single cancer driver genes and their local ancestry in a highly admixed long-lived population of Northeast Brazil. Genet Mol Biol. 2022 Feb 2;45(1):e20210172. doi: 10.1590/1678-4685-GMB-2021-0172. eCollection 2022.

30. Ghirotto B, Oliveira DF, Cipelli M, Basso PJ, de Lima J, Breda CNS, Ribeiro HC, Silva CCC, Hiyane MI, Caldini EG, Sussulini A, Kowaltowski AJ, Oliveira EML, **Zat**z **M**, Camara NOS. MS-driven metabolic alterations are recapitulated in iPSC-derived astrocytes. Ann Neurol. 2022 May;91(5):652-669. doi: 10.1002/ana.26336. Epub 2022 Mar 17.

31. Godoy JAP, Bonamino M, Melo RAP, Kondo AT, **Okamoto OK**, Kerbauy LN. CAR-T cell production. Journal of Bone Marrow Transplantation and Cellular Therapy, v. 3, p. 155, 2022

32. Godoy JAP, Kerbauy LN, Paiva RMA, Kondo AT, **Okamoto OK**, Kutner JM. Advanced Cell Therapy product release containing CAR-T cells. Journal of Bone Marrow Transplantation and Cellular Therapy, v. 3, p. 156, 2022

33. Godoy JAP, Kerbauy LN, Paiva RMA, Kondo AT, **Okamoto OK**, Bonamino M . Preclinical studies using CAR-T cells. Journal of Bone Marrow Transplantation and Cellular Therapy, v. 3, p. 154, 2022.

34. Grochowski CM, **Krepischi ACV**, Eisfeldt J, Du H, **Bertola DR**, Oliveira D, Costa SS, Lupski JR, Lindstrand A, Carvalho CMB. Chromoanagenesis Event Underlies a de novo Pericentric and Multiple Paracentric Inversions in a Single Chromosome Causing Coffin-Siris Syndrome. Front Genet. 2021 Aug 26;12:708348. doi: 10.3389/fgene.2021.708348.

35. Gurgel-Giannetti J, Souza LS, Messina de Pádua Andrade GF, Derlene MF, Meira ZMA, Azevedo BVM, Jr WC, Diniz SSL, Carvalhais MB, Oliveira JRS, Uliana L, Bráulio R, Costa PHN, Filho GB, **Vainzof M**. A Novel SPEG mutation causing congenital fiber type disproportion myopathy and dilated cardiomyopathy with heart transplantation. NeuromusculDisord. 2021 Nov;31(11):1199-1206. doi: 10.1016/j.nmd.2021.09.005.

36. Honjo RS, Monteleone VF, Aiello VD, Wagenfuhr J, Issa VS, Pomerantzeff PMA, Furusawa EA, Zanardo EA, Kulikowski LD, **Bertola DR**, Kim CA. Cardiovascular findings in Williams-Beuren Syndrome: Experience of a single center with 127 cases. Am J Med Genet A. 2022 Feb;188(2):676-682. doi: 10.1002/ajmg.a.62542.

37. Kajitani GS, Brace L, Trevino-Villarreal JH, Trocha K, MacArthur MR, Vose S, Vargas D, Bronson R, Mitchell SJ, **Menck CFM**, Mitchell JR. Neurovascular dysfunction and neuroinflammation in a Cockayne syndrome mouse model. Aging (Albany NY). 2021 Oct 10;13(19):22710-22731. doi: 10.18632/aging.203617. Epub 2021 Oct 10.

38. Kajitani GS, Quayle C, Garcia CCM, Fotoran WL, Dos Santos JFR, van der Horst GTJ, Hoeijmakers JHJ, **Menck CFM**. Photorepair of Either CPD or 4PP DNA Lesions in Basal Keratinocytes Attenuates Ultraviolet-Induced Skin Effects in Nucleotide Excision Repair Deficient Mice. Front Immunol. 2022 Mar 29;13:800606. doi: 10.3389/fimmu.2022.800606

39. Kobayashi GS, Brito LA, Moreira DP, Suzuki AM, Hsia GSP, Pimentel LF, de Paiva APB, Dias CR, Lourenço NCV, Oliveira BA, Manuli ER, Corral MA, Cavaçana N, **Mitne-Neto M**, Sales MM, Dell' Aquila LP, Filho AR, Parrillo EF, Mendes-Corrêa MC, Sabino EC, Costa SF, Leal FE, Sgro GG, Farah CS, **Zatz M**, **Passos-Bueno MR**. A Novel Saliva RT-LAMP Workflow for Rapid Identification of COVID-19 Cases and Restraining Viral Spread. Diagnostics (Basel). 2021 Aug 3;11(8):1400. doi:

10.3390/diagnostics11081400.

40. Kowaltowski A, **Naslavsky MS**, **Zatz M**. Open access: Brazilian scientists denied waivers and discounts. Nature. 2022 Mar;603(7903):793. doi: 10.1038/d41586-022-00864-3.

41. Lezirovitz K, **Mingroni-Netto RC**. Genetic etiology of non-syndromic hearing loss in Latin America. Hum Genet. 2022 Apr;141(3-4):539-581. doi: 10.1007/s00439-021-02354-4. Epub 2021 Oct 15.

42. Lima AR, Ferreira BM, Zhang C, Jolly A, Du H, White JJ, Dawood M, Lins TC, Chiabai MA, van Beusekom E, Cordoba MS, Caldas Rosa ECC, Kayserili H, Kimonis V, Wu E, Mellado C, Aggarwal V, Richieri-Costa A, Brunoni D, Canó TM, Jorge AAL, Kim CA, Honjo R, **Bertola DR**, Dandalo-Girardi RM, Bayram Y, Gezdirici A, Yilmaz-Gulec E, Gumus E, Yilmaz GC, Okamoto N, Ohashi H, Coban-Akdemir Z, Mitani T, Jhangiani SN, Muzny DM, Regattieri NAP, Pogue R, Pereira RW, Otto PA, Gibbs RA, Ali BR, van Bokhoven H, Brunner HG, Sutton VR, Lupski JR, **Vianna-Morgante AM**, Carvalho CMB, Mazzeu JF. Phenotypic and mutational spectrum of ROR2-related Robinow syndrome. Hum Mutat. 2022 Mar 28. doi: 10.1002/humu.24375.

43. Linnenkamp B, Girardi R, Rocha L, **Yamamoto GL**, Ceroni JR, Mendes AEC, Honjo R, Oliveira LA, Amemiya RB, Quaio C, de Oliveira Filho JB, Kim CA, **Bertola DR**. Vertebral segmentation defects in a Brazilian cohort: Clinical and molecular analysis focused on spondylocostal dysostosis. Clin Genet. 2022 Apr;101(4):476-478. doi: 10.1111/cge.14118.

44. Manry J, Bastard P, Gervais A, Le Voyer T, Rosain J, et al… … (de Castro MV , **Zatz M**.) The risk of COVID-19 death is much greater and age-dependent with type I IFN autoantibodies. Proc Natl Acad Sci U S A. 2022 May 24;119(21):e2200413119. doi: 10.1073/pnas.2200413119. Epub 2022 May 16.

45. Mansur F, Teles E Silva AL, Gomes AKS, Magdalon J, de Souza JS, Griesi-Oliveira K, **Passos-Bueno MR**, **Sertié AL**. Complement C4 Is Reduced in iPSC-Derived Astrocytes of Autism Spectrum Disorder Subjects. Int J Mol Sci. 2021 Jul 15;22(14):7579. doi: 10.3390/ijms2214757

46. Martins DJ, Tirman S, Quinet A, **Menck CFM**. Detection of Post-Replicative Gaps Accumulation and Repair in Human Cells using the DNA Fiber Assay. J Vis Exp. 2022 Feb 3;(180). doi: 10.3791/63448.

47. Meira JGC, Magalhães BS, Ferreira IBB, Tavares DF, Kobayashi GS, Leão EKEA. Novel USP9X variant associated with syndromic intellectual disability in a female: A case study and review. Am J Med Genet A. 2021 ;185(5):1569-1574. doi: 10.1002/ajmg.a.62141. Epub 2021 Feb 27.

48. Moreira DP, Suzuki AM, Silva ALTE, Varella-Branco E, Meneghetti MCZ, Kobayashi GS, Fogo M, Ferrari MFR, Cardoso RR, Lourenço NCV, Griesi-Oliveira K, Zachi EC, **Bertola DR**, Weinmann KS, de Lima MA, Nader HB, **Sertié A**L, **Passos-Bueno MR**. Neuroprogenitor Cells From Patients With TBCK Encephalopathy Suggest Deregulation of Early Secretory Vesicle Transport. Front Cell Neurosci. 2022 Jan 13;15:803302. doi: 10.3389/fncel.2021.803302.

49. Nani DA, Hsia GSP, **Passos-Bueno MR**, Kobayashi GS. Modeling Early Neural Crest Development via Induction from hiPSC-Derived Neural Plate Border-like Cells. Methods Mol Biol . 2022 Mar 31. doi: 10.1007/7651_2021_454.

50. **Naslavsky MS**, Scliar MO. Methods to Study Genomic DNA Sequence Variation. Chapter 3 in: Human Genome Structure, Function and Clinical Considerations. Springer, 2021**.**

51. **Naslavsky MS**, Scliar MO, **Yamamoto GL**, Wang JYT, Zverinova S, Karp T, Nunes K, Ceroni JRM, de Carvalho DL, da Silva Simões CE, Bozoklian D, Nonaka R, Dos Santos Brito Silva N, da Silva Souza A, de Souza Andrade H, Passos MRS, Castro CFB, Mendes-Junior CT, Mercuri RLV, Miller TLA, Buzzo JL, Rego FO, Araújo NM, Magalhães WCS, **Mingroni-Netto RC**, Borda V, Guio H, Rojas CP, Sanchez C, Caceres O, Dean M, Barreto ML, Lima-Costa MF, Horta BL, **Tarazona-Santos E**, **Meyer D**, Galante PAF, Guryev V, **Castelli EC**, **Duarte YAO**, **Passos-Bueno MR**, **Zatz M.** Whole-genome sequencing of 1,171 elderly admixed individuals from Brazil. Nat Commun. 2022 Mar 4;13(1):1004. doi: 10.1038/s41467-022-28648-3

52. **Naslavsky MS**, Vidigal M, Matos LRB, Cória VR, Batista Junior PB, Razuk A, Saldiva PHN, Dolhnikoff M, Schidlowski L, Prando C, Cunha-Neto E, **Condino-Neto A**, **Passos-Bueno MR**, **Zatz M**. Extreme phenotypes approach to investigate host genetics and COVID-19 outcomes. Genet Mol Biol. 2021 Mar 1;44(1 Suppl 1):e20200302. doi: 10.1590/1678-4685-GMB-2020-0302.

53. Nishi MY, Faria Júnior JAD, **Krepischi ACV**, de Moraes DR, da Costa SS, Silva ESDN, Costa EMF, Mendonca BB, Domenice S. A Small Supernumerary Xp Marker Chromosome Including Genes NR0B1 and MAGEB Causing Partial Gonadal Dysgenesis and Gonadoblastoma. Sex Dev. 2022;16(1):55-63. doi: 10.1159/000517085. Epub 2021 Sep 10.

54. Nóbrega JCL, Medeiros JB, Freitas JLGS, Silva JMM, Simões RFM, Olinda R, Santos JLF, Menezes TN, **Duarte YAO**, **Zatz M**, Matheson D, Santos S. Psychosocial aspects and support networks associated with disability in two longevous populations in Brazil: a cross-sectional study. BMC Geriatrics, 1/2, BMC Geriatr. 2022 Feb 9;22(1):110. doi: 10.1186/s12877-022-02810-4.

55. Palacios-Muñoz A, de Paula Moreira D, Silva V, García IE, Aboitiz F, Zarrei M, Campos G, Rennie O, Howe JL, Anagnostou E, Ambrozewic P, Scherer SW, **Passos-Bueno MR**, Ewer J. Mutations in trpγ, the homologue of TRPC6 autism candidate gene, causes autism-like behavioral deficits in Drosophila. Mol Psychiatry. 2022 May 2. doi: 10.1038/s41380-022-01555-1. Online ahead of print

56. Palmeira O, Larissa RB Matos LRB, **Naslavsky MS**, Heloisa MS Bueno HMS, Soler JP, Setubal JC, **Zatz M**. Longitudinal 16S rRNA gut microbiota data of infant triplets show partial susceptibility to host genetics. iScience. 2022 Feb 2;25(3):103861. doi: 10.1016/j.isci.2022.103861.

57. **Passos-Bueno MR**, Costa, CIS, **Zatz M**. Dystrophin genetic variants and autism. Discover Mental Health, volume 2, Article number: 4 (2022)

58. Pires LVL, Bordim RA, Maciel MBR, Tanaka ACS, **Yamamoto GL**, Honjo RS, Kim CA, **Bertola DR**. Atypical, severe hypertrophic cardiomyopathy in a newborn presenting Noonan syndrome harboring a recurrent heterozygous MRAS variant. Am J Med Genet

A. 2021 Oct;185(10):3099-3103. doi: 10.1002/ajmg.a.62376.

59. Pires LVL, Ribeiro RL, Sousa AM, Linnenkamp BDW, Pontes SE, Teixeira MCTV, Befi-Lopes DM, Honjo RS, **Bertola DR**, Kim CA. Nationwide questionnaire data of 229 Williams-Beuren syndrome patients using WhatsApp tool. Arq Neuropsiquiatr. 2021 Nov;79(11):950-956. doi: 10.1590/0004-282X-ANP-2020-0450.

60. Quintero-Ruiz N, Corradi C, Moreno NC, de Souza TA, Pereira Castro L, Rocha CRR, **Menck CFM**. Mutagenicity Profile Induced by UVB Light in Human Xeroderma Pigmentosum Group C Cells†. Photochem Photobiol. 2022 98(3):713-731.

61. Rezende RC, Noronha RM, Keselman A, Quedas EPS, Dantas NCB, Andrade NLM, **Bertola DR**, Malaquias AC, Jorge AAL. Delayed Puberty Phenotype Observed in Noonan Syndrome Is More Pronounced in Girls than Boys. Horm Res Paediatr. 2022;95(1):51-61. doi: 10.1159/000522670.

62. Rivas M, Johnston ME 2nd, Gulati R, Kumbaji M, Margues Aguiar TF, Timchenko L, **Krepischi ACV**, Shin S, Bondoc A, Tiao G, Geller J, Timchenko N. Cell Mol Gastroenterol Hepatol. 2021;12(5):1669-1682. doi: 10.1016/j.jcmgh.2021.06.026. Epub 2021 Jul 8.

63. Romanelli Tavares VL, Guimarães-Ramos SL, Zhou Y, Masotti C, Ezquina S, Moreira DP, Buermans H, Freitas RS, Den Dunnen JT, Twigg SRF, **Passos-Bueno MR**. New locus underlying auriculocondylar syndrome (ARCND): 430 kb duplication involving *TWIST1* regulatory elements. J Med Genet. 2021 Nov 8:jmedgenet-2021-107825. doi: 10.1136/jmedgenet-2021-107825. Online ahead of print.

64. Romanelli Tavares VL, Monfardini F, Lourenço NCV, da Rocha KM, Weinmann K, Pavanello R**, Zatz M**. Newborn Screening for 5q Spinal Muscular Atrophy: Comparisons between Real-Time PCR Methodologies and Cost Estimations for Future Implementation Programs. Int J Neonatal Screen. 2021 Aug 11;7(3):53. doi: 10.3390/ijns7030053

65. Silva MVR, de Castro MV, **Passos-Bueno MR**, Otto PA, **Naslavsky MS**, **Zatz M**. Men are the main COVID-19 transmitters: behavior or biology? Discov Ment Health. 2022;2(1):1. doi: 10.1007/s44192-022-00004-3. Epub 2022 Jan 24

66. Silva MVR, Mateus V de Castro, Maria Rita Passos-Bueno, Paulo A Otto, Michel S Naslavsky, Mayana Zatz. Men are the main COVID-19 transmitters: behavior or biology? Discov Ment Health. 2022;2(1):1. doi: 10.1007/s44192-022-00004-3. Epub 2022 Jan 24

67. Souza BTBA, Nóbrega JCL, Simões RRF, Barbosa J, Olinda RA, **Duarte YAO**, **Zatz M**, Santos S. A Comparative Study of Prevalence and Risk Factors Associated with Depressive Symptoms in Two Long-Lived Elderly Populations in Brazil. Global Journal of Health Science.1-16, 14/1/2022

68. Souza LS , Calyjur P, Ribeiro AF, Gurgel-Giannetti J, Pavanello RCM, **Zatz M**, **Vainzof M**. Association of Three Different Mutations in the CLCN1 Gene Modulating the Phenotype in a Consanguineous Family with Myotonia Congenita. J Mol Neurosci. 2021 Nov;71(11):2275-2280. doi: 10.1007/s12031-020-01785-4.

69. Asano T, Boisson B and consortium (Collaborators: **Zatz M**, **Passos-Bueno MR** et al) X-linked recessive TLR7 deficiency in~ 1% of men under 60 years old with life-threatening COVID-19. Sci Immunol. 2021 Aug 19;6(62):eabl4348. doi: 10.1126/sciimmunol.abl4348

70. Telles-Silva KA, Pacheco L, Komatsu S, Chianca F, Caires-Júnior LC, Araujo BHS, Goulart E, **Zatz M**. Applied Hepatic Bioengineering: Modeling the Human Liver Using Organoid and Liver-on-a-Chip Technologies. Front Bioeng Biotechnol. 2022 Feb 14;10:845360. doi: 10.3389/fbioe.2022.845360

71. **Vainzof M**, Gurgel-Giannetti J. Muscle regeneration in spastic muscles of children with cerebral palsy. Dev Med Child Neurol. 2021 Oct;63(10):1137. doi: 10.1111/dmcn.14953.

72. **Vainzof M**, Souza LS, Gurgel-Giannetti J, **Zatz M**. Sarcoglycanopathies: an update. Neuromuscul Disord.2021Oct;31(10):1021-1027.doi: 10.1016/j.nmd.2021.07.014. Epub 2021 Jul 28.

73. Vasconcelos, FTGR, Carvalho, LML, Souza LS, Barbosa IN, Dávila CK, **Zatz M**, **Vainzof M**. Modelos animais no estudo de doenças genéticas humanas. Genetica na Escola 17 (1), pag 26, 2022.

74. Vegas N, Demir Z, Gordon CT, Breton S, Romanelli Tavares VL, Moisset H, Zechi-Ceide R, Kokitsu-Nakata NM, Kido Y, Marlin S, Gherbi Halem S, Meerschaut I, Callewaert B, Chung B, Revencu N, Lehalle D, Petit F, Propst EJ, Papsin BC, Phillips JH, Jakobsen L, Le Tanno P, Thévenon J, McGaughran J, Gerkes EH, Leoni C, Kroisel P, Tan TY, Henderson A, Terhal P, Basel-Salmon L, Alkindy A, White SM, **Passos-Bueno MR**, Pingault V, De Pontual L, Amiel J. Futher delineation of auriculocondylar syndrome based on 14 novel cases and reassessement of 25 published cases. Hum Mutat. 2022 May;43(5):582-594. doi: 10.1002/humu.24349. Epub 2022 Mar 7.

75. **Zatz M**, Silva MVR, Castro MV, **Naslavsky MS**. The 90 plus: longevity and COVID-19 survival. Mol Psychiatry. 2022 Apr;27(4):1936-1944. doi: 10.1038/s41380-022-01461-6. Epub 2022 Feb 8

Annex 2 - Meetings, Conferences, Lectures

2.1. Abstract: National Meetings

1. Campos G, et. al. Expanding the genetics of Autism Spectrum Disorder: exome analysis of 242 Brazilian trios. Presented at the **66th Brazilian Congress of Genetics - SBG 2021**, virtual meeting from 13-17/09/2021
2. Carmo GB, Rocha K, Lazar M, Ezquina S, **Yamamoto GL**, Gollop TR, **Zatz M**, Bueno MRSP, **Krepischi ACV**, **Okamoto OK**. Variantes Germinativas em Brasileiras com Câncer de Mama e Detecção de uma Nova Deleção Patogênica no Gene ATM em Família com Câncer de Mama de Início Precoce. In: **XXXII Congresso Brasileiro de Genética Médica**, 2021, on line. Anais XXXII CBGM, 2021. p. 122-123
3. Carvalho LML, Costa SS, Campagnari F, Kaufman A, **Bertola DR** ; Da Silva IT ; **Krepischi ACV**, **Koiffmann CP**, **Rosenberg C** . Novas variantes genéticas patogênicas em MED13L: relato de um caso familial e um caso isolado.. In: **XXXII Congresso Brasileiro de Genética Médica**, 2021, On-line. Anais - XXXII Congresso Brasileiro de Genética Médica, 2021. p. 100.
4. Godoy JAP, Paiva RMA, Oliveira DC, Coa LL, Alvarez KCA , **Okamoto OK**, Marti LC, Kondo AT, Bortolini MAT, Castro R, Kutner JM. Senescence State of Mesenchymal Stem Cells in Low Culture Passages: Implications for Clinical Use In: **Congresso da Associação Brasileira de Terapia Celular e Gênica**, 2021, Curitiba. Cytotherapy, 2021. v. 23. p. 33-34. ps://doi.org/10.1016/j.jcyt.2021.02.097.
5. Latancia MT, Leandro G, Bastos AC, Moreno NC, Martins DJ, Rocha CRR, **Menck CFM**. DNA polymerase eta protects human cells against DNA damage induced by Temozolomide. Presented at the **XV Congresso da Mutagen-Brasil,** virtual meeting from 12 to 15/11/2021.
6. Leandro GS, D Mendes D, A Aguilera A, **Menck CFM**. XPD/ERCC2 mutated trichothiodystrophy patients cells present basal accumulation of DNA lesions related to R-loops and depend on homologous recombination to survive. Presented at the **XV Congresso da Mutagen-Brasi**l, virtual meeting from 12 to 15/11/2021.
7. Martins DJ, Quinet AT Vessoni, **Menck CFM**. Participation of Pol iota in the mechanisms of translesion synthesis in UV-irradiated human cells. Presented at the **XV Congresso da Mutagen-Brasil**, virtual meeting from 12 to 15/11/2021.
8. Nani D, etl al. In vitro modelling of redox signalling in human embryonic neuroectodermal specification. Presented at the **XX Congress of the Brazilian Society for Cell Biology**, virtual metting from 27-29/01/2021
9. Nani D, et.al. In vitro characterization of TCOF1 expression and redox state during human craniofacial development. Presented at **Genética 2021 - Brazilian Congress Of Genetics**, virtual meeting from 13-16/09/2021.
10. Pires SF ; Sobral de Barros J ; Costa SS. ; Scliar MO, Lengert AVH; Boldrini E ; Silva SEM, Vidal DO, **Krepischi ACV**, Maschietto M. DNA methylation and mutational signatures suggest dysregulation of developmental pathways in osteosarcomas. In: **66th Brazilian Congress of Genetics**, 2021, On-line. Abstracts - 66th Brazilian Congress of Genetics, 2021. p. 145.
11. Ramos IC, et.al. Assessment of TBCK deficiency, responsible for the neurodegenerative syndrome IHPRF3, on the neuroglutamatergic differentiation pathway. Presented at the **SBG 2021**, , virtual meeting from 13-17/09/2021
12. Santos TR, Kaid C, Araujo DD, Neville IS, Uno M,**ZatzM**,**Okamoto OK**. Ex Vivo Expansion of Tumor Infiltrating Lymphocytes (TILS) and Cancer Stem Cells From

Malignant Gliomas. In: **Congresso da Associação Brasileira de Terapia Celular e Gênica**, 2021, Curitiba. Cytotherapy, 2021. v. 23. p. 15-16.

13. Tolezano GC; Bastos GC, Costa SS,**Passos-BuenoMR**,**Koiffmann CP**, V**ianna-Morgante AM**, Jorge AAL,**Bertola DR**,**Rosenberg C**,**Krepischi ACV**. Investigating rare copy number variants in a Brazilian casuistry of 184 microcephalic patients. In: **66th Brazilian Congress of Genetics**, 2021. Abstracts - 66th Brazilian Congress of Genetics, 2021. p. 140.

2.1. Abstract: International Meetings

1. Andrade HD, Kondo AT, Kerbauy LN, Alves-Paiva RM, Castellar DCO, Coa L, Alvarez KCA, Savioli ML, Loureiro BMC, **Okamoto OK**, Hamerschlak N, KUTNER, J. M, Godoy JAP. Treatment of COVID-19 Patients: Insights into the Use of Bone Marrow-Derived Mesenchymal Stem Cells. In: **63rd American Society of Hematology (ASH) Annual Meeting**, 2021, Atlanta. Blood, 2021. v. 138. p. 4302-4304
2. Barbosa IN, Leite FS, Esposito J, Pardo MCS, Martins TMM, Olberg GGO, Pereira MCL, Bortolin RH,**Zatz M**. CRISPR-Cas9 correction of out-of-frame exon 2 duplication in iPSCs from patients with Duchenne Muscular Dystrophy. In: **Virtual European Muscle Conference**, 2021, Warsaw. Session 9: Muscle and beyond,2021.
3. Branco EV, et. al. Characterization of Phelan-McDermid brazilian cohort with small deletions and point mutations: focus on regression and behavioral changes across different ages. Presented at the **Annual Meeting of the American Society of Human Genetics**, virtual meeting from 18-22 de outubro de 2021.
4. Cabrera VIM, Santos MC, Sessa DP, Lago JH; **Netto LES**, Oliveira MA. Effects Of Natural Compounds On The Peroxidase Activity Of AhpCs From Pathogenic Bacteria In: **20th IUPAB Congress**, **45th Annual SBBf Meeting**, **and 50th Annual SBBq Meeting, 2021**, Foz do Iguaçu. 20th IUPAB Congress, 4., 2021.
5. Campos G, et. al. Expanding the genetics of Autism Spectrum Disorder: exome analysis of 242 Brazilian trios. Presented at **ASHG 2021** Virtual Meeting, from 18-22/10/2021
6. Corradi C, Vilar JB, de Souza TA, Castro LP, Munford V, De Vecchi R, Galante PA, Buzatto VC, Orpinelli F, Sotto MN, Saldiva PP, Chaibub SCW, Sarasin A, **Menck CFM**. Mutational signatures and landscape of Xeroderma Pigmentosum variant (XP-V) skin tumours. Presented as a poster and oral presentation at the Responses to DNA damage meeting, Egmond aan Zee, the Netherlands, from March 27th to April 1st, 2022.
7. Leite FS,Esposito J, Tahira A, Rodriguez-Delarosa A,**Verjovski-Almeida S**, Pourquie O, Kunkel L,**Zatz M**. Transcriptome analyses of iPSC-derived skeletal muscles of isogenic Duchenne Muscular Dystrophy (DMD) lines at different differentiation stages. In: **Virtual European Muscle Conference**, 2021, Warsaw.Suplement: Abstracts of the Virtual European Muscle Conference, Warsaw, September 20?22, 2021. v. 68.
8. Esposito J,Leite FS,Bortolin RH, Barbosa IN, Tahira A, Kaid C, Martins MM, Olberg GGO, Amaral MS, Pereira MCL, Pardo MCS,**Verjovski-Almeida S**,**Zatz M**. Differential expression of Notch pathway genes in iPSC-derived skeletal muscles from Duchenne Muscular Dystrophy patients. In: **Virtual European Muscle Conference**, 2021, Warsaw. Session 6: Myopathies: Mechanisms, modeling,medication. v. 68.
9. **Vainzof M**, Rocha de Vasconcelos FTG, Almeida CF, Bitoun M, Ishiba R, Souza LS, Ribeiro-Junior AF, Souza BW, Zogby IA, Saldys NG.Skeletal muscle injury by

electroporation – a model to study degeneration/regeneration pathways murine models for NMD. **17th International Congresso on Neuromuscular Diseases**, 5-9 july, 2022 Brussel, Belgium

10. de Mello JM, Andrade PV, Santos JM, Oliveira ASB, **Vainzof M**, Gomes do Amaral JL, Almeida da Silva HC. Predictive factors in the in vitro muscle contracture test for the diagnosis of malignant hyperthermia in a Brazilian sample. **ASHG 2022**
11. **Naslavsky MS.**. Oral presentation in Platform "Leveraging large datasets to gain insights into Mendelian disease architecture. Title: Biased pathogenic assertions of loss of function variants challenge molecular diagnosis of admixed individuals. Annual Meeting of the American Society of Human Genetics - **ASHG 2021**
12. Leandro GS, Mendes D, Aguilera A, **Menck CFM**. XPD Transcription-induced accumulation of DNA lesions in XPD/ERCC2 mutated in cells from trichothiodystrophy patients. Presented as a poster at the Responses to DNA damage meeting, Egmond aan Zee, the Netherlands, from March 27th to April 1st, 2022.
13. Latancia MT, Leandro G, Bastos AC, Moreno NC, Martins DJ, Rocha CRR, **Menck CFM**.Is Translesion Synthesis the only role of Polymerase Iota and Kappa in Temozolomide Resistance Mechanism? Presented as a poster at the Responses to DNA damage meeting, Egmond aan Zee, the Netherlands, from March 27th to April 1st, 2022.
14. Samogy Costa CI, et.al. Characterization of the genetic architecture of neurodevelopmental disorders using Duchenne Muscular Dystrophy as a model. Presented at the **Annual Meeting of the American Society of Human Genetics**, virtual meeting from 18-22 of october of 2021.
15. Hsia G, et. al. Modelling Treacher Collins syndrome in hiPSCs to investigate clinical variability, Presented at the The **ISSCR Annual Meeting 2022** (International Society of Stem Cell Research) , virtual meeting from 15-18 of june of 2021.
16. Goes CG, Genu V, Gomes F,**Netto LES**. Ahp1 is an important peroxiredoxin under stress by organic peroxide under conditions of peroxisome biogenesis in yeast In: **20th IUPAB Congress, 45th Annual SBBf Meeting**, **and 50th Annual SBBq Meeting, 2021**, Foz do Iguaçu. 20th IUPAB Congress, 4. , 2021. Resumo: 18236-1
17. Aleixo-Silva RL, Domingos RM, Trujillo M, Oliveira Filho A, Cristiano LP,**Netto LES**. Structural and biochemical characterization of LsfA, a 1-Cys Prx involved in Pseudomonas aeruginosa virulence In: **20th IUPAB Congress, 45th Annual SBBf Meeting, and 50th Annual SBBq Meeting, 2021**, Foz do Iguaçu. 20th IUPAB Congress, 4. , 2021. Resumo: 18235-1
18. Rocha LS; Pereirada Silva, B; CorreiaTML; Pereira da Silva R; Meireles DA; Pereira R; **Netto LES**; Meotti FC; Queiroz RF. The Antioxidant Peroxiredoxin AHPC1 IS A Key Protein In Pseudomonas Aeruginosa In: **20th IUPAB Congress, 45th Annual SBBf Meeting, and 50th Annual SBBq Meetin**g, 2021, Foz do Iguaçu. 20th IUPAB Congress, 4., 2021.
19. **Bertola DR**: Participation in the International Meeting for the Revision of the Nosology and classification of genetic skeletal disorders, as member of the **International Committee of Skeletal Dysplasias**, March 16th-18th of 2022, hybrid meeting, Lausanne, Switzerland.
20. Kerbauy LN, Coa L, Kondo AT, Godoy JAP, Bello I,**Okamoto OK**, Kutner J M, Hamerschlak N, Alves-Paiva RM. Umbilical Cord Blood NK Cells Stability After Cryopreservation: An Off The Shelf Strategy For Adoptive Immunotherapy Against Acute Myeloid Leukemia. In: **International Society for Cell & Gene Therapy - 28th Annual Meeting**, 2022, San Francisco. Cytotherapy, 2022. v. 24. p. s124-s124.

21. Godoy JAP,Alves-Paiva RM,Kondo AT, Kerbauy LN, Rodrigues M; **Okamoto OK**; Kutner JM. Detection of apoptosis in mesenchymal stromal cells ? In vitro? to predict their efficacy for treating graft versus host disease. In: **International Society for Cell Therapy Annual Meeting**, 2021, New Orleans. Cytotherapy, 2021. v. 23. p. s59-s59.

2.3.Conferences, Symposia, Round Tables, Lectures

1. Gomes F, Ramos A, Barros MH, **Netto, LES.** *Mechanisms of peroxiredoxins targeting to mitochondrial subcompartments*, (Simpósio,Apresentação de Trabalho).Referências adicionais: Brasil/Inglês. Meio de divulgação: Meio digital; Evento: 20th IUPAB Congress, 45th Annual SBBf Meeting, and 50th Annual SBBq Meeting; Inst.promotora/financiadora: IUPAB SBBq SBBf. 2021.
2. **Mingroni-Netto RC**, Visconti MA, Cortese JFN. *Curso de Extensão: Bioética para pesquisa em ciências da vida*, Instituto de Biociências, Universidade de São Paulo, 2021. (Organização)
3. **Okamoto OK**. *Tratamento com células CAR-T em tumores sólidos*. (palestra).XXVIII Simpósio Internacional de Hemoterapia e Terapia Celular e II Fórum Internacional de Terapia Celular. Hospital israelita Albert Einstein. 2021.
4. **Okamoto OK**. *Viabilidade de Projetos de Terapia Avançada*. 2021. (palestra).Board Review: XV Curso de Revisão em Hematologia e Hemoterapia | VII Simpósio Multidisciplinar em Hematologia, Hemoterapia e Transplante de Medula Óssea | V Simpósio de Atualizações em Oncologia Pediátrica | 9th International Symposium on Thrombosis. Hospital israelita Albert Einstein. 2021.
5. **Okamoto OK**. *Terapia oncolítica viral: oportunidades para o tratamento de tumores agressivos do SNC*. (palestra).II Fórum de Pesquisa Translacional: Conhecimento transformado em cuidado. Abordagens terapêuticas em doenças neurológicas e psiquiátricas. Hospital Sírio Libanês. 2022.
6. **Okamoto OK**. . (palestra).XXIX Simpósio Internacional de Hemoterapia e Terapia Celular | IV Fórum Internacional de Terapia Celular. Hospital israelita Albert Einstein. 2022.
7. **Okamoto OK**. Células de pluripotência induzida (iPSCs) para medicina regenerativa. (moderador de mesa redonda). XXIX Simpósio Internacional de Hemoterapia e Terapia Celular | IV Fórum Internacional de Terapia Celular. Hospital israelita Albert Einstein. 2022.
8. **Zatz M** - GenÉTICA- Conferência para a Liga de Aconselhamento Genético da *UNIFESP, 30 de junho de 2021.
9. **Vainzof M** - Conference "*Frequência e distribuição das LGMDs - Atualizações do uso de NGS (sequenciamento de nova geração) na América Latina*, no curso Expert Master classon Limb Girdle Muscular Dystrophy organizado pelo Treat-NMD, novembro 2021, 3-4 Novembro 2021.
10. **Vainzof M**- Conference *"Distrofias musculares de cintura I: epidemiología, clínica y clasificación general / Distrofias Musculares de Cintura na Escuela de Verano* Euro Latino Americana de Miologia, EVELAM 2021 Virtual". 30 de novembro a 4 de dezembro de 2021.

11. **Zatz M** -*Como ser um centenário saudável: genética ou ambiente*. Simpósio da Academia Nacional de Medicina, 16 de setembro de 2021.
12. **Zatz M** - *Mulheres na ciência*- https://biogenmedicalresearch.steeprockinc.com/login.html**Zatz M** -GenÉTICA: Como isso nos afeta, Webinar do Ivepesp, 28 de setembro https://www.youtube.com/watch?v=fdaSGF0odcI**Zatz M** -The future of Medicine- Congresso ALAG, 7 de outubro, 2021.
13. **Zatz M** -Ética em Aconselhamento genético- ICESP- 17 de novembro, 2021.
14. **Zatz M** -A medicina do futuro- Faculdade de comércio- 23 de novembro, 2021 10. 10. 9 de março: *Medicina do futuro: o que já é possível*. Aula inaugural do ciclo de residência 2022/2023 em Pneumologia e Cirurgia do Tórax da FMUSP.
15. **Zatz M** -11 de abril- ACIESP webinars | *Saúde humana e os desafios globais das doenças crônicas e infecciosas*.
16. **Zatz M** -19 de maio- VESPER: O futuro da medicina- o que já é realidade?
17. **Zatz M** -9 de junho: Estratégias para modificações genéticas em xenotransplante- Academia Nacional de Medicina.
18. **Zatz M** -15 de junho- *Fronteiras do pensamento*- Futuro da Medicina.**Zatz M** -21 de junho- seminário "*A Contribuição dos INCTs para a Sociedade*"

Annex 3 - Theses and Dissertations, Awards

3.1. PhD Theses

1. Name: **Lucila N. Kerbauy**
Title: Expansão de células NK com atividade anti-tumoral: aplicações em imunoterapia adotiva e mecanismos imunológicos envolvidos.
Supervisor: Oswaldo Keith Okamoto.
Programa de Pós-graduação Biologia/Genética, Instituto de Biociências, USP.

2. Name: **Amanda Faria Assoni**
Title: The role of neurodegeneration-associated proteins in ALS and medulloblastoma.
Supervisor: Oswaldo Keith Okamoto.
Programa de Pós-graduação Biologia/Genética, Instituto de Biociências, USP; Co-Supervisor: Floris Foijer, Post-graduation course in Biochemistry, University of Groningen, The Netherlands. (Double degree program).

3. Name: **Maria Prates Rivas**
Title: Mecanismos epigenéticos em hepatoblastomas: análise do transcriptoma e sua regulação por metilação de DNA.
Supervisor: Ana Cristina V. Krepischi
Programa de Pós-graduação Biologia/Genética, Instituto de Biociências, USP
2021/07/30

4. Name: **Angela May Suzuki**
Title: Implicações de variantes bialélicas de perda de função no gene TBCK, no transporte de vesículas de células progenitoras neurais derivadas de células-tronco pluripotentes induzidas
Supervisor: Maria Rita dos Santos e Passos Bueno
Programa de Pós-graduação Biologia/Genética, Instituto de Biociências, USP
2021/09/16

5. Name: **Samia Gomes**
Title: Fatores de risco associados à constipação intestinal e incontinência fecal em idosos do município de São Paulo - Estudo SABE
Supervisor: Yeda Aparecida de Oliveira Duate
Programa de Pós-graduação em Saúde Pública, Faculdade de Saúde Pública, USP
2022/03/07

6. Name: **Tatiana Eustaquia Magalhães de Pinho Melo**
Title: Análise longitudinal das condições de vida e saúde de idosos com histórico de câncer: Estudo Saúde, Bem-Estar e Envelhecimento
Supervisor: Yeda Aparecida de Oliveira Duate
Programa de Pós-graduação em Saúde Pública, Faculdade de Saúde Pública, USP
2021/09/22

3.2. Master Degree

1. Name: **Debora Camilotti**
Title: Comparação da heterogeneidade clínica entre portadores de desequilíbrios genômicos em 22q11.2 com base no motivo de encaminhamento para análise por microarray cromossômico
Supervisor: Carla Rosenberg
Programa de Pós-graduação Biologia/Genética, Instituto de Biociências, USP
2021/04/07

2. Name: **Igor Neves Barbosa**
Title:Edição de genes com crispr-cas9 em pacientes distróficos portadores deduplicação fora de fase (CNPq)
Supervisor: Mayana Zatz
Programa de Pós-graduação Biologia/Genética, Instituto de Biociências, USP
2022/04/06

3. Name: **Isabela Pimentel de Almeida**
Title:Pipeline OligoY para desenho de sondas oligopaint do cromossomo Y incluindo sequências repetitivas
Supervisor: Maria Dulcetti Vibranovski; Antonio Bernardo de Carvalho - (Co-supervisor)
Programa de Pós-graduação - Interunidades em Bioinformática, USP
2022/01/26

4. Name: **Sofia Lígia Guimarães Ramos**
Title: Investigação funcional do novo locus candidato, HDAC9, causativo da síndrome aurículo-condilar
Supervisor: Maria Rita dos Santos e Passos Bueno
2021/03/10

5. Name: **Gabriela Koch Alvarenga**
Title: Estudos de correlação genótipo-fenótipo em pacientes com a síndrome de Hipotonia Infantil com Retardo Psicomotor e Fácies Características 3 (IHPRF3)
Supervisor: Maria Rita dos Santos e Passos Bueno
Aconselhamento Genético e Genômica Humana, Instituto de Biociências, USP
2021/03/05

6. Name: **Vivian Romanholi Coria**
Title: Investigação clínica na interpretação de achados genômicos secundários em idosos com 80 anos ou mais
Supervisor: Mayana Zatz and Co-supervisor Michel Naslavsky
MSc Degree in Genetic Counseling and Human Genomics (IB USP)..
2021/09/29

3.3 Awards

1.**Carlos Frederico Martins Menck** - Nature Mentoring award, 2022.

2.**Luis Eduardo Soares Netto** - Travel award to Pos-Doc Carlos Tairum, Society for Redox Biology and Medicine - 2021

3.**Maria Rita dos Santos e Passos-Bueno** - Award Trajetória pela Inovação - USP - 2022

Annex 4 - Education Out Reach

4.1. Interviews to the Media

1. Abuchahla G, Amigo RG, Monteiro LF, Sanches R, **Zatz M.** Jornal Hoje "Brasil ocupa 75ª posição no ranking de capacidade de reter talentos ", por Bruna Vieira. **TV Globo - GloboPlay**, 19/10/2021. <https://globoplay.globo.com/v/9965834/>
2. Andrade T, **Zatz M**. Jornal da Cultura "Cientistas estudam pessoas resistentes à Covid-19", com Lucas Guanaes, **TV Cultura** – Youtube Channel **Jornalismo da TV Cultura**, 02/11/2021.<https://www.youtube.com/watch?v=hShseBkImW8>
3. Berkenbroch I, Debert C, Goldenberg M,Kalache A, Kairalla M, Martorelli R, Pachá A, Terra NL, Vitoy B, Winandy F, **Zatz M**. "Velhos, sim...Doentes, não! A nova cara e os desafios da velhice", by André Bernardo. São Paulo, **Veja Saúde**, 17/12/2021. <https://saude.abril.com.br/familia/velhos-sim-doentes-nao-a-nova-cara-e-os-desafios-da-velhice/>
4. Covas D, Goes J, Janine Ribeiro R**,** Nicolelis M, **Zatz M**. "25 de GloboNews" - série "documentário: Ciência e Tecnologia ", **GloboNews,** 11/10/2021. <https://canaisglobo.globo.com/assistir/globonews/especial-25-anos/v/9939691/>
5. Davidovich L, Janine Ribeiro R, **Zatz M**. Jornal Nacional, " Comunidade científica critica o corte milionário de bolsas e apoio às pesquisas", **TV Globo/ GloboPlay**, 09/10/2021. <https://globoplay.globo.com/v/9935213/> - (Access to subscribers only)
6. Dulcine M, Grupta V, Jin Lim N, Passerotti C, Salem R, **Zatz M**. Summit Saúde 2021 "O diagnóstico da saúde do futuro", online debateby Cristiane Segatto. Youtube Channel**Estadão**, 18/10/2021. <https://www.youtube.com/watch?v=bSFxm8NFlm4>
7. Dulcine M, Grupta V, Jin Lim N, Passerotti C, Salem R, Segatto C, **Zatz M**. New online debate, Summit Saúde 2021,**O Estado de S. Paulo**. "Medicina Digital" in "Nove em cada dez brasileiros confiam na vacina, diz pesquisa", by Ícaro Malta, **Portal Terra**, 18/10/2021.<https://www.terra.com.br/noticias/coronavirus/nove-em-cada-dez-brasileiros-confiam-na-vacina-diz-pesquisa,4a9dbf49f5aff38cfa2582266ebcbf8dcestatvu.html>
8. Ferreira R, Ferreira RS, Kaid C, **Okamoto OK, Zatz M**. Article "Tratamento com injeções de vírus zika destrói tumor cerebral em roedores sem causar lesão neurológica", by Luciana Constantino, **Agência Fapesp**, 26/10/2021. <https://agencia.fapesp.br/tratamento-com-injecoes-de-virus-zika-destroi-tumor-cerebral-em-roedores-sem-causar-lesao-neurologica/37149/>
9. França MFJ, **Zatz M**, **Naslavsky M**, Amaro J E., Duarte Y. Online interview about the book "O Legado dos Genes: o que a ciência pode nos ensinar sobre o envelhecimento", de Mayana Zatz e Martha San Juan França. YouTube Channel**Companhia das Letras**, 21/07/2021. <https://www.youtube.com/watch?v=X_0XIqK_wr4>
10. França MFJ, **Zatz M**, **Naslavsky M**, Amaro J E., Duarte Y. Release book "O Legado dos Genes: o que a ciência pode nos ensinar sobre o envelhecimento" e debate com participação de pesquisadores. **Agência Fapesp**, 21/07/2021. <https://agencia.fapesp.br/agenda-detalhe/lancamento-do-livro-o-legado-dos-genes-o-que-a-ciencia-pode-nos-ensinar-sobre-o-envelhecimento/36397/#:~:text=29%20de%20mar%C3%A7o%20de%202022>

11. Friedman A, Montgomery R, Raia S, Spedo M, **Zatz M.**TV show Fantástico “Um feito revolucionário, primeiro transplante de rim de porco em humano foi bem- sucedido”, **TV Globo - GloboPlay**, 24/10/2021. <https://globoplay.globo.com/v/9977426/?utm_source=whatsapp&utm_medium=share-bar>
12. **Naslavsky M**. “Cientistas da USP decifram por inteiro um genoma humano”, JR News – YouTube Channel**Record News**, 02/09/2021, <https://www.youtube.com/watch?v=XbFsxoyZ3Ok>
13. **Naslavsky M**, Oliviera LA. Live “série: Transformação decisivas: moldando um novo mundo”- Café Filosófico CPFL “Fronteiras da Medicina: Genômica e Bioética”, **TV Cultura** – YouTube Channel Café Filosófico CPFL, 21/10/2021.< https://www.youtube.com/watch?v=wKn7obmCEMc>
14. Raia S, **Zatz M**. “Pesquisadores da USP preveem 1º teste de rim de porco para humano no Brasil nos próximos dois anos”, by Estadão, **A Crítica**, 22/10/2021. <https://www.acritica.net/editorias/saude/eua-usam-pela-1a-vez-rim-de-porco-em-humano-usp-testa/558295/>
15. Raia S, **Zatz M**. “USP planeja teste de transplante de rim de porco para humano no Brasil em dois anos”, by Estadão, **BN Saúde** do Bahia Notícias, 22/10/2021, em <https://www.bahianoticias.com.br/saude/noticia/27851-usp-planeja-teste-de-transplante-de-rim-de-porco-para-humano-no-brasil-em-dois-anos.html>
16. Raia S, **Zatz M**. “Pesquisadores brasileiros já estudam transplante de rim de porco em humanos”, **CGH Saúde,** 21/10/2021. <https://gauchazh.clicrbs.com.br/saude/noticia/2021/10/pesquisadores-brasileiros-ja-estudam-transplante-de-rim-de-porco-em-humanos-ckv0zqn5d003g019mmx1n7org.html>
17. Raia S, **Zatz M**. “Brasileiros editam genes de porcos, buscam verba e planejam testes para usar rim suíno em humanos”, **GazetaWeb** - **G1**, 21/10/2021. <https://www.gazetaweb.com/noticias/ciencia-e-saude/brasileiros-editam-genes-de-porcos-buscam-verba-e-planejam-testes-para-usar-rim-suino-em-humanos/>
18. Raia S, **Zatz M**. “Rim de porco é esperança para quem aguarda por transplante”, **Jornal da USP,**by Rodrigo Tammaro. São Paulo, 03/11/2021. <https://jornal.usp.br/atualidades/rim-de-porco-e-esperanca-para-quem-aguarda-por-transplante/>
19. Roitman I, **Zatz M**. Projeto 2022/2030: O Brasil e o Mundo que Queremos, tema “Precisamos dos jovens para mudar o país”. **TvSuprenBrasília** –Youtube Channel. 18/11/2021. <https://www.youtube.com/watch?v=wuvVu9QONAU&list=PL9IsItk2XEKRqtfr7DWz4_jguc0vW6ZGN&index=226>
20. **Zatz M**. Radio columnistDecodificando o DNA. “Cientistas descobrem genes responsáveis pela longevidade e resistência em idosos”, **Rádio USP**, 03/06/2021. <https://jornal.usp.br/radio-usp/cientistas-descobrem-genes-responsaveis-pela-longevidade-e-resistencia-em-idosos/>
21. **Zatz M**. “Superimunidade à Covid não é tão rara”, diz geneticista Mayana Zatz.”**Metrópoles,** 05/06/2021. <https://www.metropoles.com/saude/superimunidade-a-covid-nao-e-tao-rara-diz-geneticista-mayana-zatz>
22. **Zatz M.**Interviewfor André Shalder “Contingenciamento proibido de fundo paralisa até pesquisa sobre a covid-19”. **O Estado de S. Paulo**, 07/06/2021.<https://saude.estadao.com.br/noticias/geral,contingenciamento-proibido-de-fundo-paralisa-ate-pesquisa-sobre-a-covid-19,70003738806?utm_source=estadao:mail&utm_medium=link>

23. **Zatz M.** "Pesquisa da USP indica que vírus da zika pode combater tumores cerebrais. **UOL**, 07/06/2021. <https://www.uol.com.br/vivabem/noticias/redacao/2021/06/07/pesquisa-da-usp-indica-que-virus-da-zika-pode-combater-tumores-cerebrais.htm>
24. **Zatz M.**Interview for Roseli Loturco "Genômica avança na cura de doenças raras". **Valor Econômico**, 07/07/2020. <https://valor.globo.com/publicacoes/suplementos/noticia/2021/06/08/genomica-avanca-na-cura-de-doencas-raras.ghtml>
25. **Zatz M.** "Virus da zika pode tratar tumores no cérebro, diz pesquisa". Magazine**Olhar Digital**. 08/06/2022. <https://olhardigital.com.br/2021/06/08/medicina-e-saude/virus-da-zika-pode-tratar-tumores-no-cerebro-diz-pesquisa/>
26. **Zatz M.** Interview by para Denise Campos de Toledo for Jornal da Gazeta. **TV Gazeta**, 17/06/2021. <https://www.youtube.com/watch?v=hrd35Qf4KFA>
27. **Zatz M.** "Após 'Estadão' mostrar bloqueio, governo libera R$ 4,8 mi para pesquisa sobre covid.", by André Shalders, **Estadão**, 23/06/2021. <https://ciencia.estadao.com.br/noticias/geral,apos-estadao-revelar-bloqueio-de-fundo-governo-libera-r-4-8-mi-para-pesquisa-sobre-covid,70003755725.amp>
28. **Zatz M.**Radio columnist Decodificando o DNA –" Mayana Zatz lança livro sobre histórias de vida de pessoas com mais de 80 anos" **Rádio USP**, 01/07/2021. <https://jornal.usp.br/radio-usp/mayana-zatz-lanca-livro-com-historias-de-pessoas-com-mais-80-anos/
29. **Zatz M.,** Kaid C**.** "Zika vírus para matar células cancerígenas. TV show The Noite, by Danilo Gentili. **SBT**, 07/07/2021. <https://www.youtube.com/watch?v=cILwggotaMo>
30. **Zatz M**. "Fatores genéticos ajudam a explicar por que alguns têm Covid grave, aponta estudo." **Amazonas Atual**, 08/07/2021. <https://amazonasatual.com.br/fatores-geneticos-ajudam-a-explicar-por-que-alguns-tem-covid-grave-aponta-estudo/>
31. **Zatz M**. "Why the Most Unusual Covid Cases Matter",**The New York Times**. 12/07/2021. <https://www.nytimes.com/2021/07/12/opinion/covid-unusual-cases-study.html>(Access to subscribers only)
32. **Zatz M**. Radio columnist Decodificando o DNA. "Quanto da nossa microbiota intestinal depende da genética?", **Rádio USP**, 15/07/2021. <https://jornal.usp.br/radio-usp/quanto-da-nossa-microbiota-intestinal-depende-da-genetica/>
33. **Zatz M**. "Mayana Zatz quer usar zika vírus para tratar tumores", site **A política em Foco**, 17/07/2021. <https://www.apoliticaemfoco.com.br/noticias/video-cientista-mayana-zatz-quer-usar-zika-virus-para-tratar-tumores/>
34. **Zatz M**. Bem-estar & Movimento, byMarcio Atalla**, Rádio CBN**, 07/08/2021. <https://www.youtube.com/watch?v=PDDa02IuxHI>
35. **Zatz M**. Oito em Ponto sobre o livro "O Legado dos Genes: o que a ciência pode nos ensinar sobre o envelhecimento", by Sergei Cobras,**Rádio Cultura**, 22/07/2021. <https://cultura.uol.com.br/radio/programas/oito-em-ponto/2021/07/22/476_mayana-zatz-lanca-livro-sobre-historias-de-vida-de-pessoas-com-mais-de-80-anos.html>
36. **Zatz M**. Radio columnist Decodificando o DNA. "Cientistas do Reino Unido mostram que é possível reverter a perda de memória em comundongos", **Rádio USP**, 30/07/2021. <https://jornal.usp.br/radio-usp/cientistas-do-reino-unido-mostram-que-e-possivel-reverter-a-perda-de-memoria-em-camundongos/#:~:text=Cientistas%20do%20Reino%20Unido%20mostraram,reverter%20a%20perda%20da%20mem%C3%B3ria>
37. **Zatz M**. "Genes incríveis não são garantia de se chegar bem aos 100 anos, diz cientista", by Ana Lúcia Azevedo**O Globo**, 30/07/2021.

<https://oglobo.globo.com/saude/genes-incriveis-nao-sao-garantia-de-se-chegar-bem-aos-100-anos-diz-cientista-25122868>
38. **Zatz M**. "Legado da influência genética sobre a longevidade", by Joyce Ribeiro, Jornal da Tarde. **TV Cultura**, 05/08/2021. <https://www.youtube.com/watch?v=e1mv5hY9Fpk>
39. **Zatz M**. Radio columnist Decodificando o DNA. "O papel da genética na fertilidade feminina é tema na pesquisa publicada pela 'Nature'", **Rádio USP**, 12/08/2021. <https://jornal.usp.br/radio-usp/o-papel-da-genetica-na-fertilidade-feminina-e-tema-de-pesquisa-publicada-na-nature/>
40. **Zatz M**, Andrade T, Soares E. "A lucky seem 'resistant' to Covid-19. Scientists want to know why", by Amitha Keaichandran. **Stat,** 23/08/2021.<https://www.statnews.com/2021/08/23/lucky-few-seem-resistant-to-covid19-scientists-want-to-know-why-2/>
41. **Zatz M**. "O instigante fenômeno a resistência natural à covid", by Leila Salim e Raquel Torres, coluna OutrasSaúde. Site **OutrasPalavras,** 24/08/2021.<https://outraspalavras.net/outrasaude/resistencia-natural-covid/>
42. **Zatz M**. "Genes de pessoas resistentes ao coronavírus podem dar pistas para futuros tratamentos", by Vera Novais. **Observador,** 23/08/2021.< https://observador.pt/2021/08/23/genes-de-pessoas-resistentes-ao-coronavirus-podem-dar-pistas-para-futuros-tratamentos/>
43. **Zatz M**. Participação para Reportagem "Homens são os principais transmissores do vírus da covid-19, sugere estudos", para futuros tratamentos", por Elton Alisson, 26/08/2021.**Agência Fapesp**. Disponível em <https://www.uol.com.br/vivabem/noticias/redacao/2021/08/26/homens-sao-os-principais-transmissores-do-virus-da-covid-19-sugere-estudo.htm>
44. **Zatz M**. "Homens são os principais transmissores do vírus da covid-19, sugere estudos", para futuros tratamentos", by Elton Alisson, Agência Fapesp – **Portal IG** 26/08/2021.<https://namidia.fapesp.br/homens-sao-os-principais-transmissores-do-virus-da-covid-19-sugere-estudo/338991>
45. **Zatz M**. "Homens são os principais transmissores do vírus da covid-19, sugere estudos", para futuros tratamentos", by Elton Alisson, Agência Fapesp - **R7**, 26/08/2021.<https://namidia.fapesp.br/homens-sao-os-principais-transmissores-do-coronavirus-aponta-estudo-brasileiro/338996>
46. **Zatz M**. "Homens são os principais transmissores do vírus da covid-19, sugere estudos", para futuros tratamentos", by Elton Alisson, Agência Fapesp - **Zero Hora online**26/08/2021. <https://namidia.fapesp.br/covid-homens-sao-principais-transmissores-do-virus-diz-estudo/338977>
47. **Zatz M**. "Homens são os principais transmissores do vírus da covid-19, sugere estudos", para futuros tratamentos", by Elton Alisson,Agência Fapesp -**Folha de Pernambuco online,** 26/08/2021.<https://namidia.fapesp.br/homens-sao-principais-transmissores-do-virus-diz-estudo/338976>
48. **Zatz M**. "Homens são os principais transmissores do vírus da covid-19, sugere estudos", para futuros tratamentos", by Elton Alisson, Agência Fapesp - **Meio Norte online (Piauí),** 26/08/2021. <https://namidia.fapesp.br/homens-sao-os-principais-transmissores-do-virus-da-covid-19-sugere-estudo/338990>
49. **Zatz M**. Bueno MRP, Vidigal M. "Homens são os principais transmissores do vírus da covid-19, sugere estudo da USP", by Fabiana Mariz,**Jornal da USP**. 27/08/2021.<https://jornal.usp.br/ciencias/homens-transmitem-mais-covid-19-do-que-mulheres-sugere-estudo-da-usp/>

50. **Zatz M**. “Estudos sugere que homens são os principais transmissores do coronavírus ”, por Elton Alisson, Agência Brasil - **Meio Diário de Pernambuco,**26/08/2021.< https://www.diariodepernambuco.com.br/ultimas/2021/08/estudo-sugere-que-homens-sao-principais-transmissores-do-coronavirus.html>
51. **Zatz M**. “ Mais da metade de Covid-19 são homens, em Ribeirão Preto”, por Lidja Matos, Agência Fapesp - **Revista Revide**, 26/08/2021. <https://www.revide.com.br/noticias/coronavirus/cerca-de-55-das-mortes-por-covid-19-sao-de-homens/>
52. **Zatz M**. “Estudo sugere que homens são principais transmissores do coronavírus”, Agência Fapesp **- Jornal do Comércio**, Porto alegre, 29/08/2021. <https://www.jornaldocomercio.com/_conteudo/especiais/coronavirus/2021/08/808845-estudo-sugere-que-homens-sao-principais-transmissores-do-coronavirus.html>
53. **Zatz M**. “Maridos transmitem Covid para as mulheres em 63% dos casos; pesquisadora explica os motivos”, **Rádio Eldorado**, São Paulo. 31/08/2021. <https://eldorado.estadao.com.br/audios/programas/jornal-eldorado/maridos-transmitem-covid-para-mulheres-em-63-dos-casos-pesquisadora-explica-os-motivos,1193400>
54. **Zatz M**. “Mapeamento completo do genoma identifica causas de doenças, diz pesquisadora“, **CNN**, São Paulo. 01/09/2021. <https://www.cnnbrasil.com.br/saude/mapeamento-completo-do-genoma-identifica-causas-de-doencas-diz-pesquisadora/>
55. **Zatz M.,** França MSJ**.** Repórter ECO **“**Como a ciência pode nos ajudar para ter um envelhecimento saudável”. **TV Cultura**, 05/09/2021, São Paulo. <https://www.youtube.com/watch?v=ouzyMSf2WQU>
56. **Zatz M.** “Homens são os principais transmissores do vírus da COVID-19, sugere estudo”. Agência Fapesp **- Portal do Governo de São Paulo**, 26/08/2021, São Paulo. <https://www.saopaulo.sp.gov.br/ultimas-noticias/homens-sao-os-principais-transmissores-do-virus-da-covid-19-sugere-estudo/>
57. **Zatz M**. Radio columnist Decodificando o DNA. “Gostar ou não de uma pessoa pode estar associado a questões genéticas, sugere estudo americano”, **Rádio USP**, 09/09/2021. <https://jornal.usp.br/radio-usp/gostar-ou-nao-de-uma-pessoa-pode-estar-associada-a-questoes-geneticas-sugere-estudo/>
58. **Zatz M**. Radio columnis Decodificando o DNA. “Microbiota intestinal pode ajudar ou dificultar perda de peso, sugere pesquisa”, **Rádio USP**, 23/09/2021. Disponível em https://jornal.usp.br/radio-usp/microbiota-intestinal-pode-ajudar-ou-dificultar-a-perda-de-peso-sugere-pesquisa/
59. **Zatz M**. “A fonte da longevidade numa conversa com Mayana Zatz”. **Veja Saúde**, São Paulo, 15/10/2021. <https://saude.abril.com.br/medicina/a-fonte-da-longevidade-numa-conversa-com-mayana-zatz/>
60. **Zatz M**. “Pesquisadores brasileiros avançam em estudo sobre super imunes à convi-19”, by Laura Pancini. **Exame**, São Paulo, 29/09/2021. <https://exame.com/ciencia/brasileiros-estudo-super-imunes-covid-19/>
61. **Zatz M**. “Estudo explica por que algumas pessoas não se infectam com Covid”. **Globo News**, São Paulo, 01/10/2021. <https://g1.globo.com/globonews/globonews-em-ponto/video/estudo-explica-por-que-algumas-pessoas-nao-se-infectam-com-covid-9908433.ghtml>
62. **Zatz M**. “Pesquisadores identificam genes de pessoas “superimunes” à Covid”. **IstoÉ Dinheiro**, São Paulo, 30/09/2021. <https://www.istoedinheiro.com.br/pesquisadores-identificam-genes-de-pessoas-superimunes-a-covid/>

63. **Zatz M**. "Estudo explica por que algumas pessoas são mais resistentes ao coronavírus ". by Simone Blanes, **Veja Saúde**, São Paulo, 30/09/2021. <Disponível em https://veja.abril.com.br/saude/estudo-explica-porque-algumas-pessoas-sao-mais-resistentes-ao-coronavirus/>
64. **Zatz M**. "Covid-19: estudo brasileiro explica por que algumas pessoas não se infectam com o vírus ". **O Globo**, 01/10/2021. <https://oglobo.globo.com/saude/ciencia/covid-19-estudo-brasileiro-explica-por-que-algumas-pessoas-nao-se-infectam-com-coronavirus-25218929>(Access to subscribers only)
65. **Zatz M**. "Pesquisadores identificam genes de pessoas 'superimunes' à Covid-19 ". **Rádio Bandeirantes**, 02/10/2021. <https://www.band.uol.com.br/noticias/pesquisadores-identificam-genes-de-pessoas-superimunes-a-covid-19-16452343>
66. **Zatz M**. Radio columnist Decodificando o DNA. "Pesquisa americana avalia a capacidade de algoritmo prever doenças em jovens", **Rádio USP**, São Paulo, 07/10/2021. <https://jornal.usp.br/radio-usp/pesquisa-americana-avalia-a-capacidade-de-algoritmo-prever-doencas-em-jovens/>
67. **Zatz M**. " Entidades criticam o corte de 600,00 milhões em investimentos: 'ciência agoniza'", by Lúcio Borges, **Enfoque MS,** Campo Grande, 09/10/2021. <https://www.enfoquems.com.br/entidades-criticam-corte-de-r-600-milhoes-em-investimentos-ciencia-agoniza/>
68. **Zatz M**. "Ciência brasileira em frangalhos ". **Correio Braziliense**, São Paulo, 19/10/2021. <https://www.correiobraziliense.com.br/opiniao/2021/10/4956240-ciencia-brasileira-em-frangalhos.html>
69. **Zatz M**. Radio columnist Decodificando o DNA. "Como é ser voluntário de pesquisa científica?", **Rádio USP**, 21/10/2021. <https://jornal.usp.br/radio-usp/como-e-ser-voluntario-de-pesquisa-cientifica/>
70. **Zatz M**. "O porco é a solução", por Fernando Levieri, Revista **IstoÉ,** 29/10/2021. <https://istoe.com.br/o-porco-e-a-solucao/>
71. **Zatz M**. Radio columnist Decodificando o DNA. "Pesquisa da USP testa segurança eficácia no tratamento do câncer cerebral com zika vírus.", **Rádio USP**, 04/11/2021. <https://jornal.usp.br/radio-usp/pesquisa-da-usp-testa-seguranca-e-eficacia-no-tratamento-de-cancer-cerebral-com-o-zika-virus/>
72. **Zatz M**. "A saúde no pós-pandemia". São Paulo, **Estadão**, 03/11/2021. https://opiniao.estadao.com.br/noticias/notas-e-informacoes,a-saude-no-pos-pandemia,70003887601 (Access to subscribers only)
73. **Zatz M**. Podcast "Um manual para nos ajudar a viver mais". São Paulo, **Época Negócios**, Globo.com, 03/11/2021. <https://epocanegocios.globo.com/colunas/50-Vida-e-Trabalho/noticia/2021/11/um-manual-para-nos-ajudar-viver-mais.html>(Access to subscribers only) **Zatz M**. Participação na reportagem da Agência Fapesp "Injeções do vírus zika interrompem câncer cerebral em cobaias". **Portal Diário da Saúde**, 05/11/2021. <https://www.diariodasaude.com.br/news.php?article=injecoes-virus-zika-interrompem-cancer-cerebral-cobaias&id=15007>
74. **Zatz M**. "Pesquisa analisa casais que tiveram reações diferentes ao coronavírus ". **TV Record – R7**, 12/11/2021. <https://noticias.r7.com/jr-na-tv/videos/pesquisa-analisa-casais-que-tiveram-reacoes-diferentes-ao-coronavirus-12112021>
75. **Zatz M**. Podcast da Bandeirantes, Ciência e Saúde "#31-Mayana Zatz, a pesquisadora que carrega a ciência no gene". São Paulo, **Grupo Bandeirantes**, 11/11/2021. <https://www.spreaker.com/user/grupo_bandeirantes/podcast-ciencia-e-saude-1111>
76. **Zatz M**. "Pesquisadores comprovam existência de pessoas com capacidade imunológicas contra o Coronavírus". São Paulo, Jornal da Cultura - **TV Cultura – Canal**

– Canal do Jornalismo da TV Cultura no YouTube 13/11/2021. <https://www.youtube.com/watch?v=n78fDPhSRiM>
77. **Zatz M**. Radio columnist Decodificando o DNA. “Pesquisa do Reino Unido investiga papel das células de memória em indivíduos assintomáticos expostos à covid-19”, **Rádio USP**, 18/11/2021. <https://jornal.usp.br/radio-usp/pesquisa-realizada-no-reino-unido-investiga-o-papel-das-celulas-de-memoria-em-individuos-assintomaticos-expostos-a-covid-19/>
78. **Zatz M**. “As antienvelhecineto funciona? A ciência é que responde”, by Cristiane Segatto. São Paulo, **O Estado de S. Paulo**, 28/11/2021. <https://saude.estadao.com.br/noticias/geral,as-dietas-funcionam-a-ciencia-e-que-responde,70003910886> (Access to subscribers only)
79. **Zatz M**. Radio columnist Decodificando o DNA. “Estudo americano traz esperança para quem sofreu lesão na coluna vertebral”, **Rádio USP**, 02/12/2021. <https://jornal.usp.br/radio-usp/estudo-americano-traz-esperanca-para-quem-sofreu-lesao-na-coluna-vertebral/>
80. **Zatz M**. Radio columnist Decodificando o DNA. “Como estão as gêmeas que tiveram seus genomas editados há três anos?”, **Rádio USP**, 16/12/2021. <https://jornal.usp.br/radio-usp/como-estao-as-gemeas-que-tiveram-seus-genomas-editados-ha-tres-anos/>
81. **Zatz M**. “Capes encerra repasses de verbas a institutos de pesquisa e cientistas relatam surpresa”, por Júlio Marques. São Paulo, **O Estado de S.Paulo**, 16/12/2021. <https://educacao.estadao.com.br/noticias/geral,capes-encerra-repasse-verba-institutos-pesquisa,70003927754>(Access to subscribers only)
82. Achatz MI, Giugliani R, **Zatz M**. “Teste genético: quando é indicado e quais cuidados deve ter, segundo médicos”, by André Biernath, **BBC News - Brasil**, 13/04/2022. <https://www.bbc.com/portuguese/geral-61085700>
83. Almeida de Oliviera PS, Brandalise SR, Harb-Gama A, Raia S, **Zatz M**. “Médicos provam que é possível envelhecer e seguir se destacando na profissão”, by Fernando Laviere, **Revista IstoÉ**, 08/04/2022. <https://istoe.com.br/em-medicina-idade-nao-e-sinonimo-de-aposentadoria/>
84. Atala A, Kaczorowski D, Raia S**, Zatz M**. “Vida em reconstrução: a ciência avança no implante de órgãos artificiais”, by Paula Felix, **Revista Veja**, 18/03/2022. <https://veja.abril.com.br/saude/a-vida-em-reconstrucao-os-avancos-da-ciencia-para-implante-de-orgaos/>
85. Bennet JD, Fernandes PP, Griffith B, Mohiuddin M, Raia S, **Zatz M**. TV show Fantástico “Transplante inédito de coração de porco em humanos pode mudar a história da medicina”, by Sonia Bridi, **TV Globo – GloboPlay**, 16/01/2022. <https://g1.globo.com/fantastico/noticia/2022/01/16/transplante-inedito-de-coracao-de-porco-em-humanos-pode-mudar-a-historia-da-medicina.ghtml?utm_source=twitter&utm_medium=social&utm_content=post&utm_campaign=fant>
86. Brandão PE**, Zatz M**. “Por que algumas pessoas nunca pegaram Covid-19”, by Fabiana Schiavon, São Paulo, **Revista Veja**, 18/04/2022. <https://saude.abril.com.br/medicina/por-que-algumas-pessoas-nunca-pegaram-covid-19/ >
87. França MSJ, **Zatz M**. “Saiba o que ciência diz para conseguir um envelhecimento saudável”, **Correio**, por Vinicius Nascimento, 14/02/2022, <https://www.correio24horas.com.br/noticia/nid/saiba-o-que-ciencia-diz-para-conseguir-um-envelhecimento-saudavel/>

88. Kowaltowski A, **Zatz M**. “Acesso aberto a artigos científicos volta à discussão após mudanças no grupo Springer Nature”, by FolhaPress, **Portal Mix Vale**, São Carlos, 31/01/2022. <https://www.mixvale.com.br/2022/01/31/acesso-aberto-a-artigos-cientificos-volta-a-discussao-apos-mudancas-no-grupo-springer-nature/>
89. **Naslavsky M**. “No sequenciamento soluciona quebra-cabeças sobre o genoma humano, diz professor”, by Amanda Garcia e Bel Campos, **CCN Brasil**, 04/04/2022. < https://www.cnnbrasil.com.br/saude/novo-sequenciamento-soluciona-quebra-cabecas-sobre-o-genoma-humano-diz-professor/>
90. **Naslavsky M**. Café Filosófico CPFL “Fronteiras da Medicina: Genômica e Bioética”, TV Cultura – YouTube Channel Café Filosofico CPFL, 01/05/2022.<https://www.youtube.com/watch?v=RkFn_dfyvF0>
91. **Zatz M**. “How do some people avoid getting Covid?”, **Jornal The Times**, 08/01/2022. <https://www.thetimes.co.uk/article/the-covid-mystery-how-do-some-people-defy-the-virus-68c6bfxsk>(Access to subscribers only)
92. **Zatz M**. “É #Fake que vacinas contra Covid-19 são produtos de terapia gênica”, by Roney Domingos, **O Globo – G1**, 10/01/2022. <https://oglobo.globo.com/fato-ou-fake/e-fake-que-vacinas-contra-covid-19-sao-produtos-de-terapia-genica-25350369>
93. **Zatz M**. “Por que algumas pessoas não se infectam com Covid-19 mesmo tendo contato com um doente?”, **GloboNews – G1**, 24/01/2022. <https://g1.globo.com/saude/noticia/2022/01/24/por-que-algumas-pessoas-nao-se-infectam-com-covid-19-mesmo-tendo-contato-com-um-doente.ghtml>
94. **Zatz M**. Roda Viva, interviewers Righetti S, Garcia R, Teixeira M, Biernath A, Pivetta M ”, by Vera Magalhães. **TV Cultura** – YouTube Channel Roda Viva, 31/01/2022. <https://youtu.be/vjR0JkShpDo>
95. **Zatz M**. Radio columnisto Decodificando o DNA. “Primeiro transplante de coração de porco para humano vivo é realizado com sucesso”, **Rádio USP**, 03/02/2022. <https://jornal.usp.br/radio-usp/primeiro-transplante-de-coracao-de-porco-para-humano-e-realizado-com-sucesso/>
96. **Zatz M** . “Pesquisas de universidades públicas descobre como o sistema imunológico funciona contra a covid”, by Carlos Tramontina, SP1 -**TV Globo – GloboPlay**, 05/02/2022. < https://globoplay.globo.com/v/10273945/>
97. **Zatz M** . “Mulheres têm menos chances de ter Covid-19, diz pesquisa”, by Anna Grabriela Costa e Layane Serrano, **CNN Brasil,** 06/02/2022. <https://www.cnnbrasil.com.br/saude/mulheres-tem-menos-chances-de-ter-covid-19-diz-estudo/?amp>
98. **Zatz M** . “Mulheres têm menos chances de ter Covid-19, aposta estudo”, **JPNews,** 07/02/2022. < https://jovempan.com.br/programas/jornal-da-manha/mulheres-tem-menos-chances-de-contrair-covid-19-aponta-estudo.html>
99. **Okamoto OK**, Campregher P, Khayat AS, Sakamoto L. Podcast do Comitê de Medicina de Precisão da Sociedade Brasileira de Oncologia Pediátrica, tema: “Biomarcadores no tratamento e prognóstico do câncer infanto-juvenil”. **Precision Cast SOBOPE**, 18/03/2022. < https://app.podcastguru.io/podcast/precision-cast-sobope-1610169483/episode/ep-002-biomarcadores-no-tratamento-e-progn-stico-do-c-ncer-infantojuvenil-aef5e8e732923614654dfa245393892e>
100. **Zatz M** . “Estudos indica que mulheres são mais resistentes à covid-19”, por repórter da Rádio Nacional, **RadioagênciaNacional**, 07/02/2022, <https://agenciabrasil.ebc.com.br/radioagencia-nacional/saude/audio/2022-02/estudo-indica-que-mulheres-sao-mais-resistentes-covid-19 >
101. **Zatz M**. Radio columnist Decodificando o DNA. “Projeto Germina vai acompanhar o desenvolvimento de 500 bebês durante três anos e meio”, **Rádio USP**, 17/02/2022.

<https://jornal.usp.br/radio-usp/projeto-germina-vai-acompanhar-o-desenvolvimento-de-500-bebes-durante-tres-anos-e-meio/>

102. **Zatz M**. Radio columnist Decodificando o DNA. “Pesquisa da USP vai investigar de que forma a genética contribui na formação da microbiota intestinal”, **Rádio USP**, 03/03/2022. Disponível emhttps://jornal.usp.br/radio-usp/pesquisa-da-usp-vai-investigar-de-que-forma-a-genetica-contribui-na-formacao-da-microbiota-intestinal/
103. **Zatz M**. “Banco genômico brasileiro permitirá aprimorar o diagnóstico de doenças genéticas no país”, by Elton Alisson, **Agência Fapesp**, 07/03/2022. <https://agencia.fapesp.br/banco-genomico-brasileiro-permitira-aprimorar-o-diagnostico-de-doencas-geneticas-no-pais/38069/>
104. **Zatz M** . “Cientistas criam o 1º banco genômico de idosos do Brasil para decifrar envelhecimento saudável”, by Roberta Jansen, **Estadão**, 04/03/2022. <https://saude.estadao.com.br/noticias/geral,estudo-da-usp-buscar-formar-1-banco-genomico-de-idosos-no-brasil-e-a-entender-melhor-a-longevidade,70003997365?utm_source=estadao:whatsapp&utm_medium=link(Access to subscribers only)
105. **Zatz M** . “Banco de dados brasileiro permitirá aprimorar diagnóstico de doenças genética”, Agência Fapesp **- CNN Brasil**, 04/03/2022. <https://www.cnnbrasil.com.br/saude/banco-de-dados-brasileiro-permitira-aprimorar-diagnostico-de-doencas-geneticas/>
106. **Zatz M**. “Envelhecimento saudável: cientistas criam o 1º banco genômico de idosos do Brasil”, by Estadão - **PortalBem Paraná**, 04/03/2022. <https://www.bemparana.com.br/noticia/envelhecimento-saudavel-cientistas-criam-1o-banco-genomico-de-idosos-do-brasil-870#.YpwpG6hKiUl>
107. **Zatz M**. “Envelhecimento saudável: cientistas criam o 1º banco genômico de idosos do Brasil”, by Estadão, **GAZ** (Gazeta do Sul), 05/03/2022. <https://www.gaz.com.br/envelhecimento-saudavel-cientistas-criam-1o-banco-genomico-de-idosos-do-brasil/>
108. **Zatz M**. “Banco genômico brasileiro vai aprimorar diagnóstico de doenças genética ”, by Estadão - **RevistaGalileu**, 06/03/2022. <https://revistagalileu.globo.com/Ciencia/Saude/noticia/2022/03/banco-genomico-brasileiro-vai-aprimorar-diagnostico-de-doencas-geneticas.html>
109. **Zatz M**. “Why do some people never get Covid?”, **The New York Times**, 08/03/2022. <https://www.nytimes.com/2022/03/08/opinion/people-never-get-covid.html?referringSource=articleShare>
110. **Zatz M**. “Mayana Zatz: ‘Enquanto tiver verba continuarei pesquisando’”, **Revista Época**, 07/03/2022. <https://epocanegocios.globo.com/Profissionais-50/noticia/2022/03/enquanto-eu-tiver-verba-continuarei-pesquisando.html(Access to subscribers only)
111. **Zatz M**. “Técnica de transplante com órgão de animal avança; entenda como funciona”, by Leon Ferrari, **Estadão**, 14/03/2022. <https://ciencia.estadao.com.br/noticias/geral,tecnica-de-transplante-com-orgao-de-animal-avanca-entenda-como-funciona,70004007740>
112. **Zatz M**. “Técnica de transplante com órgão de animal avança; entenda como funciona”, by Estadão, **Portal Terra**, 14/03/2022. <https://www.terra.com.br/noticias/ciencia/tecnica-de-transplante-com-orgao-de-animal-avanca-entenda-como-funciona,b160cb084ed7828d41851874072786d9kjrguhwq.html>

113. **Zatz M**. “Técnica de transplante com órgão de animal avança”, by Estadão, **Jornal Correio do Povo**, 14/03/2022. <https://correiodopovo-al.com.br/geral/tecnica-para-transplante-com-orgao-de-animal-avanca>
114. **Zatz M**. Radio columnist Decodificando o DNA. “USP cria o primeiro banco genômico de idosos brasileiros”, **Rádio USP**, 17/03/2022. <https://jornal.usp.br/radio-usp/usp-cria-o-primeiro-banco-genomico-de-idosos-brasileiros/>
115. **Zatz M**. “Pesquisa explica por que pessoas não pegam Covid, mesmo dormindo juntas”, MyNews, by Mariane De Luca, YouTube Channel **MyNews**, 29/03/2022. <https://veja.abril.com.br/saude/brasileiros-identificam-2-milhoes-de-novas-variantes-geneticas-em-idosos/>
116. **Zatz M**. Radio columnist Decodificando o DNA. “Pessoas que contraíram covid-19 podem ter atrofia cerebral, sugere estudo inglês”, **Rádio USP**, 31/03/2022. <https://jornal.usp.br/radio-usp/usp-cria-o-primeiro-banco-genomico-de-idosos-brasileiros/>
117. **Zatz M**. “14 minutos de saúde”, by Fernanda Venturini, **Canal Fernanda Venturini** no YouTube, 07/04/2022. <https://www.youtube.com/watch?v=pIQ0ROWSm_A>
118. **Zatz M**. Radio columnist Decodificando o DNA. “Consórcio de cientistas descobre 2 milhões de variantes genéticas do genoma humano”, **Rádio USP**, 14/04/2022. <https://jornal.usp.br/radio-usp/consorcio-de-cientistas-descobre-dois-milhoes-de-variantes-geneticas-do-genoma-humano/>
119. **Zatz M.** Programa sinais vitais? https://www.cnnbrasil.com.br/ao-vivo. 25 de abril?
120. **Zatz M** radio USP: https://jornal.usp.br/radio-usp/testes-genomicos-para-investigar-doencas-embrionarias-pre-implantacao-precisam-ser-discutidos/28 de abril
121. **Zatz M** - folha de S.Paulo: https://www1-folha-uol-com-br.cdn.ampproject.org/c/s/www1.folha.uol.com.br/amp/ciencia/2022/04/brasileiro-deve-comecar-a-receber-transplante-de-orgaos-de-porcos-a-partir-de-2025.shtml; 30 de abril
122. **Zatz M.** VEJA-SAÚDE: Covid-19: como explicar as pessoas que nunca pegaram a doença? – Fatos Desconhecidos 30 de abril 2022
123. **Zatz M.** radio USP: https://jornal.usp.br/radio-usp/de-que-forma-a-genetica-interfere-no-comportamento-do-seu-cao/12 de maio-
124. **Zatz M**. Por que algumas pessoas não contraíram a Covid? - BIT magazine25 de maio-
125. **Zatz M.** radio usp: https://jornal.usp.br/radio-usp/cliquido-cerebral-de-camundongos-jovens-melhora-a-memoria-em-camundongos-mais-velhos/26 de maio
126. **Zatz M.** Com investimento de R$ 89 milhões, novos centros de ciência vão buscar soluções para problemas da sociedade – Jornal da USP27 de maio
127. **Zatz M.** Folha de SP- Café da manhã: https://open.spotify.com/episode/78kLolzlxMyk6qxRChJOSw, 6 de junho:
128. **Zatz M.** Veja saúde: Medicina | Veja Saúde (abril.com.br) 6 de junho:
129. **Zatz M.** https://jornal.usp.br/radio-usp/edicao-de-genes-em-tomates-pode-transforma-los-em-produtores-de-vitamina-d/ 9 de junho:
130. **Zatz M.** https://www.fatosdesconhecidos.com.br/como-virus-podem-ser-armas-poderosas-para-a-cura-do-cancer/16 de junho?
131. **Zatz M.** Estudo associa falta de vitamina D à demência - ISTOÉ DINHEIRO 17 de junho

4.2. Science Dissemination

1. **Mingroni-Netto RC**, Silveira RVM, Teixeira M. Podcast Segredos de Família “Ana Maria e os testes de ancestralidade”. Youtube Channel **Genoma USP Genoma USP,** 28/07/2021. < https://www.youtube.com/watch?v=pbAF6B-ZLPE>
2. **Mingroni-Netto RC**, Silveira RVM, Teixeira M. Podcast Segredos de Família “Hugo e o câncer colorretal”. Youtube Channel **Genoma USP**, 28/07/2021. <https://www.youtube.com/watch?v=YiMQjD62ZEA>
3. **Mingroni-Netto RC**, Silveira RVM, Teixeira M. Podcast Segredos de Família “Ingrid e a Hemofilia”. Youtube Channel **Genoma USP**, 28/07/2021. <https://www.youtube.com/watch?v=Dqa3NULimYg>
4. **Mingroni-Netto RC**, Silveira RVM, Teixeira M. Podcast Segredos de Família “Joana e o teste do pezinho”. Youtube Channel **Genoma USP**, 28/07/2021. <https://www.youtube.com/watch?v=RBraSe2cJag>
5. **Mingroni-Netto RC**, Silveira RVM, Teixeira M. Podcast Segredos de Família “Marcelo e a doença de Huntington”. Youtube Channel **Genoma USP**, 28/07/2021. <https://www.youtube.com/watch?v=a4UxbXmmLC8&t=992s>
6. **Mingroni-Netto RC**, Silveira RVM, Teixeira M. Podcast Segredos de Família “Maria e a distrofia muscular de Duchenne”. Youtube Channel **Genoma USP**, 28/07/2021. <https://www.youtube.com/watch?v=i9x8Jzx0msQ>
7. **Naslavsky M**. “ABC da Ancestralidade”, video: “Você sabia que seu teste genético pode ser usado contra você?”. Youtube Channel **Genoma USP**, 14/03/2022. <https://www.youtube.com/watch?v=NaxpHRPayd8&list=PLRxLNUL6CtpXirTTsdgtSlDZfVvWbulV7&index=6>
8. **Naslavsky M.** “ABC da Ancestralidade” do video: “Testes de ancestralidade são certeiros?”, **Canal Genoma USP** do YouTube, 26/01/2022. <https://www.youtube.com/watch?v=bhLttCHkz24>
9. **Naslavsky M.** “ABC da Ancestralidade” do video:,”Você precisa saber disso para escolher seu teste de ancestralidade!”.Youtube Channel **Genoma USP**, 10/02/2022. <https://www.youtube.com/watch?v=BncjnOpum5M&list=PLRxLNUL6CtpXirTTsdgtSlDZfVvWbulV7&index=12>
10. **Naslavsky M**. “ABC da Ancestralidade”, para o video: “Como as mutações podem informar sua ancestralidade genética”. Youtube Channel **Genoma USP**, 01/12/2021. <https://www.youtube.com/watch?v=TgJmeoNS3_8&list=PLRxLNUL6CtpXirTTsdgtSlDZfVvWbulV7&index=4>
11. **Naslavsky M**. “ABC da Ancestralidade”, video: “O número que nunca te contaram: somos no máximo 0,03% diferentes!”. Youtube Channel **Genoma USP**, 15/12/2021. <https://www.youtube.com/watch?v=NaxpHRPayd8&list=PLRxLNUL6CtpXirTTsdgtSlDZfVvWbulV7&index=6>

1.3. Tables

Table 1. Laboratory Class Project - Training of 37 High School teachers from Educational Directory of Osasco Region, March 9th, 2022 and Educational Directory Center-West Region, March 10th, 2022.

High School	Teachers	Educational Directory
EE Antonio Carlos da Trindade	Rodrigo de Oliveira	Osasco
EE Antônio Raposo Tavares	Érika Cristiane	Osasco
EE Cel Antonio Paiva Sampaio	Ivone Luzia Simões Santos	Osasco
EE Dr. Aureliano Leite*	Rosemary Valli	Osasco
EE Educador Paulo Freire	Rômulo de Carvalho*	Osasco
EE Gloria Azedia Bonetti	Stephanie Vitoria Castro Martins Silva	Osasco
EE Graciliano Ramos	Maria de Lourdes de Mendonça Miwa	Osasco
EE Jardim Cipava	Cristiana Soares Silva	Osasco
EE Jardim Santa Maria III	Ester Alves Correa*	Osasco
EE José Edson Martins Gomes	Antonio Reis de Sousa	Osasco
EE Julia Lopes de Almeida	Edna Célia Silvestrini Assis	Osasco
EE Maria Augusta Siqueira	Leticia Martines	Osasco
EE Prof. Benedito Caldeira	Rômulo de Carvalho*	Osasco
EE Prof. Eloi Lacerda	Vera da Silva	Osasco
EE Prof. Ernesto Then de Barros	Ester Alves Correa	Osasco
EE Prof. João Batista de Brito	Elivelton dos Santos	Osasco
EE Prof. José Jorge	Jarredes Domingos da Silva Peres	Osasco
EE Prof. Josué Benedito Mendes	Bruna Gabriele Aguiar da Silva	Osasco
EE Prof. Lucy Anna Carrozo Latorre	Fluviam Campos	Osasco
EE Prof. Newton do Espirito Santo Ayres	Gabriele Milani E R da Silva	Osasco
EE Ricardo Genésio da Silva	Cristiana Soares Silva*	Osasco
EE Rosa Bonfiglioli	Camila Candelo	Osasco
EE São Paulo Da Cruz	Fernanda F de Almeida	Osasco
EE.Prof. Orlando Geribola	Rubileide Santos	Osasco
EE Prof. Almeida Junior	Diego Arruda Filgueira	Center West
EE Prof. Aristides de Castro	Mayla Beyer	Center West
EE Prof. Daniel Paulo Verano Pontes	Madalena Rosa Chaves	Center West
EE Prof. Manuel Ciridião Buarque	Cezane Odette Kiss Natti	Center West
EE Samuel Klabin	Alcione Silva Santana	Center West
EE Solon Borges dos Reis	Pamela Tavares da Silva	Center West
EE Thomázia Montoro	Neide Miwako Hossokawa	Center West
	Juliana C Gobbo	
EE Virgílio Rodrigues de A. Carvalho Pinto	Dhiego Botelho	Center West
EE Prof. Andronico de Mello	Fernanda Hernades Siqueira Mariani	Center West
EE. Prof. Architiclino Santos	Raquel Martins	Center West
EE Dr Kyrillos	Carla Wanessa Caffagni	Center West

*Teacher teaching at two High Schools

Table 2. Instructional Material Project – Training of 47 Biology High School teachers from Educational Directory of Osasco Region (May, 2nd, 2022) and Educational Directory of Center West region (May, 3th, 2022)

High School	Teachers	Educational Directory
EE Alice Velho Teixeira	Francisco Antonio Silva	Osasco
EE Antônio Raposo Tavares	Érika Cristiane	Osasco
EE Deputado Guilherme Oliveira Gomes	Keila Soares Lima	Osasco
EE Dr. Américo Marco Antonio	Alex O. de Mello	Osasco
EE Dr. Luiz Lustosa da Silva	Viviane dos Reis Silva	Osasco
EE Educador Paulo Freire	Rômulo de Carvalho*	Osasco
EE Francisco Casabona	Marcel Yuki Fujita	Osasco
EE Francisca Lisboa Peralta	Sabrina Pareico Neves	Osasco
EE Francisco Matarazzo Sobrinho	Cristina Maria ferreira Lopes	Osasco
EE Gloria Azedia Bonetti	Renan Daves Tostes	Osasco
EE Horacio Quaglio	Leyla Bastos Paulino	Osasco
EE José Edson Martins Gomes	Antonio Reis de Sousa	Osasco
EE Julia Lopes de Almeida	Maria Valderez da Silva	Osasco
EE Maria Augusta Siqueira	Leticia Martines	Osasco
EE Prof. Alcyr Oliveira Porciuncula	Guilherme N Martins	Osasco
EE Prof. Benedito Caldeira	Rômulo de Carvalho*	Osasco
EE Prof. Eloi Lacerda	Vera Cotrim da Silva	Osasco
EE Prof. João Batista de Brito	Elivelton dos Santos	Osasco
EE Prof. José Jorge	Benedita de Souza	Osasco
EE Prof. José Liberati	Edna Vriina S Santos	Osasco
EE Prof. José Maria Rodrigues Leite	Vanessa M Zago	Osasco
EE Prof. Josué Benedito Mendes	Bruna Gabriele Aguiar da Silva	Osasco
EE Prof. Newton do Espirito Santo Ayres	Gabriele Milani E R da Silva	Osasco
EE Ricardo Genésio da Silva	Cristiana Soares Silva*	Osasco
EE São Paulo Da Cruz	Cristiane F Gomes	Osasco
EE.Prof. Orlando Geribola	Rubileide Santos	Osasco
EE Prof. Vicente Peixoto	Antonio Carlos dias Junior	Osasco
EE Prof. Almeida Junior	Diego Arruda Filgueira	Center West
EE Prof. Aristides de Castro	Mayla Beyer	Center West
EE Prof. Daniel Paulo Verano Pontes	Madalena Rosa Chaves	Center West
EE Prof. Manuel Ciridião Buarque	Cezane Odette Kiss Natti	Center West
EE Samuel Klabin	Alcione Silva Santana	Center West
EE Solon Borges dos Reis	Pamela Tavares da Silva	Center West
EE Thomázia Montoro	Neide Miwako Hossokawa Juliana C Gobbo	Center West
EE Virgílio Rodrigues de A. Carvalho Pinto	Dhiego Botelho	Center West
EE Prof. Andronico de Mello	Fernanda Hernandes Siqueira Mariani	Center West
EE. Prof. Architiclino Santos	Raquel Martins	Center West
EE Dr Kyrillos	Carla Wanessa Caffagni	Center West
EE Pereira Barreto	Lilian Colombini Etchebehere	Center West

*Teacher teaching at two High Schools

Tables 3 – Production delivered on Instagram: 59 posts on feed, 62 videos on IGTV, 8 Reels and 374 Stories. (June/2021 to May/ 2022)

YouTube (production of 69 videos)

Subject matter	Videos produced	Views
ABC - Genetic Counseling	4	213
ABC - Cancer and virus	4	658
ABC – Central dogma of Molecular Biology	3	626
ABC - Ancestry	16	7.591
Decoding DNA - Program by Mayana Zatz on Rádio USP	20	2.338
Family Secrets Podcast	6	3.214
CINEgenoma	3	1.878
Best Moments of CINEgenoma	12	906
"Journal USP no Ar" newspaper with the participation of Mayana Zatz	1	95
Total views		**17.519**

Instagram (production of 59 posts in feed, 62 videos in IGTV, 8 Reels and 374 Stories)

Subject matter	Posts	Videos IGTV/ Reels
Genetic Counseling	2	2
Genetic tests	1	
Cancer and virus	4	4
Announcement of grants, events, calls for volunteers and petitions	7	-
Secrets of Family podcast	7	-
CINEgenoma	9	17
Autism	-	1
Cancer	-	1
Genetic deseases	4	2
Commemorative dates	1	-
Ancestry	16	16
Central dogma of Molecular Biology	3	4
Xenografts	1	1
Decoding DNA - USP Radio Program	-	20
Cultural tips	3	-
Retinoblastoma	-	2
Covid-19	1	-

Facebook (84 posts)

Subject matter	Posts
Videos from the GenomaUSP channel on Youtube	30
Links to journalistic content in the area of activity of Genome USP published in the media	21
Posts from Instagram	30
Lives of CINEgenoma	3

Annex 5 – Personnel

Scientific Initiation - IS

Supervisor	Student
Ana Cristina V. Krepischi	Davi Mendes Campos Fialho
	Giovanna Civitate Bastos
Luis Eduardo Soares Netto	Lene Clara de Melo dos Santos
	Júlia Maria de Almeida Silvino
	Rebeca Bandeira Candia
Maria Rita Passos Bueno	Diogo Nani
	Gabriele Campos
	Igor Cabreira Ramos
	Isabela Nobrega
Mariz Vainzof	Brandow Willy Souza
	Isabela de Aquino Zogbi
	NathaliaGagliardiSaldys
	Gabriella Azevedo Chagas Santos
Mayana Zatz	Lara Borges Pacheco
	Sabrina Kaori Kadowaki Komats
Michel Naslavsky	Camila Hosoe
	Evelyn Lima
	Marvin Alexandria
Regina Célia Mingroni Netto	Ianca Rosa Dias
Oswaldo Keith Okamoto	Isabela Fonseca de Oliveira Granha

Master MSc

Supervisor	Student
Ana Cristina V. Krepischi	Amanda Shinzato
	Luíza Dias Chaves
	Gustavo Dib Dangoni
Debora Romeo Bertola	Taccyanna Mikulski
Maria Dulcetti Vibranovsk	Carolina de Athayde Mendonça
	Henry Bonilla Bruno
Maria Rita Passos Bueno	Camila Galvão

	Sofia Ligia Guimarães Ramos
Merari de Fátima Ramires Ferrari	Alan Moreira Henrique.
	Luann Fostter
	Romina Horianski
Michel Naslavsky	Adolfo Rojas(2)
	Airi Carvalho
	Gabriel do Nascimento Santos
	Gustavo Augusto(1)
	Luciana Nasciben
	Mariana Bardella
	Samantha Paco
Regina Célia Mingroni Netto	Beatriz Cetalle Schiavo
	Camila Cristina Avila Martins
	Jennifer Leôncio
	Stella Diogo Cavassana
Oswaldo Keith Okamoto	Alice Kei Endo
	Ianaê Ichikawa Ceschin.
	Lucas Carvalho Price
	Maria Susana J. Marodin
	Rodolfo Sanches Ferreira.
	Thais Regina dos Santos
	Thiago Giove Mitsugi

(1) Mestrado profissional
(2) student Universidad de Chile (co-orientador)

Doctorate - PhD

Supervisor	Student
Ana Cristina V. Krepischi	Laura Machado Lara Carvalho
	Gabriel Bandeira do Carmo
	Sara Ferreira Pires
	Giovanna Cantini Tolezano
Carlos Frederico Martins Menck	Matheus Molina Silva
	Livia Luz Nascimento
	Davi Jardim Martins,

	Davi Mendes
	Marcela Latância
	Camila Corradi
Debora Romeo Bertola	Ricardo di Lazaro Filho
	Giovanna Cantini Tolezano
Edson Amaro Jr	Liana Guerra Sanches da Rocha
	Mariana Athaniel Silva Rodrigues
Luis Eduardo Soares Netto	Rogério Luis Aleixo Silva
	Angélica Ramos
	Caroline Gonçalves de Góes
	Maria Tereza Oliveira Batista
Maria Dulcetti Vibranovsk	Camila CorreiaAvelino
	Frederico Monfardini
	Gabriel Nassar Reich Goldstein
Maria Rita Passos Bueno	Claudia Ismania Samogy Costa
	Debora Correa
	Elisa Varela
	Gabriella Hsia
	Angela May Suzuki
Mayana Zatz	Joyce Esposito de Souza
	Kayque Alvez Telles Silva
	Raiane Ferreira
Regina Célia Mingroni Netto	Vinícius Magalhães Borges

Pos Doctorate/Visiting Researcher

Supervisor	Name
Ana Cristina V. Krepischi	Talita Aguiar
	Anne Teixeira Barbosa
Carla Rosenberg	Darine Vilella
Carlos Frederico Martins Menck	Andre Uchimura Bastos
	Giovana Leantro
Luis Eduardo Soares Netto	Ana Luiza Dorigan de Matos Furlanetto
	Helena Gabriela Turano
	Carlos Abrunhosa Tairum
	Fernando Gomes

Maria Rita Passos Bueno	Daniela de Paula Moreira
	Gerson Kobayashi
	Lucas Alvizi Cruz
	Luciano Abreu Brito
Mariz Vainzof	André Luis Fernandes dos Santos
Mayana Zatz	Carolini Kaid Davila
	Danyllo Felipe Oliveira
	Ernesto da Silveira Goulart
	Felipe de Souza Leite. Início
	Luiz Carlos Caires Junior
	Lylyan Fragoso Pimentel
	Mateus Vidigal de Castro
	Thalita Figueiredo Cunha
Oswaldo Keith Okamoto	Elisa Helena Farias Jandrey

Laboratory Technicians and Assistants

Supervisor	Funding Source	Name
Ana Cristina V. Krepischi	USP	Maria Raimunda L. S. Pinheiro
Celia Koiffmann	USP	Cláudia I. Emilio de Castro Fabris
Eliana Maria B. Dessen	HUG-CELL/FUSP	Andrea Grieco
	CEPID/IB-USP	Marici Leite Salviano
	USP	Job Carvalho Bezerra
Luis Eduardo Soares Netto	USP	Simone Vidigal Alves
	USP	Thiago Geronimo Alegria
Maria Rita Passos Bueno	HUG-CELL/FFM	Ana Girardi
	HUG-CELL/FFM	Bruno de Oliviera Stephan
	HUG-CELL/FFM	Carolina Régoli Dias
	HUG-CELL/FFM	Daiane Gil Franco
	HUG-CELL/FUSP	Guilherme Lopes Yamamoto
	HUG-CELL/FFM	Jaqueline Yu Ting Wang
	USP	Kátia Maria da Rocha
	HUG-CELL/FFM	Kelly Bagatini
	HUG-CELL/FFM	Marília de Oliveira Scliar
	HUG-CELL/FFM	Monica C. V. Rodrigues da Silva
	USP	Monize Lazar Magalhães
	USP	Naila Cristina V. Lourenço

	USP	Roberto Rivelino de Camargo
	USP	Simone Gomes Ferreira
	HUG-CELL/FUSP	Fabiane Felisberto
	USP	Vanessa Naomi V. O. Takahashi
Mariz Vainzof	HUG-CELL/FUSP	LetíciaNogueiraFeitosa
Mayana Zatz	HUG-CELL/FUSP	Heloísa Maria de Siqueira Bueno
	USP	Marta Canovas
	HUG-CELL/FFM	Thais Oliveira de Andrade
	HUG-CELL/FFM	Vivian Landini
	HUG-CELL/FFM	Vivian Romanholi Coria
Merari R. F. Ferrari	USP	Andressa Y. Silvestre Sakugawa
Oswaldo Keith Okamoto	USP	Patrícia Semedo

Bioinformatics Support / Information Technology

Supervisor	Funding Source	Name
Maria Rita Passos Bueno Michel Naslavsky	HUG-CELL/FAPESP	Carlos Eduardo da Silva Simões
	USP	Ricardo Nonaka
	HUG-CELL/FAPESP	Victor Hugo Calderon
	HUG-CELL/FAPESP	José Franklin Calderon

Administrative/ Finance

Supervisor	Funding Source	Name
Ana C. V. Krepischi	USP	Maraisa de Castro Sebastião
Celia P. Koiffmann	USP	Luceleni da Silva
Eliana M.B. Dessen	USP	Luciana Cristina A.Oliveira
Maria Rita Passos-Bueno	HUG-CELL/FUSP	Caissa Santos C. da Silva
Mayana Zatz	HUG-CELL/FUSP	Márcia Góes Teixeira
	USP	Marta Rita Celestino de Macêdo
	USP	Wagner Falciano